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High Blood Pressure Increases the Risk of Cerebral Microbleeds in Hypertensive Individuals

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Abstract

Introduction: Hypertension is the leading preventable risk factor for major cardiovascular diseases worldwide. Recently, compelling evidence has emerged associating hypertension with cerebral microbleeds (CMBs), which are sub-clinical hemorrhages in the brain resulting from structural abnormalities in the small vessels that supply the brain. In addition to overall elevated blood pressure (BP), elevation in individual parameters such as systolic BP, diastolic BP, pulse pressure and mean arterial pressure could also individually be important risk factors for CMBs. This study aimed to assess the association between CMBs and blood pressure, and assess blood pressure parameters that could be possible risk factors for CMB. **Methods:** A retrospective case-control study was conducted from August 2021 to September 2022 on patients who underwent MRI due to primary complaints of limb disorders, loss of consciousness, persistent dizziness, and intermittent headaches. The patients were divided according to MRI results into 52 cases (those who had CMBs) and 52 controls (those who had no CMBs). Extracted data were analyzed in SPSS. Chi-square test, binary logistic regression, and Spearman's correlation analysis were conducted. **Results:** In total, 104 cases and control patients were assessed, with mean (\pm SD) age 70.6 ± 8.56 vs 68.9 ± 8.93 years respectively ($p > 0.05$). CMB patients had more cases of stroke, hyperlipidemia and diabetes than non-CMB patients. Systolic blood pressure (SBP), diastolic blood pressure, pulse pressure (PP) and mean arterial pressure (MAP) were all considerably raised in CMB patients than non-CMBs patients. Blood pressure grades were positively correlated with the severity of CMBs ($r = 0.22$; $p = 0.044$). Logistic regression analysis showed that SBP and MAP were in-

dependent risk factors for CMBs (age and sex adjusted odds ratio = 1.420; 95% CI: 1.030 - 1.851, and 1.310; 95% CI: 1.011 - 1.631 respectively). **Conclusions:** In summary, this study found that hypertension was positively correlated with CMBs severity, and that SBP and MAP are independent risk factors for CMBs in patients with hypertension.

Keywords

Hypertension, Pressure, Risk, Cerebral, Microbleeds

1. Introduction

Hypertension is the leading preventable risk factor for major cardiovascular diseases (CVD) worldwide [1]. It is defined as systolic blood pressure (SBP) \geq 140 mmHg and/or diastolic blood pressure (DBP) \geq 90 mmHg [2]. Due to an aging world population, the global prevalence of hypertension has risen sharply and continues to rise [3]. It is estimated that the global prevalence of elevated systolic BP (\geq 140 mmHg) rose by 3.2% from 17.3% in 1990 to 20.5% in 2015 [1], while in China, it ranges between 18.0% - 44.7% [4]. Hypertension is known to cause several CVDs including stroke [5]. Recently, compelling evidence has emerged associating hypertension with cerebral microbleeds (CMBs) [6] [7] [8] [9]. While insidious hypertension has long been known to induce intracranial hemorrhage (ICH) [10], and CMBs are one of the causes of ICH [11], it is until recently that links between hypertension and CMBs have been documented.

Cerebral microbleeds (CMBs) are tiny subclinical hemorrhage in the brain that occurs as a result of structural abnormalities in the small vessels that supply the brain [12]. The mechanism for the development of CMBs is still not fully understood, and patients often do not present with specific signs and symptoms [12]. They are identified when lesions made of small perivascular hemosiderin deposits are detected on MRI using susceptibility-weighted imaging [13]. CMBs occur in approximately 29.4% of patients > 65 years of age [14] and have, most recently, been increasingly seen among hospitalized Covid 19 patients ([15], p. 19).

Hypertension has emerged as a crucial risk factor for CMBs. A population based cohort study involving 344 randomly selected 70 to 87 years old hypertensive individuals in Sweden revealed that 26% of the cohort had CMBs, increasing from 19% among individuals in their 70s to 30% among those in their 80s [8]. Similarly, a study involving 218 patients without any history of cerebrovascular disease revealed that 16.1% of the participants had CMBs, and each standard deviation increase in ambulatory blood pressure increased the risk of CMBs by 1.9-fold [16]. Other studies by Lyu *et al.* [7], Yamashiro *et al.* [17] and Reddy *et al.* [6] conducted among hospital patients have all linked hypertension to the occurrence of CMBs. Evidence suggests that as a person ages, functional changes occur in the heart, such as diastolic and systolic dysfunction, and electrical dys-

function (45). These changes are insidious and, in the long term, lead to vasculopathies that eventually disproportionately triggers CMBs in the elderly patients more frequently than in the relatively young ones.

While linkages between hypertension and stroke or ICH are well documented globally, there are still limited studies on its association with CMBs. Moreover, there is evidence to suggest that blood pressure parameters could also individually be important risk factors for CMBs; for instance, the Framingham study revealed that knowing systolic blood pressure (SBP) alone correctly classified 99% of hypertension [18], while Tully *et al.* [19] showed that elevated SBP raised the odds of developing cerebrovascular disease 3 folds. More recently, Jiang *et al.* [20] showed that elevated pulse pressure (PP) was associated with a significant increase in cardiovascular mortality in old age. All these studies suggest that certain individual blood pressure parameters could be more associated with cardiovascular or cerebrovascular diseases than others.

In this retrospective observational study, we explored the association between hypertension and CMBs in a cohort of patients at our hospital. We further individually assessed systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) and mean arterial as potential independent risk factors for CMBs. Other risk factors analyzed were age, gender and other CMB comorbidities.

2. Materials and Methods

This study was conducted in accordance with the STROBE guidelines [21]. A retrospective case-control study was conducted at the first affiliated Renmin Hospital of Wuhan University. Patients recruited were those who underwent brain MRI scan using susceptibility weighted imaging (SWI) following primary complaints of limb disorders, loss of consciousness, persistent dizziness, and intermittent headaches. Permission to conduct the study was sought from Renmin Hospital of Wuhan University Research Ethics Committee. The committee waived patient's rights to consent since it was a retrospective study. A total of 104 patients (72 males and 32 females, aged 18 - 95 years) were recruited from August 2021 to September 2022. Patients were divided according to MRI results into 52 cases (those who had CMBs) and 52 controls (those who had no CMBs). Recruited cases were those who had radiologically confirmed CMBs as seen on MAGNETOM Avanto & Prisma 3T MRI systems (Siemens, Germany) using SWI sequence, with parameters were set as: 800 ms repetition time, 20 - 50 ms echo time, 20 - 30 flip angles, 256 × 256 matrix, 240 × 100 vision, 7-mm scan slice thickness, and 2.5 mm spacing. These data were extracted from the hospital electronic medical database and the picture archiving and communication system (PACS). Cerebral microhemorrhages were defined as a loss of circular signal with a uniform diameter of 2 - 5 mm, possessing a clear margin, with no edema around the circular punctate non-sulcus area. Those excluded were subjects with no record of blood pressure measurements, those who had radiologically con-

firmed CMB but diagnosed with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), cerebral amyloid angiopathy (CAA) or Moyamoya disease.

2.1. Blood Pressure Measurements and Comorbidities

For blood pressure measurements, we retrieved single recordings from the database for each patient. Hypertension was defined according to the International Society of Hypertension (ISH) [22] as blood pressure readings $\geq 140/90$ mmHg. Pulse pressure (PP) was calculated Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) as the arithmetic difference between the former and the latter. Blood pressure measurements were classified according to the International Society of Hypertension (ISH) as: normal ($<139/89$ mmHg); grade 1 hypertension ($140 - 159/90 - 99$ mmHg); and grade 2 hypertension ($\geq 160/100$ mmHg) [22]. Other comorbidities collected were diabetes, hyperlipidemia, and stroke, all defined by the World Health Organization criteria for diagnosing hypertension, diabetes, and hyperlipidemia. Furthermore, smoking history, and history of alcohol intake were also extracted. Stroke diagnosis was conformed based on definitive diagnosis and treatment from Renmin Hospital of Wuhan University, and image findings of obsolete cerebral lesions. Other important data collected were: subject demographic information, clinical and medical characteristics, and treatment details. Cardiovascular risk factors assessed were systolic and diastolic blood pressure, pulse pressure, mean arterial pressure, gender, age, cholesterol levels, diabetes, and smoking and alcohol consumption [23].

2.2. Brain MRI Scan Results

All brain MRI results retrieved were conducted and interpreted by highly qualified radiologists. When viewed on MAGNETOM Avanto & Prisma 3T MRI systems (Siemens, Germany) using SWI sequence, CMBs were seen as small homogenous, and round foci with low signal intensity, having a diameter < 10 mm and without peripheral edema. Similar structures such as vascular gap, cavernous hemangioma, calcified plaque of atherosclerosis, hemosiderin deposition on the pia mater, and calcification of the globus pallidus were excluded. Location of CMBs were categorized into; lobar (cortical gray and subcortical or periventricular white matter), deep (deep gray matter: basal ganglia and thalamus; and the white matter of the corpus callosum, internal, external, and extreme capsule), and infratentorial (brain stem and cerebellum). CMBs were defined as: non-CMB (0), mild (1 - 2), moderate (3 - 10) and severe (>10) and patients grouped accordingly.

2.3. Statistical Analysis

Statistical data analysis was conducted using SPSS version 25 software (IBM Inc. USA). Mean \pm SD was used to summarize continuous variables while categorical variables were presented as counts and percentages. Independent student's t test

was used to examine the differences between means of continuous variables, while Pearson's Chi-square test was used to analyze categorical data. Spearman's rank test was used to conduct correlation analysis. Logistic regression analysis was conducted to examine risk factors associated with CMBs. Statistical significance was set at p -value < 0.05 .

3. Results

3.1. Summary of Patient Characteristics

Patient characteristics are summarized in **Table 1**. A total of 104 patients were recruited, 52 with CMBs and 52 without, Mean (\pm SD) ages 70.6 ± 8.56 vs 68.9 ± 8.93 respectively ($p > 0.05$). No significant difference in age was observed between the two groups, but significant difference was observed in gender as presented in **Table 1**. Stroke, hyperlipidemia and diabetes were more common in the CMB group than the non-CMBs group, while history of smoking and alcohol consumption were more common in the non-CMBs group. Systolic blood pressure (SBP), diastolic blood pressure, pulse pressure (PP) and mean arterial pressure (MAP) were all considerably raised in the CMBs group than in the non-CMBs group (**Figure 1**). The prevalence of CMBs increased with increase in age. Similarly, a patient having more than one CMB also increased with age. In the age group 50 to 59 years, 33.3% had at least 1 microbleed, which increased to 50.9% after 70 years of age (**Table 2**).

Table 1. Characteristics of the patients.

Characteristic	Case, N = 52	Controls, N = 52	p
Gender (male), n (%)	43 (82.7)	38 (73.1)	$<0.001^*$
Age, y (Mean \pm SD)	70.6 ± 8.56	68.9 ± 8.93	0.76
SBP (mmHg)	140.0 ± 20.6	133.0 ± 19.2	0.02*
DBP (mmHg)	79.2 ± 14.2	76.8 ± 11.8	0.14
PP (mmHg)	61.0 ± 17.0	56.0 ± 14.0	0.06
MAP (mmHg)	99.4 ± 14.5	95.4 ± 13.1	0.04*
Co-morbidities			
Hypertension grade			0.12
No hypertension	25 (48.1)	34 (65.3)	
Mild hypertension	17 (32.7)	14 (26.9)	
Severe hypertension	10 (19.2)	4 (7.8)	
Stroke, n (%)	4 (7.7)	2 (1.9)	0.16
Diabetes mellitus, n (%)	1 (1.9)	0 (0)	0.31
Hyperlipidemia, n (%)	4 (5.8)	3 (5.8)	0.98
Smoking, n (%)	22 (44.2)	31 (57.7)	0.18
Alcohol, n (%)	11 (21.2)	21 (40.4)	0.03*

SBP: Systolic blood pressure. DBP: diastolic blood pressure. PP: Pulse pressure. MAP: Mean arterial pressure. *represents significant results.

Table 2. Age-specific prevalence of cerebral microbleeds (10-year strata).

Age range	Patient number	CMBs, N (%)	Multiple CMBs, N (%)
40 - 49 years	1	0 (0)	0 (0)
50 - 59 years	15	5 (33.3)	3 (20)
60 - 69 years	33	19 (57.5)	15 (45.4)
≥70 years	55	28 (50.9)	23 (41.8)
Total	104	52 (50.0%)	41 (39.4%)

CMBs: Cerebral microbleeds.

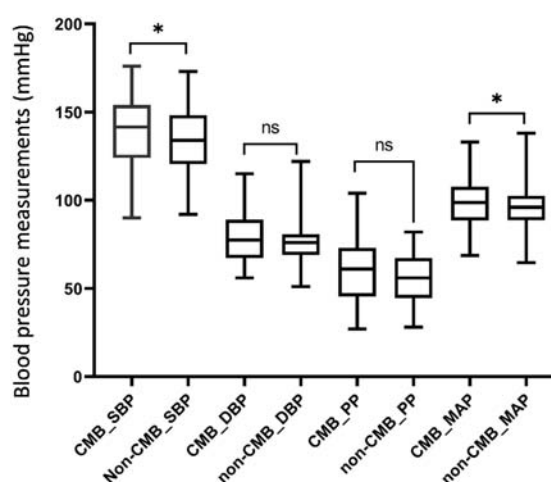


Figure 1. Comparison of blood pressure parameters between the CMB and non-CMB patients.

