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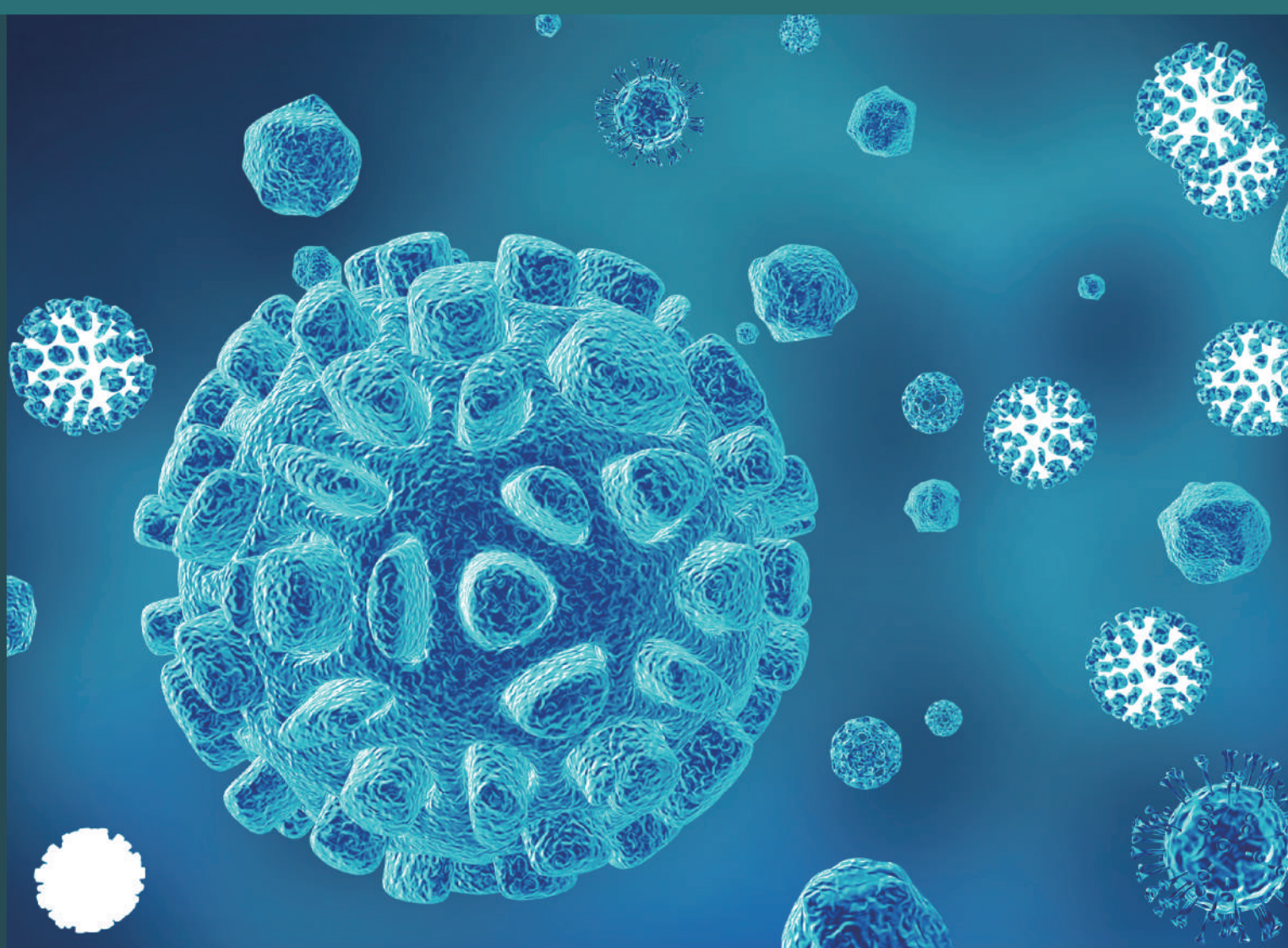
Volume 1 Issue 3

Journal of Oncology Research

Volume 1 Issue 3 · October 2019 · ISSN 2630-5267



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Price: S$30.00

Volume 1 Issue 3 • October 2019 • ISSN 2630-5267 (Online)

Journal of Oncology Research

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REVIEW

Unusual Metastases to Diaphragm and Spleen from Adenocarcinoma of Lung Detected by ^{18}F-FDG PET/CT Imaging: A Case Report

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ARTICLE INFO

Article history
Received: 23 December 2019
Accepted: 14 January 2020
Published Online: 31 March 2020

Keywords:
PET/CT
Lung carcinoma
Diaphragm metastasis
Splenic metastasis

ABSTRACT

Globally, carcinoma of lung is the predominant cause of cancer death among both men and women. While hematogenous spread from primary lung cancer to multiple other organs is frequently reported, metastases of malignant tumors to diaphragm and spleen are rare. Nowadays, Positron emission tomography (PET) with ^{18} F- fluorodeoxyglucose (FDG) has emerged in such a way that it has become an effective imaging technology for the evaluation of different carcinomas, particularly for cancer staging and follow up after therapy. PET scan is able to provide metabolic information. In this case, we present an attractive unified PET/CT scan image in a patient with lung carcinoma having unusual diaphragm and splenic metastases. So, PET/CT imaging could strongly identified rare and unusual metastatic sites of cancer and added more appropriate staging in patient with carcinoma of lung.

1. Introduction

Globally, carcinoma of lung is the predominant cause of cancer death among both men and women [1]. While there has been advancements in imaging modalities in the last twenty years, the maximum carcinoma of lung are still only identified due to evolvement of remote metastases. The spread of blood-borne metastases to numerous organs is usually identified and documented. The most common metastatic sites from carcinoma of lung are liver, adrenal glands, bone and brain [1]. Metastases of malignant tumors to spleen and diaphragm are rare [2,3]. Nowadays, Positron emission tomography (PET) with ^{18} F- fluorodeoxyglucose (FDG) has emerged in such a way that it has become an effective imaging technology for the evaluation of different carcinomas, particularly for cancer staging and follow up after therapy. PET scan is able to provide metabolic information [2]. In this case report, we introduce an attractive unified PET/CT scan image in a patient with lung carcinoma having unusual diaphragm and splenic metastases.

2. Case Report

This 50 years-old patient was referred to Institute of Nuclear medical Physics, Savar for initial staging of adenocarcinoma in left lung (upper Zone). PET/CT scan image was taken 45 min after 5 mCi FDG injection (Figure 1). Maximum Intensity Projection (MIP) image of PET/CT (a), Coronal view of PET/CT fusion image (b) and cross

