Functional Medicine

Oddities Sporadic Neurofibroma of the Urinary Bladder. A Case Report

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ABSTRACT

Neurofibromas of the urinary bladder are an exceedingly rare entity and are considered mostly in conjunction with the disease of neurofibromatosis type 1. The fortuitous discovery of vesical plexiform neurofibromas without other stigmata of the disease is presented in a 57-year-old male patient. The course of his condition, modalities of investigation and a non-precedent treatment plan are demonstrated.

Introduction

Neurofibroma (Schwannoma, Neurilemmoma) of the urinary bladder is an extremely rare tumor. Gerhardt described the first neurofibroma case of the bladder during an autopsy in 1878. Urogenital involvement arises from the pelvic and bladder nerves, and the prostatic plexus. The most frequently affected organ of the urinary tract is the urinary bladder. The diagnosis is confirmed histopathologically and immunohistochemically. Treatment is usually conservative although surgical treatments have been reported. The patient should be worked-up and followed-up to evaluate any development of new lesions.

Case presentation

We report a male patient of 57 years of age complaining of severe nocturia and pollakisuria with a moderate difficulty of voiding urine and straining despite TURP but no history of incontinence. Clinical examination was unremarkable with a normal neurological examination of the perineum and a firm prostate on DRE. An ultrasound revealed a prostatic volume of 10 g and a PVR of 60 mL. Detrusor overactivity was suspected and the patient was treated with anticholinergics with no improvement.

An urodynamic study showed a limited bladder capacity of 250 mL with a painful sensation at this filling volume. The bladder was compliant and a forceful urination with a maximal flow rate of 24 mL/s of 210 mL. The study concluded a non-specific cystalgia. The patient was put under surveillance using USP (Table 1) and 24-h bladder diaries (Table 2). A urinary cytology was unremarkable.

A cystoscopy showed flat sessile lesions found on the right and left lateral walls of the bladder and dome. TURBT was indicated and done. The left lateral biopsies showed a proliferation of fusiform eosinophilic cells in a collagenised and vascularized background. The tumor cells were located in the lamina propria. The detrusor was not seen. There were no mitotic figures, no necrosis nor cellular atypia. A moderate inflammation was
present composed of lymphocytes and rare eosinophils. Immunohistochemistry showed a positive staining for S100 protein and neurofilament but was negative with smooth muscle actin (see Fig. 1). Dome biopsies were unfortunately not interpretable because of artifacts. The right lateral biopsies also showed a similar pattern.

Subsequently, a decision was made to treat the patient using intravesical botulinum toxin injections of 50 IU but no improvement was seen (Table 1). The second attempt with 100 IU was accomplished and showed a short but remarkable improvement of symptoms (Tables 1 and 2). A third attempt using 100 IU was redone with some improvement especially on the level of urinary incontinence and also a non-negligible increase in voiding volumes (Tables 1 and 2). Follow-up urine cytology and pelvic MRI were normal.

### Discussion

Benign epithelioid nerve sheath tumors, in general, are rare and have only recently begun to be characterized. Their classification as either neurofibromas or schwannomas remains unclear. Neurofibromas arise from Schwann cells in nerve sheaths and may be benign or malignant and are often associated with the NF-1 disease. The likelihood of malignant degeneration increases with advancing age, and after an operation for benign neurofibromas. Neurofibromas of the genito-urinary tract most commonly affect males than females by a ratio of 3:1, and commonly affect the bladder, but there are also reports of neurofibromas involving the penis, clitoris, prostate, urethra, testis, spermatic cord and ureter. The patient should be always worked-up to rule out other manifestations of NF-1 disease and followed to evaluate the development of new lesions.

Sporadic cases of this tumor are even more rare. They represent <0.1% of all bladder tumors. Isolated schwannomas have also been discovered in other areas such as the kidney and retroperitoneum but rarely in the bladder. Bladder neurofibromas may present with voiding and/or storage symptoms, flank pain or incontinence. The radiological aspects of neurofibromas are characteristic; especially on MRI and they can frequently evoke the diagnosis, which is confirmed by biopsy. We believe MRI could be an excellent tool for non-invasive follow-up. It may occur as an isolated focal mass within the bladder wall or as a diffuse infiltrating process with wall thickening described as a plexiform lesion.

A differential diagnosis of leiomyosarcoma, ganglioneuroma and paraganglioma should always be considered in isolated cases. Histopathologically, they stain positive for protein S100 with immunohistochemical techniques and this is the pathognomonic pathology finding of schwannomas.

### Table 2

| 24-h urine diary | Pollakisuria | Nocturia | Minimum (mL) | Maximum (mL) | mL/Day Median (mL in 24 h) | Mean (mL in 24 h) |
|------------------|-------------|---------|--------------|-------------|---------------------------|------------------|
| Post oral Rx     | 17          | 7       | 50           | 150         | 2300                      | 100              |
| Post oral Rx     | 14          | 8       | 50           | 150         | 2200                      | 125              |
| Post oral Rx     | 14          | 7       | 50           | 150         | 1925                      | 50               |
| Post 1st botox 100 IU | 15   | 6       | 50           | 150         | 2025                      | 100              |
| Post 1st botox 100 IU | 15   | 6       | 50           | 150         | 1145                      | 100              |
| Post 1st botox 100 IU | 15   | 6       | 50           | 150         | 1365                      | 100              |
| Post 1st botox 100 IU | 8    | 5       | 50           | 150         | 1370                      | 110              |
| Post 2nd botox 100 IU | 12  | 6       | 80           | 300         | 2860                      | 160              |
| Post 2nd botox 100 IU | 11  | 5       | 80           | 300         | 2870                      | 180              |
| Post 2nd botox 100 IU | 12  | 4       | 80           | 300         | 2490                      | 150              |
| Post 2nd botox 100 IU | 11  | 4       | 80           | 320         | 2180                      | 120              |

Figure 1. A. Hematoxylin and eosin stain (Positive), B. S100 Protein stain (Positive), C. Neurofllament stain (Positive), D. Smooth muscle actin stain (Negative), Magnification x20.
Treatment of these tumors has included cystectomy, transurethral resection, observation, radiotherapy, chemotherapy, and urinary diversion. To our knowledge, this is the first case treated using Intravesical botulinum toxin injections. Although there is no evidence linking the lesions with the patient’s symptoms and thus the use of botulinum toxin injections, we were intrigued by the clinical improvement following the second and third injections. We believe that this management strategy warrants further investigations.

**Conclusion**

A conservative approach is more appropriate unless complications occur. We suggest using our method of treatment before using a more invasive one. Careful follow-up is necessary to detect upper urinary tract obstruction, which may be a sign of progressive tumor growth with possible malignant transformation. The tumor should be resected if it increases in size. The management of these tumors is not yet resolved; no guidelines are available for its management.

**Conflict of interest**

There is no conflict of interests.

Consent has been taken from the patient.

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