3.2. Location and Severity of Cerebral Micro Bleeds

Of the 52 patients with CMBs, the total number of CMB lesions was 320, majority of them, 110 (34.3%) occurred in the lobar region of the brain, followed by 93 (29.1%) in deep region, and 65 (20.3%) in infratentorial region (**Figure 2**). We then graded the CMB lesions according to severity as follows; grade 0 (no lesions), grade 1 (1 - 2 lesions), grade 2 (3 - 10 lesions) and grade 3 (>10 lesions), and determined possible association with gender and age groups of the patients. Chi-square analysis showed no association between both gender and age groups and severity of CMBs (all $p > 0.05$) (**Table 3**).

3.3. Association between Blood Pressure and Cerebral Microbleeds

To assess the association between blood pressure and severity of cerebral microbleeds, blood pressure was categorized into normal, grade 1 and grade 2 according to the ISH classification [22], and Spearman's correlation analysis conducted among the blood pressure grades and severity of CMBs. The results revealed that blood pressure was correlated with CMB severity; $r = 0.22$; $p = 0.044$ (**Table 4**). Preliminary multicollinearity analysis showed no significant association among

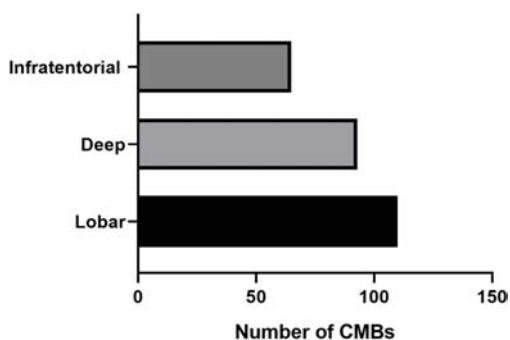


Figure 2. Distribution of CMBs in the different parts of the brain.

Table 3. Association between CMBs and age and gender.

	CMB grade				N	p
	0 (0)	1 (1 - 2)	2 (3 - 10)	3 (>10)		
Gender						0.08
Male	36	18	13	5	72	
Female	16	2	10	4	32	
Total	52	20	23	9	104	
Age group						0.21
40 - 49 years	1	0	0	0	1	
50 - 59 years	10	3	2	0	15	
60 - 69 years	14	10	5	4	33	
≥70 years	27	7	16	5	55	
Total	52	20	23	9	104	

Table 4. Association between CMBs and blood pressure.

CMB grade	BP classification			N
	Normal	Mild	Severe	
0 (0)	34	14	4	52
1 (1 - 2)	9	7	4	20
2 (3 - 10)	11	8	4	23
3 (>10)	5	2	2	9
Total	59	31	14	104

Spearman's $r = 0.22$; p -value = 0.044.

independent variables, and binary logistic regression analysis revealed that systolic blood pressure (SBP), and mean arterial pressure (MAP) were significantly associated with the presence of CMBs (all $p < 0.05$), demonstrating that SBP and MAP are independent risk factors for CMBs (age and sex adjusted odds ratio = 1.420; 95% CI: 1.030 - 1.851, and 1.310; 95% CI: 1.011 - 1.631 respectively) (**Table 5**).

Table 5. Univariate analysis of CMBs and blood pressure.

	B	SE	Wald	df	Sig	OR	95% CI
SBP	0.024	0.010	5.094	1	0.02*	1.420	1.030 - 1.851
DBP	0.023	0.016	2.181	1	0.14	1.024	0.992 - 1.056
PP	0.22	0.013	2.857	1	0.09	1.022	0.997 - 1.048
MAP	0.31	0.015	4.034	1	0.04*	1.310	1.011 - 1.631
Age	0.003	0.021	0.023	1	0.88	1.003	0.962 - 1.046

SBP: Systolic blood pressure. DBP: Diastolic blood pressure. PP: Pulse pressure. MAP: Mean arterial pressure. *represents significant results.

4. Discussion

We conducted this study to examine the association between blood pressure (BP) and the occurrence of cerebral microbleeds (CMBs) among our patients who underwent MRI examination using the 3T MRI susceptibility-weighted imaging technique. It should be noted that the MRI sequence used in detecting CMBs determines the rate of detection of microbleeds [12]. We also assessed age, systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP), and mean arterial pressure (MAP) as independent risk factors for the occurrence of CMBs. Blood pressure parameters are non-invasive, easy to measure and economically cheap measurements that could be used to predict CMBs.

Previous studies have already shown that an association exists between CMBs and hypertension. Igase *et al.* [24] showed that SBP is positively correlated with CMBs, while Fan *et al.* [25] demonstrated that DBP is also exhibits a positive correlation with the occurrence of CMBs. More recently, Lyu *et al.* [7] showed that SBP, DBP and age are all independent risk factors for CMBs. In our study, we used Spearman's rank correlation analysis of BP grade based on CMB severity, and found that a rank correlation indeed existed between BP grade and CMB severity ($r = 0.22$, $p = 0.044$). Further assessment using a logistic regression analysis, revealed that systolic blood pressure and mean arterial pressure are independent risk factors for CMBs. However, we did not observe a statistically significant relationship between CMBs and age, diastolic blood pressure and pulse pressure, although all the three parameters appeared to be raised in CMB patients compared to non-CMB patients. Chronic hypertension leads to weakening of small vessel walls, and forces the vessel smooth muscles to be replaced by fibrous or necrotic tissues. This eventually induces atherosclerotic plaque formation, and rupture which may cause cerebral thrombosis and sometimes aneurysms [26]. In this regard, CMBs can also be considered as a type of target organ damage induced by hypertension. Presence of multiple CMB is an indication of a terminal micro-vascular lesion prone to bleeding [27].

Although our study did not find a statistically significant association between age and CMBs, we noticed that the prevalence of CMBs increased with age, and that a patient having more than one CMB also increased with age, 33.3% for pa-

tients in 50 to 59 years age group and 50.9% in patients 70 years and above (**Table 2**). This finding is consistent with Lyu *et al.* [7], who also did not find an association between age and severity of CMBs. However, unlike us, they showed that age is an independent risk factor for CMBs. We think that the difference could be in our small sample size and the slight difference in age stratification we applied compared to theirs. In addition to Lyu *et al.* [7], Imaizumi *et al.* [28], and Horita *et al.* [29] have also demonstrated that old age is indeed an independent risk factor for CMBs.

CMBs were distributed in multiple areas of the brain. Majority of them (34.3%) occurred in the lobar region consisting of the brain cortex, and sub-cortex or periventricular white matter. This was consistent with the findings by Lyu *et al.* [7] and Poels *et al.* [30] who both reported that CMBs occurred in higher frequency in the cortical and sub-cortical regions of the brain. Furthermore, majority of the patients had between 2 to 10 CMBs per patient also consistent with previous findings by Lyu *et al.* [7]. Recent evidence suggests that occurrence of CMBs could be associated with cognitive impairment in the affected individuals [31] [32], whether this is correlated with the location of the CMB lesions needs to be determined.

Our study had a few limitations. First, we did not assess medication use among the hypertensive patients. Being a chronic disease with long term medication, this could also have an effect on the blood pressure parameters, so the results should be interpreted accordingly. Second, the study sample size was small, and this could have affected the power of the study. Third, the study was retrospectively conducted and so carried all the inherent limitations of a retrospective study, and so larger scale prospective cohort studies are needed to verify these findings. Lastly, the blood pressure measurements used were single measurements extracted from the electronic database. 24 hour ambulatory blood pressure measurement could have been more reliable to use.

5. Conclusion

In summary, our study demonstrated that CMBs, as determined by the 3T MRI susceptibility weighted imaging, were associated with hypertension and that systolic blood pressure (SBP) and mean arterial pressure (MAP) were independent risk factors for CMBs. Furthermore, the CMBs were more likely to occur in the lobar region of the brain compared to the deep and infratentorial regions. In light of the limitations of the study, further studies, preferably large prospective cohorts, are needed to verify these results.

Author Contributions

- (1) Concept or design: Yahya Abdullahi Ali;
- (2) Acquisition of data: Yahya Abdullahi Ali and Xi Wang;
- (3) Analysis or interpretation of data: Yahya Abdullahi Ali and Erick Thokerunga;
- (4) Drafting of the article: Yahya Abdullahi Ali;

(5) Critical revision for important intellectual content: Erick Thokerunga, Xi Wang and Zakaria Ahmed Mohamed.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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Ethics Approval

This study was approved by the Wuhan University Renmin Hospital Research Ethics Committee.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Is There Any Relationship between Total Hip Arthroplasty and Urinary Incontinent?

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Abstract

Introduction: In my daily practice as a hip surgeon, I have observed some circumstances where urinary incontinence (UI) improves after total hip arthroplasty (THA). We investigated UI symptoms before and after THA at our facility and considered the factors that influence UI. **Patients and Method:** The subjects were 113 female patients who underwent primary THA in our facility. An anterior lateral approach was used in all cases. Using the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF), we conducted an investigation into the presence of UI before and 2 weeks after THA. An improvement in UI was defined as a decrease of 1 point or more, a worsening is defined as an increase of 1 point or more. **Results:** The responses from the 113 subjects were analyzed. Of the 113 patients, prior to THA, UI was prevalent among 59 patients and was absent among 54 patients. In the group where UI was prevalent, it improved after THA in 50 patients (85%), remained unchanged in 5 (8%) and worsened in 4 (7%). In the group where UI was absent, 49 patients (91%) remained unchanged and UI appeared in 5 (9%). Compared with the non-prevalence group (62 patients), the prevalence group (50 patients) had a noticeable improvement rate of internal rotation of the surgical hip side ($P < 0.01$). **Conclusion:** UI greatly reduces the quality of life (QOL). In this study, there is a possibility that THA improves UI.

Keywords

Total Hip Arthroplasty, Urinary Incontinence, Obturator Internus

1. Introduction

The majority of Japanese osteoarthritis patients have secondary osteoarthritis

mainly due to congenital dislocation of the hip joint or acetabular dysplasia [1]. Hip joint disorders from osteoarthritis greatly reduce the quality of life (QOL), and QOL improves markedly within three months after total hip arthroplasty (THA) [2]. The prevalence of hip osteoarthritis is particularly high among middle-aged and elderly women [3]. The term lower urinary tract symptoms (LUTS) which was introduced in 1994, many adults experience, and the prevalence of these symptoms increases with age [4]. LUTS are highly prevalent in Japan, and few subjects seek treatment [5]. UI is significantly under-diagnosed, and many people suffer from life-disrupting consequences of a condition that is largely treatable [6]. Furthermore, it is expected that patients with hip osteoarthritis are hesitant to say they have LUTS symptoms to a hip surgeon. Although in such a situation, in daily practice as a hip surgeon, we have observed that there are some circumstances in which UI improves after THA. THA is a great option that relieves pain and improves mobility, and as a result, improves QOL. The improvement in symptoms is amazing for patients suffering from hip dysfunction and UI.

We acknowledge that Tamaki *et al.* [7] first submitted the information that patients with UI before THA improved by 64% 3 months after THA using the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF). Okumura *et al.* [3] reported that for patients with hip-joint disorder, hip-joint treatment could prove to also be a useful treatment for UI. Baba *et al.* [8] reported that symptoms of UI were significantly improved in anterior approach (AA) group and aggravated in the posterior approach (PA) group. In our institution, anterior lateral approach was adopted at the time of THA. We investigated whether UI improves after THA in our facility.

2. Methods

Information on the existence of UI and hip function limitations was collected on 113 female patients with an average age of 63.5 years. All patients had suffered from hip osteoarthritis and underwent primary THA in the period from July 2019 to December 2021. 11 of them were given simultaneous bilateral THA. All the arthroplasty procedures employed the anterolateral muscle-sparing approach in a 60-degree half-lateral position. No dislocation and no infection were reported in two weeks after THA. And patients were immediately followed by postoperative rehabilitation on the first day. Rehabilitation included both active and passive motion exercises on the affected joints. Patients were allowed to put their full weight on these joints. Prior to surgery and 2 weeks after, we requested all members of the group to fill out the ICIQ-SF.

An improvement of UI was defined as a decrease of 1 point or more, a worsening is defined as increase of 1 point or more. Range of movement (ROM) was measured before and after surgery, and the number of births, age, body mass index (BMI), intraoperative bleeding, and surgery time were listed. No patient received medication for UI. The Mann-Whitney U test was applied to evaluated difference, and the level of statistical significance applied was $P < 0.05$.

3. Results

3.1. Patient Background

Of the 113 patients, prior to THA, UI was prevalent among 59 (52%) patients (incontinent group) and was absent among 54 (48%) patients (continent group).

There was no significant difference in the number of births, age, body mass index (BMI), intraoperative bleeding, or surgery time.

Concerning ROM, there was no significant difference in flexion, abduction, adduction, external rotation, or internal rotation. However, there was a significant difference in extension ($P < 0.05$).

In the incontinent group, the symptoms of UI improved in 50 (85%) patients, remained unchanged in 5 (8%) and worsened in 4 (7%) after THA.

In the continent group, the symptoms of UI remained unapparent in 52 (96%) patients, and worsened in 2 (4%) (Table 1).

Among the 113 patients, the number of patients whose UI improved was 50 (group A), and whose UI remained unchanged or worsened was 63 (group B). Characteristics of the 2 groups are listed in Table 2. There were no significant differences in age, height, number of births, unilateral or bilateral THA. There were significant differences in weight and BMI ($P < 0.05$, $P < 0.01$ respectively). In response to the question, “when does urine leak?” for the patients who had UI symptoms before surgery, 44 (75%) replied “when coughing or sneezing” the most frequently (Figure 1).