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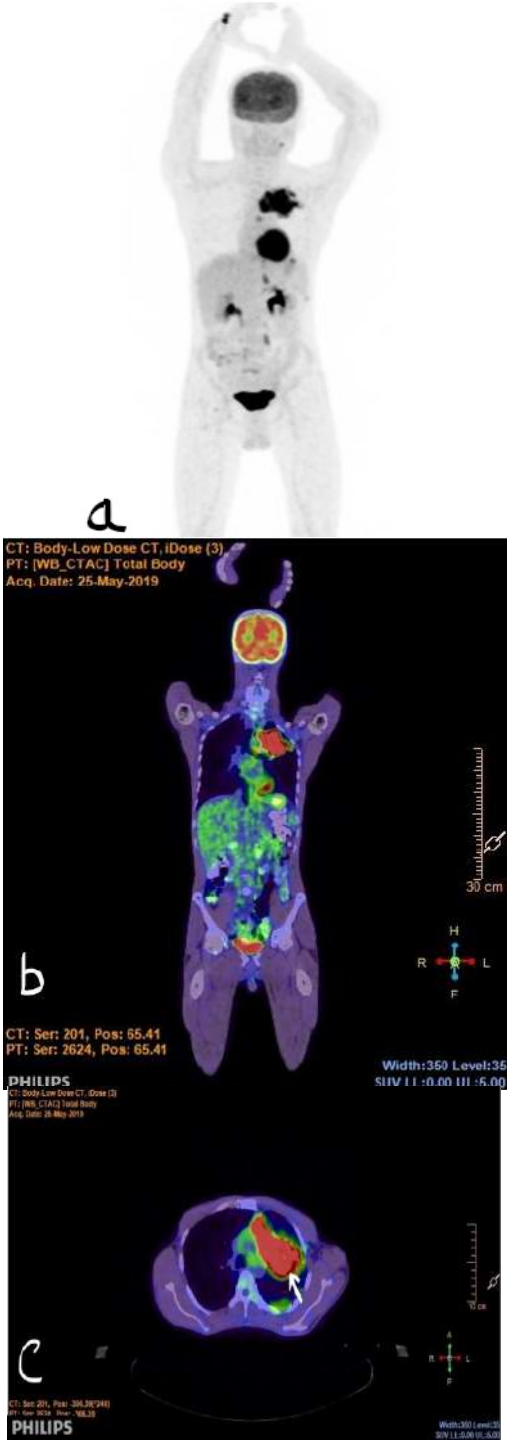
 DOI: https://doi.org/10.30564/jor.v1i3.1586

sectional image at thorasic level (c) demonstrated a 87 × 44 mm left upper lobe mass with intense hypermetabolism (SUVmax 12.8). PET/CT image (d) and corresponding CT image (e) showed thickening (8.5 mm) of left crus of the diaphragm with SUVmax 13.5. Additionally, a 18 mm subcapsular hypodense lesion on spleen with moderate hypermetabolism were detected (SUVmax 6.7) (e, f). PET/CT imaging can identify definite metastatic lesions into the diaphragm and spleen (d, f).



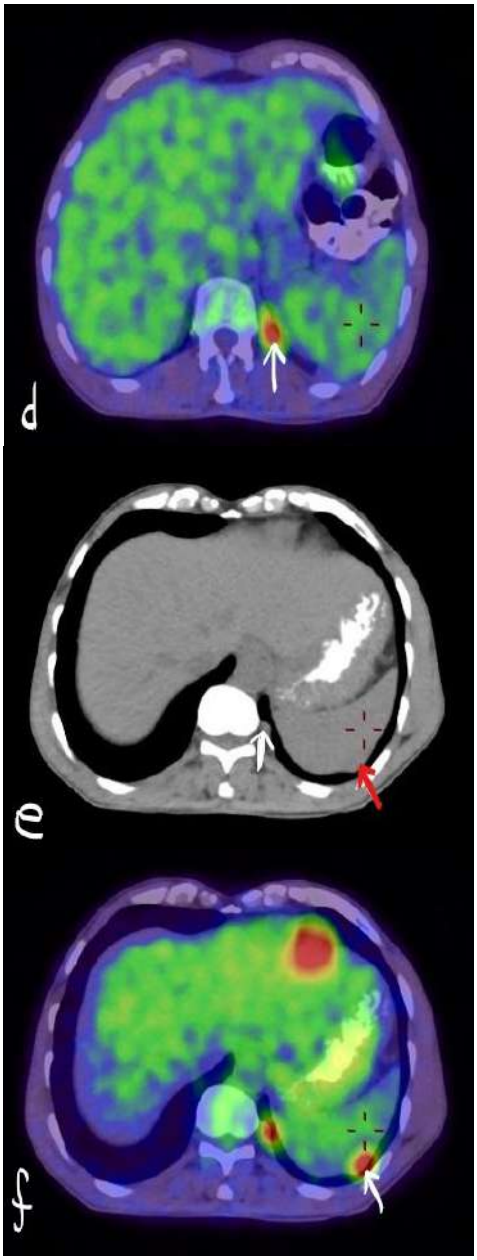


Figure 1. Positron Emission Tomography (PET-CT) scan image of this Case patient

Note: MIP view of PET-CT scan (a) Coronal view of PET-CT hybrid image (b) and cross sectional view at thorasic level (c) demonstrated a 87 × 44 mm mass with intense hypermetabolism (SUVmax 12.8) in left lung upper lobe. PET-CT image (d, White arrow) and corresponding CT image (e, White arrow) showed thickening (8.5 mm) of left crus of the diaphragm with SUVmax 13.5. Additionally, a 18 mm subcapsular hypodense lesion on spleen with moderate hypermetabolism were detected (SUVmax 6.7) in PET-CT image (f, white arrow) and corresponding CT image (e, red arrow).

3. Discussion

Neither diaphragm nor splenic invasion was verified histologically on a stage IV lung carcinoma patient having distant metastases. This is because an invasive biopsy

DOI: https://doi.org/10.30564/jor.v1i3.1586

would be required. The pattern of FDG uptake in benign pathologic conditions, as well as physiological variants and metastatic disease is clearly different without any histopathological diagnosis. Recognising hypermetabolic foci at diaphragm in patients having pulmonary pathology is quite significant. Bilateral high FDG uptake at the crura of diaphragm is usually due to hyperventilation but in this case FDG uptake occurs unilaterally [4]. Asymmetrical hypermetabolic focus which is not on the expected physiological area in the upper abdomen is difficult to diagnosis on PET/CT image [5]. Furthermore, PET/CT fusion imaging has ability to detect the benign nature of focal normal fatty tissue uptake.

Carcinoma of lung can be classified histopathologically into small cell lung carcinoma (SCLC-15% to 20%) and non-small cell lung carcinoma (NSCLC-80%). Adenocarcinoma (50% of cases), squamous cell carcinoma (40% of cases), large-cell carcinoma (almost 10% of cases), and rarely adenosquamous carcinoma are histological subtypes of NSCLC. PET/CT is an accepted modern imaging technology for both mediastinal and distant staging of NSCLC. Presence of widespread metastatic involvement identifies and categorizes the patient as having stage IV disease. The usual metastatic sites from NSCLC are liver, adrenal glands, bone and brain [6]. Rarely, it has been reported that NSCLC metastases are present in soft tissue, kidney, peritoneum, spleen, pancreas, intestine, bone marrow, eye, ovary, thyroid, heart, breast, nasal cavity, and tonsils [7]. Unusual diaphragm and splenic metastases from lung carcinoma were depicted in this case report. Invasion of malignant tumors to spleen and to diaphragm are rarely observed [2,3]. Currently the documented incidence of splenic metastasis from primary lung cancer is 1.2–5.6%. Metastasis to spleen is predominantly noted in the extreme stage as part of a widespread metastatic disease. Generally at this stage 3–6 other organs are also involved as well [3].

4. Conclusion

Although the patient in this case was already at stage IV, PET/CT could strongly identified rare and unusual metastatic sites of cancer and added more appropriate staging. PET/CT fusion image was able to find out lesions to a greater extent than where either PET or CT was used alone. Whatmore, PET-CT imaging provides excellent anatomic information of pathological FDG uptake.

