ISSN: 2325-7075 Volume 11, Number 7, July 2022

Scientific Research Publishing

Case Reports in Clinical Medicine

ISSN: 2325-7075

https://www.scirp.org/journal/crcm

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ISSN Print: 2325-7075 ISSN Online: 2325-7083
https://www.scirp.org/journal/crcm

Editorial Board

Case Reports in Clinical Medicine, 2022, 11, 245-272
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

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Volume 11 Number 7 July 2022

Case Reports in Clinical Medicine (CRCM)
Journal Information

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Case Reports in Clinical Medicine, 2022, 11, 245-252
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ISSN Online: 2325-7083
ISSN Print: 2325-7075

Selinexor, Carfilzomib, Pomalidomide, and Dexamethasone as a Salvage Regimen for Refractory and Relapsed Multiple Myeloma with Plasma-Cell Leukemia Transformation: A Case Report and Literature Review

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How to cite this paper: Zhang, Y.F., Ying, C., Zhang, Y.C. and Deng, J.C. (2022) Selinexor, Carfilzomib, Pomalidomide, and Dexamethasone as a Salvage Regimen for Refractory and Relapsed Multiple Myeloma with Plasma-Cell Leukemia Transformation: A Case Report and Literature Review. *Case Reports in Clinical Medicine*, **11**, 245-252.
https://doi.org/10.4236/crcm.2022.117036

Received: June 5, 2022
Accepted: July 8, 2022
Published: July 11, 2022

Abstract

Refractory and relapsed multiple myeloma (RRMM) with plasma-cell leukemia (PCL) transformation is highly aggressive and resistant to conventional therapy. Novel therapeutics are needed for RRMM-transformed PCL. Selinexor [an oral exportin 1 (XPO1) inhibitor], carfilzomib (a second-in-class proteasome inhibitor), pomalidomide (third generation of immunomodulatory drug) are usually used for RRMM, but there are no reports on their application in PCL transformation. We describe a 62-year-old male initially diagnosed with MM IgD-lambda type with complex karyotype and extramedullary plasmacytoma in 2020, and relapsed after five months of autologous stem cell transplantation. Despite the use of various therapies, the patient rapidly developed into PCL over a 4-month period. The patient was started on selinexor, carfilzomib, pomalidomide, and dexamethasone (XKPd) combination as a salvage regimen in July 2021. He achieved fast response in first cycle. Then, he fulfilled third cycle of consolidation treatment and got four-month remission. The success of XKPd therapy in achieving a good response suggests its utility in RRMM transformed-PCL patients, who have exhausted various combinations of drug regimens and have historically poor survival outcomes.

Keywords

Selinexor, Carfilzomib, Multiple Myeloma, Plasma Cell Leukemia

1. Introduction

Multiple myeloma (MM) has witnessed significant advances due to the approval of many novel agents such as proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), monoclonal antibodies (mAbs), which have profoundly improved the prognosis of MM. Despite all these new developments, multiple myeloma remained an incurable hematological malignancy, and most patients would eventually relapse [1]. The patients who had received several treatments would have poorer outcomes as resistance emerges, especially the disease transformed into plasma-cell leukemia (PCL), which was the most aggressive form of MM. Treatment options for RRMM with PCL were limited [2]. While the advance of novel agents to treat MM in recent years have likely prolonged the survival of PCL. The following case report described a patient with RRMM who had stubborn to PIs, IMiDs, daratumumab and finally progressed into PCL, who demonstrated an excellent response to selinexor, carfilzomib, pomalidomide, and dexamethasone combination treatment. To our knowledge, this is the rare case report of combination treatment in an RRMM-transformed PCL.

2. Case Report

A 62-year-old man was admitted to our hospital in March 2020 due to lumbar pain. The MRI examination suggested anterior spinal neoplastic lesions in the posterior mediastinum (**Figure 1**), and postoperative pathology revealed extramedullary myeloma involvement. The blood routine test revealed anemia with hemoglobin 87 g/L. He was transferred to our department. The patient had 10-year diabetes history. Laboratory examinations revealed serum calcium, albumin, globulin levels, and renal function test results were normal. The β2 microglobulin level was 8.57 mg/l (normal 0.70 - 1.3 mg/l). Immunoelectrophoresis

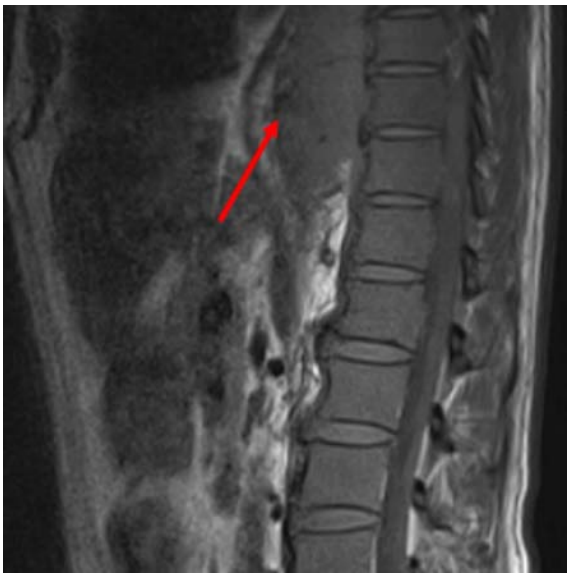

Figure 1. The MRI examination showed anterior spinal neoplastic lesions in the posterior mediastinum.

fixation revealed abnormal IgD-lambda immunoglobulin in the serum. Bone marrow smear (BMs) showed 59% of plasma cells (PCs), and flow cytometry (FCM) revealed 52.29% abnormal PCs with restrictive lambda light chain expression. Fluorescence in situ hybridization (FISH) analysis had a complex karyotype, including gain1q, deletion 13q, deletion 16q, and deletion 17p. Accordingly, the patient was diagnosed with IgD-lambda type MM (Internatinoal Staging System stage III) having a complex karyotype.