Table 1. Changing of urinary incontinence after total hip arthroplasty.

	Total	Improvement	No change	Worsening
Incontinent group	59	50 (85%)	5 (8%)	4 (7%)
Continent group	54	-	52 (96%)	2 (4%)
Total	113	50	57	6

Table 2. Group A (improvement) 50 patients; Group B (no change + worsening) 63 patients; patients' back ground.

	Group A	Group B	P value
Age	64.6 ± 9.6	62.6 ± 10.4	0.34
Height	153.5 ± 6.1	153.9 ± 5.4	0.43
Weight	59.7 ± 11.1	55.7 ± 8.66	<0.05
BMI	25.5 ± 4.3	23.5 ± 3.6	<0.01
Number of births	1.8 ± 0.8	1.9 ± 1.0	0.38
Unilateral THA: bilateral THA	45:5	57:6	0.93

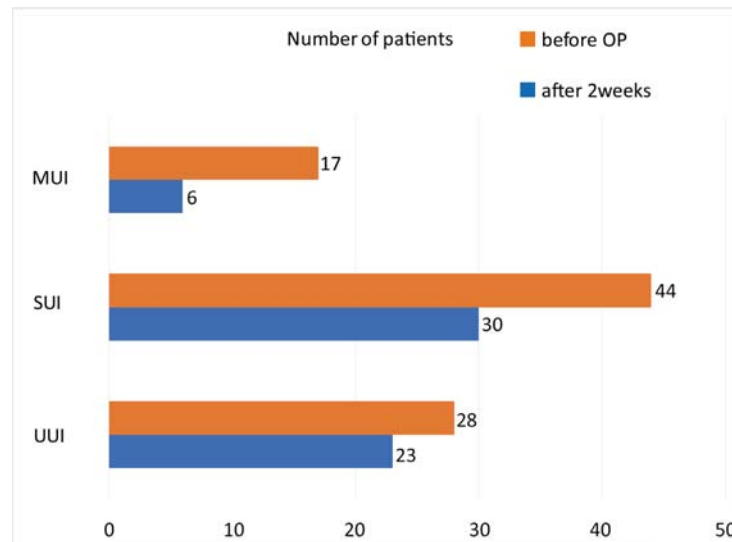


Figure 1. Response to the question, “when does urine leak?”.

3.2. Evaluation of Hip Range of Movement

-Group A-

Flexion significantly improved from 85.5 ± 20.1 before THA to 91.6 ± 9.5 at 2 weeks after ($P < 0.05$).

Extension significantly improved from -3.4 ± 7.8 before to 0.6 ± 5.4 at 2 weeks after ($P < 0.01$).

Internal rotation significantly improved from 13.2 ± 12.9 before to 27.8 ± 11.9 at 2 weeks after ($P < 0.01$).

There was no significant difference in abduction, adduction, or external rotation (**Table 3**).

-Group B-

Extension significantly improved from -2.5 ± 7.9 before to 2.8 ± 6.2 at 2 weeks after ($P < 0.01$).

Abduction significantly improved from 13.3 ± 0.9 before to 15.9 ± 4.8 at 2 weeks after ($P < 0.01$).

Internal rotation significantly improved from 17.2 ± 15.9 before to 26.4 ± 11.3 at 2 weeks after ($P < 0.01$).

There was no significant difference in flexion, adduction, or external rotation (**Table 4**).

3.3. Comparison between Group A and Group B in Range of Movement

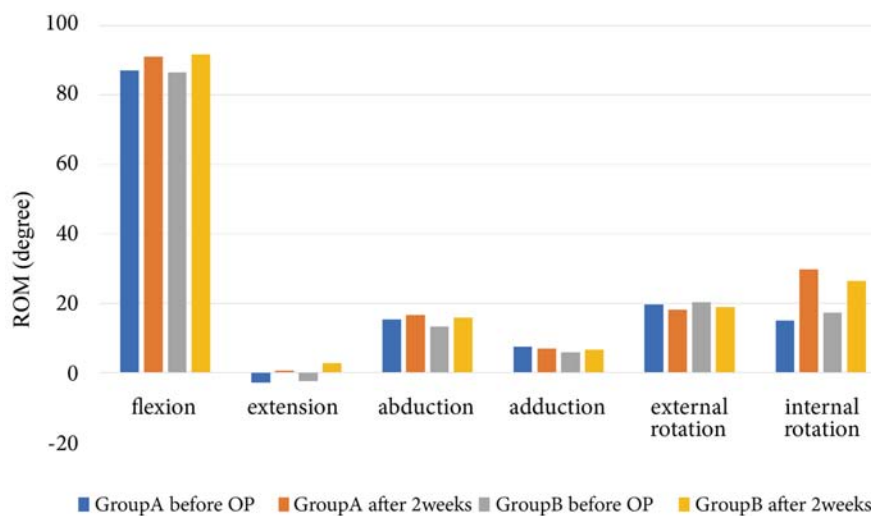
Improvement in ROM was compared between the 2 groups (**Figure 2**). Flexion, extension and internal rotation were significantly improved at 2 weeks after THA in group A. In group B, extension, abduction and internal rotation were significantly improved at 2 weeks after THA. The difference between unilateral and bilateral arthroplasty was compared, and there were no significant differences in terms ROM. We determined improvement rate by dividing the ROM

Table 3. Group A: Evaluation of hip ROM.

	Before	After 2 weeks	P value
Flexion	85.5 ± 20.1	91.6 ± 9.5	<0.05
Extension	-3.4 ± 7.8	0.6 ± 5.4	<0.01
Abduction	15.4 ± 8.1	16.3 ± 5.6	=0.20
Adduction	7.1 ± 5.4	6.9 ± 3.8	=0.82
External rotation	19.6 ± 9.6	18.1 ± 7.6	=0.16
Internal rotation	13.2 ± 12.9	27.8 ± 11.9	<0.01

Table 4. Group B: Evaluation of hip ROM.

	Before	After 2 weeks	P value
Flexion	86.5 ± 18.5	91.7 ± 8.5	=0.11
Extension	-2.5 ± 7.9	2.8 ± 6.2	<0.01
Abduction	13.3 ± 0.9	15.9 ± 4.8	<0.01
Adduction	5.8 ± 4.6	6.6 ± 2.9	=0.08
External rotation	20.3 ± 10.2	18.8 ± 9.1	=0.28
Internal rotation	17.2 ± 15.9	26.4 ± 11.3	<0.01

**Figure 2.** Comparison between group A and group B in ROM.

before THA by the ROM after 2 weeks THA. Using the improvement rate of ROM, statistically there was a significant difference between 2 groups, only in internal rotation ($P < 0.05$). Improvement rate of internal rotation was significantly higher in group A.

3.4. Case Presentation

The patient was a 55-year old woman who was suffering from right hip pain be-

cause of her osteoarthritis of the hip. According to her questionnaire before THA, she leaked a moderate amount of urine two or three times a week. And her leaking urine interfered with her life by level 4. Her Points of ICIQ-SF was 10 before THA. 2 weeks after the THA, she never leaked urine, and it interfered with her life by level 1. Her point of ICIQ-SF was 1, 2 weeks after the THA (Figure 3).

4. Discussion

4.1. Prevalence of Urinary Incontinence

Kikuchi *et al.* [9] investigated the prevalence of UI using ICIQ-SF in 676 Japanese men and women aged > 70 years who were living in the Tsurugaya area of Sendai, one of the major cities in the Tohoku area of Japan. In the study, the prevalence of UI was 25% (34% in women and 16% in men), and the shown high physical activity level was independently related to a lower self-reported prevalence of UI in a community-dwelling elderly population aged > 70 years.

Tamaki *et al.* [7] reported the prevalence rate of UI in patients with hip osteoarthritis before THA was 43%, using ICIQ-SF.

Baba *et al.* [8] reported the prevalence rate of UI in patients with hip osteoarthritis before THA was 47% using ICIQ-SF.

Okumura *et al.* [3] reported the prevalence of UI in patients with hip osteoarthritis before THA was 67% using a core lower urinary tract symptom score (CLSS).

In our study, the prevalence of UI in patients with hip osteoarthritis before THA was 52%.

In the case of hip joint disorders, physical activity levels might be lower, and the prevalence of UI in patients with hip dysfunction may be higher than in people without hip dysfunction.

4.2. Type of Urinary Incontinence

Hannestad *et al.* [10] reported half of the incontinent women were experiencing symptoms of stress incontinence (SUI) alone, symptoms of urge incontinence (UII) alone affected only one in ten, while mixed incontinence (MUI) was



Figure 3. 55-year old patient whose UI improved after THA.

reported by one in three in 6501 of UI patients. In our study, stress incontinence was the most frequent. (Figure 1) Bo K reported that pelvic floor muscle training is effective in the treatment of female stress incontinence (SUI) and mixed urinary incontinence and therefore, it is recommended as a first-line therapy.

The stress continence system includes the sphincteric closure mechanism consisting of urethral striated muscle, urethral smooth muscle, and vascular elements and the remainder of the bladder support system consisting of the anterior vagina, endopelvic fascia, tendinous arch of levator ani, and bony pelvis [11]. The consequence of levator ani muscle damage might depend on which or how many elements have been damaged [12]. If the tendinous arch of levator ani falls, the ipsilateral side of the vagina falls, carrying with it the bladder and the urethra, and thus contributing to urinary incontinence. The tendinous arch of levator ani is at the bottom of the fascia obturator.

Tamaki *et al.* focused on the obturator internus muscle, which originates from the pelvic floor and has a close relationship with the levator ani muscle [7]. Okumura *et al.* reported that THA is performed to improve hip-joint function and recovery of levator ani function that is connected to the obturator internus [3].

Baba *et al.* [8] reported that since the short external rotator may have been atrophied due to hip joint dysfunction before surgery, support of the pelvic organs and UI may be improved if the strength of this muscle group recovers. And, symptoms of UI were significantly improved in the anterior approach group without dissecting the short external rotators, and aggravated in the posterior approach group [8].

The superior gemellus, inferior gemellus, and obturator internus muscle have been regarded as a single muscle unit and called the “rotator triceps muscle” [13]. The gemelli converge onto the tendon of insertion of the obturator internus muscle and because the three muscles terminate at the same common bony attachment, the medial aspect of the greater trochanter [13]. Their functions are also common; they act synergistically to rotate the pelvis and/or femur [13]. The obturator internus muscle arise over a wide area of the lesser pelvis, converges to the lesser sciatic notch, changes its course, and is inserted into the medial aspect of the greater trochanter [13].

In our institution, all the arthroplasty procedures employ the anterolateral muscle-sparing approach in the 60-degree half lateral position. At the time of stem insertion, we may cut the conjoint tendon as little as possible if it is hard to insert the stem.

4.3. Improvement Rate of Urinary Incontinence

In our study, UI improved in 50 (85%) patients. In other studies, Tamaki *et al.* [7] reported the symptoms of UI ameliorated in 52 (64%) patients which was done by the muscle-sparing direct anterior approach using ICIQ-SF. Okumura *et al.* [3] reported in total, patients were better than improved (72%). The rate of cured and improved patients was 76%, for stress UI, 100% mixed UI, and 50%

urge UI. Baba *et al.* reported UI improved after THA in 8 patients (22%), slightly improved in one (2.8%) in the anterior approach group using the distal part of the Smith-Petersen approach. In the posterior approach group, by dissecting the short external rotators, UI improved after THA in one (2.5%). Patients with hip disorder have limited range of motion, and those muscles around hip reduce tension. In our study, improvement rate of internal rotation of group A (improvement of UI group) was high. Think about why UI improved after THA, and the internal rotation movement became possible after that, external rotators including the obturator internus are able to stretch, and preserve the original musculature. As a result, the obturator internus can exert tension. The obturator internus is closely related to the levator ani. In addition, thinking of the approach of THA which preserves the obturator internus, it could be advantageous for the improvement of UI.

Pelvic floor dysfunction is a common problem that leads to significant suffering among women [14]. Pelvic floor muscle training is effective in the treatment of female stress (SUI) and mixed urinary incontinence and, therefore, it is recommended as a first-line therapy [11]. Hip joint disorders from osteoarthritis and UI both greatly reduce the QOL. And both ages of onset are the same for middle age and older [7]. Tamaki *et al.* hypothesizes that a loose pelvic floor could be improved by THA [7]. In our study, 85% of the THA patients' UI improved just 2 weeks after THA. That suggests THA might have the same effect as pelvic floor muscle training and might be more immediately effective than muscle training.

5. Limitations

This study had some limitation. Firstly, because the study was only two weeks, the long-term results are unclear. Secondly, a pain scale wasn't used; therefore the patients' pain levels were unknown.

Thirdly, only orthopedic doctors got involved in this study, no urologists were involved.

Fourthly, the number of patients studied was low. Finally, the anterior and posterior THA approaches were not compared.