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DOI: 10.1186/s12885-016-2169-5

 DOI: https://doi.org/10.30564/jor.v1i3.1586

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REVIEW

Case Report: Granular Cell Tumor In Breast

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ARTICLE INFO

Article history
Received: 7 February 2020
Accepted: 1 April 2020
Published Online: 20 April 2020

Keywords:
Breast cancer
Benign neoplasm
Unusual
Differential diagnosis

ABSTRACT

Granular cell tumor (GCT) of the breast is an unusual neoplasm, tipically benign, it represents between 5-6% of all GCT cases. These tumors are more common in middle-aged premenopausal women with a greater predilection African American race [1]. Nevertheless, there are also cases described in men [2-4]. Almost all of them are favorable, the malignant cases are uncommon (only 1-3%). Sometimes it could be clinically and radiologically confused with a malignant breast tumor; so it's very important to make a differential diagnosis. The choice therapy is an extensive local extirpation with free margins [5], without the need for adjuvant chemotherapy or radiotherapy. Our case is a 61-year-old woman with a GCT, and three years ago a history of breast carcinoma in the same breast.

1. Introduction

Granular cell tumor (GCT) of the breast is an atypical neoplasm, usually benign, it represents between 5-6% of all GCT cases.

In the firs instance it was described in 1854 by Weber; and then, in 1926, it was described in detail by Abrikossoff, who supposed a myogenic origin and determinated it as "granular cell myoblastoma [6]". Later researchers described its origin in schwann cells, due to the positivity of the S-100 protein and the similarity of tumor cells to schwann cells [7].

Although GCT is a well established identity, it very often presents a clinical, radiological and even anatomopathological aspects very similar to breast carcinoma or fibroadenoma, being a diagnostic challenge for gynecologists, oncologists, radiologists and pathologists.

Our case is a 61-year-old woman with a GCT, and three years ago a history of breast carcinoma in the same breast.

2. Case Report

61-year-old woman with menarche at age 12, menopause at age 47. Denies use of oral contraceptives pill or hormone replacement therapy. Two full-term pregnancies.

As an important history, four years ago she was diagnosed with breast cancer (infiltrating ductal carcinoma of the right breast, Nottingham's grade II, pT1c pN0 M0, luminal immunophenotype B) Treated by breast-conserving surgery (quadrantectomy). Oncotype 11%. Followed by whole-breast irradiation (50 Gy) and a boost to the tumour bed (16 Gy) and then a hormone therapy.

She performs medical check-ups until a control mammogram describes a new 9 mm nodule/lymph node, BI-RADS 4a in the right breast.

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DOI: https://doi.org/10.30564/jor.v1i3.1695

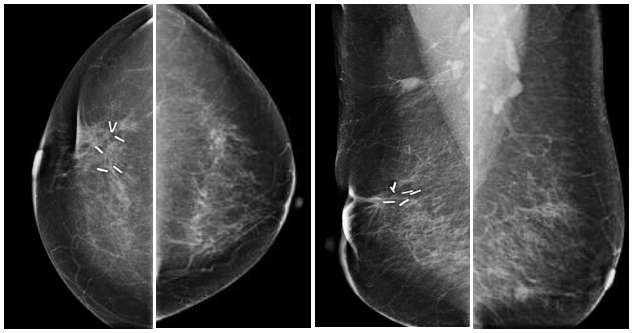

Figure 1. Mammogram (CC and MLO view). MLO view of the right breast showed well defined mass-forming in the upper quadrant (arrow)

An ultrasound-guided breast biopsy is performed and in the pathological anatomy, proliferation of solid lobed pattern with fibrovascular tracts is described, consisting of rounded cells of granular broad cytoplasm PAS+ and round or oval nucleus with scarce anisonucleosis, compatible with GCT (It is likewise recognised as Abrikossoff's tumor).

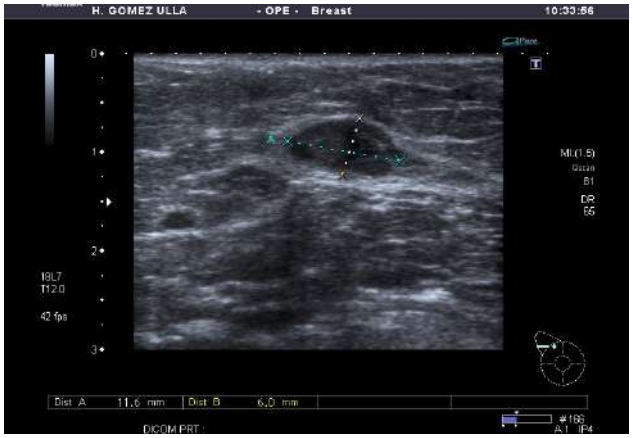

Figure 2. Ultrasound of the right breast showed a regular hypoechoic lesion

Later, a lumpectomy was performed, and the diagnosis was confirmed by the histological study. The postoperative period was without incidents and the patient remains asymptomatic at present. She continues her medical revisions [8] due to her oncological history of breast cancer.

3. Discussion

GCT is an unusual tumor that can emerge anywhere in the body, but the most common origin is the tongue, followed by the soft tissues [9-10]. Appears on the breast the breast only in In 5–6 % of cases and it represents around 1/1000 of all breast tumors.

These tumors are more common in middle-aged premenopausal women with a greater predilection African American race[] [11]. Nevertheless, there are also cases described in men [12-14].

Almost all of the are favorable, the malignant cases are uncommon (only 1-3%) [15-16].

Sometimes it could be clinically and radiologically confused with a malignant breast tumor, so it's very important to make a differential diagnosis [17] because, although they have similarities in diagnosis, the treatment and the prognosis are very different [18,19]. In young women the clinical and radiological presentation may simulate the characteristics of a fibroadenoma [20-21].

Appears as a painless single node, with a size less than 3 cm, but also can be presents as a multifocal. It is usually appear in the top internal quadrant, in contrast to breast carcinoma, which is more usually located in the top external quadrant, but it can appear in any location.

On mammography, it presents as an ill-defined or spiculated lesions, comparable to breast carcinoma.

It is not possible to differentiate a GCT from a carcinoma without a biopsy, so the ultrasound-guided biopsy of the lesion is the diagnosis of choice [22].

It is essential to know the immunochemistry to confirm the diagnosis, it is fimly immunoreactive for the S-100 protein, they also exhibit positivity for the specific neuronal enolase (NSE), CD68 and vimentin. Tumor cells are negative for epithelial markers like cytokeratin and epithelial membrane antigen and carcinoembryonic antigen [23].

The choice therapy is an extensive local extirpation with free margins [24], without the need for adjuvant chemotherapy or radiotherapy.

4. Conclusion

Although GCT is an unusual neoplasm it is very important to make the differential diagnosis due to they can simulate malignant breast tumors.

A diagnosis error can lead to unnecessary treatment, like a mastectomy, which has great physical and emotional impact.

The choice treatment is always a surgical excision with extensive margins, due to cases of malignancy have been described.