The patient was initially treated with bortezomib, thalidomide, cyclophosphamid, dexamethasone (VTCd) for a total of four cycles, and achieved a complete remission (CR). He underwent autologous hematopoietic stem cell transplant (ASCT) with 200 mg/m^2 melphalanin in October 2020. After ASCT, lenalidomide was given as maintenance treatment. After 5 months, he experienced morphological recurrence, with 20% of PCs in BMs in March 2021. He subsequently started daratumumab, ixazomib, dexamethasone (DId) therapy. After 5 weeks, his platelet count rapidly declined to less than 20 × 10^9/L, BMs showed 28% of PCs, and FISH test remained the same as that the disease diagnosed. The patient proceeded to liposome doxorubicin, pomalidomide, ixazomib, dexamethasone (PIDd) regimen, the disease was still progressing. Taken the nature of the disease and resistance to conventional therapy, he initiated selinexor [an oral exportin 1 (XPO1) inhibitor], pomalidomide, dexamethasone (XPd) regimen, selinexor 60 mg once a week, in combination with pomalidomide 2 mg days 1 - 21, and dexamethasone 20 mg once a week. During the first course of XPd therapy, the PCs rapidly disappeared from the PB. Soon after, the treatment regimen failed to achieve control, with approximately 35% monoclonal PCs in PB (**Figure 2**), 72% of bone marrow PCs and secondary myelofibrosis. It appeared that MM had progressed to PCL.

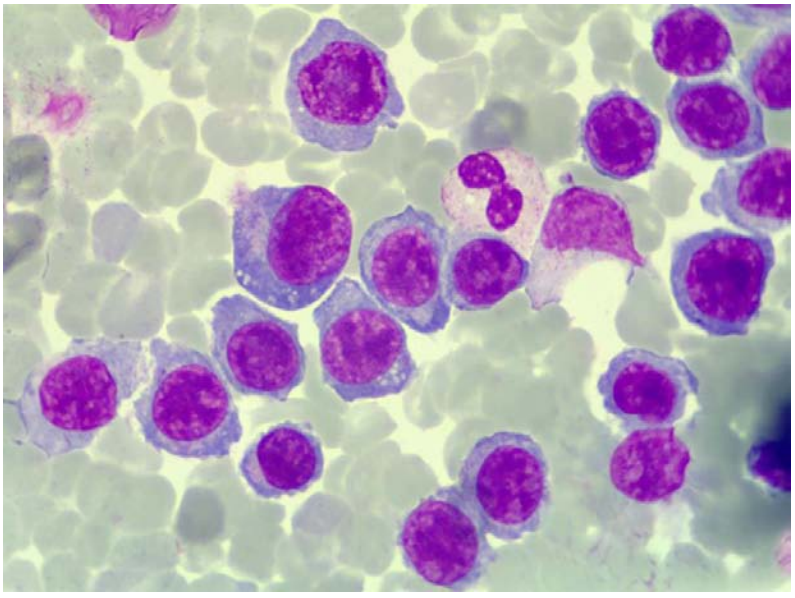

Figure 2. Circulating plasma cells as evident on the peripheral smear (1000×) in June 2021.

Despite responses to various therapies, the patient continued to experience relapses and exhausted options of many novel agents seen in MM treatment. He was not eligible for CAR-T clinical research. After detailed communication with the patient and his family, they accepted the treating doctor advice to receive the salvage therapy including selinexor, carfilzomib, pomalidonide and dexamethasone (XKPd) in July 2021. The dose of carfilzomib was 20 mg/m^2 twice a week, selinexor was 60 mg once a week, pomalidomide was 2 mg on days 1 - 21, and dexamethasone 20 mg on twice a week. After the first week of treatment PB plasma cells disappeared remarkably. Only one cycle of therapy finished we evaluate the efficacy revealed BMs had no PCs, bone marrow MRD was 0.0%, and immunoelectrophoresis fixation revealed IgD immunoglobulin was negative and the serum FLC ratio returned to normal range. The PET-CT scan showed extramedullary myeloma was disappeared (**Figure 3**). He achieved CR. The treatment-related adverse events including slight fatigue and grade 3/4 myelosuppression, which were managed with appropriate supportive care and dose modifications. Then, he fulfilled three cycles of XKPd consolidation and got four-month remission. The patient refused to undergo allogeneic hematopoietic stem cell transplantation. XKPd therapy was continued, and his condition was evaluated as very good response with negative MRD tests after three cycles of chemotherapy. A summary report of clinical and treatment assessments is presented in **Table 1**. However the patient eventually died of severe pneumonia during the fourth cycle.

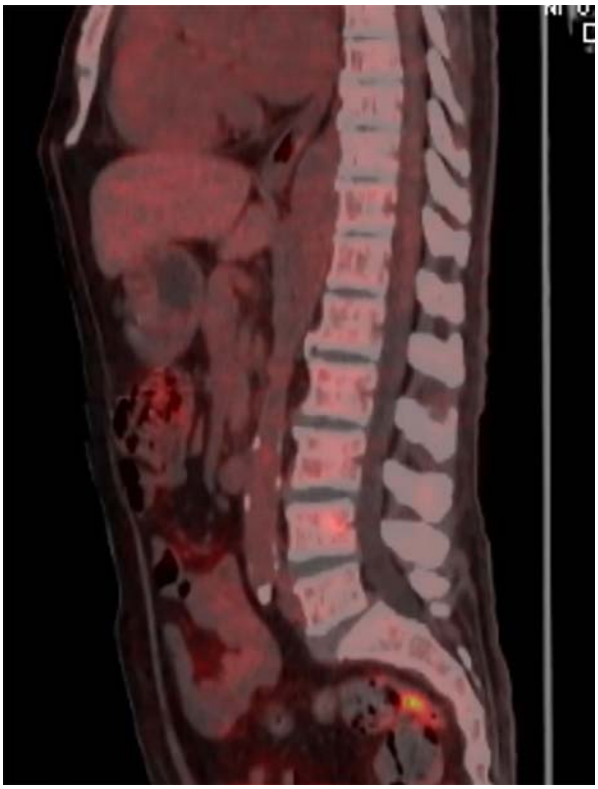

Figure 3. The PET-CT scan showed extramedullary myeloma was disappeared.

