CASE REPORT
Pathology

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Chronic Urinary Outflow Obstruction Resulting from Prostatic Neurofibromatosis

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Abstract

Neurofibromatosis type 1 is a disorder characterized by tumors of autonomic peripheral nerve sheaths. Visceral involvement is infrequent, with genitourinary involvement being rarer. Presented here is a case of a 52-year-old male who presented with an acute renal injury secondary to renal tract obstruction. Transurethral resection of the enlarged prostate demonstrated neurofibromatosis with no signs of malignant transformation.

Keywords: Neurofibroma, prostatomegaly, bladder outflow obstruction

Introduction

Genitourinary manifestations of neurofibromatosis type 1 are rare, with purely prostatic involvement being even rarer. We report a case of prostatic neurofibromatosis presenting with acute renal failure due to bladder outlet obstruction.

Case Presentation

A 52-year-old male was admitted to the intensive care unit for type 2 respiratory failure requiring non-invasive ventilation in the setting of urosepsis with an *Escherichia coli* bacteremia. His past medical history was significant for obstructive sleep apnea, hypertension, type 2 diabetes and neurofibromatosis type 1. He had an associated acute kidney injury with creatinine of 193 umol/L from a baseline of 60 umol/L (Reference range: 60-110), prompting a non-contrast computerized tomography scan of the renal tract, which demonstrated gross hydroureternephrosis bilaterally and prostatomegaly (Figure 1). Upon further history, he had longstanding symptoms of urinary frequency, urgency and nocturia. On digital rectal examination, he had an enlarged, but soft and benign prostate. He improved clinically following the insertion of an indwelling urinary tract catheter and intravenous antibiotics. He was weaned off oxygen and discharged one week later. Ultrasound following this demonstrated a markedly enlarged 100 cc prostate. Cystoscopy and transurethral resection of the prostate were performed approximately six weeks following his initial admission; the bladder mucosa was moderately trabeculated, and the prostate was enlarged and occluded. Histopathological analysis revealed pieces of a spindle cell tumour with elongated and bent nuclei that appeared diffusely infiltrative. There were a few scattered mast cells and eosinophils in the stroma with no normal prostatic glands. Immunohistochemistry confirmed that the spindle cells were positive for the neural markers, SOX10 and S100 (Figure 2). The patient successfully passed a trial of void post-operatively with the return of normal renal function, and resolution of his lower urinary tract symptoms after six weeks.

Discussion

Neurofibromatosis type 1 (NF1) is an inheritable autosomal dominant disorder with nearly 100% penetrance and markedly varied expressibility (1-4). It is caused by genetic mutations of the tumour-suppressor gene located on 17q11.2, which result in increased cellular proliferation.

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It is relatively common, with an incidence of 1 in 3000 live births and affects both sexes and races equally. It is characterized by multiple neurofibromas, which are tumors of autonomic peripheral nerve sheaths, mainly arising from Schwann cells, but may also originate from the perineurium or endoneurium.

Diagnosis involves two or more of the following seven criteria: six or more café au lait macules, two or more neurofibromas or one plexiform neurofibroma, axillary or inguinal freckling, optic pathway glioma, two or more iris hamartomas (Lisch nodules), bony dysplasias, or a first-degree relative with NF1 (3).

Visceral involvement is infrequent, but if present, the gastrointestinal tract is the most common site of occurrence (2). Genitourinary tract involvement is even rarer, with approximately only 70 cases reported in the literature, approximately 50 of these involving the bladder (2). To date, there have only been 10 cases of neurofibromatosis of the prostate reported in the literature (3). Neural tumors that involve the genitourinary tract have been postulated to arise from the anatomically adjacent autonomic plexuses, which innervate the tract. With time, the tumors enlarge and extend into the contiguous organs (1-3).

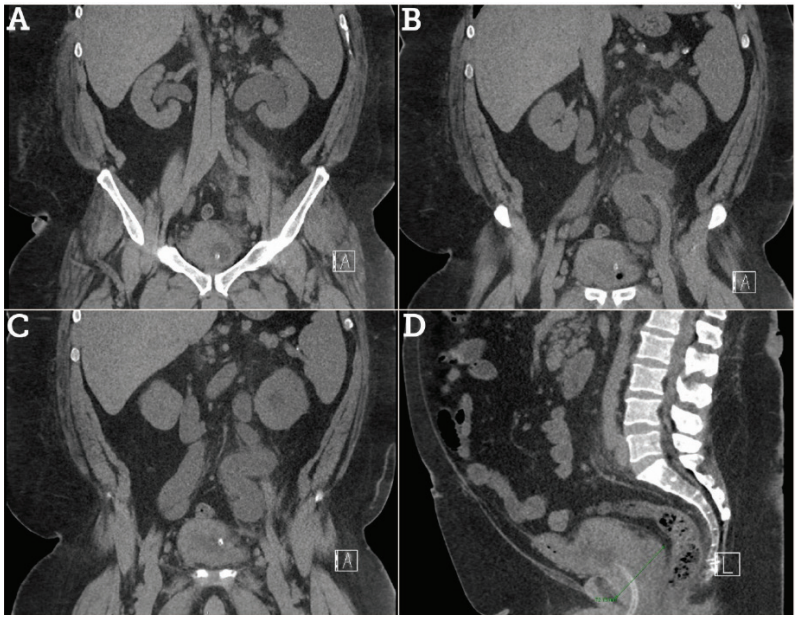

Figure 1. Coronal (A, B and C) and sagittal (D) computed tomography images demonstrating severe bilateral hydroureternephrosis and prostatomegaly

