International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

Primary Bladder Lymphoma in an Elderly Asian Female: A Rare Case of Diffuse Large B-Cell Lymphoma

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Abstract: ***In the United Kingdom, Bladder cancer is the seventh most diagnosed cancer in the male population. Bladder cancer remains one of the most- costly cancers to treat to date and continues to be a profoundly significant contributor to cancer-related mortality rates within the United Kingdom, with an alarming statistic indicating that approximately 5,600 individuals succumb to it each year, which constitutes a striking 3% of the total number of deaths attributable to various forms of cancer. While it is widely acknowledged within the realm of oncological pathology that Transitional Cell Carcinoma represents the predominant histological variant of bladder cancer, accounting for an impressive percentage that exceeds 90% of all diagnosed cases, it is with great scholarly interest that we present a rather uncommon and exceptional case involving primary lymphoma of the bladder, which was diagnosed in an elderly female patient of Asian origin. Primary bladder lymphoma is a rare urological malignancy that is often frequently misdiagnosed due to presentation with nonspecific lower urinary tract symptoms, since it was first described in 1885 by Eve and Chaffey, it remains a rare cancer with fewer than 150 cases documented in existing literature. This academic report comprehensively outlines a case study related to a manifestation of diffuse large B Cell lymphoma in an elderly female patient. It is imperative to recognize that numerous management strategies are accessible including, but not confined to, surgical intervention, radiotherapeutic approaches, and various chemotherapeutic regimens. It is essential to emphasize that these treatment modalities may be implemented as standalone therapies or in synergistic combinations. In the specific instance of our patient, she underwent surgery (Transurethral Resection of Bladder Tumour, TURBT, which was subsequently followed by an extensive chemotherapy regimen - RCHOP. For our patient, it is significant to highlight that the follow-up included clinical evaluations, annual PET CT scans, which has revealed no metastasis after 3 years, thereby affirming that the patient is currently in a state of remission. Additionally, our review also incorporates a thorough literature analysis that clarifies the current management modalities and explore future possibilities.***

Keywords: Haematuria, Primary bladder lymphoma, Diffuse large B cell lymphoma, RCHOP chemotherapy, Urological malignancy

1. Introduction

Bladder carcinoma indisputably represents a significant and urgent public health concern, engendering substantial difficulties not only within the confines of the United Kingdom but also reverberating its consequences throughout the global landscape, impacting innumerable individuals and healthcare infrastructures in a similar manner.

In the United Kingdom, bladder carcinoma is acknowledged as one of the ten most frequently diagnosed neoplasms, illustrating a notable statistic of approximately 10,500 to 11,000 newly cases reported annually, which corresponds to an estimated 3% of all newly identified cancer occurrences according to Cancer Research UK. 90% of bladder cancers are Urothelial cancer (Transitional cell carcinoma) with other types being squamous cell carcinoma, and rarely primary bladder lymphomas.

Lymphomas are a heterogeneous group of cancers originating from the lymphatic system. They are among the most common cancers in the UK, with significant variations in incidence, survival, and prevalence across subtypes. Lymphomas are broadly classified into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL), while the majority of Hodgkins lymphoma present with nodal involvement, extra nodal involvement is rare [1,2].

Non-Hodgkin lymphoma encompasses a diverse group of lymphoid malignancies, classified into various subtypes based on histology, genetics, and clinical behaviour. The World Health Organization (WHO) classification system is widely used to categorize NHL into distinct entities such as diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, and marginal zone lymphoma (MZL) [3,4] . Gurney & Cartwright [5] reported Extranodal Non Hodgkins Lymphoma accounts for 25-35% of all NHL cases, with common sites including the stomach, small intestine, central nervous system and skin.

Clinically, Primary bladder lymphoma (PBL) most often presents in a more common presentation of bladder disease, such as hematuria, dysuria, and frequency. These presentations are nonspecific, leading to misdiagnosis and further delay in appropriate intervention. Computerised Tomography (CT) and ultrasonography are imaging tools primarily used to identify bladder masses and underscore the need for appropriate diagnostic tools. Cystoscopy, however, is the primary diagnostic tool for PBL. This is because, it allows for direct visualization of the bladder mucosa and facilitates collection biopsies for histopathological evaluation which ultimately confirms the diagnosis of PBL, distinguishing it from other malignancies.