Table 1. Evolution of therapy in our patient.

Regimen	Duration of therapy (month range)	Best response	Reason for stopping
Bortezomib/thalidomide/cyclophosphamide/dexamethasone (VTCD)	5 (May-Oct 2020)	CR	Started ASCT
ASCT	Oct 2020	CR	Started maintenance
Lenalidomide	5 (Oct 2020-Mar 2021)	CR	PD
Daratumumab/ixazomib/dexamethasone (DId)	1 (Mar-Apr 2021)	PD	PD
liposome doxorubicin/pomalidomide/ixazomib/dexamethasone (PIDd)	2 (Apr-Jun 2021)	PD	PD
Selinexor/pomalidomide/dexamethasone (XPd)	1 (Jun-Jul 2021)	PD	PCL
Selinexor/carfizomib/pomalidonide/dexamethasone (XKPd)	4 (Jul-Nov 2021)	CR	Died

Abbreviations: CR: complete remission; ASCT: autologous hematopoietic stem cell transplant; PD: progressive disease; PCL: plasma-cell leukemia.

3. Discussion

In MM, the triple cytogenetic abnormalities combined with del17p, IGH translocation and gain (1q) were associated with particularly inferior prognosis and a median OS is only 9.1 months [3]. Bortezomib and carfilzomib treatment appear to abrogate the negative impact of del (17p), improve complete response [4]. In contrast, patients with multiple adverse cytogenetic abnormalities do not benefit from these agents [5]. PCL was the end stage of MM with high drug resistance, which highlights its aggressive and advanced stage, and historical median survival was only one month [6] [7]. A multicenter retrospective study including 101 patients with PCL revealed that over-all survival (OS) who received therapy was 4.2 months, 1-year OS only 19% [8]. Because PCL patients were often heavily pretreated, studies are minimal, only a few cases of successful treatment have been reported. Such as the venetoclax-based therapy in some cases of RRMM and transformed into PCL, harboring the (11; 14) translocation, had shown single-agent activity [9] [10]. Our patient did not have the t (11; 14) abnormity, so the venetoclax-based therapy may have limited effects.

As for the new upcoming studies, we focused on selinexor, a selective inhibitor of the nuclear export compound that blocks exportin 1 (XPO1), which is a novel potential treatment for RRMM [11] [12]. In STORM study utilized the selinexor with dexamethasone for RRMM, 68% of patients were penta-refractory, the overall response rate (ORR) was 26%, of note, response rates appeared to be consistent across subgroups, including patients with high-risk cytogenetics [13] [14]. In many studies, selinexor with dexamethasone as skeleton combined with various drugs such as ixazomib, liposomal doxorubicin, bortezomib, pomalidomide, carfilzomib, daratumumab, had shown modest activity in a heavily refractory patient population [15]. Carfilzomib is a new irreversible proteasome inhibitor targeting the chymotrypsin like activity of the 20 S proteasome [16]. An Phase IIb study PX-171-003-A1 evaluating carfilzomib in patients with

RRMM, demonstrated the ORR was 23.7%, with a median duration of response lasting 7.8 months and median OS was 15.6 months [17]. The common adverse effects of carfilzomib included fatigue (55.5%), anemia (46.8%), nausea (44.9%), and thrombocytopenia (36.3%) [17]. An phase 3 clinical trial ASPIRE showed carfilzomib combination with lenalidomide and dexamethasone in RRMM, the median progression-free survival (PFS) was 26.3 months, the median time to response was 1 month, duration of response was 28.6 months [18]. The combination of Selinexor, carfilzomib, pomalidomide and dexamethasone (XKPd) in the treatment of RRMM is rare, and the toxicity may greater.

Our patient's baseline characteristics and treatment experience were more complex and had all high-risk factors. Ultimately, the patient proceeded to a salvage regimen of XKPd, and achieved CR with only one cycle of treatment. Although the CR status lasted for only 4 months, the patient died of severe pneumonia eventually. This therapy still gave the patient 4-month follow-up treatment opportunities.

To our knowledge, this is the first case report describing the XKPd regimen usage in RRMM that has progressed to PCL. The above case highlights the refractory, aggressive nature of PCL and limited treatment options. Based on the successful outcome seen in this case, future clinical studies are warranted in exploring selinexor, carfilzomib, pomalidomide, in combination with other therapies for the treatment of RRMM and PCL.

The limitation of this case was that we failed to take effective consolidation measures after the PCL remission status, and the patient died of treatment complications finally.

Acknowledgements

Thank Dr HuanLi for providing purely technical help and writing assistance.

Conflicts of Interest

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

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Case Reports in Clinical Medicine, 2022, 11, 253-260
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

Peripheral Hematological Parameters in Sudanese Women with Polycystic Ovary Syndrome

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How to cite this paper: Mohammed, S., Elhaj, E.T., Ahmed, M.A., Eltayeb, R. and Adam, I. (2022) Peripheral Hematological Parameters in Sudanese Women with Polycystic Ovary Syndrome. *Case Reports in Clinical Medicine*, **11**, 253-260.
https://doi.org/10.4236/crcm.2022.117037

Received: June 6, 2022
Accepted: July 12, 2022
Published: July 15, 2022

Abstract

The aim of this study is to assess the association between polycystic ovarian syndrome (PCOS) and hematological parameters [hemoglobin, red cell parameters, white blood cells (WBCs), platelets volume (MPV)]. This is a matched case-control study (60 women in each arm of the study) which was conducted in Saad Abualila infertility center Hospital in Khartoum, Sudan. Infertile women with PCOS were the cases and healthy non pregnant women were the controls. The gynecological characteristics were gathered through questionnaire and blood samples were analyzed for different blood parameters by automated hematology analyzer. While the two groups were matched in their age; body mass index was significantly higher in women with PCOs compared to the normal control. The investigated different hematological parameters (hemoglobin, RBCs, RDW, WBCs, platelets and MPV) showed no statistical difference between the women with PCOS and the controls.

