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Malignant peripheral nerve sheath tumour in an unusual location of the urinary bladder: case report and review of literature

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Abstract

Background: Malignant peripheral nerve sheath tumour (MPNST) is a rare malignant soft tissue neoplasm of ectomesenchymal origin. They usually arise from a major or minor peripheral nerve branch or its sheath and also from somatic soft tissues. The most common sites of origin include the extremities and trunk but can sometimes arise an unusual site resulting in the demise of the patient before any intervention.

Case presentation: We report a case of 58-year-old male who presented with complaints of weight loss of a year duration, abdominal swelling of 10 months duration and easy fatigability of 3 weeks duration. Digital rectal examination revealed a huge firm mass 6 cm from the anal verge which was non-tender. Abdomino-pelvic ultrasound scan revealed an irregular heterogeneous mass in the posterior wall of the urinary bladder measuring 15.1cmx 14.0 cm with bilateral dilatation of the renal pelvi-calyceal system and ureters. His clinical condition continued to deteriorate while on hospital admission, and he died on the12th day of admission. Post-mortem examination showed a rough ovoid tumour mass firmly adherent to the posterior wall of the bladder with compression of both ureters. Histological and immunohistochemical analysis of the tumour revealed the diagnosis of a MPNST. The final anatomical diagnosis and cause of death was that of a malignant peripheral nerve sheath tumour of the urinary bladder with obstructive uropathy and severe sepsis.

Conclusion: MPNST can arise at unusual sites other than its common location in the extremities and the existence of neurofibromatosis may not be present. High index of suspicion of MPNST should be raised in rapidly growing painless tumour in and around a nerve tissue. Prompt radio-imaging with biopsy and expert immunohistochemical analysis of lesions will lead to early diagnosis and intervention. Molecular targeted therapies following surgery for MPNST should be developed to improve prognosis and patient outcomes.

Keywords: Post-mortem, Malignant peripheral nerve sheath tumour, Urinary bladder

1 Background

Malignant peripheral nerve sheath tumour (MPNST) is a rare malignant soft tissue neoplasm of ectomesenchymal origin [1]. It usually arises from a major or minor peripheral nerve branch or its sheath and also from somatic soft tissues [2]. It is the malignant counterpart of benign nerve sheath tumours like neurofibromas and schwannomas and it may also arise secondarily from them [1]. The most common sites of origin include the extremities and trunk; usually involving the sciatic nerve, brachial plexus and the sacral plexus [1]. MPNSTs involving other body parts or organs are extremely rare, and only few of such lesions have been reported till date. The incidence of MPNSTs in the general population is 0.001%; however, it can increase to 5–42% in individuals with neurofibromatosis type 1 (NF 1) [1]. MPNST is more common in adult within an age range of 20 to 50 years and they

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represent approximately 10% of all soft tissue sarcomas [3]. MPNST is among the rarest sarcomas arising in the urinary bladder [4]. Only few cases have been reported and some of these cases arose in the setting of neurofibromatosis type 1, probably originating from neurofibromas of the autonomic nerve plexuses of the bladder wall [5, 6]. We report a case of malignant peripheral nerve sheath tumour arising primarily at an unusual site of the urinary bladder without features of neurofibromatosis type 1.

2 Case presentation

A 58-year-old male cleric presented with complaints of weight loss of a year duration, abdominal swelling of 10 months duration and easy fatigability of 3 weeks duration. There was associated change in micturition pattern occasioned by straining and pain. There was also history of intermittent episodes of diarrhoea and constipation. He was diagnosed of hypertension a year ago. He had no history of diabetes or asthma. There was no history of cancer treatment. He neither smoked nor consumed alcohol. There was no family history of similar complaints.