The rarity and nonspecific presentation of PBL mandate a high index of suspicion on the part of clinicians. Given the rarity of reported cases in the literature, treatment regimens for PBL are not clearly established and are based on case reports and small series. Early diagnosis and appropriate treatment, nonetheless, are associated with good outcomes.

Highlighting rare cases like primary bladder lymphomas is essential to improve early recognition and treatment in the absence of standardized protocols. More awareness and studies on PBL are needed to improve patient outcomes. This report aims to present a rare case of primary bladder lymphoma and evaluate current diagnostic and treatment approaches through a literature-supported discussion.

2. Case Report

A 81 year old female patient was reviewed in the HOS (Haematuria One Stop Clinic on account of painless visible haematuria ongoing for a year. She reported no abdominal pain, burning sensation, vulvar itchiness or fever. she did not report any significant irritative LUTS (lower urinary tract symptoms) such as frequency, urgency, nocturia, urge incontinence, no Voiding LUTS such as weak stream or incomplete emptying. Patient did not report any constitutional symptoms of malignancy such as weight loss, loss of appetite, easy fatigability or weakness in limbs. Neither did she have any recognized risk factors for urothelial malignancy such as smoking, occupational or significant family history. She had recently been started on iron tablets for Iron deficiency anaemia and also known to have well controlled Type 2 diabetes and hypertension.

She was evaluated in the HOS with flexible cystoscopy and Ultrasound of the Urinary tract. Ultrasound showed normal upper tract while the flexible cystoscopy showed debris in the bladder and normal bladder wall, however, could not exclusively rule out an underlying malignancy and patient subsequently scheduled to have a further Computerized tomography (CT) . Computerized Tomography showed bladder lesion mainly involving the wall of the bladder

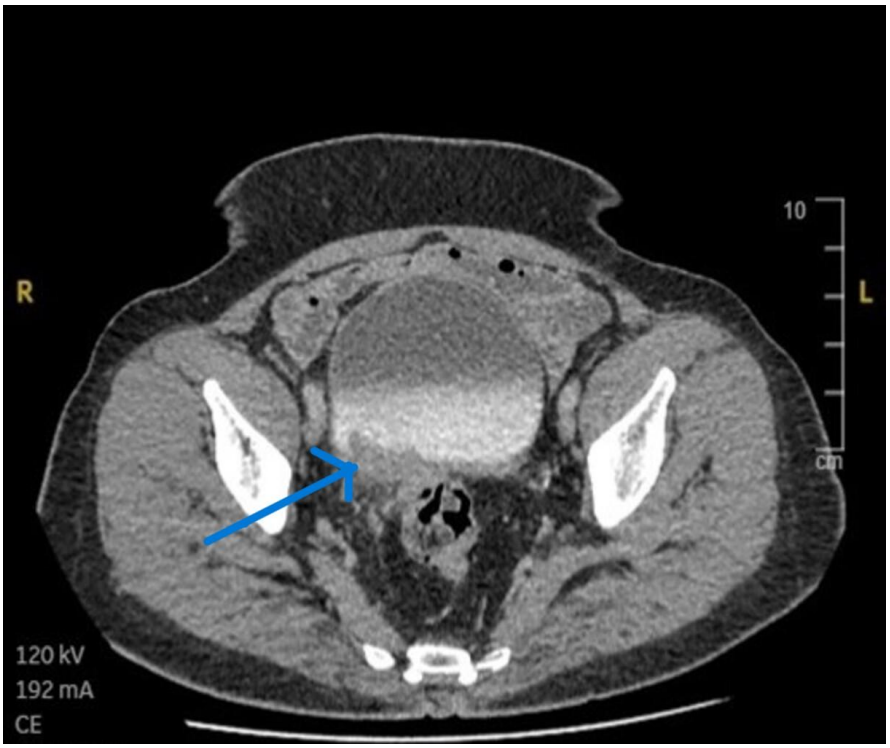

Figure 1: Pre TURBT Axial CT scan showing right lateral wall filling defect

TURBT (transurethral resection of bladder tumour) under general anaesthesia was performed after imaging findings . TURBT revealed a histological finding of Diffuse Large B Cell Lymphoma, germinal centre type.

