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Testicular Burkitt's Lymphoma: A Case Report and Literature Review

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Abstract

Background: Burkitt's lymphoma of the testis (TBL) is a rare and extremely aggressive malignant usually diagnosed in front of a testicular mass. We describe an interesting single case of TBL managed by a combined multimodal approach with a review of the literature. **Case Report**: A patient aged 69-year-old male, newly hypertensive, who presented with a twelve-month history of right testis progressive painful scrotal swelling, which worsens following a motorbike accident. Clinical examination revealed a large tender mass in an erythematous right scrotal bursa. A scrotal ultrasound showed a right heterogenous intra-testicular mass. The patient underwent unilateral (right) radical orchiectomy. Histopathological examination revealed presence of monomorphic lymphoid cells, with moderate to increased size, dissociated inconstantly by macrophages consistent with a Burkitt's-like non-Hodgkin Lymphoma. After surgery, the patient was transferred to oncologist for adjuvant chemotherapy. **Conclusion**: A testicular mass is a usual circumstance for the discovery of a primary tumour of the testicle. Burkitt's testicular lymphoma is a rare tumour whose diagnosis is based on histological findings. There are non-consensual etiological or predisposing factors. The treatment depends imperatively on the stage of the disease. Therapeutic modalities relay on in surgical excision, chemotherapy and radiation therapy but the accurate procedures are not standardized.

Keywords

Burkitt's Lymphoma, Orchidectomy, Testis

1. Introduction

Testicular lymphoma was first reported by Malassez and Curling in 1866 [1]. Burkitt's lymphoma is an uncommon form of non-Hodgkin lymphoma (NHL) in adults and represents less than 5% of lymphoma cases [2]. Burkitt's Lymphoma (BL) is a highly aggressive, rapidly growing B cell non-Hodgkin's Lymphoma, which manifests in several subtypes including: Epstein-Barr virus endemic, sporadic, and immunodeficiency-associated types [2]. These clinical variants are recognised with different epidemiology, risk factors, and clinical presentations. The endemic subtype is found in equatorial Africa and New Guinea with a near 50-fold higher incidence than that seen in the US [3], the distribution corresponds to areas where malaria and Epstein Barr virus are prevalent.

Primary testicular lymphoma is a rare tumour accounting for 1% of all testicular non-Hodgkin lymphoma [4]. It is defined by the primary localization of the tumour in the testis at presentation. Diffuse large B-cell lymphoma is the most common histological variety [5]. Testicular lymphoma is the most common testicular tumour in men aged over 50 (26% to 44% of testicular tumours) [6]. It is the most frequent testicular malignancy in men over 60 years of age. Its prognosis is usually poor, characterized by spreading to non-contiguous extranodal sites, especially in central nervous system and high recurrence [7].

In Cameroon, between 1999-2008, 20 cases of primitive urogenital lymphoma were found in the urology and andrology unit of Yaoundé Central Hospital, with a remarkable predominance for Burkitt's Lymphoma [8]. The management of this tumour is a multidisciplinary purpose, and relies mainly on a radical upper inguinal orchidectomy mostly associated with chemotherapy.

We hereby present a case report of Burkitt's Lymphoma, of the right testicle of a 69-year-old patient who presented following an external genitalia trauma, as well as our results on: local literature review, the socio-demographic study, means of diagnosis, means of treatment and the prognosis of this uncommon pathology.

2. Case Report

We report a case of a 69-year-old black male with a medical history of hypertension noncompliant to treatment. He presented with an eighteen-month history progressive increase in right testicle initially without associated pain until his motorbike accident, all evolving in the context of a slight decline in general condition. He was the middle passenger on a motorbike with 3 passengers hooked between the driver and the third passenger, which had a head-on collision with a touristic car three-day prior to consultation. The sweeling increase along with pain onset prompted consultation in our unit. The clinical examination revealed an ulcerative and necrotic right scrotal skin lesion measuring 3 × 4 cm of diameter with an underlying large tender irreducible nonfluctuating testicular mass in the right scrotal bursa extending to the inguinal region, the lymph nodes were free. There was no splenomegaly or hepatomegaly. A scrotal ultrasound

showed an enlarged, heterogenous testis with multiple hypoechoic masses, discretely polylobed, hypervascularized right intra-testicular mass suggestive of a seminoma. The ultra-sound examination showed an enlarged, heterogeneous testis with diffusely hypoechoic parenchyma and irregular edge measuring 66 × 67 mm, the contralateral testis was increased in size too without a particular architectural change. There were also multiple lymphadenopathies in the inguinal and iliac regions, raising our suspicion for a malignant tumour of the right testis. A Kidney-Ureter-Bladder (KUB) Ultrasonography and transrectal prostate Ultrasonography (TRUS) showed bilateral uretero-hydronephrosis, a significant post-residual volume (PRV) of 175 ml and a normal prostate with a volume of 28.6 ml (**Figure 1**).

