Original Article

Clinicopathologic Features of Benign Neurogenic Tumor of Urinary Bladder

International Journal of Surgical Pathology
2018, Vol. 26(3) 221–228

DOI: 10.1177/1066896917742722
journals.sagepub.com/home/ijs
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Abstract

Background. Benign neurogenic tumor involving the urinary bladder is a very rare and heterogeneous disease group. The clinical and radiological diagnosis may be difficult because of the disease's rarity and the histological similarities of each disease especially in needle biopsy specimens. However, accurate diagnosis is very important because the clinical course of each disease, even within the same diseases, is quite variable. In this study, we investigated 7 benign neurogenic tumors to better understand the rare disease entity in the urinary bladder by analyzing histological and immunohistochemical findings and comparing clinicopathologic features. *Methods*. We collected the cases by searching the medical records database of Seoul National University Hospital from 2000 to 2016. *Results*. We identified 3 ganglioneuromas, 2 schwannomas, 1 neurofibroma, and 1 granular cell tumor involving the urinary bladder. There were some limitations for the initial clinical and radiological diagnosis and even pathologic diagnosis using needle biopsy specimens. One infant patient was diagnosed radiologically with rhabdomyosarcoma, but the final diagnosis changed to ganglioneuromatosis. The initial needle biopsy diagnosis of 2 ganglioneuroma cases showed neurofibroma. All patients underwent a local resection, and 1 granular cell tumor patient suffered with pain because of a recurrent tumor. One neurofibromatosis patient had a lesion appear 34 months after the bladder operation, so he underwent repeated debulking operations, but he was diagnosed with malignant transformation after 8 years. *Conclusions*. An understanding of benign neurogenic tumors involving the urinary bladder and the sharing of rare experiences surrounding them are required to provide accurate diagnoses.

Keywords

urinary bladder, neurofibroma, neurilemmoma, ganglioneuroma, granular cell tumor

Introduction

Benign neurogenic tumor involving the urinary bladder is rare and includes several disease entities. Neurofibroma is a benign nerve sheath tumor characterized by the proliferation of Schwann and perineurium-like cells, as well as fibroblasts and intermediate type cells.[1] Benign neurogenic tumor involves the urinary bladder in a wide patient age range[1,2] and is especially associated with neurofibromatosis type 1 (NF1) in the pediatric age group.[3] The urinary bladder is known as the most involved organ in the genitourinary system for NF1 patients.[3] Neurofibromas are benign but plexiform neurofibromas and solitary intraneural neurofibromas arising in sizeable nerves are precursor lesions of a majority of malignant peripheral nerve sheath tumors associated with NF1.[4]

Schwannoma of the urinary bladder is much less common than neurofibroma, with only limited cases reported.[2] It is composed entirely of differentiated neoplastic Schwann cells[4] and is often confused with neurofibroma, even though it is a completely different disease. The etiology of sporadic schwannoma is not known, but multiple schwannomas are a feature of neurofibromatosis type 2 (NF2), which is commonly present before the age of 30.[4] Schwannomas are benign, and malignant transformation of conventional schwannoma is exceptionally rare, unlike neurofibromas.

Ganglioneuromas are rare benign neoplasms that originate from neural crest cells of sympathetic ganglia or adrenal medulla. Ganglioneuromas are known to occur mostly in the posterior mediastinum (41.5% of cases), retroperitoneum (37.5%), and adrenal gland (21%), but they may occur

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anywhere that contains sympathetic nervous tissue including, although rarely, in the urinary tract, which includes the urinary bladder.[5,6] These tumors are at one end of the neuroblastic tumor spectrum,[6] and they may arise primarily or differentiate from neuroblastic tumors, consisting of mature Schwannian stroma and fully mature ganglion cell.[7]

A granular cell tumor is of Schwann cell origin and is composed of large polygonal cells with abundant granular cytoplasm.[3] The head and neck, including the tongue, is a common location, but there have been rare cases reported of these tumors affecting the genitourinary system including the urinary bladder.[8] Most tumors are benign but may rarely recur after excision, and 2 cases of malignant granular cell tumor of the urinary bladder have been reported.[3,9,10]