6. Conclusion

In conclusion, UI doesn't affect a patient's life span; however, it affects their QOL later in the future. Our study has shown that THA can be beneficial for treating UI. We would like to continue this study more using X-rays to consider how patients' femoral offset changes after THA.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Personalized Management of Chronic Myeloid Leukemia Presenting with Ovarian Apoplexy and Review of Health Emergency Cases

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Abstract

Introduction: Chronic myeloid leukemia (CML) may significantly affect quality of life and life expectancy in the accelerated and acute phases, especially if presented with health emergencies. **Objective:** The purpose of the study was the evaluation of the personalized management milestones in CML cases presented with ovarian apoplexy and the analysis of the international experience on health emergencies in this leukemia. **Materials and Methods:** An original, case-report study was performed. The diagnosis was confirmed by cytological, cytogenetic and molecular examinations of the peripheral blood and bone marrow at the comprehensive research cancer center—Institute of Oncology from Moldova. The real-time PCR was performed for quantitative detection of BCR-ABL gene p210 and p190 transcripts. The ECOG Scale and complete hematologic response (CR) estimated the short-term results. The ECOG performance status served as a measure of functional status. Its scores range from 0 to 5 and correlate with the level of patient functioning. CR is the disappearance of all detectable clinical and hematological signs of malignant neoplasm in response to treatment. CR span was assessed in months. The overall and relapse-free survivals asserted the long-term results of treatment, and were evaluated in months as a case. **Results:** CML may be manifested by life-threatening conditions, including infections and thrombotic events, splenic infarcts and ruptures, bleedings, etc. CML with the uncommon onset under the form of the ovarian apoplexy is described. The hematological CR was obtained under the treatment with imatinib mesylate. The molecular CR and the long-lasting overall survival (197.5 months) were achieved after the treatment with nilotinib. Under the treatment with tyrosine kinase inhibitors, the patient did not experience the disease burden and side effects, and resumed her work, with a good life quality (ECOG score is 0).

Discussion: CML may be manifested by life-threatening health emergencies, especially thrombotic events, splenic infarcts and ruptures, bleedings, etc. The CML patients with high leukocyte and platelet counts may experience also different symptoms of hyperviscosity: tinnitus, priapism, stupor, visual abnormalities and cerebrovascular accidents. However, the management of CML with the life-threatening conditions, especially in the accelerated and acute phases, should be realized with participation of the multidisciplinary teams. **Conclusions:** The ovarian apoplexy may serve as a presenting feature of CML in young females with a highly elevated leukocyte count. The reported CML case underwent successful personalized management with 2 generations of tyrosine kinase inhibitors, even if designated with Social intermediate-risk score and complicated by a health emergency.

Keywords

Leukemia, BCR-ABL Gene Transcripts, Health Emergencies, Ovarian Apoplexy, Tyrosine Kinase Inhibitors, Survival

1. Introduction

Chronic myeloid leukemia (CML) is registered in up to 20% of all cases with leukemias in adults and emerges from a clonal malignant myeloproliferation of the stem cell [1] [2] [3] [4] [5]. This hematological malignancy develops mostly in a working-age population with the age of 40 - 55 years. The total number of CML patients grew annually by 2% between the years 2007-2016, and the total number of deaths declined annually by 1% during the years 2008-2017. Higher morbidity by CML was observed among persons exposed to radiation in high doses, including the survivors of the atomic blasts in Japan, Ukraine and patients undergoing radiotherapy, and in those with obesity [6] [7] [8]. The course of this leukemia comprises 3 succeeding phases: chronic, acceleration and acute, and each of them may be associated with the life-threatening emergencies, including the ovarian apoplexy as a presenting feature [4] [5] [9] [10] [11] [12] [13]. The patients with advanced phases and relapses of CML may manifest a sizable disease burden and negative effect on their life quality, working productivity and daily living activities, especially if complicated with health emergencies. The unusual cases of CML were reported in the literature, which evolved into the medical emergencies and required a multidisciplinary approach. Arulkumaran S. et al were among the first, who provided a detailed description of a female patient presented to the gynecological unit as a case of septic abortion [14]. The history and clinical examination suggested the occurrence of double pathology of septic abortion and CML. The histological investigation of the tissues removed from the uterus detected leukemic infiltrates. The diagnosis of CML was proved by the bone marrow aspiration and biopsy. Most careful clinical and laboratory examinations, thus, helped in diagnosis and appropriate treatment of CML presented

as a gynecological emergency. The purpose of our study was the evaluation of the personalized management milestones in CML cases presented with the ovarian apoplexy and the analysis of the international experience on health emergencies in this leukemia.

2. Materials and Methods

Herewith, we evaluated the management milestones in CML case presented with the ovarian apoplexy and reviewed the literature concerning the health emergencies in CML. The patient follow-up was related to the in-patient and ambulatory care. The type of hematological malignancy was identified according to the International Revised 2017 WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues [15] [16]. The diagnosis was confirmed by cytological, cytogenetic and molecular examinations of the peripheral blood and bone marrow [1] [3] [5] [7] [10] [12] [13] [17]. The real-time PCR with the usage of sequence-specific DNA probes was performed for quantitative detection of p210 and p190 transcripts of BCR-ABL fusion gene while proceeding with CML diagnosis. The bone marrow cytogenetic and molecular analyses were accomplished every 6 - 12 months until the complete cytogenetic remission was achieved, and annually thereafter [1] [13] [16] [17]. Main outcome measures [18]: The ECOG Scale and complete hematologic response (CR) estimated the short-term results. The ECOG performance status served as a measure of functional status. Its scores range from 0 to 5 and correlate with the level of patient functioning. CR is the disappearance of all detectable clinical and hematological signs of malignant neoplasm in response to treatment. CR span was assessed in months. The overall and relapse-free survivals asserted the long-term results of treatment [18], and were evaluated in months as a case. The whole research protocol for CML studies was approved by the Research Ethic Board of the State University of Medicine and Pharmacy “N. Testemitanu”. The informed consent was obtained from the patient to assure the researcher and Research Ethic Board that the participant knows every aspect of participation in the study.

3. Results

The CML patient has been followed up and treated from 2006 to 2022 at the Institute of Oncology in the hematology and outpatient departments. This patient was a 21-year-old female, initially hospitalized in the hematology department in June 2006 with the left upper abdominal discomfort and fatigue. She denied fever and any weight loss. During the interrogation the patient mentioned the rough onset of the disease on 8th of June 2006, with the intensive pain in the projected zone of the left ovary. The same day this patient was admitted to the National Research and Practical Emergency Medicine Center with the diagnosis of left-sided ovarian apoplexy. The saturation of the left ovary was performed. The following clinical and laboratory findings were revealed: splenomegaly, anemia (Hb 85 g/L) and elevated leukocyte count ($165.0 \times 10^9/L$) with the shift

to the left. These suggestive findings served the indication for an appointment at hematologist from the Institute of Oncology. On June 23 clinical examination showed mild anemic syndrome, moderate splenomegaly (palpable at the level of +1 cm below the costal arch) and minor hepatomegaly. The spleen and liver surfaces were smooth and painless at palpation. Peripheral and intraabdominal lymph nodes weren't enlarged at palpation. Cardiovascular, respiratory and nephrouinary systems proved without abnormal findings. ECOG performance score was 2. Complete blood count identified the following changes at the time of diagnosis: hemoglobin 85 g/l, erythrocytes $3.4 \times 10^{12}/L$, leukocytes $430.0 \times 10^9/L$, platelets $510.0 \times 10^9/L$, erythrocyte sedimentation rate 4 mm/h, blasts 9%, promyelocytes 8%, myelocytes 33%, metamyelocytes 12%, band neutrophils 16%, segmented neutrophils 8%, eosinophils 2%, basophils 2%, monocytes 8%, lymphocytes 7%. Bone marrow aspiration revealed the increased cellularity, myeloid hyperplasia (84.0%), and normal percentage of blast cells (1.0%). Cytogenetic analysis and real-time quantitative PCR of the bone marrow cells detected 100% and 42% expression of Ph-chromosome and BCR-ABL p210 transcript, respectively. BCR-ABL p210 transcript subtype was b3a2. BCR-ABL p190 transcript proved to be negative. Biochemical test detected the slightly elevated lactate dehydrogenase value—297 U/L. Thus, the diagnosis of late chronic phase of CML was confirmed. Social prognostic score was 1.16, placing this patient into the intermediate-risk group. The ultrasound scanning of the abdomen found moderate splenomegaly (length = 16 cm) and insignificant hepatomegaly, regional lymph node enlargement.

The patient underwent single-agent cytoreduction therapy with hydroxyurea 3000 mg daily, with the achievement of partial hematological remission. Since 2007 she underwent the targeted therapy with imatinib mesylate at a daily dosage of 400 mg, with the achievement of complete hematological remission and minor cytogenetic remission in December 2008 (Ph-chromosome = 60%). ECOG performance score was recovered up to 0. Due to the persistence of Ph chromosome and BCR-ABL p210 transcript in the bone marrow cells, the daily dosage of imatinib mesylate was boosted up to 600 mg. In December 2009 the follow-up cytogenetic analysis of the bone marrow cells did not detect Ph-chromosome. The follow-up real-time quantitative PCR proved a major/optimal molecular response in January 2014: BCR-ABL p210 transcript was 0.03%. The patient continued targeted therapy with imatinib mesylate at a daily dose of 600 mg, followed by nilotinib at a daily dose of 600 mg due to the persistence of BCR-ABL p210 transcript. The repeated real-time quantitative PCR didn't reveal BCR-ABL p210 transcript under the therapy with nilotinib. Thus, the complete molecular remission was achieved. By January 2022, the overall survival accounted 197.5 months, and the relapse-free survival—154.5 months. Under the treatment with tyrosine kinase inhibitors, the patient did not experience the disease burden and side effects, and resumed her work, with a good life quality (ECOG score is 0). The reversal of the unfavorable medical and social patterns of

CML improved the individual productivity and could be considered as an optimizing factor of patients' management.

4. Discussion

The narrative review of the bibliographic sources was fulfilled in the form of a synthesis. The accumulation of information for this study was performed by analyzing the data from the specialized international references and official statistics concerning CML. The scientific publications were searched over the Google Search, PubMed, NCIB, Medscape, Z-library, and Hinari database, by the keywords: "chronic myeloid leukemia", "incidence", "health emergencies", "ovarian apoplexy", "BCR-ABL gene transcripts", "diagnosis", "management", "treatment", "molecular response", "survival", "prognosis". We studied more than 50 bibliographic reference sources in order to accomplish the Discussion section. Twenty-eight essential primary sources were determined and selected, according to the relevance of the impact score.

CML may be manifested by the life-threatening health emergencies, especially thrombotic events, splenic infarcts and ruptures, bleedings (after dentistry procedures, epistaxis, cerebral), etc. [5] [9] [19]. The CML patients with high leukocyte and platelet counts also may experience different symptoms of hyperviscosity: tinnitus, priapism, stupor, visual abnormalities and cerebrovascular accidents [4] [5].

Leukemias associated with spontaneous hemoperitoneum are the uncommon events and generally involve leukemic cell infiltration of female genital tract [20]. CML, other leukemias and lymphomas may affect genital tract but there is a scarcity of literature pertaining to leukemia resulting in corpus luteal cyst rupture leading to hemoperitoneum without histopathological involvement of female genital tract with leukemic cells. Ovarian cyst hemorrhage in CML patient had been first reported by Valentsik in 1951 [21]. Chaudhar *et al.* reported a 32-year-old, multiparous female who presented with hypovolemic shock with hemoperitoneum, splenomegaly, and was subsequently diagnosed with a chronic myeloproliferative disorder [20]. The splenic hemorrhage was initially thought to be the cause of hemoperitoneum but an ultrasound scan proved corpus luteal hemorrhage as the etiological cause. Emergency ultrasonography and Doppler scan revealed hemoperitoneum and splenomegaly without any site of rupture. An empty normal sized uterus with echogenic lesion (3.8 × 2.7 cm) in left ovary suggestive of corpus luteal cyst was observed. Thus, the final diagnosis of corpus luteal hemorrhage with myelo-proliferative neoplasm was made. Conservative management was successful thereby averting surgery. Patient was started on imatinib after diagnosis of CML was established by real-time PCR test of the peripheral blood RNA. She conceived while on treatment and delivered a healthy newborn with her disease being under remission.

Another case report of 39 years old female, who presented with the evidence of intra-abdominal bleeding to the emergency department of the University

Hospital of North Midlands (UK), proved to be related to CML [22]. An urgent CT-scan revealed a massive intra-abdominal hematoma with the suggestion of a gynecological origin. The patient was then transferred immediately to the operating theatre where she had an emergency laparoscopy to evacuate the hematoma and identify the source of bleeding. In view of persistently elevated leukocyte ($54.8 \times 10^9/L$) and platelet ($695.0 \times 10^9/L$) counts, a multidisciplinary team of gynecologists, general surgeons and hematologists decided to perform a bone marrow biopsy under the care of the hematology team. The biopsy and real-time PCR revealed BCR/ABL1 re-arrangement, strongly suggestive of a Philadelphia chromosome, typically associated with CML. This article highlighted the critical role of Multi-Disciplinary Team involvement in elaborating management plans to achieve the best possible outcomes for those patients.

In 2008 Joseph D.E. and Durosinmi M.A. performed an attempt to describe the non-reversal neurological deficiencies complicating CML [23]. Patients' case folders and hematological malignancies register of CML cases followed-up in Jos University Teaching Hospital between 1995 and 2005 were retrospectively studied. Thirty-three cases of CML had been seen within the study period. Five (15.15%) of them had one or more sensori-neural defects. Fundoscopy revealed leukemic depositions on the retina. The authors reported about the regression of the hyperleucocytosis-induced complications under the conventional therapy. Nevertheless, the complications due to other pathogenetic mechanisms such as leukemic depositions did not recovered to their pre-morbid condition followed disease control despite the usage of the accessible contemporary treatment programs.

CML initial presentations, thus, were considered as the extramedullary myeloid blast crises involving the central nervous system and multiple lymph nodes, with no findings of the acceleration phase or blast crisis in the peripheral blood or bone marrow [24]. Although the induction therapy was not consolidated with allogeneic stem cell transplantation, the complete cytogenetic and molecular remission was maintained under a single-agent therapy with dasatinib for 3.5 years since the diagnosis with no evidence of the active extramedullary disease. The authors suggested that dasatinib might play an important role in controlling not only chronic phase of CML, but also its extramedullary central nervous system blast crisis, especially when combined with whole-brain radiation therapy.