Tumour markers assay showed normal levels of serum alpha-fetoprotein (αFP), serum lactate dehydrogenase (LDH), and serum beta human chorionic gonadotropin (βHCG). Laboratory tests, especially, serum testosterone, Prothrombin ratio, urine culture, activated partial thromboplastin time were all normal except for the renal function which was altered, with a plasma urea of 52 mg/dl, and a creatinaemia of 3.03 mg/l. He has also had a microcytic hypochromic moderate anaemia with a haemoglobin level at 6.7 g/dl (Normal value (NV): 14.1 - 18.1 g/dL), which was corrected with a transfusion of 03 units of group O positive whole blood. HIV serology was negative.

Following a multidisciplinary team meeting including urologists, oncologist, pathologist, anaesthesiologist, radiologist, a treatment strategy was adopted. The patient then underwent a unilateral (right) inguinal orchidectomy under spinal anaesthesia with complete excision of the testis. Intraoperatively, the right testicle was found to be completely replaced by tumour, with extension into the gubernaculum and epididymis. The specimen was sent for histopathology studies (**Figure 2**).

Figure 1. Macroscopic view of the inguino-scrotal swelling and the necrotic layer.

Thoracic abdomen pelvic scan performed after the surgery due to financial constraints found a diffused retroperitoneal infiltration, suggesting an important lymph node invasion consider as probable secondary locations, a diffuse condense peritoneal fat tissues alongside with a residual ascites and the presence of a bladder tumoral mass of 37 mm diameter to sought out. (**Figures 3(a)-(c)**)

Using Ann Arbor Staging System The patient was staged stage IVA.

Histopathology revealed extensive involvement and replacement of testicular parenchyma by a tumour composed of large discohesive sheets of cells with pleomorphic, hyperchromatic nuclei and prominent nucleoli suggestive of a Burkitt's-like lymphoma (**Figure 4** and **Figure 5**).

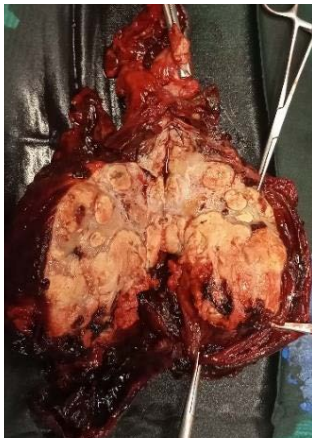
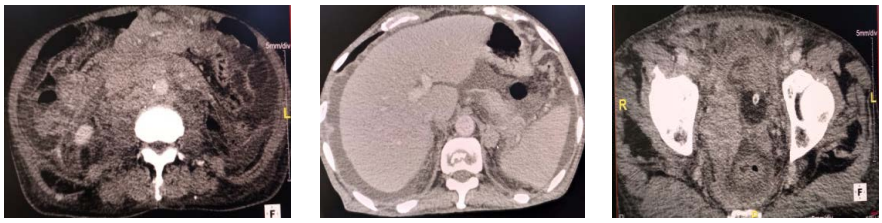


Figure 2. Macroscopic view of the excised right testis.



(a) (b) (c)

Figure 3. (a)-(c): Intra-abdominal leak of lymphadenopathies (a), diffused condensation of the peritoneal fat tissue (b), bladder tumoral mass (c).

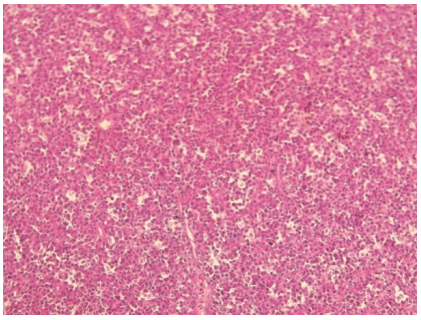


Figure 4. Microscopic view of the Burkitt's-like non-Hodgkin Lymphoma (HE ×10). (Note the presence of monomorphic lymphoid cells, with moderate to increased size, dissociated inconstantly by macrophages).