Keywords

Hemoglobin, Platelets Volume, Polycystic Ovarian Syndrome, Red Blood Cells, White Blood Cells

1. Introduction

Polycystic ovary syndrome (PCOS) is essentially a group of endocrine disorders, with a complex of metabolic, endocrinological and genetic factors that commonly affect women during reproductive age [1]. This syndrome is characte-

rized by irregular, anovulatory menstrual cycles, features of hyperandrogenism, and polycystic ovaries. PCOS can lead to poor obstetric outcomes such as infertility, pregnancy loss, gestational diabetes and macrosomia which are affecting 5% - 20% of women with reproductive age [2] [3] [4]. Moreover, PCOS is associated with various changes such as metabolic syndrome, insulin resistance, hypertension, dyslipidemia and increased cardiovascular disease [5] [6].

In spite of the advance in the many disciplines (genetic, environmental and inflammatory biomarker), the exact etiology and pathophysiology of PCOS are not yet fully elucidated [7]. Several recent researches have reported inconsistent association between PCOS and the different components of the hematological parameters [8]-[19]. Thus, association between hematological parameters and PCOs is still an area of active research. Hence there is a need to conduct further research on blood parameters and PCOs. Moreover, the analyses of the peripheral blood parameters were previously performed using manual procedure which was a time consuming and needs personnel with high technical skills and its results might be doubtful. Nowadays the analyses and interpretation of peripheral blood parameters are conducted using automated analyzers. PCOS is the main cause of female infertility in Sudan [20]. Previous studies have shown that different metabolic and hormonal factors were associated with PCOS in Sudan [21] [22]. In Sudan, there are no published data concerning the relation between PCOS and complete blood count (CBC). Thus, the current study was conducted among Sudanese women to describe the relation between PCOS and different hematological parameters Saad Abualila infertility center (Khartoum, Sudan).

2. Methods

This was a case-control study carried out at Saad Abualila infertility center (Khartoum, Sudan) during the period of May to December 2019. Saad Abualila Hospital is a tertiary semi-private hospital governed by the Faculty of Medicine, University of Khartoum. Cases were women with confirmed PCOS based on Rotterdam criteria [3]. Women with systemic disease (cardiovascular disease and diabetes mellitus), on medication for 6 months prior to the study (oral contraceptives, glucocorticoids, ovulation induction agents, and estrogenic or anti-androgenic) were excluded from the cases and controls.

After signing an informed consent the socio-demographic, medical and gynecological history was taken from each patient using questionnaire. The detailed medical and gynecological history was taken (menstrual, fertility, hirsutism, acne, acanthosis nigricance, scalp, hair loss or thinning) were taken from all patients included in the study. Then full general and pelvic examinations were performed.

Body weight (kg), height (cm), was measured in all women and BMI was calculated by dividing the weight (in kg) by the height (m^2). Thereafter, two 2 mL of blood was withdrawn (under aseptic condition) from every participant in an ethylene diamine tetra acetic acid by a trained technician. The sample was ana-

lyzed for a complete blood count using an automated hematology analyzer guided by the manufacturers' instructions (Sysmex KX-21, Japan) previously described [23] [24].

A total sample size of 60 women in each arm of the study (cases and controls) was calculated according to the expected difference in the mean of the investigated variables (WBC, hemoglobin, platelets RBCs and RDW) that would provide 80% power to detect a 5% difference at $\alpha = 0.05$ and assumed that 10% of women would not respond or have incomplete data.

3. Statistics

Data were entered in computer using SPSS for data analyses and expressed as proportions, mean (SD) and median (interquartile). The continuous variables were assessed for normality using Shapiro test. *T*-test and Mann-Whitney *U*-test were used to compare the continuous data between the cases and the controls when the data were normally and abnormally distributed, respectively. X^2 test was used to compare the categorical variables. Two-tailed tests were used and $P < 0.05$ was considered statistically significant.

4. Results

During the study 60 women in each arm of the study were enrolled in the study. There was no significant difference between the cases and the controls in their age, residence and education. The BMI was significantly higher in women with PCOs compared to the normal controls, Table 1.

There was no significant difference in all of the hematological parameters (hemoglobin, RBCs, WBCs, platelets), Table 2.

5. Discussion

The current study showed no significant difference in the various hematological values between the women with PCOs and the controls. In our neighbor Kingdom of Saudi Arabia, recently ALhabardi *et al.*, have shown that the hematological

Table 1. Comparing the socio-demographic characteristics in women with polycystic ovarian syndrome with the controls.

The mean (*SD*)	Polycystic ovarian syndrome (n = 60)	Controls (n = 60)	P
Age, years	24.2 (3.9)	24.7 (5.2)	0.541
Body mass index, kg/m^2	30.5 (7.8)	27.8 (5.8)	0.031
Number (%) of			
Rural residence	16 (26.6)	12 (20.0)	0.388
Education level ≤ secondary level	11 (18.3)	14 (23.3)	0.500
Housewives	34 (56.6)	36 (60.0)	0.711

Table 2. Median (interquartile range) of hematological values in women with polycystic ovarian syndrome and the controls.

