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Bladder Ganglioneuroma: A Rare Case Report

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ABSTRACT

Ganglioneuromas are neurogenic tumors that often stem from sympathetic ganglion cells, and less frequently from the adrenal medulla and peripheral nerves. These tumors are slow-growing and have a more benign character compared to other cell types. Herein we present a pure ganglioneuroma of a 50-year-old male patient as the third case reported in the urinary bladder. At cystoscopy a 6 cm x 6 cm tumor was found on the posterior wall of the bladder and resected. Histologically, the tumor was composed of mature and immature ganglion cells and Schwann cells. Since the neuroblasts did not consist of an evident bundle structure, it was diagnosed as a ganglioneuroma. To our knowledge, 5 cases of composite paraganglioma-ganglioneuroma have been reported in the English literature. However, there are only 2 documented cases of bladder-located, pure ganglioneuromas.

INTRODUCTION

Peripheral neuroblastic tumors are classified into neuroblastomas (NBs), ganglioneuroblastomas (GNBs), and ganglioneuromas (GNs). These tumors are categorized according to their stage of maturation in a spectrum, which starts from NB, the most primitive form, and extends to GN, the most mature form. GNs are neurogenic tumors that often stem from sympathetic ganglion cells, and less frequently from adrenal medulla and peripheral nerves. These tumors are slow-growing and have a more benign character compared to other cell types [1]. They are most commonly located in the retroperitoneum (52%), mediastinum (39%), pelvis, and neck (9%) [2]. Almost 60% of cases are in patients under 20 years of age [3,4].

So far, 5 case reports in the existing literature have documented bladder-located, composite paraganglioma-ganglioneuromas [5-9]. However, since there are only 2 documented cases of bladder-located, pure GN [10,11], we present this tumor of neurogenic origin with a benign clinical prognosis, which is identified for the third in the bladder.

CASE REPORT

A 50 year-old male presented to the general surgery polyclinic with abdominal pain. An abdominal ultrasonogram identified a 6 cm x 6 cm solid mass on the posterior bladder wall. Urology was then consulted. The patient denied hematuria. No pathology was identified on physical examination. Serum biochemistry, hematological test results, and urine microscopy were normal. A transurethral tumor resection was planned with a presumptive diagnosis of a bladder tumor. On cystoscopy, a dirty gray-colored, hard, dense, lobulated lesion covering the posterior bladder wall was identified. This varied in appearance from a bladder tumor, which is typically either solid or papillary (Figure 1a). Resection and fulguration of the 6 cm x 6 cm lesion was performed, which did not affect the ureteral orifice (Figure 1b). Post-procedure, a 3-way urethral catheter was inserted and then removed on the third postoperative day. The patient was discharged without evidence of postoperative complications and was asked to follow up with the pathology report.

The patient has been followed every 3 months in our clinic. During the 12-month period of postoperative follow-up with no additional treatment, neither clinical nor radiological tumor recurrence has occurred.

KEYWORDS: Ganglioneuroma, urinary bladder

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Figure 1. a) The cystoscopic appearance of the 6 cm x 6 cm dirty gray-colored, hard, dense, lobulated lesion on the posterior bladder wall. b) The cystoscopic appearance of the lesion after resection and fulguration.