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DOI: https://doi.org/10.30564/jor.v1i3.1695

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ARTICLE

Leiomyoma Of Urinary Bladder a Rare Entity: Series Of 3 Cases And Review Of Literature

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ARTICLE INFO

Article history
Received: 13 January 2020
Accepted: 19 February 2020
Published Online: 31 March 2020

Keywords:
Leiomyoma
Benign tumor
Bladder outlet obstruction
Benign bladder tumor
LUTS

ABSTRACT

Introduction: Leiomyoma of urinary bladder is a rare entity and comprises 0.43% of all bladder tumors. Here we present our series of 3 cases and the related review of literature. **Methods:** 3 cases of bladder leiomyoma presented over a period of 16 months in Osmania Medical College and Hospital. Detailed history was taken, physical examination, routine blood, urine and radiological investigations were done. Patients were treated by Trensurethral Resection (TUR) of the mass and histopathological analysis with Immunohistochemistry was done for all cases. **Results:** All 3 cases were females with mean age of 31.6 years. All cases were endovesical type, mass near bladder neck and presented with obstructive symptoms. Two cases presented with acute retention of urine. Radiological investigations in all patients suggested a possibility of leiomyoma and all cases had reduced urinary flow rates. Histopathology confirmed the diagnosis in all cases. No recurrence was found at one year of follow up. **Conclusion:** Leiomyoma of urinary bladder is a rare disorder which frequently occurs in middle aged females. Symptoms are related to its size and location, diagnosis is confirmed by histopathological analysis. Treatment is by surgery (mainly TUR). Prognosis of the disease is excellent.

1. Introduction

Benign mesenchymal tumours of urinary bladder are rare and represent about 1-5% of all neoplasms [1]. Leiomyoma is the most common benign neoplasm among them accounting for 35% of mesenchymal bladder tumours and 0.43% of all bladder tumours [2]. They are frequently encountered in middle aged females [3]. Endovesical variety with obstructive symptoms is the most common presentation [3, 4]. Around 300 cases have been reported till date and among them very few have reported more than 2 cases [2, 3]. We present our series of three cases and the related review of literature.

2. Case Report

We report three cases which presented to urology department of Osmania Medical College and Hospital during October 2017 to January 2019. Written and informed consent was taken from all three cases for treatment, use of the data and pictures for the purpose of publication.

Case 1:

27 year female presented with intermittent stream of urine, straining during micturition and dysuria since 3 months

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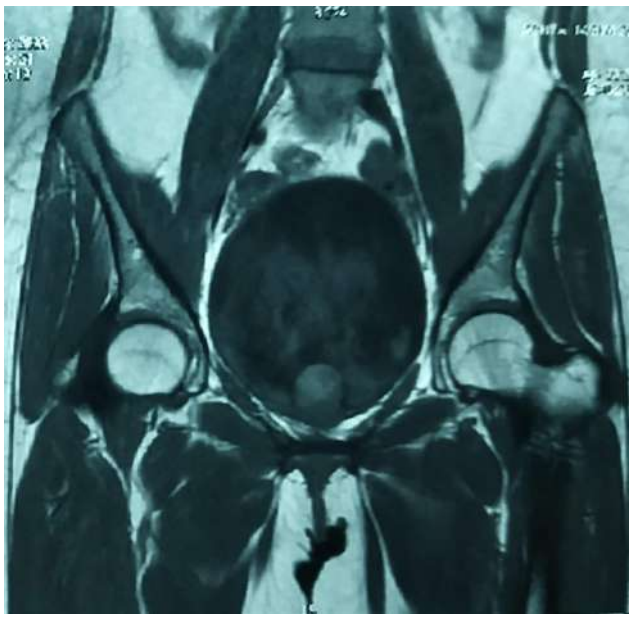
 DOI: https://doi.org/10.30564/jor.v1i3.1642

which increased with passage of time. There was no other urinary or general complaint. Patient had no other co-morbidities and the physical examination was unremarkable. All laboratory values were in normal limit and routine urine examination showed pus cells (4-5) and plenty of Red Blood Cells (RBC) and the urine culture was sterile.

Uroflowmetry recorded max urinary flow rate (Q_{max}) of 5.6 ml/sec and average urinary flow rate (Q_{avg}) of 2.5 ml/sec. Ultrasonography (USG) of abdomen showed 2×2×3 cm homogeneous mass at the bladder neck with mild increase in vascularity. Magnetic Resonance Imaging (MRI) abdomen and pelvis reported 29×25×24 mm^3 polypoidal lesion arising from the urethra and base of the bladder, protruding into the bladder lumen ,iso-to-hyper intense in T1 and hypointense in T2 sequence (figure 1). Cystoscopy showed a pedunculated mass hanging down from the bladder neck at 12 o'clock position with prominent vessels on its surface (figure 2). Mild bladder trabeculations were present.



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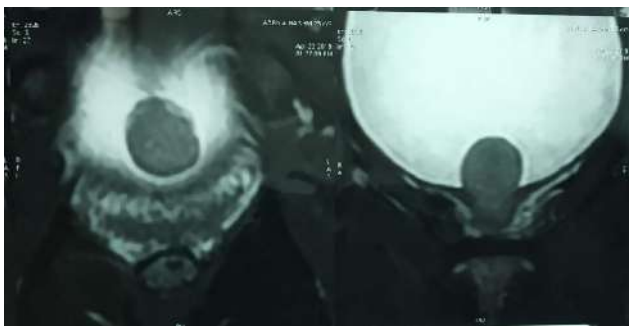


(B)

Figure 1. (A) T1 image of bladder showing mass at the bladder neck, (B) corresponding T2 images

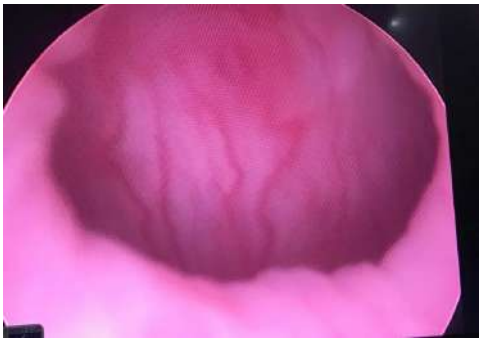


Figure 2. cystoscopic image of the pedunculated mass hanging down from 12 o'clock near bladder neck with prominent surface vessels

Case 2:

30 year female presented with obstructive lower urinary tract symptoms for 6 months and acute retention of urine since 2 days. There was no history of hematuria, fever, increased frequency of urine or pain abdomen. Patient had no other co-morbidities and the physical examination was unremarkable. All laboratory values were in normal limit and routine urine examination showed pus cells (4-5), no RBCs and the urine culture was sterile. She was catheterised on presentation and catheter was removed after 2 days after which she was able to void but with difficulty.

Uroflowmetry recorded Q_{max} of 12 ml/sec and Q_{avg} of 5 ml/ sec. USG abdomen showed 2.2×1.5×1.6 cm^3 homogeneous mass at the bladder neck with mild increase in vascularity (figure 3). Contrast Enhanced Computed Tomography (CECT) abdomen and pelvis reported 27×16×17 mm^3 mass arising from the base of the bladder near the bladder neck, protruding into the bladder lumen. The bladder wall was thickened and she had right mild hydronephrosis (figure 4). Cystoscopy showed a broad base mass near the bladder neck extending from 10 o'clock to 2 o'clock position and abutting the posterior wall of the bladder neck with prominent vessels on its surface (figure 5). Mild bladder trabeculations were present.