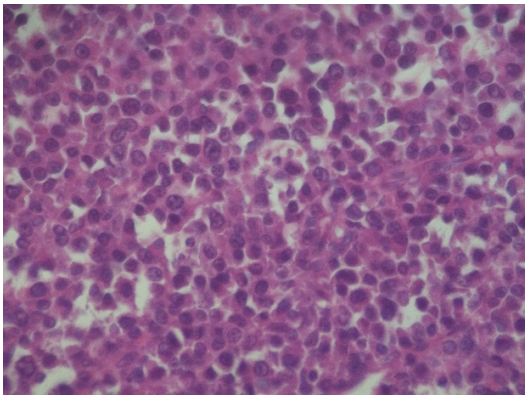


Figure 5. Microscopic view of the Burkitt's-like non-Hodgkin Lymphoma (HE ×40). (Note the presence of monomorphic lymphoid cells, with moderate to increased size, dissociated inconstantly by macrophages).

The patient was referred for further management to the oncology unit of the Yaoundé General Hospital on the third day post-operative, and was subsequently scheduled for adjuvant chemotherapy. Unfortunately, he died on the 32nd post-operative day.

3. Discussion

Burkitt's lymphoma is a highly aggressive B-cell NHL, with a doubling time of 24 hours [9]. While the sporadic BL is observed in North America, Europe, and East Asia with an annual incidence of 2 per 1 million, endemic type of BL is usually seen in the African subcontinent and is more commonly associated with Epstein-Barr virus and malaria [10]. In endemic region, Burkitt's lymphoma represents 10% of all testicular lymphoma [11]. There are non-consensual etiological or predisposing factors. Various reports have implicated prior trauma, chronic orchitis, cryptorchidism and filariasis of the spermatic cord as risk factors [12].

Testicular lymphoma may be the primary and only manifestation of malignant lymphoma, the initial sign of generalized disease, or it may occur during the clinical course of a patient with established lymphoma. Primary Testicular Lymphoma (PTL) concerns mainly men over 50 years of age as shown by most prospective and retrospective studies [13] with a median age of 65 years [14]. Secondary involvement of the testis in patients with lymphoma is far more common than primary testicular lymphoma [15].

These highly aggressive tumours are rare, this can be illustrated by the diagnosis of this case in our unit more than 20 years after Mamadou Sow *et al.* work in the same unit [8].

Even if our patient was HIV negative, international literature suggest that the incidence of this tumour is favoured by a state of immunodepression (HIV etc.), tuberculosis, and EBV infections [11].

Diagnosis of testicular lymphoma begins with a thorough medical history and physical exam of the entire body. Additional diagnostic tests include imaging,

blood tests, and tests performed on cancer tissue. The usual presentation is a unilateral painless progressive increase in size testicular mass over several months [13] [14] [15] [16]. However, at presentation, a bilateral involvement is noticed in up to 10% of the cases [16]. Constitutional symptoms such as fever, weight loss, anorexia, night sweating and fatigue are seen in 25% to 40% of the patients [4]-[16]. The presence of these systemic signs is predictive of tumour aggressiveness and is observed in 25% to 41% of patients with advanced disease [13] [14]. The classic physical sign in the localized stage is a solid testicular mass of variable size. This mass can be unilateral or bilateral. It is synchronous in 10% and asynchronous in 30% - 35% [17]. Our patient initially had a painless unilateral scrotal swollen which became painful following an external genitalia trauma but general signs were absent. Complementary paraclinical investigations help to determine the unilateral or bilateral nature and the extent of the disease. Scrotal ultrasonography often coupled with Doppler is the first-line investigation for an enlarged scrotum which demonstrates focal or diffuse areas of hypoechogenicity with hypervascularity in an enlarged testis [18]. LDH levels have been correlated with tumor aggressiveness, whereas other tumor markers such as βHCG and αFP are rarely elevated in TNHL cases [19]. In our case, LDH, βHCG and αFP levels were normal.

Due to the differences between early and advanced stages of testicular lymphoma, a complete lymphoma workup should be performed including bone marrow biopsy and CT scan of the thorax, abdomen and pelvis. In recent years, CT or magnetic resonance imaging (MRI) has also played an important role in the diagnosis of primary testicular tumors by simultaneously evaluating the structure of the testis and epididymis [20]. At the same time, there is growing interest in using fluorescence in situ hybridization (FISH) as the gold standard for diagnosis [20]; however, this method is rarely employed because of availability, patient preference and economic conditions in our case. CT remains the modality of choice for assessing retroperitoneal lymph nodes [21].