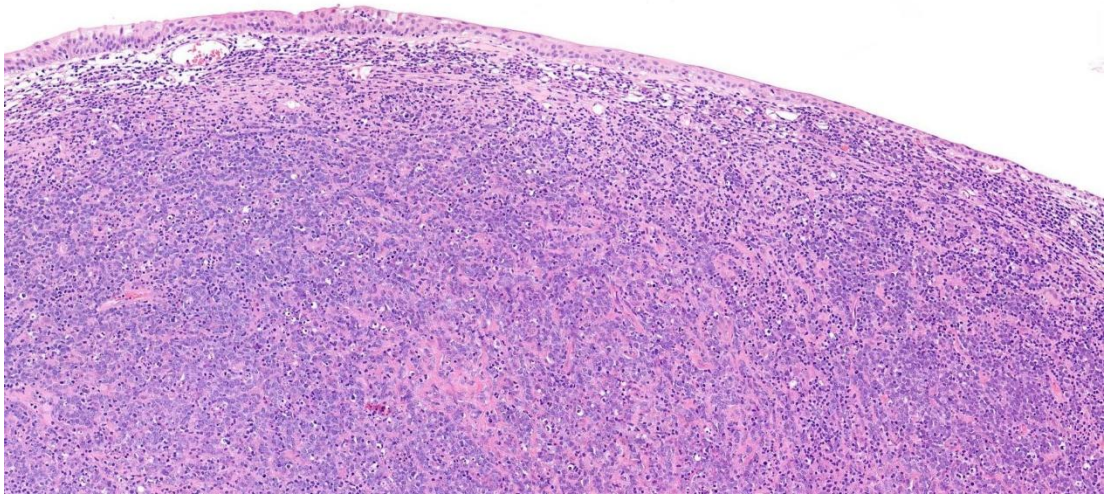

Figure A: H&E stain x10 power. Diffuse large B cell lymphoma, germinal centre type. Compose of sheets of large to medium size cells

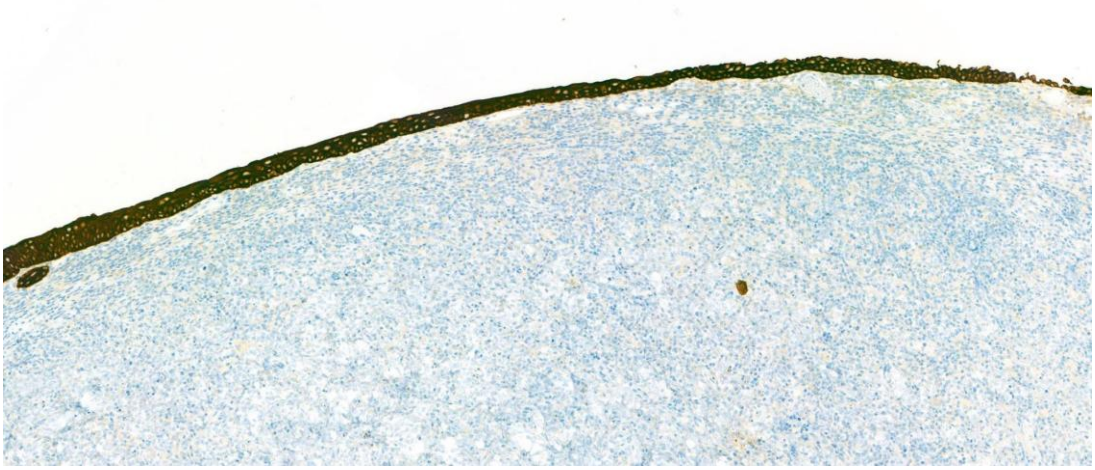

Figure B: AE/AE3 stain x10 power. Pankeratin highlight the surface urothelium while negative in the DLBCL lymphoma.

Figure C: CD45 stain x10 power. Leukocyte cimmom antigen (LCA) confirm hematopoietic nature of tumour

Figure D: CD20 stain x10 power. Common B cell marker highlighting the B-cell phenotype of the neoplastic cells.(Immunostain, 100x magnification)

Images in FIGURES A, B, C, D showing Microphotographs of the bladder mucosa infiltrated by sheets of monotonous medium sized cells which have vesicular nuclei, some prominent nucleoli and apoptosis.

PET CT scan undertaken and revealed no further actively metabolic site.