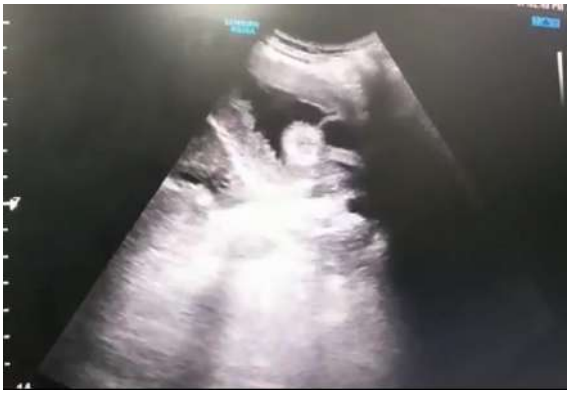
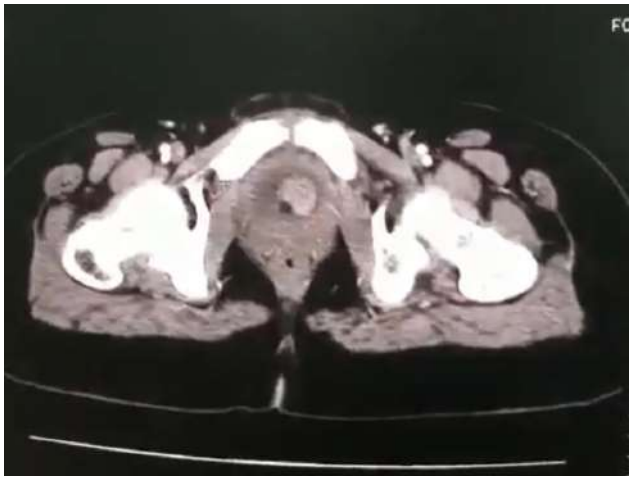
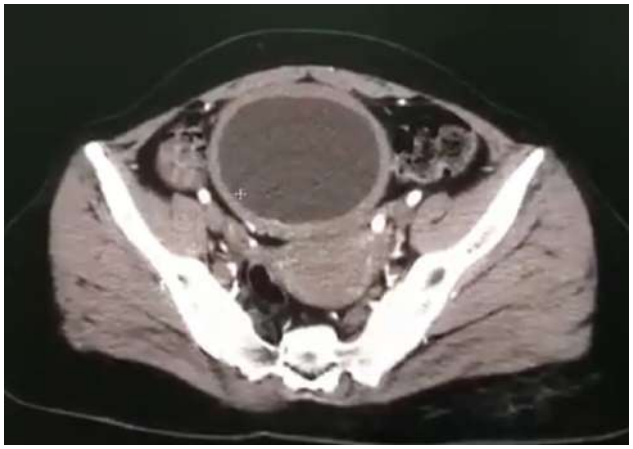


Figure 3. USG showing bladder and homogeneous mass near the bladder neck adjacent to foleys catheter

DOI: https://doi.org/10.30564/jor.v1i3.1642



(A)



(B)

Figure 4. CECT showing mass at the bladder neck (A) and thickened bladder wall (B)

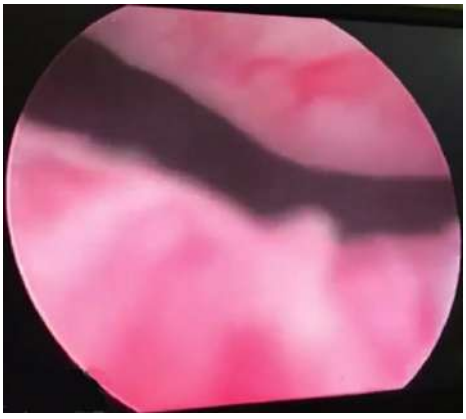


Figure 5. cystoscopic picture showing mass which is broad base arising from the anterior wall of bladder near the bladder neck

Case 3:

35 year female presented with difficulty in voiding since 2 months and acute urinary retention since 1 day. She had no other urinary or general symptoms, no co-morbidities and an unremarkable physical examination. She was catheterised on presentation and later given a catheter free trial but was not able to void. All other laboratory parameters were normal. Urine routine showed few pus cells, plenty of RBCs and urine culture was positive for Escherichia coli $>10^5$ colony forming units.

USG showed 3.5×2.5×3 cm homogeneous mass at the bladder neck with mild increase in vascularity (figure 6). MRI abdomen and pelvis reported 37×26×31 mm^3 mass arising from the base of the bladder near the bladder neck, protruding into the bladder lumen (figure 7). Cystoscopy showed a broad base mass near the bladder neck extending from 9 o'clock to 3 o'clock position, abutting the posterior wall of the bladder neck and completely closing it, with prominent vessels on its surface (figure 8). Moderate bladder trabeculations were present

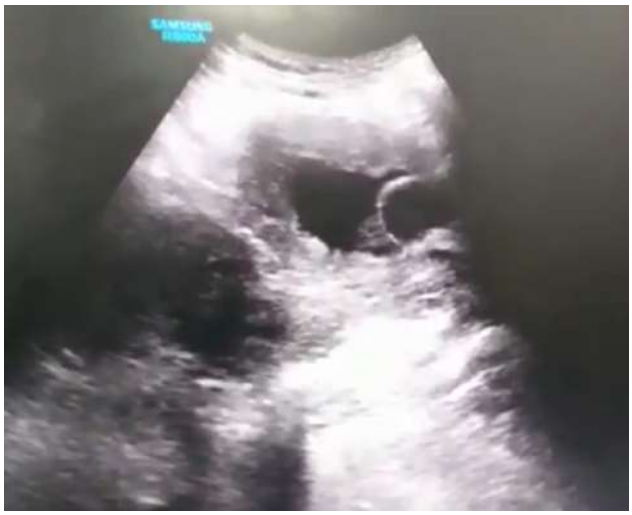


Figure 6. USG showing large homogeneous mass at the bladder neck

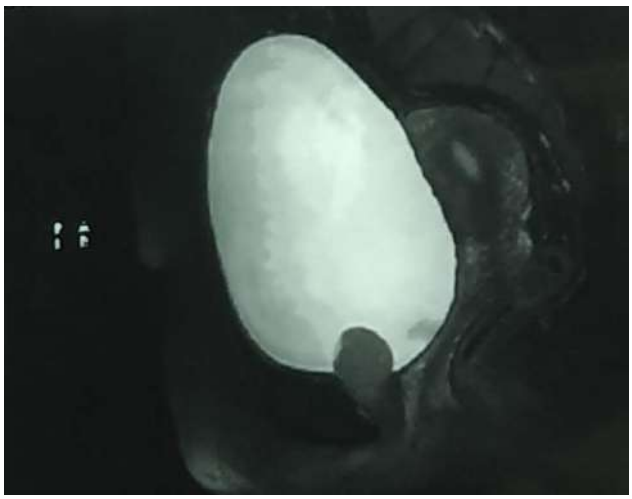


Figure 7. T2 images of MRI showing mass near the bladder neck

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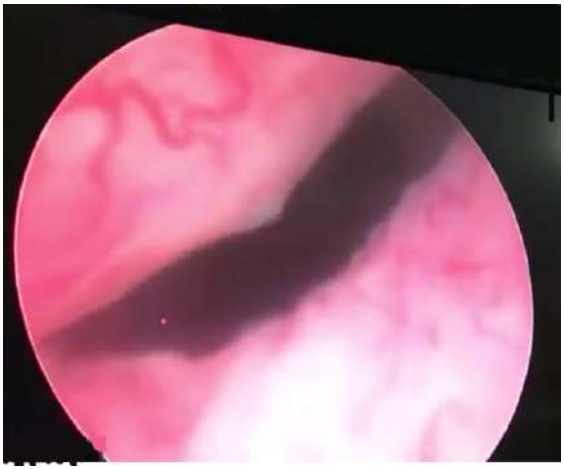

Figure 8. Cystoscopic image of the mass, broad base and almost abutting the posterior wall of bladder neck

None of the three cases had incidental finding or past history of uterine leiomyoma. All patients underwent Trans-Urethral Resection (TUR) with 26 French Resectoscope using bipolar loop working element with normal saline irrigation. Complete clearance of mass was done in all cases. Tumour in the third case bled profusely during resection but was controlled. None of the cases required any blood transfusion. Foleys catheter was removed on day 3 in all the cases and they were able to void. Follow up was done on day 14 with USG abdomen and Uroflowmetry, all cases showed marked improvement in flow rates reaching near normal values.