Variables	Polycystic ovarian syndrome (n = 60)	Controls (n = 60)	P
White blood cell, cells × 10^9/l	6.550 (5.210 - 7.675)	6.550 (5.525 - 7.700)	0.854
Neutrophils, cells × 10^9/l	3.050 (2.100 - 4.475)	3.250 (2.100 - 4.650)	0.974
Lymphocytes, cells × 10^9/l	2.400 (1.915 - 2.975)	2.400 (1.800 - 2.700)	0.445
Hemoglobin, gm/dl	12.6 (11.3 - 13.7)	11.95 (10.525 - 13.25)	0.076
Haematocrit, %	38.7 (35.32 - 41.6)	37.300 (34.15 - 39.675)	0.351
Red blood cell cells	4.600 (4.37 - 4.90)	4.800 (4.500 - 5.000)	0.103
MCV	83.9 (76.25 - 88.000)	81.400 (71.472 - 88.200)	0.326
MCH	28.200 (25.525 - 29.475)	27.000 (23.425 - 28.600)	0.099
MCHC	32.300 (30.2 - 33.350)	32.300 (31.100 - 33.000)	0.735
Red cell distribution width, %	13.2 (12.6 - 14.5)	13.45 (12.4 - 17.32)	0.264
Platelets count, 10^3/µl	305.5 (247.5 - 355.2)	330.0 (260.0 - 353.0)	0.511
Mean platelet volume, f	8.2 (7.8 - 9.0)	8.8 (8.0 - 9.8)	0.257
Platelet distribution width, %	15.4 (15.1 - 15.7)	15.5 (14.9 - 15.7)	0.861

parameters were not different between women with PCOS and health controls [8]. Moreover, Kałużna *et al.*, have shown that WBC were not different between women with PCOS and controls [9]. Our findings were consistent with Ucakturk *et al.*, findings who observed no significant difference in the homological parameters namely hemoglobin, RBCs, platelets count and WBCs between the women with PCOS and women without PCOS [25]. Likewise, It has been reported previously reported that serum iron levels were not different between women who had PCOs and the controls of women who had no PCOS [26].

A significantly higher of hemoglobin has been reported in women with PCOS compared with the healthy women (control) [27]. This finding (high hemoglobin) has been explained by the hormone levels in PCOS women which might in-

fluence on hemoglobin levels through a dose-dependent stimulatory effect on erythropoiesis [28] [29]. Furthermore, androgen receptor in the bone marrow might lead to increase in hemoglobin level [30]. The reduced frequency of menstruation in women with PCOS group is thought to cause the differences of hemoglobin level between PCOS and control groups.

Our results showed no significant difference in the WBCs counts between the women with PCOS compared with women without PCOS. Several previous studies have shown that WBC count was significantly higher in the women with PCOS group [12] [17] [18]. Moreover, a positive predictive effect of WBCs as well as a negative predictive effect of lymphocytes on insulin resistance has been reported in women with PCOS [31]. It is worth to be mentioned that an aerobic exercise might reverse the higher WBCs in women with PCOS [32].

Although, we did not show a significant difference in the MPV, RDW in women with PCOS and controls, previous studies have shown that MPV, NLR, neutrophil count, neutrophil to total leucocyte ratio were significantly higher in women with PCOS compared with the controls [13] [14] [33].

6. Conclusion

The current study showed no significant difference in the hematological parameters in Sudanese women with PCOS and the healthy controls. A study with larger sample size is required in the future to confirm this finding and we did not assess many other hematological variables e.g. serum ferritin as well as other inflammatory markers e.g. C-reactive protein and insulin resistance.

Conflicts of Interest

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

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Case Reports in Clinical Medicine, 2022, 11, 261-267
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

Evaluating Hospital Utilization Late in the Epidemic

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How to cite this paper: Lagoe, R. and Littau, S. (2022) Evaluating Hospital Utilization Late in the Epidemic. *Case Reports in Clinical Medicine*, **11**, 261-267.
https://doi.org/10.4236/crcm.2022.117038

Received: June 8, 2022
Accepted: July 17, 2022
Published: July 20, 2022

Abstract

This study evaluated present and future impact of the coronavirus on hospitalization as the virus winds down in the metropolitan area of Syracuse, New York. The study compared adult medicine and adult surgery discharges between January-May 2019 and 2022. The data indicated that 69 percent of the reduction in medical-surgical discharges that occurred since 2019 was offset during 2022. The remaining 31 percent remained at levels experienced in 2020 and 2021. The study clearly demonstrated that medical and surgical discharges increased significantly since 2019. An important question is whether these will continue or if they will level off.

Keywords

Hospitals, Infectious Diseases, Hospitalization

1. Introduction

In recent years, increased attention has focused on the utilization of health care in the United States. This has resulted from the need to accommodate the requirements of populations in the current system as well as concerns regarding the costs of care.

The need to address chronic diseases has become a major part of the mission of the health care system. During 2020 and 2021, the advent of coronavirus placed increased emphasis on the treatment of infectious diseases [1].

For the health care system and especially hospitals, dealing with the coronavirus has involved large provider expenses without regard for the size of these costs. This approach has worked on a short-term basis, however, it may not be sustained over longer periods of time [2] [3].

Between 2020 and 2022, the coronavirus exerted a major impact on the utili-

zation of health care at the community level. The most visible part of this impact was exerted on inpatient beds, both medical-surgical and critical care [4] [5] [6].

This impact was also exerted on inpatient care for other diagnoses such as heart disease and stroke. In many communities, the need to treat patients with coronavirus has limited the resources available to deal with these conditions [7].

As the most recent wave of the coronavirus winds down, local hospitals are attempting to evaluate their remaining medical and surgical capacities. These resources need to be available for the diagnoses that were treated before the advent of the virus.

A major issue for the future of hospital care is the size of inpatient capacity that will be available at the community level. This capacity will be necessary to treat chronic diseases after the epidemic has passed. It will be identified based on medical and surgical conditions that require hospital care, as well as resources that are available to treat them at the community level. This study suggests an approach to this subject.

2. Population

This study focused on hospital utilization in the metropolitan area of Syracuse, New York. This area includes three large hospitals, Crouse Hospital (18,217 inpatient discharges excluding well newborns, 2021); St. Joseph's Hospital Health Center (20,720 inpatient discharges, 2021); and Upstate University Hospital (32,245 inpatient discharges, 2021).

These hospitals provide primary and secondary acute care to an immediate service area with a population of approximately 600,000. They also provide tertiary services to the eleven county Central New Yok Health Service Area with a population of 1,400,000 [8].