Benign neurogenic tumors involving the urinary bladder are a very rare and heterogeneous disease group. The clinical and radiological diagnosis is sometimes difficult because of their rarity, and even a pathological diagnosis because of the histological similarities of each disease, especially in a needle biopsy specimen, can be difficult too. Some of these tumors, particularly in the pediatric cases associated with NF1, occur in multiple sites including the urinary bladder. Benign neurogenic tumors are typically cured by surgical treatment, but some cases of local recurrence and multiple occurrences, as previously mentioned, and malignant transformation, have been difficult to treat, especially when associated with NF1. Thus, the clinical course of benign neurogenic tumor is variable, even within the same disease.

In this study, we investigated 7 benign neurogenic tumors to better understand the rare disease entity in the urinary bladder by analyzing histological and immunohistochemical findings and comparing clinicopathologic features. The sharing of these rare experiences will allow for the more accurate diagnosis of these diseases in the future.

Material and Methods

We obtained cases by searching the medical records database of The Seoul National University Hospital from 2000 to 2016 and reviewing all available hematoxylin and eosin slides and immunohistochemical stained slides. Clinical and pathological information were collected from electronic medical records and pathologic reports. This study was approved by the Institutional Review Board of Seoul National University Hospital.

Results

Clinical Features and Follow-up Information

We identified 3 ganglioneuromas, 2 schwannomas, 1 neurofibroma, and 1 granular cell tumor involving the urinary bladder. The clinical features and follow-up information are summarized in Table 1. The age at diagnosis of the 7 patients (2 males, 5 females) ranged from 4 months to 51 years. Three cases, 2 ganglioneuromas and 1 neurofibroma, were pediatric, and all 3 patients were associated with NF1. Initial patient presentations were variable, such as microscopic hematuria, right flank pain, health screening for localized adult cases, vomiting for 1 infant case, and paraplegia for 1 neurofibromatosis pediatric patient. We identified cystoscopic findings in 3 patients. Two schwannoma patients showed an extrinsic mass-like lesion or submucosal mass. One infant ganglioneuromatosis patient showed a huge mass involving mucosa.

There were some limitations for the initial radiological diagnosis. One infant patient was diagnosed with rhabdomyosarcoma radiologically, but the diagnosis was ultimately changed to ganglioneuromatosis. She was diagnosed with neurofibromatosis type 1 after the pathologic diagnosis of the urinary bladder. Clinically or radiologically benign neurogenic tumors were occasionally misdiagnosed as leiomyoma because it is the most common benign mesenchymal tumor of urinary bladder; however, leiomyoma actually accounts for less than 1% of all bladder tumors.[3] Preoperative pathologic diagnosis by needle biopsy was performed for 3 patients. The initial needle biopsy diagnosis of 2 ganglioneuroma cases was neurofibroma because of morphologic similarity (Figure 1A and B). One granular cell tumor patient was diagnosed by needle biopsy because of unique morphologic features, even though it is a very rare tumor.

The urinary bladder was a secondary involved organ for one ganglioneuroma patient, the initial involved organ for the others, and one of multiple involved organs for the secondary ganglioneuroma and one neurofibroma patients. Three patients were diagnosed with NF1. As previously mentioned, one infant patient was diagnosed with NF1 after the pathologic diagnosis of a urinary bladder lesion. She already had a pigmented skin lesion in the inguinal area, but it had been overlooked until that point. In that case, the splicing defect of *NF1* gene was found via direct sequencing (c.1641+1G>A (IVS10c), heterozygote).[11] The other 2 cases are too old to find specific mutation records. All 3 cases were clinically appropriate to NF1. There were no cases with other predisposing genetic condition including NF2.

All patients underwent local resection, and 6 patients had clinical follow-up information available. One granular cell tumor patient had suffered with pain because of a recurrent tumor adjacent to the right pubic bone that showed no response to radiotherapy after 55 months from the initial diagnosis. One ganglioneuroma patient, for whom urinary bladder was the secondary involved organ, had a remnant lesion at the time of operation and newly appeared mass lesions during follow-up. She was under observation without any treatment. Another neurofibromatosis patient had a newly appeared lesion 34 months after