General physical examination revealed a conscious and alert man with no focal neurologic deficits. He was severely pale, anicteric and not cyanosed. There was no significant peripheral lymphadenopathy. There were no external features indicative of neurofibromatosis 1. He was tachypneic with a respiratory rate of 28 cycles per minute, breath sounds were vesicular with few crepitations heard bi-basally. There was suprapubic fullness. Digital rectal examination showed a huge firm mass 6 cm from the anal verge which was non-tender. The upper limit of the mass was not palpable. Abdomino-pelvic ultrasound scan revealed an irregular heterogeneous mass in the posterior wall of the urinary bladder measuring 15.1cmx 14.0 cm with bilateral dilatation of the renal pelvi-calyceal system and ureters. His full blood counts revealed severe anaemia with a packed cell volume of 16.3%. He had mildly elevated white blood cell count of 12,000 cells/mm3 (normal is 400–11,000 cells/mm3) with relative neutrophilia (80% neutrophils). He also had deranged renal function tests with a moderately elevated blood urea of 66 mg/dl (normal is 15–45 mg/dl), elevated creatinine of 2.9mgldl (normal is 0.5–1.5 mg/dl) and low glomerular filtration rate (GFR) of 26.4 ml/min/1.73m2 (normal GFR $\geq$ 90 ml/min/1.73m2). Serum sodium, potassium and calcium levels were within normal range. The serum prostate specific antigen value was within normal range. Abdomino-pelvic ultrasound scan revealed an irregular heterogeneous mass in the posterior wall of the urinary bladder measuring 15.1 $\times$ 14.0 cm with bilateral dilatation of the renal pelvi-calyceal system and ureters.

An assessment of a bladder mass with chronic kidney disease secondary to obstructive uropathy was made. He was initially planned for biopsy of the bladder mass but his clinical condition continued to deteriorate while on hospital admission. He developed features of sepsis and complete intestinal obstruction with worsening azotaemia. He had a session of haemodialysis and blood transfusion. He also had a sigmoid loop colostomy done on the 10th day of admission under local anaesthesia to relieve intestinal obstruction. Despite all these interventions, he eventually suffered a fatal cardiopulmonary arrest from septic shock 2 days post-colostomy and was certified dead on the 12th day of hospital admission.

3 Post-mortem examination

Post-mortem examination revealed a rough ovoid tumour mass firmly adherent to the posterior wall of the urinary bladder and loosely adherent to the anterior surface of the distal sigmoid colon and rectum weighing 2000 g and measuring 16 $\times$ 16 $\times$ 10 cm. The mass was seen compressing the terminal ends of both ureters. Cut sections through the mass showed firm greyish-white lobulated surfaces with extensive areas of necrosis. The mucosal surfaces of the bladder appeared mildly congested. The right and left kidneys were within normal limits. The capsules of both kidneys striped with difficulty to reveal rough sub-capsular surfaces with multiple depressed scars. Cut sections of both kidneys show attenuation of the cortex and medulla with dilatation of the renal pelvi-calyceal systems and proximal ureters.

Histological analysis of the tumour showed a malignant mesenchymal neoplasm composed of spindle-shaped cells disposed in sheets, fascicles and focal storiform patterns. The cells have elongated to wavy hyperchromatic nuclei and moderate eosinophilic cytoplasm. Mitotic count is 8 per10 high power fields. There was stromal desmoplasia with extensive areas of necrosis.

Immunohistochemical analysis of the tumour cells was positive for S-100 protein and Vimentin but negative for Desmin, Myogenin and AE1/AE3 pancytokeratin markers. The overall features were consistent with the diagnosis of a malignant peripheral nerve sheath tumour.

4 Discussion

Malignant peripheral nerve sheath tumour (MPNST), previously referred to as malignant schwannoma or neurofibrosarcoma, is a rare cancer that arises from the nerve sheaths of major or minor peripheral nerves [7]. MPNSTs occur mainly in adults with no sex predilection [8], and only 10–20% of cases occur in individuals less than 20 years of age [1]. About half of the cases are diagnosed

in patients with type 1 neurofibromatosis and in this population, the incidence is 0.1% while the total risk of developing MPNST is 13–16%, compared with the incidence of 0.001% in the general population [8, 9]. Practically what this means is that the risk of developing MPSNT in carriers of the NF1 gene mutation is 4600 times higher than what obtains in the general population [9]. The age of the patient in this index case is still within the peak age for MPNST (the 5th and 6th decades of life), it is noted to be considerably higher than the average age for African patients with MPNSTs as documented by Nthumba et al. [10]. This may likely be due to the sporadic nature of the tumour in this index case. Although the tumour was not subjected to genetic analysis to check for NF1 mutations, there were no peripheral or systemic stigmata of neurofibromatosis type 1 documented clinically and none was found at autopsy. Apart from hereditary mutations in the NF1 gene, the main risk factors for developing MPNST are existing benign plexiform neurofibromas and previous radiotherapy which were not seen in this patient [9].

The location of the tumour in the posterior bladder wall as seen in this patient suggests an origin from one of the branches of the inferior hypogastric plexus. The bladder is an extremely rare location for MPNST, and only few cases have been reported in the literature [5, 6, 11–15]. Some of these cases were malignant degeneration of pre-existing neurofibromas in patients with Von Recklinghausen disease [11, 12]. Two cases were reported to be sporadic [13, 15], which is similar to what we found in our index case.