Histopathology (HPE) was done in all three cases. Grossly they were grey white to grey brown and soft. Microscopic examination showed interlacing fascicles & bundles of uniform spindle cells with elongated nuclei, minimal or absent cytological atypia (figure 9). The epithelium over the tumour was maintained and consisted of mostly transitional cell and in few places stratified squamous epithelium. This might indicate possibility of urethral origin of these tumours which have grown into the bladder lumen. Immunohistochemistry was done for desmin (positive) (figure 10A), Smooth Muscle antigen (SMA) (strong positive) (figure 10B), Ki67 (low) (figure 10C), Anaplastic Lymphoma Kinase (ALK) (negative), P63 (negative), CD34 (negative), Vimentin (negative). These confirmed the tumour as benign leiomyoma.

All cases were followed up for a minimum duration of 1 year. 3 monthly USG abdomen, Uroflowmetry and Cystoscopy was done. There were no signs of recurrence.

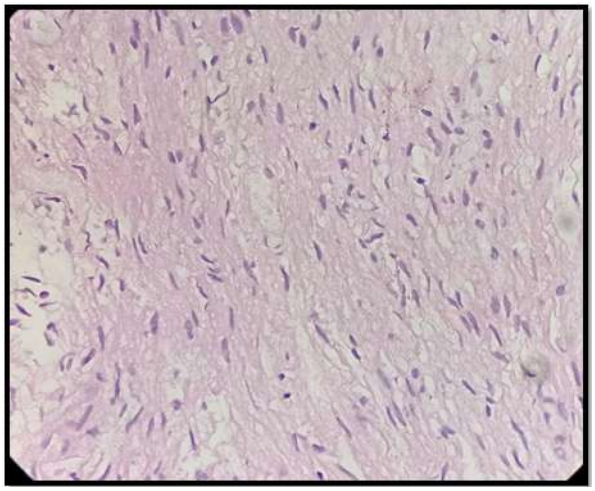

Figure 9. Microscopic examination showed interlacing fascicles & bundles of uniform spindle cells with elongated nuclei, minimal or absent cytological atypia

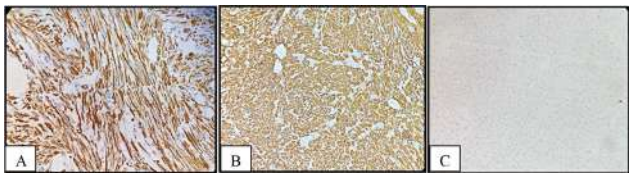

Figure 10. Immunohistochemistry of the tumour, A) Desmin- positive, B) SMA-strong positive, C) Ki67- low

3. Discussion

Leiomyomas can occur at any site in the genitourinary system and most common site of occurrence is Renal capsule [1,2]. Around 95% of the bladder tumours are of epithelial origin and only around 5% constitute the mesenchymal tumours. Leiomyoma of bladder is the most common mesenchymal tumour comprising one third of them and accounts for only 0.43% of all bladder tumours [3,4].

The occurrence of leiomyoma was initially thought to be equal among males and females [3,4]. But Goluboff et al [3] in their review of 37 patients, reported female preponderance (76%) and occurrence of most of the cases in the third to sixth decades (59%) with mean age of 44 years. In our series all patients were females with mean age of 31.6 years.

Bladder leiomyoma can occur at different locations with endovesical (63-86%) being the most common one followed by extravesical (11-30%) and intramural (3-7%) locations [3, 5]. Symptomatology ranges from being totally Asymptomatic (19%) to a variety of other symptoms like, obstructive (49%), irritative (38%), hematuria (11%) and flank pain (13%), which depend mainly on their location and the size they attain [3,6]. The endovesical type most commonly produces obstructive or irritative symptoms

DOI: https://doi.org/10.30564/jor.v1i3.1642

depending on the size [6]. Very few case reports of leiomyoma presenting with acute retention of urine have been reported [6,7]. Hydronephrosis can also result from the increased intravesical pressure created by the ball valve effect of the endovesical leiomyomas [7]. Matsusmiha et al [6] reported the urodynamic changes which occur due to a leiomyoma causing bladder outlet obstruction. In our series all three patients had obstructive symptoms, one had irritative symptoms, microscopic hematuria was present in one case, two cases presented with acute retention of urine and mild degree of hydronephrosis was present in one case.

Teran and Gambrell [8] proposed 4 theories for the pathophysiology of these lesions: (1) hormonal influences, (2) embryonic rests of the tissues residing in the bladder, (3) perivascular inflammation and metaplastic transformation, (4) infection and inflammation of the bladder musculature. But the exact pathophysiology is still unknown.

The female predominance of these leiomyomas is also a matter of debate and theories of association with female hormones have been advocated [8, 9, 10]. These tumours are most commonly encountered during fourth to fifth decades when the female hormones are released abundantly. The increased use of the ultrasonography in females could account for the pickup of asymptomatic cases [7]. The occurrence is rare before puberty and decrease in size after menopause have been reported. So the influence of female hormones in the development of leiomyoma can be considered a possibility [11]. In our series all cases were females of child bearing age.

Ultrasonography is the most common and initial tool for the diagnosis of leiomyomas of bladder. They appear as a homogeneous mass with smooth outline which is usually solid but few cystic appearing lesions have also been reported [12,13]. MRI is a very useful tool in the current era for the accurate depiction of the anatomic location, morphology and the extent of leiomyomas. MRI will show an intermediate signal intensity on both T1 weighted images and intermediate to low signal intensity on T2 weighted images with smooth surface. Few degenerate leiomyomas may have heterogeneous signal intensity. After injection of gadolinium contrast, a variable pattern of enhancement is observed, some enhance heterogeneously and some do not [6, 14]. In our series MRI was done in two cases which clearly delineated the mass and the relationship to bladder and surrounding structures. The signal intensity and enhancement pattern was consistent with the classical descriptions. Imaging modalities cannot confirm the exact diagnosis and cannot differentiate a benign leiomyoma from a malignant leiomyosarcoma, so histopathological studies are needed to confirm the diagnosis [15].

Treatment methods depend on the size, extent and location the tumour and involvement of other structures. Small endovesical tumours are best managed by TUR but the larger endovesical, intramural and the extravesical will require segmental resection [7]. Other approaches of resection like transvaginal, laparoscopic, cystoscopic assisted laparoscopic and robot assisted laparoscopic techniques have also been reported [2,16,17]. Few surgeons advocate reserving surgical treatment only for symptomatic tumours based on the good diagnostic accuracy of imaging and the benign nature of the tumour [5,7]. But the bladder leiomyomas often mimic malignant lesions and can be definitely diagnosed by histopathological analysis only; the ease of TUR resection for diagnosis and treatment favours surgical removal [2].