Our first line imaging study was a doppler scrotal ultrasonography associated with an abdominopelvic ultrasonography which confirm our suspicions of a testicular tumour. Subsequently, after the surgery we could carry out a CT scan of the chest, abdomen and pelvis, which the family could only afford by that time. Whereas, the diagnosis was confirmed by an anatomopathological examination of the surgical biopsy specimen. Unfortunately, the diagnosis remains late in our context due to various reasons contributing to a poor prognosis for the patient, as illustrated by our case where the patient consulted because of the posttraumatic testicular pain while his testis has been swollen for several months.

In case of PTL suspicion, inguinal orchiectomy is required to achieve optimal disease control and adequacy of a pathologic specimen which has both diagnostic and therapeutic purposes [13]. It removes the so-called sanctuary site [13]. When the blood-testicular barrier is present, it's difficult for drugs to penetrate the testes, therefore chemotherapy effect is not ideal [22]. On the other hand, testicular tumoral cells may express high levels of drug-resistant proteins, such

as P-glycoprotein (PGP) and breast cancer drug-resistant protein (BCRP), resulting in resistance to chemotherapy [22].

Given the rarity of this tumour, the treatment is not standardised. A multimodal therapeutic approach is needed. The multidisciplinary team includes urologists, haematologists and radiation oncologists [23]. Histological examination is the only means of diagnosis. It can be made on biopsy or surgical specimen. Until to 1995, a combined modality therapy was recommended to PTL, which consists of orchiectomy, systemic chemotherapy, scrotal radiotherapy, and prophylaxis intrathecal chemotherapy [24]. Treatment regimens vary widely, as many studies on testicular lymphoma were done retrospectively, most advocates a phased-management approach for testicular lymphoma with all patients receiving multi-agent chemotherapy (doxorubicin, cyclophosphamide, vincrisitine and a corticosteroid) [14]. Patients treated with orchiectomy followed by chemotherapy without scrotal radiotherapy have a significant risk of relapse, especially in the contralateral testis, estimated at 25% [23]. Indeed, chemotherapy drugs have a low penetration in the healthy testis [13]. However, the results of numerous studies attest that scrotal irradiation is associated with a better survival [13].

We did a multidisciplinary team review of this case to propose an adequate and feasible therapeutic plan, we then opted for an inguinal orchidectomy under spinal anaesthesia and the surgical specimen was send for histopathology studies for determination of tumour type and diagnosis confirmation. Immunochemistry studies were not done in this case because his family couldn't afford sending his sample abroad for complementary analysis. Base on histopathology result, we opted for adjuvant chemotherapy with cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone regimen (CHOP), which is done in another centre leading to his transfer for follow-up by the oncologist. This therapeutic attitude is consistent with that proposed by a large number of authors in the literature. [1]-[20]. The most important factors determining the prognosis are stage and histological grade. Testicular lymphoma carries a poor prognosis compared to other NHL and extranodal lymphomas and may require a more prolonged course of chemotherapy compared to other extranodal lymphomas [14]. Stage and pathologic grading are the most important predictive factors for outcome [14]. Insufficient organ functions due to advanced age, presence of the constitutional symptoms, tumour burden higher than 9 cm, spermatic chord and bilateral testicular involvement, vascular invasion, degree of sclerosis and high level of LDH affects the prognosis negatively [25]. Of the known poor prognostic factors, our patient had involvement of the epididymis and spermatic chord, advance age, delay presentation and advanced diseases. Unfortunately, our patient short nor long term outcome can't be assessed since he died in the course of treatment at the 32nd postoperatively day during chemotherapy. This is consistent with data from the literature, which highlights the fact that the prognosis depends on early diagnosis and the presence or absence of secondary locations [26].

4. Conclusion

Burkitt's Lymphoma is a rare aggressive testicular tumour which should be considered as a diagnosis for elderly male over 60 years presenting with a progressive painless testicular mass whether constitutional signs are present or absent. Presence of normal testicular tumour markers should not be an exclusion criterion of testicular tumour. Doppler scrotal ultrasound is the first line imaging study for exploration of testicular mass. The definitive diagnosis is base on histopathology results from the surgical specimen. Management is multidisciplinary, mainly through an inguinal radical orchiectomy the earlier as possible and associated with chemotherapy. The prognosis remains poor and depends on early diagnosis and management.

Conflicts of Interest

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

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