CML is known to trigger nephrotic syndrome. A case of CML patient with nephrotic syndrome was reported by Yoshizaki N *et al.* in 1989 [25]. The renal biopsy with histological examination revealed membranous proliferative glomerulonephritis. Other published case reports also established an association between nephrotic syndrome and CML. The histology of the renal biopsies was either minimal change disease or membranous glomerulonephritis. Nephrotic syndrome is a well-recognized documented complication after allogeneic peripheral stem cell transplantation [26]. It commonly emerges due to the autoimmune glomerulonephritis and is supposed to be a clinical sign of the graft versus host disease. The authors analyzed several case reports of nephrotic syndrome occurring after the peripheral stem cell transplantation. Most of those cases were

membranous nephropathy. Other pathologic conditions were due to the diffused proliferative glomerulonephritis and minimal change disease. All of the cases had concomitant findings of the graft versus host disease, either acute or chronic. The authors suggested that graft versus host disease in those cases generated an autoimmune response, thereby triggering immune-complex deposition in the glomeruli.

Priapism is a complication uncommonly observed in leukemia [27] [28]. Nevertheless, about 20% of all priapism cases are related to hematological diseases. The incidence of priapism in adult leukemic patients is about 1% - 5%. Leukemia is commonly manifested by painful priapism. Four different mechanisms were described: sludging of leukemic cells in the corpora cavernosa and the dorsal veins of penis; venous congestion of the corpora cavernosa due to the mechanical pressure on the abdominal veins by massive splenomegaly; infiltration of the sacral nerves with leukemic cells; leukemic proliferation in the central nervous system. The following case characterized priapism as an uncommon manifestation of CML. A 21-year-old male with a steady painful erection of penis for 19 hours at home was reported in the medical literature. The patient underwent immediate irrigation and decompression of priapism by urologist at the emergency department. This approach led to a flaccid penis later. During hospitalization, the diagnosis of CML was confirmed by the peripheral blood smear exam and bone marrow aspiration. No impotency and other consequences were registered after his departure from the hospital.

The described cases proved the usefulness of participation of multidisciplinary teams consisting of clinicians of different specialties in management of patients with uncommon onsets of hematological malignancies. However, the management of CML with the life-threatening conditions, especially in the accelerated and acute phases, should be realized in the specialized inpatient wards with the support of Multi-Disciplinary Teams. Imatinib mesylate remains the first-line therapeutic option in chronic phase with low and intermediate Socal prognostic score, being superior to the conventional antineoplastic therapy and α -interferon due to the opportunity of achievement of a fast complete hematological remission, complete cytogenetic and molecular responses and due to the significant increase of the life quality and individual productivity, overall and relapse-free survival of CML patients [1] [3] [5] [6] [8] [9] [13]. Our study analyzed the uncommon onset of CML under the form of the ovarian apoplexy in a young female patient with Socal intermediate-risk score. Surgical treatment (sutation of the left ovary) was performed in order to manage this life-threatening health emergency prior to CML diagnosis. The targeted therapy with imatinib led shortly to a complete hematological remission, complete cytogenetic and major molecular response. The complete molecular response, thus, was achieved after a personalized targeted therapy with 2nd generation TKI nilotinib.

5. Conclusions

CML is a clonal myeloproliferative BCR-ABL-positive neoplasm, which some-

times may be complicated with the life-threatening emergencies, especially hemorrhagic and thrombotic events, infarct and rupture of the spleen, ovarian apoplexy, that require the involvement of the multidisciplinary team.

The ovarian apoplexy may serve as a presenting feature of CML in young females with a highly elevated leukocyte count. The reported CML case underwent successful personalized management with 2 consequent generations of TKIs, even if designated with Social intermediate-risk score and complicated with ovarian apoplexy.

Author Contributions

Conceptualization, methodology, formal analysis, investigation, resources, data curation, writing-original draft preparation, writing-review and editing, visualization, project administration.

Institutional Review Board Statement

The whole research protocol for CML studies was approved by the Research Ethic Board of the State University of Medicine and Pharmacy “N. Testemitanu”.

Informed Consent Statement

The informed consent was obtained from the patient to assure the researcher and Research Ethic Board that the participant knows every aspect of participation in the study.

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Conflicts of Interest

The author declares no conflict of interest. The author does not have any financial relationships that might bias the content of this manuscript.

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One Case of Diabetes Nephropathy Stage V, Combined Valvular Disease, Total Heart Failure with Diabetes Foot Gangrene

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Abstract

The patient was found to have 4+urine sugar by physical examination 14 years ago and was treated with oral hypoglycemic drugs. Insulin was injected intramuscularly nine years ago. Two and a half years ago, it was found that the color of the thumb, index and middle toe of the left foot became black. He went to a third-class hospital in Beijing and was diagnosed as “diabetes foot”. He was treated with “balloon dilation of lower limb blood vessels of diabetes foot”. Half a year ago, the third toe on the right side was broken and treated in the hospital again. “Popliteal artery stent implantation” was given for the diagnosis of “double kidney insufficiency, diabetes foot, left heart failure, combined heart valve disease”, “Hemofiltration therapy” and anti-inflammatory, amino acid supplementation, kidney function protection, anticoagulation, anemia correction and other treatments. Later, he went to our hospital and was diagnosed by the TCM diagnosis: category of consumptive disease, toe or finger gangrene (syndrome/pattern of qi and yin deficiency). Western medicine diagnosed: stage V of diabetes nephropathy, type II diabetes foot gangrene, combined with heart valve disease, hypoalbuminemia, double kidney cyst, moderate anemia, pleural effusion, hyperkalemia, pulmonary infection, and total heart failure. The patient was treated by the Qi-acupuncture therapy of TCM in combination with Chinese and Western medicine Medical treatment made the patient significantly better and discharged.

Keywords

Diabetic Nephropathy Stage V, Diabetic Foot Gangrene, Uremia, Combined Valvular Heart Disease, Total Heart Failure, The Qi-Acupuncture Therapy of the TCM

1. Introduction

After dialysis and treatment with traditional Chinese medicine and Western medicine, the patient's condition gradually worsened, and it was a miracle that the patient was significantly improved by the use of the Qi-acupuncture therapy of the TCM.

2. Case

The patient, a male, 74 years old, from Yangquan City, Shanxi Province, was admitted to the hospital on March 3, 2022. Mainly due to diabetes for more than 14 years, edema of both lower limbs with gangrene of feet, and an increase of serum creatinine for 1 month. The patient was given oral metformin tablets and Acarbose tablets after finding urine sugar 4+ in the local hospital 14 years ago. 9 years ago, due to poor control of fasting blood glucose, it was changed to intramuscular insulin (dosage form and dosage were ominous). Two and a half years ago, it was found that the color of the left foot's big toe, index toe and middle toe became black. After treatment in a top three hospital in Beijing, it was diagnosed as "type II diabetes foot gangrene", and was treated with "balloon dilatation of lower limb blood vessels of diabetes foot" and other treatment for improvement. Half a year ago, he was treated again in the above-mentioned Beijing hospital because of the ulceration of the middle toe of his right foot. Blood biochemistry: albumin 29.23 g/L, creatinine 526 $\mu\text{mol/L}$, urea 41.24 mmol/L, uric acid 458 $\mu\text{mol/L}$, total cholesterol 2.96 mmol/L, calcium 1.81 mmol/L; Sputum culture: find gram-negative cocci and bacilli 4+, gram-positive cocci and bacilli 4+. Blood routine test: WBC $11.27 \times 10^9/\text{L}$, L $0.76 \times 10^9/\text{L}$, N $10 \times 10^9/\text{L}$, RBC $2.97 \times 10^{12}/\text{L}$, HGB 86 g/L; Interleukin 6: 16.39 pg/mL; Urine routine: urine occult blood 3+, urine protein 2+, Glu 1+, WBC 45.2/UL, RBC 677.6/UL, WBC 8.13 HPF, RBC 121.87 HPF; B-type natriuretic peptide was more than 35000 pg/mL; ECG: 1. Sinus rhythm, 2. ST-T changes. Color ultrasound: bilateral renal cyst; Left ventricular dilation, left ventricular wall stage motion abnormality, aortic regurgitation (mild), mitral regurgitation (moderate to severe), tricuspid regurgitation (mild), left ventricular systolic and diastolic dysfunction, aortic sinus dilation. Chest film: bilateral pulmonary edema and infection, bilateral pleural effusion. He was diagnosed as "double kidney insufficiency, type II diabetes foot gangrene, left heart enlargement, combined alvular heart disease, cardiac insufficiency, multiple pulmonary nodules, double kidney cysts, hypoproteinemia, moderate anemia, bilateral pleural effusion", and was given "popliteal artery stent implantation", hemofiltration treatment, antibacterial and anti-inflammatory, amino acid supplementation, renal function protection, anticoagulation, anemia correction and other treatments. Continue to take levofloxacin tablets, sodium bicarbonate tablets, benzbromarone tablets and compound α Ketonic acid (Kaitong) tablets, mecobalamin tablets, Duqing granules (毒清颗粒), Miqu enzyme tablets, Qumei pudding tablets, folic acid tablets, furosemide tablets, aspirin tablets, hydrocopyrigrel tablets, etc. The renal function rebounded significantly; the

condition worsened and came to our hospital for treatment. The outpatient department was admitted to hospital with “diabetes nephropathy, foot gangrene”. Main symptoms: chest tightness, wheezing, shortness of breath, anorexia, cough, white sputum, moderate and mild finger concave edema in the lumbosacral region, severe edema in both lower limbs below the groin, half sitting position, aggravation at night, shallow and fast breathing. Since the onset of the disease, the patient has no disturbance of consciousness, can eat well, has normal stool, and has a urine volume of about 800 mL/24h. He has no history of hypertension, trauma or surgery. He was born in his native country, has lived in the local area for a long time, and has not been to pastoral areas or epidemic areas. He has no known history of COVID-19, viral hepatitis, typhoid, tuberculosis and other infectious diseases, nor any special medication history. For over 20 years, he smoked 20 cigarettes a day, but later he had already quit smoking. He has no long-term heavy drinking history, but one of his sisters has a history of diabetes. He also has a history of exposure to non toxic substances, due and radioactive substances. The spouse and 2 children are healthy with T36.1°C, P161 times/min, R18 times/min, BP97/61 mmHg. Cooperate in the physical examination, be clear and articulate, not in good spirits, pale and colorless, answer to the point, passive posture, and push into the ward. The mouth and lips are dark, the tongue is in the middle, the tongue is fat, the fur is white and greasy, and the pulse is heavy. The skin of the whole body is free of yellowing, bleeding spots and ecchymosis, liver palm and spider nevus are negative, and the superficial lymph nodes around the body are not touched and swollen. There is no edema on both sides of the eyelids, pale palpebral conjunctiva, no yellow staining on the sclera, no varicocele of the jugular vein, symmetry and deformity of the thorax, decreased respiratory activity of the right thorax, shallow and fast breathing, decreased right lung language fibrillation, and dullness in the lower lung field. The dullness boundary of the lung and liver is located in the fourth intercostal space of the right midline of the clavicle, small rales can be heard in both lungs, no protuberance in the precordial area, mass pulsation of the cardiac apex, heart rate 161 beats/minute, arrhythmia, and diastolic galloping rhythm can be heard in the apical area. The abdomen is flat and soft, there is no varicose veins in the abdominal wall, no tenderness and rebound pain, Murphy’s sign is negative, the liver and spleen are not reached under the ribs, the mobility dullness is negative, the bowel sounds are normal, the lumbosacral part is slightly edema, the lower extremities below the groin are severely concave edema, and the shoes and socks cannot be worn for a long time, and the self-made footpads are wrapped. After debridement of broken dorsum of foot due to loss of thumb, indication toe and middle toe of left foot; after debridement of gangrene of the right foot, the wounds of both feet were ulcerated and the pulsation of the dorsal artery was weakened. Blood routine test: RBC $2.01 \times 10^{12}/L$, Hb 59 g/L, hematocrit 19%, L $0.46 \times 10^9/L$, N 88.9%; Renal function: UREA 45.46 mmol/L, Cr 947.5 $\mu\text{mol}/L$, UA 570 $\mu\text{mol}/L$, cysC 3.96 mg/L; Electrolyte: K^+ 6.20 mmol/L, Na^+ 130.01

mmol/L, Cl 92.48 mmol/L, nCa 0.89 mmol/L, TCa 1.73 mmol/L, TCO₂ 20.28 mmol/L; Liver function: Tp 59 g/L, ALB 29.8 g/L, A/G 1, CHE 2.51 kU/L, CRP 41.7, PCT 0.34 ng/mL; ESR: 92 mm/h, Pi 2.47 mmol/L, CK 132 U/L; Blood type: Rh (D) blood type B is positive, irregular antibody negative; GHb 5.1%; GLU 8.91; Fasting C-peptide 14.703 ng/mL; Plasma lipids: TC 3.43 mmol/L, TG 2.73 mmol/L. ECG: 1) Sinus rhythm; 2) ST-T changes. Chest film: bilateral pulmonary edema and infection, bilateral pleural effusion. Chest CT; Thorax is symmetrical, multiple patchy high-density shadows can be seen in both lungs, large high-density shadows can be seen in the left upper lobe of the lung, uneven density, blurred edge, flocculent slightly high-density shadows can be seen in the left lower lobe and right upper lobe of the lung, local consolidation, large right hilar, atrophy of the inner segment of the right lower lobe of the lung, and gas-containing bronchial shadows can be seen inside; The heart shadow is enlarged, a small amount of watery density shadow is found in the pericardium, no swollen lymph nodes are found in the mediastinum, and watery density shadow is found in both sides of the chest, especially in the right side. Color Doppler ultrasound: 1) Bilateral pleural effusion (+), the anteroposterior diameter of the right pleural lamellar dark area is about 13.6 cm; 2) Fatty liver, widened portal vein and enlarged light spots in liver parenchyma; 3) Spleen enlargement; 4) Bilateral renal cysts, with enhanced echo in the collecting part of both kidneys; 5) The prostate volume increases; No abnormality is found in ureter and bladder; 6) Left atrium enlarged and left ventricular diastolic function decreased; 7) Mitral valve—moderate to severe insufficiency; 8) Moderate tricuspid insufficiency; 9) Mild aortic insufficiency; 10) Aortic sinus dilation; 11) A small amount of pericardial effusion.