3. Method

This study evaluated the impact of the coronavirus on inpatient hospital utilization at the community level in the metropolitan area of Syracuse, New York in the United States. It also suggested potential future developments concerning this subject.

The study was based on adult medicine and adult surgery inpatients in the Syracuse hospitals. These patients were those aged 18 years and over excluding pediatrics, obstetrics, neonates, and mental health.

In the United States, adult medicine and adult surgery are the largest hospital inpatient populations. During 2021, they accounted for 70.1 percent of inpatients in the Syracuse hospitals. This information was available from Hospital Executive Council data.

Data for the study were obtained from the Syracuse hospitals on a daily basis by the Hospital Executive Council. Through this approach, the study included the most current information available.

The study was based on adult medicine and adult surgery utilization between

January and May 2019 and 2022. The 2019 data were used because they constituted the most recent inpatient population before the advent of the coronavirus in the Syracuse hospitals during 2020. They amounted to a discrete population whose utilization was not affected by the coronavirus.

The 2022 data were employed because they included the most recent populations available as the coronavirus has receded. With the 2019 data, they amounted to the most recent populations available for projecting the future impact of the coronavirus on hospital inpatients.

The first component of the analysis focused on comparison of numbers of medical and surgical inpatients admitted to and discharged from the Syracuse hospitals between January and May 2019 with adult medicine and adult surgery inpatients admitted to and discharged from the hospitals between January and May 2022. Within the five month periods, this information was identified for weekly intervals.

The separation between the 2019 and the 2022 made it possible to compare the impact of the coronavirus on medical-surgical utilization during the two five month periods. These differences suggested the extent to which hospitals will be able to return to inpatient utilization before the coronavirus.

The second component of the analysis focused on emergency department utilization characteristics in the Syracuse hospitals between January and May 2019 and 2022. This analysis was based on differences in weekly numbers of ambulances dispatched to hospital emergency departments in the community.

The analysis of numbers of ambulances dispatched extended to comparison of health care utilization beyond inpatient care. It included ambulance utilization generated by patients who were admitted and those who were not.

4. Results

The first component of the study focused on differences in inpatient medical-surgical patients discharged from the Syracuse hospitals by week between January and May 2019 and 2022. Relevant data are summarized in **Table 1**.

This information demonstrated that numbers of inpatient medical and surgical discharges were relatively consistent during the weekly periods in 2019. Numbers of inpatients ranged between 1100 and 1200. The data also indicated that numbers of weekly inpatients increased during the same periods in 2022. Actual numbers ranged from 755 - 760 to 974 - 994.

Comparison of the weekly data for 2019 and 2022 identified downward developments in the differences between the two years. These differences delineated a return to inpatient utilization characteristics before the advent of the epidemic. The data indicated that 69 percent of the reduction in medical-surgical discharges that occurred during the epidemic had been offset by 2022. Another 31 percent remained.

The study did not determine the extent which the increases in medical-surgical utilization in the Syracuse hospitals would continue. It demonstrated that more

Table 1. Inpatient medical/surgical discharges, Syracuse hospitals.

Week of	2019	2022	Difference
Jan 6-12	1198	755	−443
Jan 13-19	1238	760	−478
Jan 20-26	1078	852	−226
Jan 27-Feb 2	1154	805	−349
Feb 3-9	1183	772	−411
Feb 10-16	1156	815	−341
Feb 17-23	1164	873	−291
Feb 24-Mar 2	1105	864	−241
Mar 3-9	1200	863	−337
Mar 10-16	1146	904	−242
Mar 17-23	1186	866	−320
Mar 24-30	1167	925	−242
Mar 31-Apr 6	1155	921	−234
Apr 7-13	1209	870	−339
Apr 14-20	1147	902	−245
Apr 21-27	1162	946	−216
Apr 28-May 4	1204	918	−286
May 5-11	1181	984	−197
May 12-18	1155	980	−175
May 19-25	1262	928	−334
May 26-Jun 1	1033	902	−131
Jun 2-8	1170	974	−196
Jun 9-15	1129	994	−135

Source: Hospital executive council daily inpatient census report.

than half of the reduction in utilization that occurred during the epidemic has already returned.

Additional experience with inpatient utilization in the Syracuse hospitals will be necessary to determine future inpatient utilization characteristics. This information should suggest whether 2019 utilization characteristics will return.

The second component of the study focused on differences in ambulances dispatched to area hospitals between January and May 2019 and 2022. Relevant data are summarized in Table 2.

This information identified changes in health care utilization characteristics between the two time periods. The data indicated that weekly numbers of ambulances dispatched were relatively consistent during 2019. Most of the utilization ranged between 1200 and 1300. The data also indicated that numbers of

Table 2. Hospital emergency department ambulances dispatched, Syracuse hospitals.

Week of	2019	2022	Difference
Jan 6-12	1239	1222	−17
Jan 13-19	1198	1076	−122
Jan 20-26	1301	1039	−262
Jan 27-Feb 2	1143	1080	−63
Feb 3-9	1283	1053	−230
Feb 10-16	1271	1091	−180
Feb 17-23	1259	1201	−58
Feb 24-Mar 2	1215	1145	−70
March 3-9	1296	1252	−44
March 10-16	1227	1207	−20
March 17-23	1357	1195	−162
March 24-30	1304	1219	−85
March 31-April 6	1287	1238	−49
April 7-13	1202	1203	1
April 14-20	1208	1164	−44
April 21-27	1207	1211	4
April 28-May 4	1260	1184	−76
May 5-11	1192	1143	−49
May 12-18	1233	1225	−8
May 19-25	1230	1137	−93
May 26-Jun 1	1251	1226	−25
Jun 2-8	1174	1205	31
Jun 9-15	1192	1195	3

Source: Hospital executive council daily emergency department report.

ambulances dispatched were slightly lower in 2022. For most of the weeks, utilization was below 1200 patients.

