CASE REPORT

Leiomyoma of the bladder in a patient with von Recklinghausen's neurofibromatosis

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Leiomyomas are an uncommon manifestation of neurofibromatosis type 1 (NF-1) and occur most often in the gastrointestinal tract. Here, they have a proclivity for the proximal small bowel and tend to be multiple. Urinary tract involvement by NF-1 is usually in the form of neurofibromas, and leiomyomas are exceptionally rare. This report describes a case of solitary leiomyoma occurring in a 49 year old woman with NF-1. The patient had symptoms related to a lower urinary tract infection and on examination was found to have a distended bladder. Imaging of the bladder showed a mass involving the posterior wall, neck, and trigone causing bilateral hydronephrosis. The mass was excised with part of the bladder. Microscopic examination revealed typical features of a leiomyoma and there was strong immunoreactivity for desmin and smooth muscle actin. Leiomyoma must be considered in the differential diagnosis of spindle cell neoplasms in patients with NF-1.

A 49 year old woman presented with dysuria and lower abdominal pain that had been present for several months. On examination, she was found to have neurofibromatosis type 1 (NF-1), with multiple neurofibromas on her trunk, extremities, and face together with axillary café au lait freckling. She had a tender, slightly distended lower abdomen. Her blood results were within normal limits and there was no growth on urine culture. Abdominal ultrasound revealed a bladder mass and bilateral hydronephrosis. The excretory urogram showed pronounced hydronephrosis and hydroureter on the right. The left ureter was not well visualised. A cystogram followed, which showed a polypoidal mass indenting the right posterior wall of the bladder base and neck. Cystoscopy showed an irregular erythematous mucosa and the biopsy revealed mucosal ulceration and a chronic active cystitis. Computed tomography scan demonstrated a well defined hypodense mass in the region of the bladder neck and a neurofibroma was considered the most likely clinical and radiological diagnosis. The patient then underwent a partial cystectomy and the mass at the bladder trigone was excised. No other tumours were seen at this time. She made an uneventful postoperative recovery and was subsequently discharged. She is well at six weeks follow up.

PATHOLOGICAL FINDINGS

On macroscopic examination, the bladder trigone showed a central, well circumscribed tumour, which surrounded and compressed the ureters with a resultant right hydroureter. The tumour measured 25 × 25 × 24 mm and had the characteristic uniform white whorled appearance of a leiomyoma. Microscopy revealed a well demarcated tumour composed of interlacing fascicles of monotonous spindle cells with blunt ended, cigar shaped nuclei and eosinophilic cytoplasm. There

Figure 1 The tumour is composed of interlacing fascicles of uniform spindle shaped cells. No mitotic activity, pleomorphism, or necrosis is evident (haematoxylin and eosin stained; original magnification, ×100).

Figure 2 The spindle cells are strongly immunoreactive for desmin (anti-desmin immunohistochemistry; original magnification, ×400).

was no evidence of hypercellularity, pleomorphism, mitotic activity, or necrosis (fig 1). Immunohistochemical stains confirmed the smooth muscle nature of the tumour with strong diffuse positive staining for smooth muscle actin and desmin (fig 2). The tumour was negative for the S100 protein, whereas resident nerves were strongly immunoreactive.

DISCUSSION

Benign smooth muscle tumours of the urinary tract are uncommon to rare, and most arise in the urinary bladder.¹ Vesical leiomyomas have been detected in all age groups from 1.5 to 75 years, with a peak age in the 4th to 6th decades.¹ There is a female predominance (76%), and patients present most commonly with obstructive urinary symptoms (49%), irritative symptoms (38%), haematuria (11%), or flank pain (13%).² Three forms have been described, namely: endovesical (86%), extravascular (11%), and intramural (3%), which are dependent on the predominant location of the tumour.² The endovesical form is more common because it protrudes into the bladder and is therefore more apt to cause

symptoms, thereby resulting in the patient seeking medical attention.² Local excision of the neoplasm is curative.² NF-1 is an autosomal dominant disorder characterised by multiple neurofibromas, multiple cutaneous café au lait spots, axillary freckling, optic nerve gliomas, pigmented nodules of the iris (Lisch nodules), and skeletal abnormalities.³ It is one of the more common genetic disorders, with a frequency of 1 in 3000.³ Involvement of the urinary tract is uncommon and is usually by neurofibromas.⁴ A review conducted by Blum and colleagues states that urogenital manifestations of NF are rare and can be categorised thus: (1) retroperitoneal neurofibromas affecting the upper and lower urinary tract, (2) hypertension as a result of renal artery stenosis or a pheochromocytoma, and (3) a large variety of genital neurofibromas.⁵ Leiomyomas in patients with NF-1 are very rare and usually involve the gastrointestinal tract.⁶⁻⁹ It is said that one of the least frequent manifestations of NF-1 in the gastrointestinal tract is the occurrence of leiomyomas.⁶ When they do occur, they tend to be multiple and preferentially involve the proximal small bowel.⁶⁻⁹ The usual mode of presentation is as a result of haemorrhage, but ulceration, intussusception, perforation, and obstruction can occur.⁶ The patient described by Hamanaka *et al* had multiple small bowel leiomyomas, together with a leiomyoblastoma,⁹ whereas the patient reported by Ishizaki and colleagues showed the spectrum of smooth muscle tumours, from leiomyomas through to epithelioid leiomyoma to leiomyosarcoma.⁸ The occurrence of leiomyoma in NF is not the result of serendipity.

"It is probable that leiomyomas occurring in the bladder and/or remainder of the urogenital tract are pathogenetically related to those in the gastrointestinal tract in neurofibromatosis"

The subdivision of NF into types 1 and 2 has both a clinical and molecular basis.¹⁰ Other rare types of NF have also been described, including a so called syndrome consisting of multiple naevi, multiple schwannomas, and multiple vaginal leiomyomas.¹⁰ Hence, multiple smooth muscle tumours at different sites are part of the spectrum of tumours encountered in NF.

The presence of smooth muscle tumours in the bladder is exceedingly rare and, to date, there is only one case report in the literature of a leiomyosarcoma arising in a leiomyoma of the urinary bladder in a patient with von Recklinghausen's disease.¹¹ It is probable that leiomyomas occurring in the bladder and/or remainder of the urogenital tract are pathogenetically related to those in the gastrointestinal tract in NF. It is quite possible that alterations in the NF-1 gene, together with growth factors, are responsible for the development of mesenchymal tumours, some of which show smooth muscle differentiation. Therefore, it is important to bear this diagnosis in mind when dealing with a patient suffering from NF. Although the case described in our report was a solitary lesion, one should be aware that multiple lesions are usually the rule, especially in the gastrointestinal tract. In addition, evidence of malignant change or malignancy should be sought. Although

Take home messages

- Leiomyomas are an uncommon manifestation of neurofibromatosis type 1 (NF-1) and occur most frequently in the gastrointestinal tract
- To the best of our knowledge, this is the first report of a solitary leiomyoma of the bladder in a patient with NF-1
- Leiomyoma must be considered in the differential diagnosis of spindle cell neoplasms in patients with NF-1

the histopathological criteria to distinguish between a vesical leiomyoma and leiomyosarcoma are not well established in the literature, Martin *et al* suggest that the diagnosis of urinary bladder leiomyoma should be reserved for non-infiltrative smooth muscle tumours lacking mitotic activity, cytological atypia, and necrosis.¹²

To the best of our knowledge, the case reported here is the first documentation in the English language of a solitary leiomyoma of the bladder in a patient with NF-1.

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