Western medicine diagnosis: stage V of diabetes nephropathy, type II diabetes foot gangrene, combined heart valve disease (3-valve disease, moderate to severe), hypoproteinemia; Bilateral renal cyst, moderate anemia, massive pleural effusion, hyperkalemia, pulmonary infection, and heart failure. The TCM diagnosis: category of consumptive disease (虚劳病), toe or finger gangrene (脱疽病) (syndrome/pattern of qi and yin deficiency, 气阴两虚证). On the basis of integrated treatment of traditional Chinese medicine and western medicine, the treatment of the Qi-acupuncture therapy of the TCM (中医气针疗法) is added. Take a low-salt, high-quality and low-protein diet, record the 24-hour urine volume, and measure the weight every day. De-leucocyte suspension red blood cells (Hebei Provincial Blood Center) were given a static point, 2 units of treatment dose/time, two times in total; Three times of continuous intravenous hemodialysis; Give blood purification treatment for detoxification and drainage for 6 times intermittently; Thoracic drainage and drainage for 4 times drained 2363 ml of pleural fluid; Folic acid tablets (Tianjin Lisheng Pharmaceutical Co., Ltd.; GYZZ H12020215; 5 mg) 5 mg orally, 3 times/day; Recombinant human erythropoietin injection (North China Pharmaceutical Jintan Biotechnology Co., Ltd.; GYZZ S20133012; 5 mL: 5000 IU), 0.5 ml subcutaneous injection, twice a

week; Polysaccharide iron complex capsule (Shanghai Pharmaceutical Qingdao Guofeng Pharmaceutical Co., Ltd.; GYZZ H120030033; 0.15 mg [calculated by iron]) 0.15 g/time, oral, 1 time/day; Cefoperazone sulbactam sodium for injection (Pfizer Pharmaceutical Co., Ltd.; GYZZ H12020527; 1.5 g) 1.0 g static point, once/12 h; Jingdian Danhong Injection (Shandong Danhong Pharmaceutical Co., Ltd.; GYZZ H120026866; 20 mL/piece), 40 ml/time/day; Furosemide injection (Tianjin Jinyao Pharmaceutical Co., Ltd.; GYZZ H20020527; 2 mL: 20 mg), static point, 40 ml/time/day. “Reyan package (中药热奄包)” of the TCM (consisting of coix seed, rhubarb, salvia miltiorrhiza, etc., one pair per day) is applied externally. The Qi-acupuncture therapy of TCM is based on the acupoints of upper limbs and abdomen, and the acupoints of Hegu, Neiguan, Zhongwan, Jianli, lower wrist, water, and Tianshu are selected. After 4 times of treatment, the edema of both lower limbs disappeared below the knee joint, and gradually increased the number of Liangqiu, Xuehai, Zusanli, Shangjuxu, Fenglong, Sanyinjiao and other acupoints. There were 15 times of treatment before and after treatment, and the condition was significantly improved and discharged. T36.7°C, P74 times/min, R18 times/min, BP115/68 mmHg. With clear mind, clear language and good spirit, he walked out of the ward with fair complexion, pale red lips, pale tongue, white and greasy fur, and deep pulse. The respiratory activity of both lungs is consistent, the speech tremor is equal, and the respiratory sound of both lungs is clear. There is no protuberance in the precordial area, the heart rate is 74 beats per minute, and the rhythm is uniform. The abdomen is flat and soft, the liver and spleen are not reached under the ribs, and there is no edema in the lumbosacral region and both lower limbs. The thumb, index and middle toes of the left foot are missing, the five toes of the right foot are present, the skin of both feet is wrinkled, the edema is eliminated, and the wound has been healed. The pulsation of the dorsal arteries of both feet is normal. Blood routine test: RBC $2.44 \times 10^{12}/L$, Hb 72 g/L; Renal function: UREA 20.98 mmol/L, Cr 428.4 $\mu\text{mol}/L$, cysC 4.18 mg/L; Liver function: TP 61.1 g/L, A 30.5 g/L, CHE 4890 U/L; Four items of blood coagulation: fibrinogen 4.53 g/L. Bacteria and drug sensitivity test: no bacterial growth. Routine cytological examination of pleural fluid: proliferative mesothelial cells and inflammatory cells can be seen, but no cancer cells can be seen. Chest CT: no abnormality in both lungs and chest. On April 10, local chest CT re-examination showed no abnormality in both lungs and chest. There was no recurrence in the follow-up for nearly one year.

3. Discussion

Diabetes kidney disease (DKD) is also known as Diabetes Nephropathy (DN). It's one of the common microvascular complications of diabetes. Its clinical manifestations are fatigue, edema and other symptoms, characterized by proteinuria. On this basis, progressive renal function damage, hypertension, edema and severe renal failure occur in the late stage. According to the Chinese Guidelines for

the Prevention and Treatment of diabetes Nephropathy (2021) [1], DKD refers to chronic kidney disease caused by diabetes, mainly manifested as urinary albumin/creatinine ratio (UACR) ≥ 30 mg/g and/or estimated glomerular filtration rate (eGFR) < 60 ml·min⁻¹·(1.73 m²)⁻¹, which lasts for more than 3 months. Huang Shixiong *et al.* [2] believed that DKD is one of the most common chronic complications or complications in diabetes, and also the primary cause of end-stage renal disease, which seriously affects the quality of life of patients, has a poor prognosis, and is one of the main causes of death in diabetes patients. According to the GFR stage, chronic kidney disease is currently divided into 1 - 5 stages according to the guidelines formulated by the Kidney Disease Prognosis Quality Initiative (K/DOQI) [3]. DKD stage V is an end-stage renal disease, which is a progressive impairment of renal function. With the gradual decline of renal function, it eventually evolves into uremia. For advanced uremia, dialysis treatment or kidney transplantation is required. Patients with uremia are prone to severe infection due to low immune function and abnormal leukocyte function. The decrease of immunity may be related to uremic toxin, acidosis and malnutrition. Pulmonary infection is the most common. Dialysis patients may have arteriovenous fistula or peritoneal entrance infection, hepatitis virus (hepatitis B, hepatitis C) infection. Diabetes foot gangrene, also known as diabetes limb gangrene, is lower limb infection, ulcer formation and (or) destruction of deep tissue caused by diabetes combined with neuropathy and various degrees of lower limb vascular disease (lower limb artery occlusion and local ischemia). Wei Hanlin *et al.* [4] believed that diabetes foot gangrene is one of the serious complications of diabetes. It is common in clinical practice and has a poor prognosis, often leading to amputation, toe amputation, or even death. The symptoms include lower limb pain, sensory abnormalities, intermittent claudication, skin ulcer, limb gangrene, etc. The treatment methods of western medicine mainly include balloon expansion, stent implantation, bone removal, etc., and the curative effect is not ideal. Traditional Chinese medicine generally adopts the method of activating blood circulation and removing stasis to improve blood circulation and increase local blood supply, clearing heat and detoxification to remove systemic or local infection, and on the basis of strict disinfection and debridement, traditional Chinese medicine is used to remove pus and saprophytic muscle for wound treatment, which has a positive effect, a short course of treatment and avoids amputation. Renal cysts can be divided into simple renal cysts and complex renal cysts. Generally, it is unilateral, and it is rare that it occurs simultaneously on both sides. It is usually a benign disease, with smooth wall and transparent fluid. Simple renal cyst is the most common disease in human kidney diseases, and its incidence rate ranks first in cystic renal diseases. It is the manifestation of kidney aging, not heredity. The number of cysts may increase with age. Its etiology is still unclear. The patients generally have no symptoms, more than those found in the health examination or other diseases when they were examined by B-ultrasound and CT. The most common clinical manifestations are abdominal or back pain on the affected side, hematuria, ab-

dominal mass, elevated body temperature and general discomfort. It has little impact on renal function and little chance of malignant transformation. Complex cysts may be congenital, such as polycystic kidney is a genetic disease. This patient suffered from diabetes for a long time, consuming qi to hurt yin, damaging yin and yang, imbalance of qi and blood yin and yang, and damage to the five internal organs, of which the deficiency of kidney is the root cause, coupled with old and weak body, leading to deficiency of both qi and yin, coupled with local feeling of external evil, on this basis, the disease products such as water dampness, phlegm turbidity, blood stasis and other diseases occur, and cause and effect each other, forming the extremely critical and severe syndrome of deficiency and excess.

Combined valvular heart disease, also known as multi-valvular disease, refers to the simultaneous existence of two or more valvular diseases of the heart. The most common pathological change is a rheumatic disease, followed by degenerative disease. Infectious endocarditis and other causes are rare. When more than one valve is damaged, the overall hemodynamic abnormality is more serious than that of each valve alone. The valve damage with two lighter signs may have obvious symptoms. At the same time, the combined existence of valvular disease often makes the diagnosis difficult due to the change of typical signs of a single valvular disease. Zhang Baoren *et al.* [5] found that combined valvular disease accounted for about 15% of heart valvular disease, including 80% of combined aortic and mitral valve disease, about 20% of mitral and tricuspid valve disease or combined aortic valve disease, and rare aortic valve and tricuspid valve disease. In the same period, only one case of valve disease was reported. When mitral regurgitation combined with aortic regurgitation, the left heart's diastolic blood volume is greatly increased, the left heart is very easy to expand and fail, and the blood flow back into the left atrium during systole is increased, which is easy to cause the left atrium decompensation. Tricuspid valve insufficiency is often accompanied by pulmonary hypertension, which will cause the enlargement of the right atrium and right ventricle. The enlargement of the right atrium and right ventricle will lead to the symptoms of right heart failure. The symptoms of right heart failure mainly include swelling of the upper and lower extremities, varicosity of the jugular vein, enlargement of the liver and spleen, and in severe cases, pleural effusion and ascites. Both tricuspid valve diseases can cause total heart failure in the late stage. Combined valvular disease, total heart failure and other organic heart diseases have early diastolic galloping rhythm, which is not affected by body position. Most of them originate from the left ventricle. The clearest part of auscultation is at the apex of the heart. The causes of aortic sinus dilatation include arteritis, ascending aortic aneurysm and aortic valve stenosis. It can affect coronary artery and cardiac function, change the direction of aortic hemodynamics in diastole, affect the blood supply of coronary artery, and can be manifested as palpitation, shortness of breath, chest tightness and other symptoms. Medical treatment is mainly to prevent the deterioration of cardiac function and the occurrence of complications. Surgery is the main me-

thod of treatment. TCM treatment based on syndrome differentiation has a certain effect, but systematic studies of large cases are rare. In this case, 3 valvular diseases were combined with aortic sinus dilatation at the same time. No relevant report was found after consulting relevant data.

DKD is associated with hypoalbuminemia, uremia and other protein loss or reduced synthesis diseases, resulting in the decrease of plasma albumin, the decrease of plasma colloid osmotic pressure in the capillaries of the chest model, and the formation of pleural effusion; Cardiac valvular disease and total heart failure lead to increased hydrostatic pressure in the capillaries of the chest mold, resulting in leakage pleural effusion; Pulmonary infection leads to pleural inflammation, which increases the permeability of the capillaries of the chest model, and a large number of cells, proteins and liquids in the capillaries infiltrate into the peritoneal cavity. The protein content in the pleural fluid increases and the osmotic pressure of the pleural fluid colloid increases result in exudative pleural effusion. The respiratory amplitude caused by pulmonary infection, total heart failure and pleural effusion becomes shallow, usually accompanied by increased respiratory rate, and shallow and fast breathing is formed at this time. The gas stays in the alveolus for too short a time, and the gas is exhaled before it can exchange gas, resulting in hypoxia in the body and affecting the respiration of cells. The Chinese expert consensus on diagnosis and treatment of lung nodules [6] defines lung nodules as focal, quasi-circular, high-density solid or sub-solid lung shadows with diameter ≤ 3 cm, which can be solitary or multiple, without atelectasis, hilar lymph node enlargement and pleural effusion. This patient's hypoproteinemia, lung infection, and total heart failure are the causes of bilateral pleural effusion and pericardial effusion, so it is very important to improve immunity and resist infection.