Histopathological analysis is the definite diagnosis, grossly the tumour is well circumscribed, white to grey and fleshy. There have been descriptions of few milimeters to 30 cm and few grams to 9 kg in literature [7]. Microscopically they are composed of interlacing fascicles and bundles of uniform spindle cells containing moderate to abundant eosinophilic cytoplasm. The nuclei are elongated, minimal to absent cytological atypia and mitotic figures are absent [15]. Immunohistochemistry is being used routinely to distinguish from the other differential diagnosis like leiomyosarcoma, inflammatory mayofibroblastic tumour, solitary fibrous tumour, perivascular epithelial tumours. Leiomyomas are desmin positive, SMA positive, Ki67 is low, ALK negative, P63 negative, CD34 negative and Vimentin negative [18].

Prolonged follow up of these patients is not mandatory because of the excellent prognosis and no reports of malignant transformation till date. Few cases of recurrences have been reported, probably because of incomplete excision [2,9]. The recurrence rates may increase after widespread use of TUR which has more possibility of incomplete resection. We followed all the patients by three monthly USG, Uroflowmetry and Cystoscopy for the first year to detect any recurrence. We propose some duration of follow up after TUR, preferably a year. Further studies are needed to find the causes and patterns of recurrences and define the treatment and follow up protocol.

4. Conclusion

Leiomyoma of urinary bladder is a rare disorder which frequently occurs in middle aged females. Symptoms are related to its size and location, the endovesical location and obstructive symptoms are the most common finding. Imaging modalities can diagnose the condition but histopathological analysis is confirmatory. A number of sur-

 DOI: https://doi.org/10.30564/jor.v1i3.1642

gical modalities of treatment have been described, TUR being the most common modality now. Prognosis of the disease is excellent.

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DOI: https://doi.org/10.30564/jor.v1i3.1642

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ARTICLE

Primary Malignant Melanoma of Female Urethra: A Case Report and Review of Literature

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ARTICLE INFO

Article history
Received: 22 April 2020
Accepted: 18 June 2020
Published Online: 30 June 2020

Keywords:
Female
urethra
melanoma

ABSTRACT

We report a very rare case report of female diagnosed with primary malignant melanoma. A 65 years old diabetic elderly postmenopausal female presented with a history of intermittent blood spots on undergarments for few days. Genital examination revealed a single, tan colored, soft chestnut size and polypoidal non ulcerated mass lesion protruding through the urethral meatus. Mass biopsy revealed poorly differentiated epithelial malignancy and immuno-histological analysis revealed positive with HMB 45 and protein S-100 suggestive of melanoma. Metastatic work up for the malignancy was negative. Complete urethrectomy with Mitrofanoff procedure with inguinal lymph node dissection was performed. Histopathological examination was suggestive of malignant melanoma of urethra. Here we discuss the clinicopathological features and management option possible in this scenario.

1. Introduction

Primary malignant melanoma of female urethra is very uncommon tumour and constitutes 0.1 - 0.2% of all melanoma [1-5]. Urethral melanoma can be sub classified based on its origin type into mucosal melanomas or cutaneous melanomas. Urethral melanomas are usually under reported clinically and it inherits grave prognosis with poor five year survival rates [6]. Here we present a case of an elderly female diagnosed with primary malignant melanoma of urethra in and its surgical management at our center along with review the literature.

2. Case Report

A 65 years old diabetic elderly female came with a history of intermittent blood spots on undergarments for few days. She had no complaints of difficulty in micturition, hematuria, flank pain, lithuria. She has attained post menopause and had no history of postmenopausal syndrome. At primary center she was diagnosed with urethral mass and biopsy of mass suggestive of poorly differentiated epithelial malignancy. Immnuohistological analysis revealed positive with HMB 45 and protein S-100 which were suggestive of melanoma.

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 DOI: https://doi.org/10.30564/jor.v1i3.1975

Genital examination revealed a single, tan colored, soft chestnut size and polypoidal shape non ulcerated mass lesion measuring 2 x 2 x 1 cm protruding through the urethral meatus (Figure 1). Her per vaginal and speculum examination was normal. Abdominal examination revealed no organ enlargement of no regional lymphadenopathy.

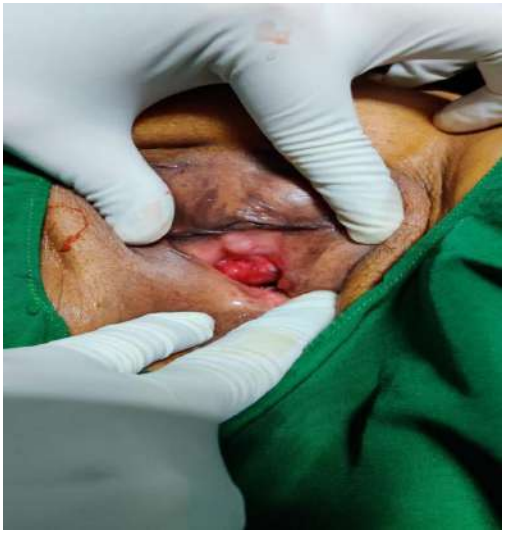

Figure 1. Urethral malignant melanoma presenting as a mass protruding from external urethral meatus on genital examination

Abdomen-pelvis contrast enhanced computed tomography (CECT) along with MRI T2W saggital sequence revealed that single enhancing lesion of 2 x 1.3 cm in urethra with not involvement of periurethral tissue, bladder, regional or distant lymphadenopathy.

Initially urethral meatus was difficult to visualize but with suprapubic pressure gush of urine flow was seen and the glide wire was passed in urethra followed by its serial dilatation up to 16 Fr. Cystourethroscopy examination revealed polypoidal reddish brown growth involving the distal urethra and urethral meatus. Bladder was unremarkable. Vaginoscopy showed compression of anterior vaginal wall with mass however no any evidence of invasion seen on inspection. Complete urethrectomy with formation of continent catheterizable stoma using the appendix (Mitrofanoff procedure) with inguinal lymph node dissection was performed. Mass was removed along with the normal appearing surrounding tissue. Frozen section of proximal urethral margin and adjacent vaginal mucosa were free of tumour.

Gross examination of specimen showed a polypoidal solid mass of 2 x 1.8 x 1.5 cm with brownish cut surface without any ulceration on surface. Histopathological analysis showed loosely cohesive nests of epitheloid cells with dusty brown melanin pigments. Malignant cells had abundant eosinophilic cytoplasm, large nuclei with prominent nucleoli along with mitotic figures. No lymphovascular invasion was seen (Figure 2). Immuno-histochemical analysis of the malignant cells was positive for protein S-100 (Figure 3) and HMB-45 (Figure 4) which are markers for melanocyte differentiation.

