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Case Report

Pathology Section

Primary Bladder Neurofibroma: A Rare Case with Clinical Implications and Diagnostic Challenges

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ABSTRACT

Neurofibroma of the genito-urinary tract is rare. Urinary bladder is the commonest organ involved in cases of urinary tract involvement. Patients present early in life and there is male preponderance. We discuss here a case of primary neurofibroma of the urinary bladder in a 52-year-male presenting with haematuria, irritative bladder symptoms and pelvic mass. Cystoscopy showed a swelling in the left lateral wall. A transurethral biopsy revealed neurofibroma of the urinary bladder. Immunohistochemical studies confirmed the diagnosis.

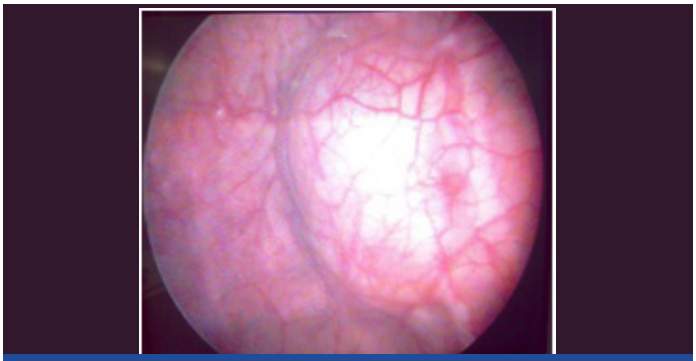
Keywords: Imaging studies, Immunostains, Urinary tract

CASE REPORT

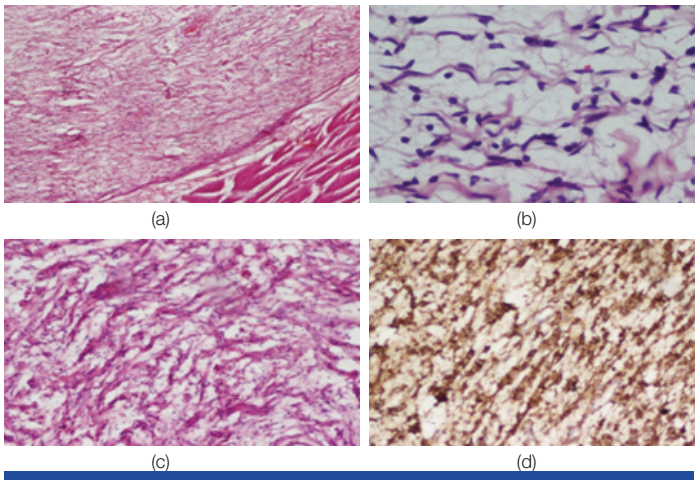
A 52-year-old male presented with symptoms of haematuria, increased urinary frequency and fullness in the lower abdomen. His general physical examination was unremarkable. No neurological deficiency was observed. Per rectal examination did not reveal any abnormality. Imaging studies were performed to further investigate the cause of urinary symptoms. Pelvic MRI revealed a well-defined lesion involving the left lateral wall of the urinary bladder. On cystoscopy, a swelling of around 1 cm was noted in the left lateral wall near the ureteric orifice. The mucosa of the bladder wall over the swelling was smooth and continuous [Table/Fig-1]. Based on the small size of the swelling and smooth bladder mucosa, suspicion of benign bladder tumour was raised on imaging which required histopatholgic examination for confirmation. An image guided transurethral biopsy of the bladder wall lesion was performed and submitted to histopathology. Grossly, we received only fragments of tissue measuring 1 x 0.5 x 0.5 cm and on microscopy revealed a non-encapsulated, moderately cellular, circumscribed lesion composed of thin spindle cells with elongated wavy nuclei, loosely spaced in a collagenous matrix extending up to the muscular layer [Table/Fig-2a-c]. The spindle tumour cells where positive for protein S-100 by immunohistochemistry (Biogenix, Envision method) [Table/Fig-2d]. A final diagnosis of neurofibroma was rendered. The patient was posted for conservative excision, but he failed to follow up. The tumour was picked up due to initial symptomatic manifestation, which was investigated further by imaging modality and confirmed by histopathological examination.