The patient is an elderly man in his 70s, who has been suffering from thirst and has been ill for a long time, resulting in foot gangrene, chest tightness, shortness of breath, cough, cough, white sputum, and severe edema in the lower body, half sitting, and shallow and fast breathing. Clinically, there are more than a dozen syndromes at the same time, and any one of them is critical and serious, which will endanger life. Together, it is even more dangerous. This belongs to the categories of gangrene, chest pain, edema, clearance, suspended drinking and so on secondary to diabetes in traditional Chinese medicine, and is considered as asthenia and fatigue syndrome. Minimally invasive surgery, western medicine and hemodialysis, creatinine and urea continue to rise, and edema gradually worsens, entering the uremic stage. On the basis of Chinese and Western medicine treatment, the author added Chinese medicine Qi medicine therapy. Increase the oxygen carrying capacity of cells, continuous venous hemodialysis treatment to drain water and relieve the symptoms of heart failure; Give intermittent blood purification treatment for detoxification and drainage; Thoracic drainage to relieve dyspnea and improve myocardial blood supply; Blood transfusion improves anemia; Anti-infection with intravenous antibiotics; It can

promote water and reduce swelling. The Chinese medicine “Reyan package” is applied externally to tonifying replenishing the spleen and kidney (补益脾肾), activating blood and resolving stasis (活血化瘀); Director Xu Yubo [7] [8] [9] of the Chinese medicine Qi-acupuncture therapy, believes that the disease is based on deficiency of spleen and kidney, deficiency of both qi and yin, blood stasis blocking collaterals, and water dampness, dampness and turbidity, damp heat, and turbidity. The disease is located in the spleen, lung and kidney. The kidney is the key, involving the heart and liver. Treating the tip in acute disease (急则治标), the upper limbs and abdominal acupoints should be the main points. The large intestine of Hegu point in the prescription converges here through qi and blood. It has the effects of clearing the lung and water, regulating the water channel, clearing the collaterals and relieving pain, clearing the heat and relieving the exterior, opening the mind, invigorating the qi and strengthening the exterior, and promoting qi and activating blood. This point is good at treating fever caused by acute fever and exogenous diseases. It has a high prevention and treatment effect on patients with infectious inflammation, strengthens the body’s defense function, has a two-way adjustment effect on white blood cells, can significantly increase the platelet in the blood, can increase the content of globulin in the serum, can adjust the blood circulation function, and can reduce the content of cholesterol in the blood of hypertensive patients. Wu Yanying [10] *et al.* electroacupuncture at Zusanli and Hegu can reduce the sensitivity of intestinal pain in IBS rats and improve gastrointestinal motility. Neiguan acupoint can nourish qi and blood, calm the heart and calm the nerves, calm the stomach and reduce the adverse reactions, relieve arthralgia, relieve depression, broaden the chest and regulate qi, relieve asthma, relieve pain, regulate yin and yang qi and blood, dredge meridians, etc. It connects the upper, middle and lower triple energizers and can treat palpitation, chest pain and chest tightness of the upper energizer; Mid-focus stomach pain and vomiting; lower focus urinary system disease, etc. Zhongwan point is the intersection point of the small intestine meridian of the hand sun, the triple energizer meridian of the hand shaoyang, the stomach meridian of the foot yangming, and the ren meridian, the mu point of the stomach, and the fuhui point of the eight hui points. It can coordinate with the stomach to strengthen the spleen, reduce the adverse effects and promote water, dissipate food and guide stagnation, and calm the nerves. It is a necessary point for the treatment of digestive system diseases and an important point for the treatment of nervous system diseases. The lower wrist point is the intersection point of the Ren meridian and the foot Taiyin meridian, which can strengthen the spleen and stomach, promote qi and channel, and dredge water and dampness. With Neiguan, Tianshu and Shuishui acupoints, it can treat acute bacillary dysentery, acute diarrhea, severe afterweight, lung infection, etc. Xu Yubo [11] found that replenishing the Qi of the Ren meridian is what Zhang Jingyue said in the new square eight arrays, “seeking Yang from Yin”, replenishing the blood of the governor meridian is “seeking Yin from Yang”, and those who are

good at replenishing Yang must seek Yang from Yin, and then Yang will be assisted by Yin and become infinite; Those who are good at nourishing yin must seek yin in the yang, and then yin will get yang and the source will not be exhausted. The function of Tianshu point is to regulate qi and relieve pain, promote blood circulation and remove stasis, clear away dampness and heat, and mainly treat abdominal pain, abdominal distension, constipation, diarrhea and dysentery. Water acupoints regulate water channels, regulate qi to relieve pain, strengthen spleen and diuresis, and regulate the stomach and intestines, mainly treating edema, adverse urination and other disorders of fluid distribution, abdominal pain, diarrhea, nausea and vomiting and other gastrointestinal diseases. Treating the root in chronic disease (缓则治其本). After 4 days of treatment, the edema of the lower limb subsides below the knee joint, and gradually increases the lower limb acupoints. Liangqiu point dispels wind and dampness, invigorates collaterals and relieves pain. Hegu with Taichong, called Siguan acupoint, has the effect of calming the nerves, calming the liver and calming the wind, and is mainly used to treat mania, headache, dizziness, and hypertension. Zusanli belongs to the Stomach Meridian of Foot Yangming, which is an important point for strengthening and health care. It can generate stomach qi, dry the spleen and damp, replenish the qi, strengthen the spleen and stomach, regulate qi and reduce adverse reactions, and activate blood circulation. It is mainly used to treat gastrointestinal diseases, beriberi, psychosis, asthenia and fatigue syndrome, cough, asthma, palpitation, shortness of breath, edema, etc. Shangjuxu acupoint can regulate viscera Qi, relax muscles and activate collaterals, and mainly treat digestive system diseases and motor system diseases. Zhao Rong *et al.* [12] found that acupuncture can enhance the phagocytic function of macrophages (M) in immunosuppressed rats, while the level of serum LSZ does not necessarily increase with the phagocytic function of M. Fenglong acupoint can relieve cough and asthma, dissipate phlegm and open orifices, promote qi and blood circulation, strengthen the spleen and stomach, and is the main acupoint for strengthening the spleen and eliminating phlegm. It is commonly used to treat psychosis, hysteria, hypertension, waist and knee pain, chronic bronchitis, pleurisy, urinary retention, etc. In modern research, acupuncture at Fenglong and other acupoints can cause changes in the volume of blood vessels in the lower leg and cause vasoconstriction. Huang Zhenmei [13] and others massage Fenglong and Feishu points to help expectorate patients with lung distension, reduce the risk of falling pneumonia in hospitalized patients, and improve the quality of life of patients. Lin Jie [14] acupuncture at Fenglong point has the function of regulating blood sugar and blood lipid in patients with type 2 diabetes with stomach heat. Huang Wei [15] and others found that Shuxuetong combined with Fenglong point has a positive effect and good safety in improving arteriosclerosis obliterans of lower limbs. Sanyinjiao belongs to the spleen meridian of foot Taiyin, which has the effects of activating blood circulation, regulating menstruation, supplementing qi, strengthening spleen, and nourishing

liver and kidney. Under the effect of Chinese medicine Qi acupuncture, the combination of various acupoints can make the five viscera Qi and blood supply, activate blood circulation and remove stasis, and clear the collaterals, transform qi and water, clear heat and remove dampness, and the turbid poison can be dissolved and discharged from the body, so that the critical and severe cases can be solved.

4. Brief Summary

After dialysis and treatment with traditional Chinese and Western medicine, the condition of this case gradually worsened, and the addition of traditional Chinese medicine Qi acupuncture therapy made the patient significantly improve, which is a miracle. Traditional Chinese medicine Qi acupuncture therapy has a certain therapeutic effect on critical and severe cases.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Adult Patient with Diabetic Ketoacidosis and Rhabdomyolysis

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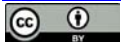
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Abstract

Rhabdomyolysis, acute kidney injury and diabetic ketoacidosis all are life-threatening conditions. Coincidence of them can be missed because the patient is usually asymptomatic or has mild symptoms related to rhabdomyolysis. The development of rhabdomyolysis as a complication of diabetic ketoacidosis is not well understood and only a few clinical studies address the phenomenon. We are reporting, along with a literature review, a 39-year-old male, who presented with diabetic ketoacidosis complicated with rhabdomyolysis and acute kidney injury. To the best of our knowledge, this is the first case reported in the United Arab Emirates. We highlight the syndrome because it is curable with early detection and proper treatment.

Keywords

Rhabdomyolysis, Diabetic Ketoacidosis, Acute Kidney Injury, Electrolytes Disturbance

1. Introduction

The world diabetes prevalence in adults in 2021 was estimated to be 10.5% [1]. Diabetic nephropathy is the leading cause of mortality in type 1 diabetes, which develops at a rate of around 2% - 3% annually [2]. Diabetes ketoacidosis is one of the common acute complications in patients with type 1 diabetes. Rhabdomyolysis is a leading cause of acute kidney injury. Emphasizing the occurrence of rhabdomyolysis in patients with diabetic ketoacidosis is vital since it will add a cumulative risk of developing renal impairment. Rhabdomyolysis is a life-threatening syndrome; the main attribute of rhabdomyolysis is the disruption of the sarcolemma and the release of creatinine kinase at a high level from the myocytes results in acute kidney injury. Electrolyte disturbance and metabolic

acidosis are common features of diabetic ketoacidosis (DKA); on the other hand, they are known to trigger rhabdomyolysis. There are a few reported cases in literature that address the existence of rhabdomyolysis and acute kidney injury in a patient with diabetic ketoacidosis. Most of the reported cases are in pediatrics. We would like to bring the physician's attention to the occurrence of rhabdomyolysis in the context of diabetes ketoacidosis, which can help in early diagnosis.

2. The Case

2.1. Case Presentation

A 39-year-old male was recently diagnosed with hypertension, for which he took an over-the-counter antihypertension medication; the patient was unsure about the name of the drug. However, he did not use it for one week prior to admission. He presented to our emergency department with generalized fatigability, nausea, and abdominal discomfort. On the clinical examination, he was conscious, slightly confused and dehydrated. His chest was clear on auscultation and his abdomen was soft and lax. In the emergency department, the patient's Venous blood gas (VBG) confirmed the diagnosis of diabetic ketoacidosis (anion gap 35 mEq/L, pH < 7.08, serum bicarbonate 6.5 mEq/L, serum ketones more than 7 mmol/L, blood Glucose 33.3 mmol/L). This is the first presentation for his diabetes. The Lab results revealed acute kidney injury and elevated creatinine kinase. Upon further history taking, he mentioned mild diffuse lower limb pain bilaterally. He denied fever, strenuous exercise or prolonged exposure to the sun. No recent use of herbal, alcohol, or recreational drugs was recorded. No history of recent trauma or abnormal movements. The Imaging studies reported a normal ultrasound scan study of the abdomen and pelvis and in the chest x-ray, there was no detectable pulmonary consolidation. The laboratory investigation on admission showed in **Table 1** and **Figure 1**.

The patient was treated according to the diabetic ketoacidosis protocol as well as alkalization of urine and his condition showed significant improvement.

2.2. Similar Case

A few cases reports in the literature have mentioned the association of hypophosphatemia, severe acidosis, and high osmolality as contributors to rhabdomyolysis in a patient with DKA.

I. A 31-year-old male presented with two weeks history of polyuria, polydipsia, and nocturia and showed up at ED with epigastric abdominal pain, nausea, and non-bloody vomiting. The patient was in a diabetic ketoacidosis episode in which rhabdomyolysis developed and complicated into acute renal failure. [3]

II. A 12-year-old female was admitted to the hospital with severe DKA, severe metabolic acidosis, hypophosphatemia, rhabdomyolysis, and oliguria ARF. [4]

III. Two type 2 diabetes mellitus (T2DM) adolescent patients who had diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS) predisposing

Table 1. Show the lab result upon admission and the following days.

Test	Result	Normal reference range
Hgb	12.40 gm/dL	13 - 17 gm/dL
Platelet	152.00 k	150 - 450 k
Sodium	123.00 mmol/L	136 - 145 mmol/L
Potassium	5.29 mmol/L (high)	3.5 - 5.1 mmol/L
Magnesium	1.1 mmol/L	0.66 - 1.07 mmol/L
Creatinine	173 decreased to 81 umol/L (high)	59 - 104 umol/L
Urea	23.10 mmol/L	2.76 - 8.07mmol/L
Calcium	2.02 mmol/L	2.15 - 2.5 mmol/L
Phosphorus	0.14 mmol/L (low)	0.37 - 1.47 nmol/L
Total CK	2356.00 increased to 14816.00 U/L ((high)	20 - 200 U/L
C-Peptide	0.289 nmol/L	0.37 - 1.47 nmol/L
HbA1C%	13.70 % (high)	4.8% - 6%
CRP	14.46 mg/L	0 - 5 mg/L
Myoglobin	705.90 ng/mL (high)	28 - 72 ng/mL