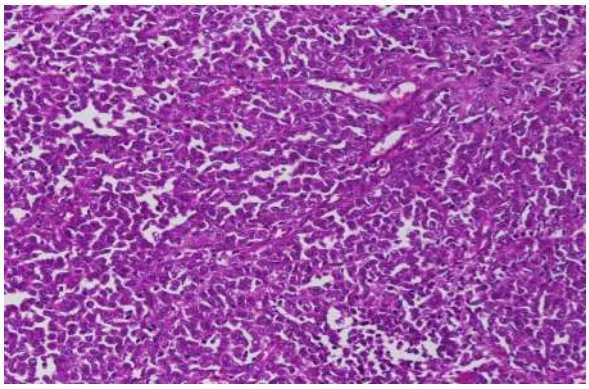

Figure 2. Microscopic findings of specimen. Large epitheloid cells with high N/C ratio.Deposition of melanin pigment could not be seen clearly

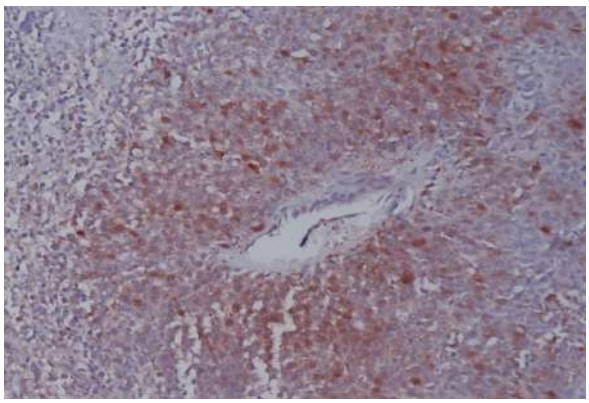

Figure 3. The immunohistochemical staining findings of the surgical specimen. The tumor cells were immunoreactive for S-100 protein

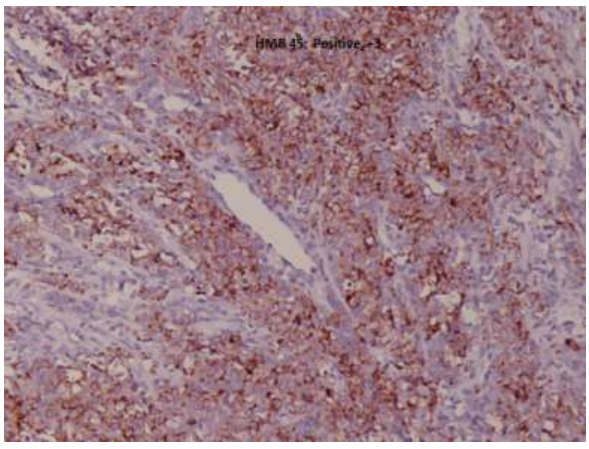

Figure 4. The immunohistochemical staining findings of the surgical specimen. The tumor cells were immunoreactive for HMB - 45

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Currently the patient is asymptomatic and is doing clean intermittent catherterization through mitrofanoff and no recurrence of disease have observed yet.

3. Discussion

Malignant melanoma of urethra was first reported in a female by Reed in 1896 [7]. Median age of presentation is 68 years [8]. Females are more commonly affected as compared to males (3:2) [9]. Urethral melanoma risk factors are not established [10].

Lack of visibility and non-specific symptoms causes delay in detection of urethral melanoma. Symptoms may include bleeding, urethral mass, pain, lower urinary tract symptoms. Clinically, differential diagnosis can be other malignant diseases or even benign lesions, including caruncle, mucosal prolapse, urethral polyps [11,12].

The diagnosis is confirmed after biopsy from the lesion. The metastatic evaluation should be done before surgical treatment for this highly invasive neoplasm. An abdominal-pelvic CECT scan provides necessary information regarding nodal involvement and metastatic foci. c-KIT mutation test is useful as it can dictate the chemotherapeutic agents [10].

Metaplasia of squamous and glandular epithelium into pigment-producing cells is proposed mechanism for melanoma originating from mucosal surface [13].

Like all mucosal melanomas, urethral malignant melanoma has grave prognosis than its cutaneous melanoma counterpart [8]. This is mostly due to significant delay in diagnosis because of its inaccessible location and also due to its vertical growth phase in urethral melanomas, lymph node metastasis [14]. Median survival in two largest series was 16 months [4,5]. Overall survival range was from 2 months to 191 months. Few case series showed five year overall survival in 10% patients [15-19].

Microscopic examination a wide histological spectrum like diffuse, nested, fascicular, and storiform growths of pleomorphic cells exists in case of urethral malignant melanomas [11]. Thus the role of immunohistochemical markers for accurate diagnosis come into existence. In clinical practice most commonly used melanocytic markers are S-100 protein and HMB-45. More than 90% of melanomas react with S-100 monoclonal antibody [20]. HMB-45, specific for melanocytic neoplasms, is less sensitive than S-100 protein for identifying melanoma [20]. Positive test with S 100 protein and subsequent testing with HMB-45 in our case confirm definitive diagnosis of malignant melanoma.

No definitive consensus or guidelines exist for management of primary malignant urethral melanoma because of its extreme rare pathology, however it depends on the tumour staging. The definite management of primary neoplasm is surgical excision with tumor-free margins to achieve control of local disease. Less radical surgical approaches are also mentioned in literature which include local excision; partial or total urethrectomy, with or without inguinal lymphadenectomy, and anterior pelvic exenteration, but neither has depicted improved survival advantage over other [10]. DiMarco et al have also advocated radical surgeries. They found high rate of urethral recurrences (69%) in their cases of partial urethrectomy patients was due to inadequate surgical margins. Overall disease-specific survival observed was 39% approximately [5].

Sentinel lymph node (SN) dissection is still controversial in primary urethral melanoma. Though the incidence of false-negative SN dissection has gone down, it is still not mandatory to perform this procedure in all cases [21].

Role of lymphadenectomy as proposed by some authors is not proper established and is debatable in various different case scenario . This procedure, though adds to the morbidity of the patient, has failed to improve disease-specific survival in affected individuals. So, role of radical surgery in case of inguinal lymph node involvement is not clear [5]. In our case we performed inguinal lymph node dissection in our case.

4. Conclusion

Urethral melanoma is an uncommon neoplasm with poor prognosis. No definitive guidelines for management exists till date. All proposed treatment are based upon case series/reports. Similar neoplastic diseases also give input for its management. Surgical excision with adequate margins is gold standard treatment of urethral melanoma. There is no basis to do inguinal lymph node dissection in all cases. Adjuvant chemotherapy and immunotherapy can be prescribed based upon surgeon preferences as no proper guidelines exists in literature.

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DOI: https://doi.org/10.30564/jor.v1i3.1975

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Ⅲ. Abstract

A general introduction to the research topic of the paper should be provided, along with a brief summary of its main results and implications. Kindly ensure the abstract is self-contained and remains readable to a wider audience. The abstract should also be kept to a maximum of 200 words.

Authors should also include 5-8 keywords after the abstract, separated by a semi-colon, avoiding the words already used in the title of the article.

Abstract and keywords should be reflected as font size 14.

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Ⅳ. Section Headings

Section headings, sub-headings, and sub-subheadings should be differentiated by font size.

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Main Manuscript Outline

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The introduction should highlight the significance of the research conducted, in particular, in relation to current state of research in the field. A clear research objective should be conveyed within a single sentence.

Ⅵ. Methodology/Methods

In this section, the methods used to obtain the results in the paper should be clearly elucidated. This allows readers to be able to replicate the study in the future. Authors should ensure that any references made to other research or experiments should be clearly cited.

Ⅶ. Results

In this section, the results of experiments conducted should be detailed. The results should not be discussed at length in

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In this section, the results of the experiments conducted can be discussed in detail. Authors should discuss the direct and indirect implications of their findings, and also discuss if the results obtain reflect the current state of research in the field. Applications for the research should be discussed in this section. Suggestions for future research can also be discussed in this section.

Ⅸ. Conclusion

This section offers closure for the paper. An effective conclusion will need to sum up the principal findings of the papers, and its implications for further research.

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Ⅺ. Glossary of Publication Type

J = Journal/Magazine

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Ⅻ. Others

Conflicts of interest, acknowledgements, and publication ethics should also be declared in the final version of the manuscript. Instructions have been provided as its counterpart under Cover Letter.

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