MPNSTs are mostly large, fleshy, often necrotic neoplasms with average sizes more than 5 cm in diameter [1]. They are usually fusiform to globular in shape and vary from white and firm to yellow and soft, depending on the absence or presence of necrosis [1]. The tumour in this case was infiltrative, greyish-white, firm and lobulated with extensive foci of haemorrhage and necrosis (Figs. 1 and 2).

The histological features of MPNSTs are those of a highly cellular, spindle-cell neoplasm with differentiation towards elements of the nerve sheath, Schwann cell, and peri-neural cell [16]. Frequent mitoses and focal areas of necrosis and haemorrhage are typical. Rarely heterologous mesenchymal or epithelial elements are present in these tumours [1]. The index case showed spindle-shaped cells disposed in sheets, fascicles and focal storiform patterns, mitosis was 8 per 10 high power fields with areas of haemorrhage and necrosis; however, no heterologous component was seen (Fig. 3).

The histological spectrum of MPNST is broad and the diagnosis rests on a combination of microscopic features, none of which is diagnostic by itself; therefore, a panel

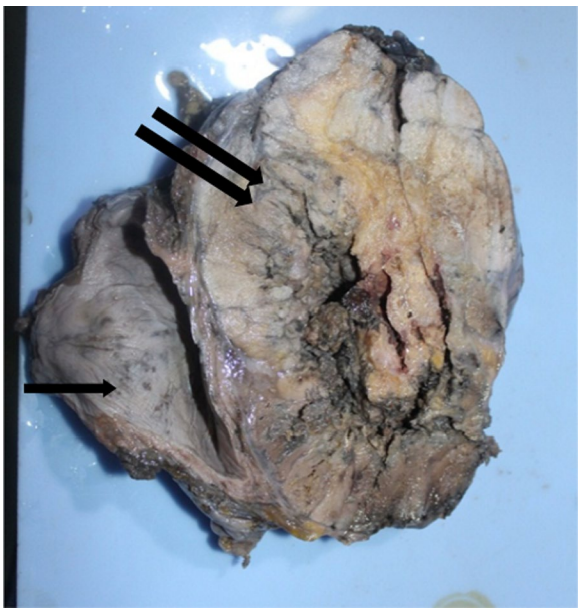

Fig. 1 Anterior view of the bladder tumour. The bladder is seen opened on the left (single arrow) while the mass is seen attached to the posterior wall (double arrows)

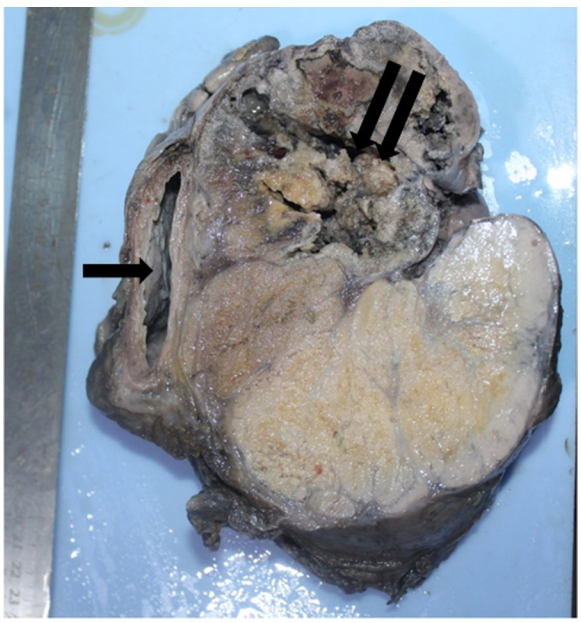

Fig. 2 Cut sections of the bladder tumour showing solid multilobulated surfaces with areas of haemorrhage and necrosis (double arrows). The bladder lumen is seen on the left (single arrow)

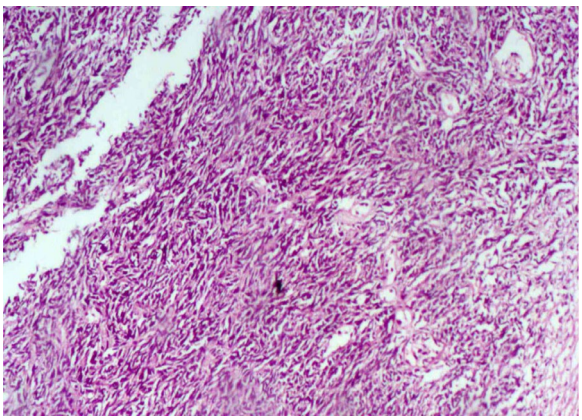

Fig. 3 Photomicrograph showing pleomorphic spindle-shaped cells disposed in sheets and short fascicles consistent with malignant peripheral nerve sheath tumour. (Haematoxylin and eosin stains, X100)