DISCUSSION

Neurofibromas of the genitourinary tract can involve the prostate, urethra, testis, spermatic cord and the ureter, but the urinary bladder is the most common site with around 70 reported cases in literature



[Table/Fig-1]: Cystoscopic findings show a swelling in the left lateral wall near the left ureteric orifice. The mucosa over the swelling was smooth and continuous



[Table/Fig-2a-d]: (a) Circumscribed tumour and normal detrusor muscle (H & E stained; original magnification, X100). (b) Wavy nuclei (H & E stained; original magnification, X100). (c) Scattered bundles of collagen forming the tumour matrix (H & E stained; original magnification, X100). (d) The spindle cells are strongly immuno reactive for S-100 protein (S-100 immunohistochemistry; original magnification, X400)

[1]. These tumours commonly arise from the pelvic, bladder nerves and prostatic nerve plexus. In the bladder, they arise from the nervous ganglia of the bladder wall. It occurs usually at a younger age group (range of 7 to 28 years) with male preponderance [2]. Common presenting clinical features include haematuria, dysuria, recurrent urinary tract infections, irritative symptoms and pelvic mass. In isolated cases of neurofibroma of bladder, a differential of leiomyosarcoma, ganglioneuroma and paraganglioma should always be considered [3].

Imaging modalities are helpful for assessing lesions in the abdomino pelvic and cranial regions, especially in case of neurofibromatosis. Imaging modalities include computed tomography (CT), MRI and cystoscopy. These are useful in early detection of neurofibromas and also in identifying possible malignant transformation which is indicated by asymmetry in size and CT heterogeneity. Bladder involvement can manifest either as a focal lesion as in our case or as a diffuse bladder wall thickening [4,5]. No malignant transformation was detected in radiological investigations in our case.

On histopathology, bladder involvement is usually generalized with diffuse proliferation of uniform neurofibroma cells. The neurofibroma cells are composed of medium sized spindle cells with elongated nuclei with S-100 positive cytoplasmic processes. The collagenized matrix are positive for Alcian blue in almost all cases. Mast cells are seen in small numbers within the stroma as seen in many soft tissue tumours. Immunostains for S-100 protein are positive in the

majority of tumour cells as seen in our case. Epithelial membrane antigen (EMA) and cytokeratin (CAM 5.2 and AE 1/3) are negative in neurofibroma [6]. The histologic appearance of neurofibroma may simulate a differential diagnosis of low grade malignant peripheral nerve sheath tumour, leiomyoma, low grade leiomyosarcoma and rhabdomyosarcoma. The distinctive clinical, histologic and immunohistochemical findings usually permit a definitive diagnosis [2].

Atypical neurofibroma which lacks mitotic figures and has assessable MIB -1 labelling index has to be differentiated from malignant peripheral nerve sheath tumour which is a life threatening condition. Ross was the first to report a case of a bladder neurofibroma with malignant transformation in a neurofibromatosis type 1 patient [7].

Loss of function mutations in the region of high linkage disequilibrium is responsible for the location of NF 1 gene. Activation of mitogen-activated protein kinase (MAPK), phosphatidylinositol 3- kinase (PI3K), protein kinase B (PKB), and mammalian target of rapamycin (m TOR) kinase generally stimulates cellular proliferation and survival.

Molecular genetic testing is necessary in cases with an atypical behaviour. Testing by fluorescence in situ hybridization, multiplex ligation dependent probe amplification is available modes in such atypical cases [8].

The management of patients with neurofibroma of the bladder is not yet resolved. Surgical intervention appears to be the treatment of choice for symptomatic patients. Conservative treatment by transurethral resection or partial cystectomy may be appropriate for patients without Upper urinary tract obstruction.

Neurofibromas have a very good prognosis and malignant transformation is very rare. Most cases reported in the literature have been treated with local excisions. Surveillance is important in cases of asymptomatic diseases [9].

CONCLUSION

Relevance to the present case is the absence of the previous diagnosis of neurofibromatosis, its occurrence in an older age group and lack of other characteristic clinical manifestation; therefore it was difficult to suspect the diagnosis clinically. Histopathologic and immunohistochemical studies offered the final diagnosis.

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