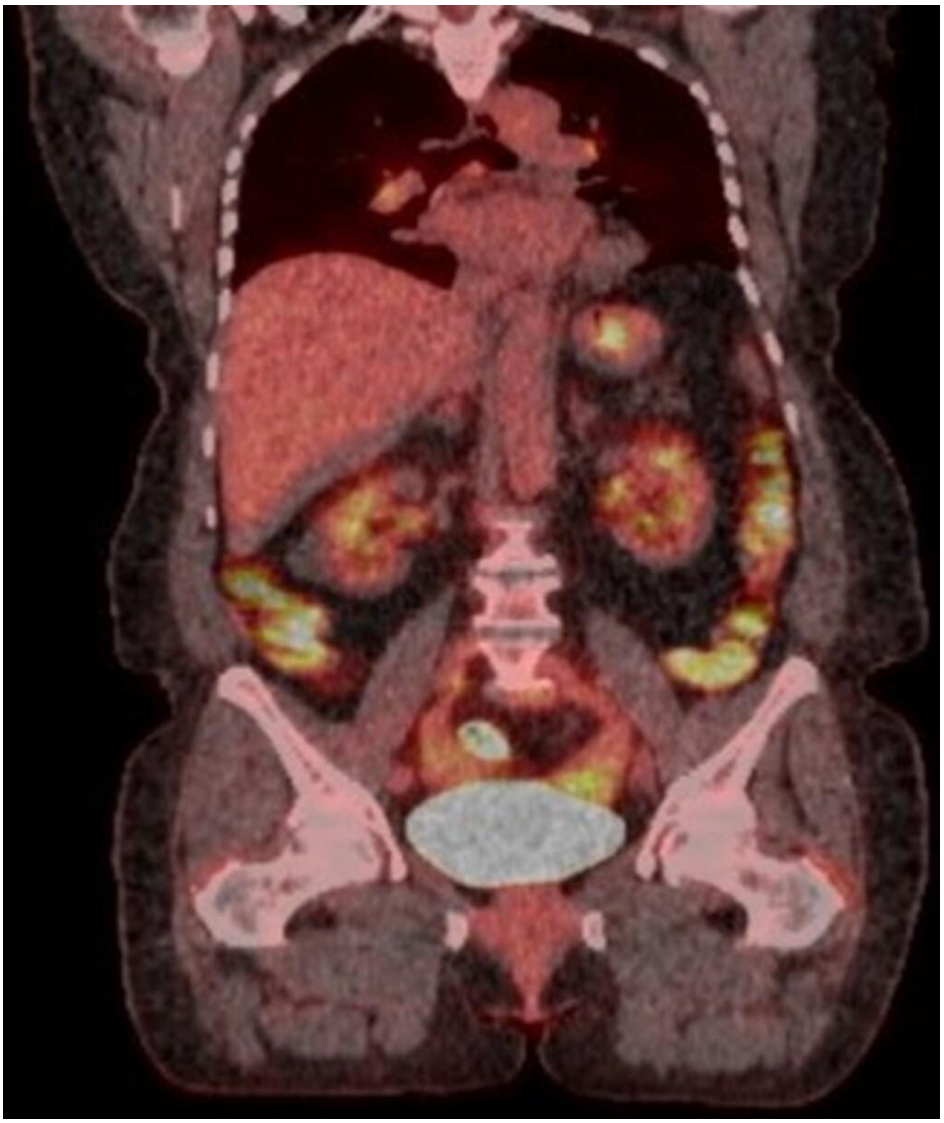

Figure 2: Post TURBT/ Pre RCHOP FDG PET CT, Coronal view, showing no metabolic active sites

Haematology MDT deliberated on the diagnosis of primary bladder lymphoma and suggested for patient to undergo chemotherapy standard R-CHOP regimen (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone) completed over six treatment cycles and patient has remained in remission for over 3 years.

3. Discussion

Primary bladder lymphoma is a rare malignancy, accounting for less than 1% of all bladder tumours and approximately 0.2% of extra nodal non-Hodgkin lymphomas [6]. The majority of cases are low-grade, with mucosa-associated lymphoid tissue (MALT) lymphoma being the most common subtype, while high grade lymphomas, such as Diffuse large B-cell lymphoma (DLBCL), are less frequent but more aggressive [7,8]. This case review focuses on treatment outcomes, chemotherapy regimens, clinical guidelines, and post-treatment follow-up strategies for primary bladder lymphoma.

Primary bladder lymphoma requires careful consideration of treatment options, especially given variation in patient responses, rarity of primary bladder lymphoma, as well as the absence of a unified central guideline in management and follow up. While Low-grade primary bladder lymphomas, particularly MALT lymphomas, are typically indolent and often associated with a favourable prognosis. Many studies have shown that these tumours respond well to less invasive therapies, such as transurethral resection of the bladder tumour (TURBT) achieving complete remission in many cases [9]. For example, Tu et al in 2023 described a case report of a patient with MALT lymphoma treated with TURBT alone and remained disease-free after one year of follow up conversely , High-grade lymphomas, such as DLBCL, are more aggressive and require systemic treatment.