The study data indicated that numbers of ambulances dispatched in 2022 were lower than in 2019. The reduction in numbers of ambulances dispatched may result from the impact of the coronavirus epidemic on patient utilization. It is not clear whether these differences were consistently increasing or decreasing.

5. Discussion

In recent years, the coronavirus and other chronic diseases have exerted a major impact on health care in the United States. This study evaluated the present and future impact as the virus winds down at the community level in the metropoli-

tan area of Syracuse, New York. It was based on adult medicine and adult surgery discharges, the largest inpatient hospital services.

The study compared adult medicine and adult surgery discharges during January-May 2019 and 2022. Utilization for 2019 has been extremely important, since it occurred before the impact of the virus. Utilization for 2022 has been an index of the extent to which health care has recovered from the coronavirus. The study also compared ambulances dispatched for the same time periods.

The inpatient data indicated that 69 percent of the reduction in medical surgical discharges that occurred since 2019 has been offset during 2022. The remaining 31 percent remained at levels experienced in 2020 and 2021. It was unclear from the data whether medical ambulances dispatched were consistently increasing or decreasing

The study data clearly demonstrated that medical and surgical discharges had increased significantly after declining during the epidemic. An important question is whether or to what extent these increases will continue or whether they will level off.

This information would require additional data concerning medical and surgical discharges and related utilization. This information is not available from existing sources.

Continued increases would suggest that the health care system could operate with additional utilization in the future. A leveling off of this experience would suggest that health care will be delivered with fewer resources. Health planners should monitor this experience during the future in order to ensure that care is delivered with the highest efficiency at the community level.

Conflicts of Interest

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

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Case Reports in Clinical Medicine, 2022, 11, 268-272
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

Dieulafoy's Lesion of the Duodenum: The Management of This Unusual Location

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How to cite this paper: Bounour, R., Mejait, A., Lahlali, M., Lamine, A., Abid, H., Mekkaoui, A., Elyousfi, M., Benajeh, D., Abkari, M.E., Ibrahimi, S.A. and Lahmidani, N. (2022) Dieulafoy's Lesion of the Duodenum: The Management of This Unusual Location. *Case Reports in Clinical Medicine*, **11**, 268-272.
https://doi.org/10.4236/crcm.2022.117039

Received: June 22, 2022
Accepted: July 17, 2022
Published: July 20, 2022

Abstract

Dieulafoy lesion (DL) is a rare source of gastrointestinal tract bleeding that can affect any site of the gastrointestinal tract, particularly the stomach and less commonly the duodenum. Early endoscopy during a bleeding episode is essential for an accurate diagnosis and sometimes multiple endoscopies are needed to establish the diagnosis. In this report, we describe a case of duodenal DL detected and treated by endoscopy. We report the case of a 65-year-old patient admitted for massive upper gastrointestinal bleeding due to a Dieulafoy lesion of the duodenum. Endoscopic diagnosis and treatment were possible and hemostasis was achieved by injecting adrenaline and placing 3 clips. Various effective endoscopic techniques are available to control bleeding, the combination of injection therapy and mechanical therapy reduces the risk of recurrence.

Keywords

Dieulafoy's Lesion, Endoscopy, Hemostatic Clips

1. Introduction

Dieulafoy's lesion (DL) is an uncommon source of gastrointestinal tract bleeding that can affect any site in the gastrointestinal tract. It accounts for 1% - 5.8% of acute gastrointestinal bleeding [1]. The most common location of this lesion is the stomach, and only 15% occur in the duodenum [2].

The diagnosis and prognosis of patients with these lesions was poor, with a mortality rate ranging from 23% to 79% before advances in endoscopy [2]. Currently, upper gastrointestinal endoscopy allows not only the diagnosis but also the treatment of DL of the duodenum.

Although, it is a life threatening condition, there are no standard guidelines

and only a few reports about duodenal lesions. In this report, we describe a case of duodenal DL that is detected and treated by endoscopy after obtaining the patient's consent.

2. Case Presentation

65-year-old patient has a history of diabetes, arterial hypertension, end-stage chronic renal failure and a previous episode of melena. An endoscopic exploration of the melena was carried out, returning in favor of a cecal angiodysplasia treated by argon plasma coagulation with a good evolution.

He was admitted to the hepato-gastroenterology departement after three days of isolated melena without hematemesis evolving in a context of anemic syndrome. The initial clinical evaluation found a conscious patient, pale, hypotensive at 10/6 mmHg, tachycardic at 100 bpm, the abdomen was soft, without pain on palpation, and without signs of portal hypertension or peritoneal irritation. A rectal examination showed melena.

Hemoglobin at admission was 4.3 g/dl, and he received 4 units of packed cell transfusion. The rest of the Laboratory investigations were without abnormality, in particular the renal function and the prothrombin level.

After patient stabilization (conditioning, vascular filling, transfusion, etc.), an upper endoscopy was performed demonstrating a massive active bleeding from the duodenum hampering optimal exploration. We doubted that it was a duodenal Dieulafoy lesion and we put a single clip with difficulty because of the importance of the bleeding. Even if the endoscopic treatment was performed, the patient still had fresh melena with deglobulization, hence the need to perform a second endoscopy.

The second upper endoscopy showed normal mucosa in the esophagus, the presence of red blood in the stomach and bulb, active bleeding in the genus superiorus of the duodenum that was compatible with Dieulafoy's lesion (**Figure 1**), adrenaline solution was injected and three hemostatic clips were placed ensuring good hemostasis (**Figure 2**).