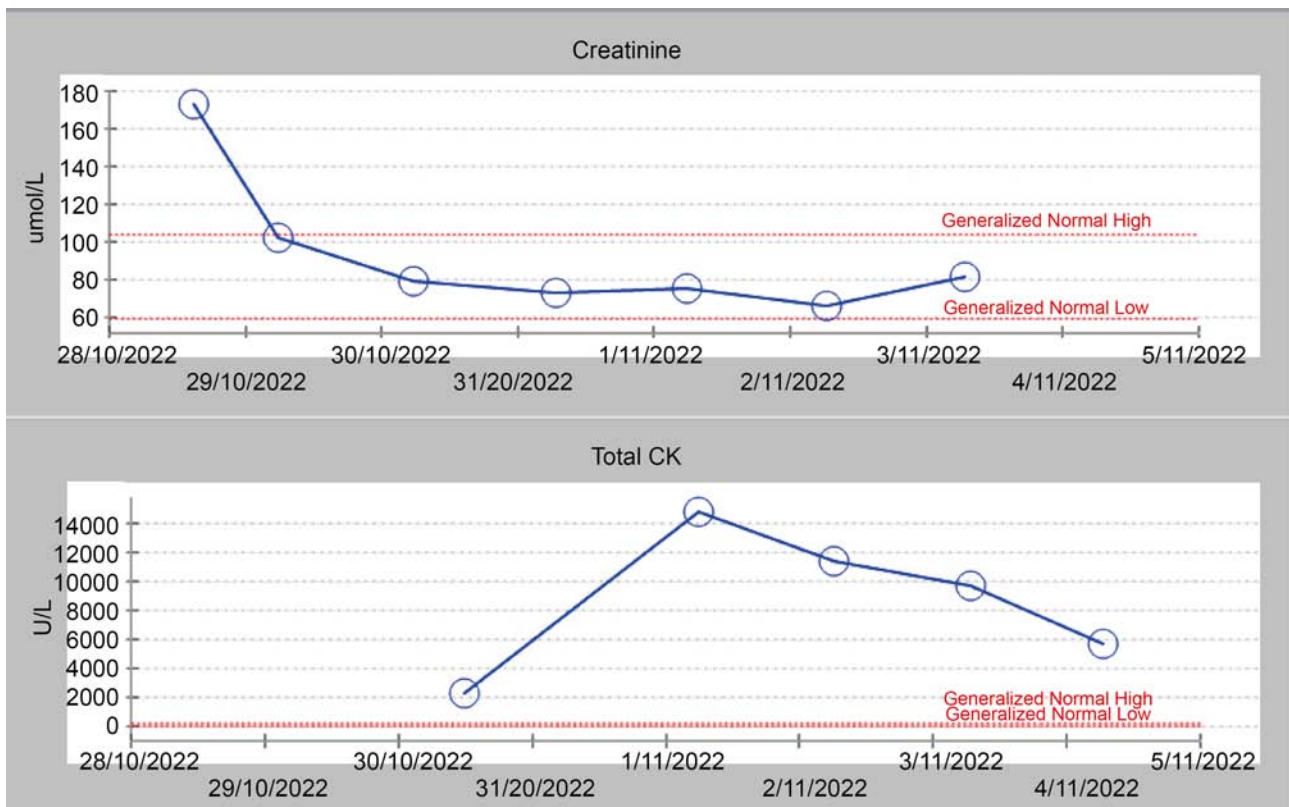


Figure 1. Show the trend of creatinine and creatinine kinase from day 29-10-2022 till 5-11-2022.

rhabdomyolysis (RM) [5].

2.3. Discussion

The Na/K-ATPase pump actively controls the transport across the cell membrane and maintained the charges gradient. These processes depend on ATP as a source of energy. ATP (adenosine triphosphate) depletion appears to be the end result of most causes of rhabdomyolysis. The depletion disrupts cellular transport mechanisms. [6] Subsequently, an increase in intracellular calcium levels will lead to the hyperactivity of proteases and proteolytic enzymes. [7] These enzymes degrade myofilaments and injure cell membrane phospholipids resulting in the leakage of intracellular contents into the plasma. However, the pathophysiology of diabetic ketoacidosis consists of marked metabolic acidosis and electrolyte disorder which theoretically can precipitate rhabdomyolysis. In a cross-sectional study carried out in the emergency department of Baghdad teaching hospital/Iraq; where 43 patients with type1 diabetes presenting with diabetic ketoacidosis were included. Rhabdomyolysis incidence in this study was 6.98%, statistically, a significant finding was observed with the duration of diabetes, higher serum creatinine, higher serum potassium, higher serum chloride, and severe acidosis. [8] The risk of renal injury is low when initial CK levels are lower than 15,000 - 20,000 U/L. However, lower CK levels may lead to renal injury in patients with sepsis, dehydration, or acidosis. [9] Based on the trend of CK and creatinine levels, we think the cause of acute kidney injury in our case is due to hypovolemia rather than rhabdomyolysis

3. Conclusion

Rhabdomyolysis in the context of diabetic ketoacidosis is usually overlooked because the patient is asymptomatic or has mild symptoms related to rhabdomyolysis. However, it may lead to permanent kidney damage and progress to chronic kidney disease. We advise focusing on the possible coincidence of Rhabdomyolysis while treating patients with diabetic ketoacidosis. Further studies to understand the underlying pathophysiology and prevalence are recommended.

Abbreviations and Acronyms

DKA: diabetic ketoacidosis; CK: creatinine kinase; ED: emergency department; ARF: acute renal failure; ATP: adenosine triphosphate.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Modified Z-Plasty for Reconstruction of Webbed Scar Contractures

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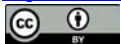
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Abstract

Rationale: Webbed scar contractures deformity caused by burns and other factors will lead to joint disorders and affect the mental health of patients, resulting in a severe decline in quality of life. Rapid, effective and less complicated surgical methods can help patients with post-burn rehabilitation. **Objective:** This article argues that a modified Z-plasty can quickly improve the range of motion caused by webbed scar contractures in joint areas, including surgical methods, postoperative care and prognosis. **Methods and Results:** The study took place from 2018 to 2022. Thirty-two patients with joint scar contracture deformity, with a mean age of 32.5 years, were included in the study. All patients underwent contracture scar revision and modified Z-plasty repair under anesthesia. All the flaps survived and the joint function was improved. Compared with the traditional Z-plasty, the duration of the operative procedure of the modified Z-plasty was significantly shorter, more surrounding scar tissue was mobilized, and the effectiveness of postoperative scar contracture release was better. **Discussions:** The modified Z-plasty for scar contracture deformity in joint area is simple, rapid, effective and easy to manage.

Keywords

Modified Z-Plasty, Surgical Flaps, Contracture, Plastic Surgery Procedures

1. Introduction

Webbing is the skin and soft tissue linking the entire path up the digits. The distal end of the web space reaches the middle of the proximal phalanx, on the same plane as the volar skin, and forms an inclined plane with the dorsal skin. The

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normal rhombus network structure of the web between the fingers is the prerequisite for adduction, abduction, arbitrary flexion and extension [1].

The hand is a part with various tissues, joints and functions. Without scientific and appropriate treatment, second-degree burns of the hand often leave a scar and even result in contracture, which affects hand function and dexterity. Post-burn contractures can lead to deformities [2]. Due to the lack of soft tissue near the contracture area, scar revision surgery, including release and defect repair, is a challenging problem.

The webbed scar of the crotch joint was released as usual using a continuous standard Z-plasty [3] [4]. The standard 5-flap Z-plasty has some limitations, such as a limited degree of scar release and extension and prolonged operative duration. At the same time, the mobilization of organizations is limited. The modified Z-plasty is an effective technique to prevent the above problems.

2. Materials and Methods

Thirty-two patients enrolled from 2018 to 2022 with joint scar contracture deformity, with a mean age of 32.5 years, were included in the study. The same surgeon, who strictly controlled the indications, performed all operations. All patients underwent incision or resection and modified Z-plasty of the scar under anesthesia. The patients suffered from contracture of the hand for at least one year, which was localized in web spaces, flexor surfaces of the digits, broad palm and extensor surfaces of the hand. The severity of contracture is classified as mild as the scar moderately restricts certain hand movements, and adequate soft tissue, according to the algorithm for releasing burn contractures described by Hudson and Renshaw [5].

2.1. Surgical Approach

In terms of design, there are some anatomical landmarks to be addressed: the arch of the normal interdigital spaces, which is the line of articulation of the metacarpophalangeal's horizontal stripes, is called the basic line (BL). The highest point of the web space scar was designed as B and the lowest as C, taking BC as the middle arm, $AB = BC = CD$. Point A is on the dorsal side. Points C and D are on the volar side (Figure 1). When the flap (A-B-C) is turned to the dorsal palmar side, point B is fixed, and point A is switched with points C and D (Figure 2). The angle between ABC is 30 to 45 degrees and BCD is 90 degrees. The shaded tissue needs to be excised to avoid affecting flap transposition (Figure 3).

1) Concerning scar blood vessel density, the dorsal palmar scar tissue should be at least tender or pliable according to the modified VSS (Vancouver Scar Scale) [6].

2) In some cases, the design needs to be changed slightly, which is when the metacarpophalangeal joint (MCP) is extended and flexed; it is guided by skin activity.

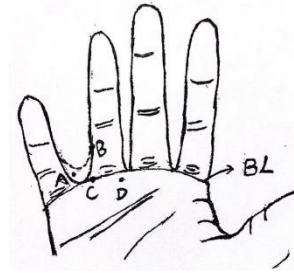


Figure 1. The highest point of the web space scar was designed as B and the lowest as C, taking BC as the middle arm, $AB = BC = CD$. Point A is on the dorsal side; points C and D are on the volar side.

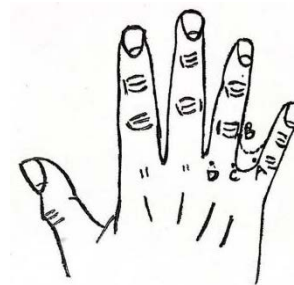


Figure 2. Point B is fixed, and point A is switched with point C and D.

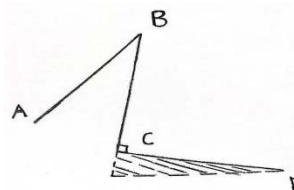


Figure 3. The shaded tissue needs to be excised to avoid affecting flap transposition.

A tourniquet was placed on the upper arm near the axilla to prevent intra-operative bleeding from affecting the operation. The incision was made toward A-B-C-D, and the skin and subcutaneous fascia were opened. Carefully separate the fascia layer to avoid finger blood vessels and nerve damage. Cut through the scar tissue. Haemostasis is achieved using bipolar electrocautery. Moving the flap, point B was transferred to point D, and point C was transferred to point A, and fixed with 5-0 Puling suture. The shape of the flap after transposition like reverse z-shape (**Figure 4**).

2.2. Postoperative Treatment

The wound was covered with a light dressing for three days. Remove blood scabs and secretions carefully during dressing change. Sutures were removed 12 - 14 days after surgery. After the sutures were removed, anti-scar treatment was performed for over half a year.

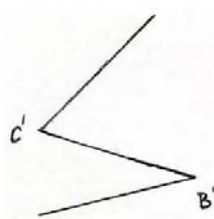


Figure 4. The shape of the flap after transposition.

3. Results

Our technique was applied to 32 patients (mostly in the upper limb) with burn contracture in the following areas: neck (5 cases), axilla (10 cases), forebreast (3 cases), thigh (2 cases), and hand (12 cases). The mean operative time for a webbed scar on the hand and other joint areas was 15 minutes and 30 minutes, respectively.

The postoperative results are shown in **Figure 5**. Sutures were removed 7 days after neck surgery, 10 days after thoracic surgery, and 12 - 14 days after limb surgery. All wounds healed well, no skin congestion, necrosis or other complications, and postoperative scar contracture was satisfactorily relieved. However, we failed to contact patients for long-term follow-up.

4. Discussion

The joint is an important fulcrum for the limb to maintain good function [7]. First, the most crucial function of joints is movement, and every joint of the human body is inseparable from movement. Second, joints act as a buffer against force. Third, joints are designed to withstand gravity, supporting weight and other stresses. Fourth, the joint can act as pivots and form a lever in the human body's activities [8].

Burns, scalds or wounds across joints may cause a hypertrophic scar or contracture scar, which may affect joint function. Webbing of scar mostly develops from the cross-joint area and requires surgery to release the tension. Webbed scar revision surgery should be performed until the scar matures and softens, which can be over half a year or longer. This can ensure the best possible surgical outcomes. Especially for the burn syndactyly, the web-space scar has little impact on the flexion and extension of the finger, making it possible to wait longer.

Examining the donor scar to understand what may be underneath it is very important. The Vancouver Scar Scale is an effective method to evaluate the condition of the scar, especially in evaluating treatment effects [9]. The more flexible the scar tissue, the greater it is potential to repair all components of the interphalangeal joints: its depth, shape, groove, and inclination to the metacarpal head.

The finger blood supply is abundant due to the modification of the Z-plasty, which has a larger Angle (the minimum angle is greater than 30 degrees), providing a reliable blood supply and avoiding necrosis of the tissue flap. If the local



Figure 5. Comparison between preoperative and postoperative contracture deformity of the web space between the fourth and fifth fingers.

flap angle is less than 30 degrees, the probability of flap necrosis increases [10] [11].

Most of the mature webbed scars were repaired by Z-plasty, multiple Z-plastics in series or the 5-flap technique. However, due to the limitation of the included angle and the force of tension, the length of the prolonged scar is limited, so the conventional Z-plasty is ineffective in treating a webbed scar. The greater the angle of the outer arm of the Z-plasty, the longer the extension of the middle arm. The angle between the outer arms is 30 degrees, and the middle arm is extended by 25%, 60 degrees is 75%, and 90 degrees is 120% [12].

5. Conclusion

The modified Z-plasty has a larger angle, more surrounding scar tissue is mobilized, the postoperative scar tissue is released, and the recurrence probability is negligible. Moreover, the operative time is significantly reduced due to the single Z-plasty. With a large angle, a flap has a sufficient blood supply. The flap is oblique in design. The adjacent fingers do not interfere with each other, which is suitable for the simultaneous operations of multiple fingers.

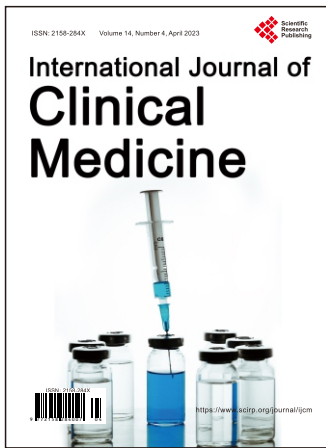
Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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