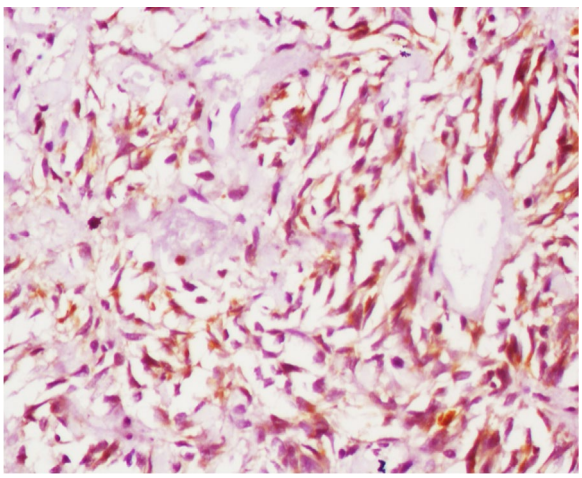

Fig. 4 Photomicrograph showing cytoplasmic S100 protein immunohistochemical positivity in tumour cells (Immunoperoxidase stain, X100)

of IHC markers is needed to exclude the differentials of other soft tissue sarcomas with similar morphology [1].

S100 protein, the most widely used antibody for nerve sheath tumour, is positive only in 50% of MPNSTs [1]. Moreover, combined immunohistochemical evaluation of potential Schwann cell markers including Leu-7, MBP, GFAP and LN3 using commercially available antibodies offers no advantage over analysis of S100-protein immunoreactivity alone [1]. The tumour in this index case showed immunopositivity with S100 protein and Vimentin (Fig. 4) and was negative for Desmin, Myogenin and AE1/AE3 pancytokeratin markers.

Effective targeted molecular therapies are still lacking; hence, surgical resection with achievement of tumour-free margins is still the mainstay of treatment [7]. If the tumour size is more than 5 cm, neo-adjuvant radiotherapy is used to shrink the size of the tumour and reduce local recurrence [17]. Chemotherapy is often preferred when either the disease is too small to detect or diffuse and for high grade and metastatic disease [7]. The recurrence rate is up to 40%, frequently with subsequent haematogenous metastasis. Five-year survival has varied in documented series from 15 to 66% [7].

This patient died from complications of the tumour before surgical resection could be done. He developed obstructive uropathy and complete obstruction of the sigmoid colon necessitating an emergency colostomy procedure. He also developed bronchopneumonia with severe sepsis and severe anaemia. The combination of the immunosuppressive effect of malignancy and prolonged hospital stay no doubt increased the risk of acquisition of hospital acquired pneumonia in this patient. Terminally he developed an oxygen refractory respiratory difficulty which eventually resulted in his demise. This was confirmed at autopsy by the finding of bilateral heavy lungs with histological features of severe bronchopneumonia.

5 Conclusion

MPNST can arise at unusual sites other than its common location in the extremities, and the existence of neurofibromatosis may not be present. High index of suspicion of MPNST should be raised in rapidly growing painless tumour in and around a nerve tissue. Prompt radio-imaging with biopsy and expert immunohistochemical analysis of lesions will lead to early diagnosis and intervention. Molecular targeted therapies following surgery for MPNST should be developed to improve prognosis and patient outcomes.

Abbreviations

MPNST: Malignant peripheral nerve sheath tumour; NF-1: Neurofibromatosis type 1; GFR: Glomerular filtration rate; GFA: Glial fibrillary acidic protein; MBP: Myelin basic protein; LN3: Mouse monoclonal HLA-DR antibody.

Authors' contributions

MAA, BLA, and IDN have made substantial contributions to the conception and design of this manuscript. All three were involved in the data acquisition and jointly drafted the work and revised it. All three were involved in the manuscript drafting, editing, and review. Manuscript was finally approved by all three contributors. MAA, BLA, and IDN have agreed to be accountable for the manuscript submitted. All authors read and approved the final manuscript.

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Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written consent for publication of this study was obtained from the study participant's next of kin. It is an autopsy study.

Competing interests
The authors declare that they have no competing interests.

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