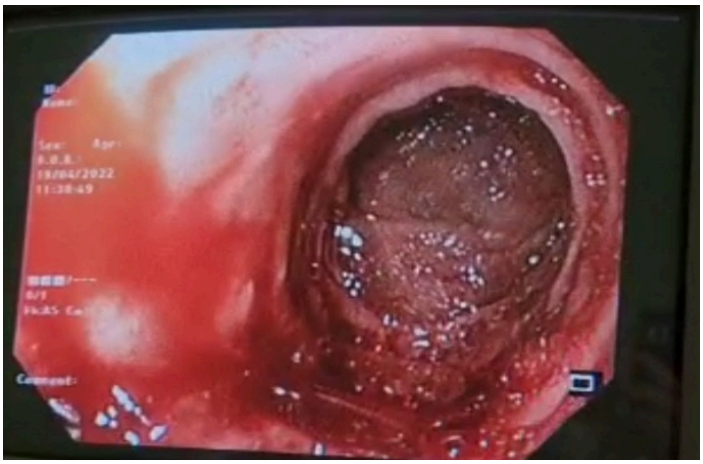

Figure 1. Dieulafoy's lesion: active bleeding from the duodenum.

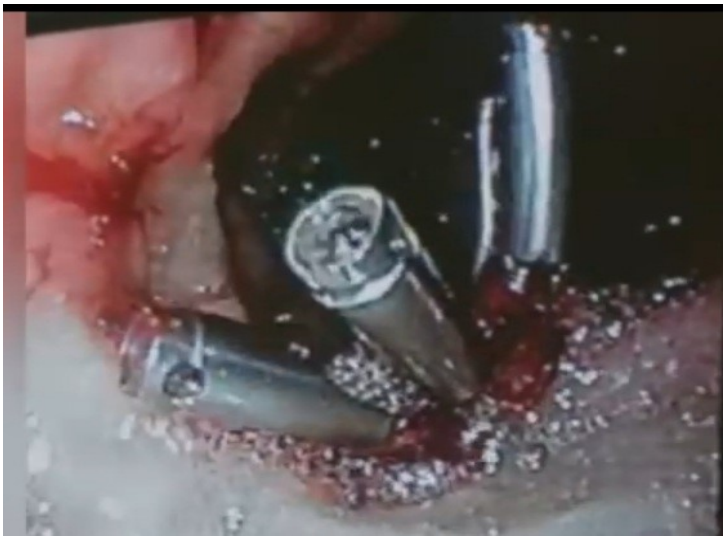

Figure 2. Treatment of Dieulafoy's lesion with three hemostatic clips.

After performing endoscopic treatment, no active bleeding was observed after washing and oral feeding with a liquid diet was initiated on the first day post-endoscopy. The patient did not develop any complications and had no further bleeding episodes during his hospitalization.

The patient was eventually discharged to home in stable condition after 8 days of hospitalization. Recovery was achieved and bleeding has not recurred in a follow-up of two months.

3. Discussion

Dieulafoy's lesion is a rare vascular abnormality characterized by a small abnormally dilated artery that runs a tortuous course in the submucosa [1].

Studies on the history of patients with DL have described that most of these patients have a history of cardiovascular disease, chronic kidney disease, hypertension, peptic ulcer disease, diabetes mellitus, and chronic use of certain medications (anti-non-steroidal inflammatory drugs (NSAIDs) and anticoagulants) [3].

The characteristic clinical presentation is often painless, massive, recurrent, intermittent hematemesis, associated with melena, hematochezia, and hypotension [4].

Previously, the diagnosis was rarely made before surgery or autopsy. It could only be made by histological examination. Currently, endoscopic findings are often sufficient to support the diagnosis by showing an isolated protruding vessel usually surrounded by normal mucosa and the diameter of the vessel stump is usually between 1 and 3 mm. Alternatively, it may show an actively bleeding lesion or completely covered by a blood clot since spontaneous hemostasis may be produced [1].

The initial endoscopy is effective for diagnosis in almost 70% of patients while approximately 6% of patients will require three or more endoscopies to establish

the diagnosis [5]. The diagnosis can be difficult to make during the first endoscopy for many reasons: first, the small size of the lesion, the normal appearance of the surrounding mucosa, and finally, due to the intermittent nature of the bleeding [2].

There is no consensus on the treatment of a Dieulafoy's lesion. Several endoscopic treatment methods are available: local injection of epinephrine, sclerotherapy, thermal or argon plasma coagulation, banding and haemoclipping [4]. The choice of therapeutic technique will depend on the clinical presentation, lesion site, and available surgical and endoscopic expertise [2].

Injection therapy mainly aims to stop bleeding from the vessels by injecting several agents such as vasoconstrictors or sclerosants. It allows temporary haemostasis, which explains the risk of re-bleeding with this technique [2].

Thermocoagulation methods carry a risk of transmural damage due to the thin wall of the duodenum. On the other hand, some Japanese groups suggest the use of vascular clips as an effective and safe method of hemostasis in thin-walled organs such as the duodenum [6].

A comparative study of hemostasis methods in patients with Dieulafoy lesions conducted by Chung *et al.* showed that mechanical techniques such as banding and hemoclipping were superior to injection methods in terms of effectiveness either to stop bleeding or to prevent re-bleeding [6].

Angiography and embolization are indicated for inaccessible lesions that are not amenable to endoscopic and/or surgical treatment. Finally, surgical resection is reserved for 5% of cases that are refractory to endoscopic management and angiographic methods [5].

4. Conclusion

Although Dieulafoy lesions are rare, especially those located at the duodenal level, they are potentially fatal and therefore increased awareness and early endoscopy during a bleeding episode are essential for an accurate diagnosis.

Various effective endoscopic techniques are available for controlling bleeding, the combination of injection therapy and mechanical therapy reduces the risk of rebleeding.

Conflicts of Interest

The authors declare that they have no competing interest.

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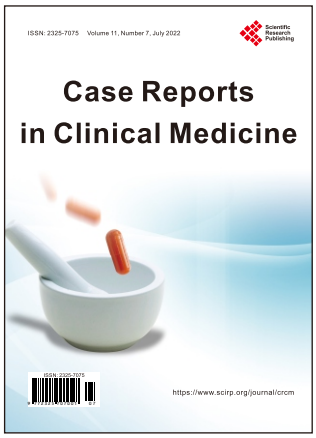

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