PRIMARY LEIOMYOSARCOMA OF URINARY BLADDER- A RARE PRESENTATION IN POSTPARTUM PERIOD

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ABSTRACT

BACKGROUND
Primary sarcomas of the urinary bladder are uncommon. Most cases of Leiomyosarcomas of the bladder are described in elderly males, years after cyclophosphamide therapy or as a second malignancy in survivors of Retinoblastoma. This case is presented due to rare presentation in young female and due to the absence of the associated factors described in the literature.

KEYWORDS
Bladder Tumours, Leiomyosarcoma, Extraterine Sarcomas.

CASE REPORT
22 years old female presented with history of haematuria of 2 weeks duration on her second month of postpartum period. On examination, there was no mass palpable per abdomen. Ultrasonogram revealed bilateral mild hydronephrosis. Cystoscopic examination was performed and a polypoid lesion in the bladder obstructing both the ureteral orifices was observed. Biopsy with transurethral resection of the tumour was done. We received a polypoid solid mass measuring 11x7x5 cm (Figure 1A). Cut surface was grey white and fleshy (Figure 1B).

Microscopic sections from bladder showed a submucosal neoplasm (Figure 2A) composed of cells arranged in fascicular pattern (Figure 2B). Individual cells were spindly with moderate amount of cytoplasm and pleomorphic vesicular nuclei. Bizarre cells and giant cells were seen (Figure 2C). Mitotic activity >10/10 HPF was noted. Areas of necrosis was also seen (Figure 2D). Diagnosis of malignant spindle cell tumour of urinary bladder was made and we proceeded with special stains and Immunohistochemistry. Masson’s trichrome stain showed red staining suggesting muscle differentiation in the tumour (Figure 3), Vimentin (Figure 4) and Smooth Muscle Actin (SMA) (Figure 5) were diffusely positive. Cytokeratin (CK) was negative (Figure 6).

A Radical Cystectomy was performed with ileal conduit Urinary Diversion. CT scan of her chest was unremarkable and a bone scan showed no evidence of metastatic disease in her skeleton. Patient is now on 3 monthly follow up and doing well two years past her surgery.

DISCUSSION
Although, Primary Leiomyosarcoma is the most common sarcoma of the urinary bladder, literature review showed less than 500 cases reported worldwide with a male predilection (male:female ratio of 2:1). Most common clinical presentation is as haematuria in elderly males more than 60 years of age. Pelvic radiotherapy, chemotherapeutic agents like cyclophosphamide and smoking are the few risk factors described in the literature. Leiomyosarcoma is the most common second malignancy in Hereditary Retinoblastoma.1,2,3,4,5

Post radiation sarcomas can occur with orthovoltage (low-energy) and megavoltage (high-energy) radiation more than 40-60 Gy. Ionising radiation is thought to act via genetic alterations including mutations of p53 and Retinoblastoma (Rb) genes.6 Cyclophosphamide is an alkylating anticancer agent causing crosslinking of DNA strands. The bladder irritant metabolite of this drug called Acrolein is considered to be the likely cause of bladder leiomyosarcoma.7

Since 1969, many cases of Gestational Leiomyosarcomas have been described in the literature in uterine and extraterine sites with maximum number of cases in uterus followed by vulva, jejunum, retroperitoneal area and other organs rich in smooth muscle tissue.8 Though Leiomyosarcoma is classically described in elderly age group, the increased incidence of this neoplasm in the uterine and extraterine locations in pregnancy and postpartum period has led to many hormone receptor studies in the tumour and serum of the affected patients. There is significant rise of hormones like oestrogen, estradiol, progesterone, relaxin,
testosterone, etc. in the antenatal and the postpartum period and all these hormones have modulating roles in the musculoskeletal system.9 The increased expression of oestrogen, progesterone and all steroid receptors in the uterine and extrauterine sarcomas is well documented.10

Macroscopically, the tumours are large, polypoid and deeply infiltrative and most commonly located in the trigone followed by vertex of bladder and lateral wall of the bladder. Most of these tumours are located in the submucosa and few are in the muscularis propria or extended outside the wall or multifocal. With the presence of atypical spindle cells of this tumour, the differential diagnosis considered are Sarcomatoid variant of Urothelial Carcinoma, Carcinoma with Pseudosarcomatous Stromal Reaction and other Sarcomas. Primary sarcomas of the urinary bladder are much rarer than Sarcomatoid Urothelial Carcinoma. The diagnosis of a Sarcoma should only be made after excluding all these possibilities. Even in the absence of epithelial component, the possibility of Sarcomatoid Carcinoma should be considered in Secondary Bladder tumours. The immunohistochemical profile of a Sarcomatoid Carcinoma notably includes positivity for epithelial markers, Cytokeratins or Epithelial Membrane Antigen at least focally. Features that are helpful in making a decision towards Carcinoma include identification of nested or clustered epithelioid tumour cells of either conventional or other types of carcinoma, lying adjacent to sarcomatoid cells. The presence of In Situ Carcinoma is also another supporting feature for epithelial origin.11,12

Positivity for Actin, Desmin and negativity for Epithelial markers and S-100 help in the definitive diagnosis of Primary Leiomyosarcoma. In our case, the histology of the bladder tumour was identical to that of a high-grade sarcoma. No past or accompanying urinary epithelial malignancy was identified, Immunohistochemistry did not demonstrate epithelial differentiation and all these findings supported a diagnosis of Primary bladder Leiomyosarcoma. Molecular studies show DNA aneuploidy in majority of cases followed by diploidy.13

CONCLUSION
Therapeutic efficacy improves with early detection of bladder tumour, early intervention and effective therapy. Partial Cystectomy as opposed to Radical Cystectomy may be a reliable option for small Bladder Leiomyosarcomas (<4 cm) in a low stage. With positive margins after surgery, adjuvant radiotherapy should be advocated for the patient. Local recurrences should be treated by Systemic Chemotherapy and/or External Pelvic RT. Salvage therapy showed to be ineffective with a median survival of 20 months after surgery.14

This case is presented due to the rare clinical presentation in female sex in unusual age group in the postpartum period.
Figure 2b. Neoplasm Composed of Spindly Cells Arranged in Fascicular Pattern. Individual Cells with Moderate Amount of Cytoplasm and Pleomorphic Vesicular Nuclei 100X

Figure 2c. Bizarre Cells and Giant Cells 400X

Figure 2d. Areas of Necrosis 100X

Figure 3. Masson’s Trichome Showed Red Staining of Smooth Muscle Fibres 100X

Figure 4. Vimentin 400X

Figure 5. Smooth Muscle Actin (SMA) 400X

Figure 6. Cytokeratin (CK) 400X
REFERENCES