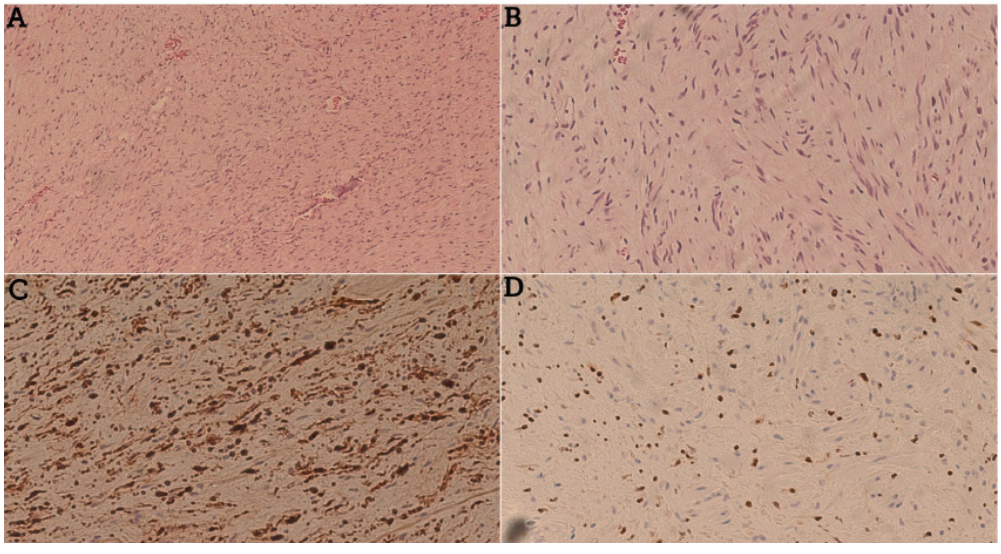

Figure 2. Microscopic prostatic chip histopathological images. H&E staining at x10 (A) and x20 (B) magnification demonstrating presence of spindle cells and scattered mast cells and eosinophils. Immunoperoxidase staining demonstrating presence of S100 (C) and SOX10 proteins (D)

The natural history of neural tumors in the pelvis is one of slow, contiguous growth, and lesions can become quite extensive before producing symptoms, such as in our case. Previous reports of prostatic neurofibromas elicit clinical histories of bladder outlet obstruction with frequency and nocturia, with some reports of prostatodynia, and a perineal or periprostatic mass palpated on a digital rectal exam (4).

Imaging techniques such as ultrasound, computerized tomography and magnetic resonance imaging, as well as the use of cystoscopy, can guide the diagnosis and determine the extent of the tumor and the presence of bladder involvement. However, a definitive diagnosis can only be obtained through histopathology, either by biopsy or the evaluation of prostatic chips obtained by resection. In many cases, diagnosis is achieved only after surgery through histopathological analysis of surgical specimens, with spindle cells expressing the S-100 protein characteristic for the tumour (4).

The mainstay of treatment remains undetermined. Chemotherapy and radiotherapy are both ineffective in managing tumor lesions (2-4), with radiotherapy being associated with the development of malignant peripheral nerve sheath lesions (4). Currently, surgical excision remains the only potential treatment for a cure, but such may not be viable when considering the removal of all cutaneous and visceral neurofibromas. Additionally, recurrence rates are high, with up to 45% of patients having local recurrences following surgical removal, many of which occur within the first year (2).

Additionally, patients with NF1 are at an increased risk of developing benign and malignant tumors, with rapid tumour growth potentially being a sign of malignant transformation. Malignant peripheral nerve sheath lesions are found in 3-15% of patients, and of these lesions, 22% present as metastases (5). Life expectancy in patients with NF1 is approximately 15 years shorter than in the general population, with the main cause of death being consequences from malignant tumors (5).

As such, the most appropriate management would be close monitoring and surgical excision of any large neurofibromas that cause bothersome symptoms or increase rapidly in size.

Conclusion

In conclusion, this is a very unusual case of a relatively young man presenting with bladder outlet obstruction and bilateral gross hydroureteronephrosis caused by prostatomegaly resulting from the presence of a neurofibroma. The diagnosis of prostatic neurofibromatosis, albeit rare, needs to be considered with those with stigmata of neurofibromatosis type 1 with urinary signs and symptoms, to organize prompt surgical management with transurethral resection and routine follow-up.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.V.B., E.H., P.G., C.S.L., Concept: S.V.B., P.G., Design: L.V., Data Collection or Processing: L.V., Analysis or Interpretation: L.V., S.V.B., E.H., P.G., C.S.L., Literature Search: L.V., Writing: L.V., S.V.B., E.H., P.G., C.S.L.

Conflict of Interest: No conflict of interest was declared by the authors.

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