In 1993, The New England Journal of Medicine published a landmark study [10] showed the efficacy of the CHOP regimen, The CHOP regimen, which encompasses cyclophosphamide, doxorubicin, vincristine (Oncovin), and prednisone, has historically constituted the foundational approach for the treatment of aggressive non-Hodgkin lymphomas, with a particular emphasis on diffuse large B-cell lymphoma (DLBCL).It however underwent several modifications which led to the development of the R-CHOP chemotherapy regimen.

The R-CHOP therapy emerged as a fundamental component in the therapeutic approach to diffuse large B-cell lymphoma (DLBCL) and various other B-cell malignancies. This regimen integrates Rituximab, a monoclonal antibody that specifically targets the CD20 antigen, with conventional CHOP regimen. The incorporation of rituximab into the CHOP regimen has markedly enhanced clinical outcomes for patients afflicted with B-cell lymphomas, providing increased therapeutic efficacy while maintaining a tolerable toxicity profile as well as survival rates. A study by Coiffier et al (2007) reported that amongst elderly individuals diagnosed with DLBCL, the complete response rate associated with R-CHOP was recorded at 76%, in contrast to 63% observed with CHOP alone [11]. This notable enhancement in clinical outcomes has established R-CHOP as the prevailing standard of care for DLBCL.

Additionally, in the context of localized malignancies, Radiotherapy is an adjuvant treatment often utilised alongside R-CHOP chemotherapy; it can also be a stand-alone treatment. In one study [12], a patient with primary bladder DLBCL treated with six cycles of R-CHOP followed by radiotherapy remained disease-free at six months post-treatment. Comprehensive irradiation of the bladder has demonstrated efficacy in achieving total remission in individuals diagnosed with MALT lymphoma, including instances characterized by high-grade histological features [13,14].

Surgical interventions, such as cystectomy, are seldom necessitated and are generally reserved for cases that exhibit resistance to treatment or complications such as in ureteric obstruction. However, cases with extravesical extension or advanced-stage disease may have poorer outcomes, highlighting the need for tailored treatment strategies [15].

Lymphoma Type	Treatment Approach	Details
Low-Grade Lymphomas (e.g MALT lymphoma)	TURBT	Often curative for localized disease
	Antibiotics	May be effective in cases with chronic inflammation
	Radiotherapy	Considered for residual disease after TURBT
High-Grade Lymphoma (e,g DLBCL)	R-CHOP or CHOP	First-line chemotherapy regimen
	Radiotherapy	Maybe added for localised disease or residual masses
	Surgery	Reserved for complicated or refractory disease

Surveilance

Regular follow-up is essential to monitor for recurrence and assess treatment response. Recommended follow-up strategies includes Cystoscopy and Imaging amongst others, Cystoscopy is deemed imperative for the accurate assessment of any potential local, such as computed tomography (CT) scans and positron emission tomography (PET) scans, are invaluable diagnostic tools for the surveillance of any distant disease dissemination. While a thorough and systematic evaluation of clinical symptoms remains essential, combined with comprehensive laboratory analyses, is fundamentally essential for the prompt and accurate identification of any potential relapse hence patients with primary bladder lymphoma is predominantly favourable, as indicated by an overall survival rate of approximately 75%, which has been documented in one specific study conducted by Hughes et al. (2005). However, it is crucial to note that the presence of high-grade lymphomas, particularly when coupled with extravesical extension, is strongly correlated with diminished outcomes, thereby underscoring the necessity for the implementation of rigorous treatment protocols and the establishment of vigilant monitoring strategies [16,17].

4. Conclusions

Primary bladder lymphoma is a rare but treatable malignancy. Low-grade lymphomas often respond well to simple therapies, while high-grade lymphomas require aggressive treatment with chemotherapy and radiotherapy. R-CHOP remains the standard of care for DLBCL, and rituximab has improved outcomes for B cell lymphomas. Regular follow-up with cystoscopy and imaging is essential for monitoring recurrence but there are currently no guidelines in place. Further research is needed to refine treatment strategies and improve prognosis for patients with aggressive or refractory disease.

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