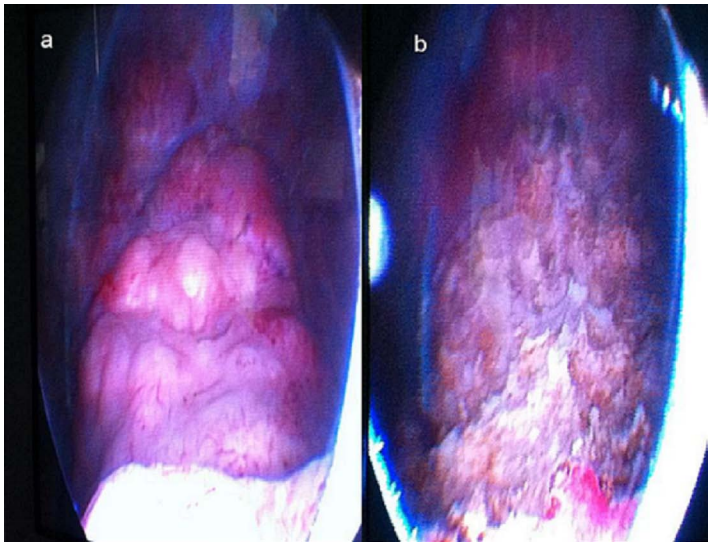
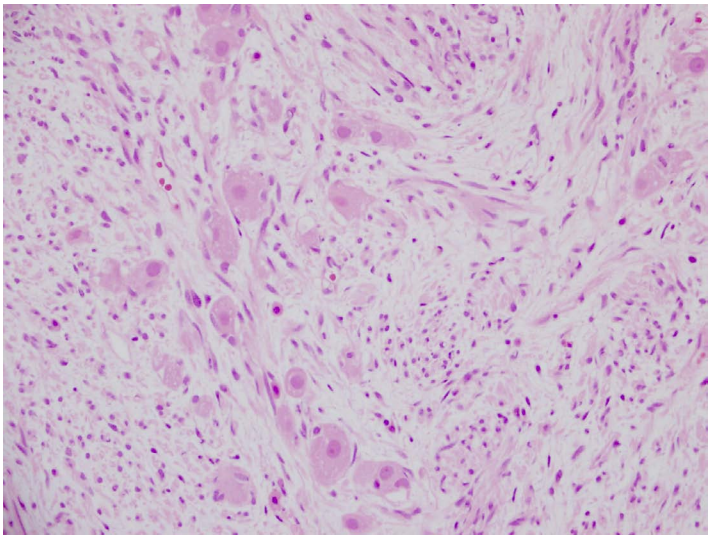


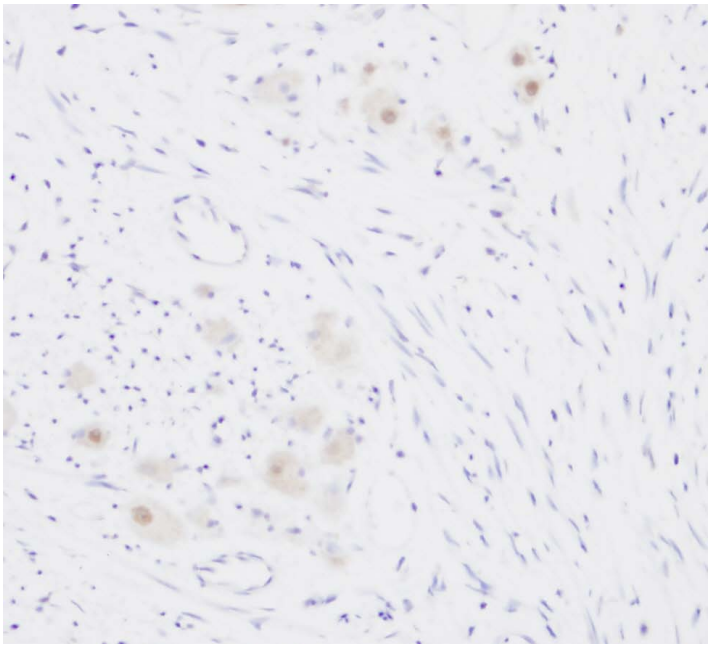
Figure 2. Mature ganglion cells deposited in a neuromatous stroma (x 20, H & E).



HISTOPATHOLOGICAL ANALYSIS

Histologically, this tumor has a uniform appearance throughout the bladder mucosa under urothelium. The tumor background consists of bundles of Schwann cells. Mature ganglion cells are scattered throughout spindle cells (Figure 2). The neuromatous portion of the tumor has a strong and diffuse expression of S-100 protein (Novocastra, NCL-L, 1:200) (Figure 3). Variable-sized mature ganglion cells exhibit immunoreactivity with neuronal nuclear antigen (Abcam, ab104225, 1:4000) (Figure 4). The presence of Ki-67 staining is under 1% at the spindle cells of the tumor.

Figure 3. Mature ganglion cells exhibit immunoreactivity with neuronal nuclear antigen (x 20, H& E).

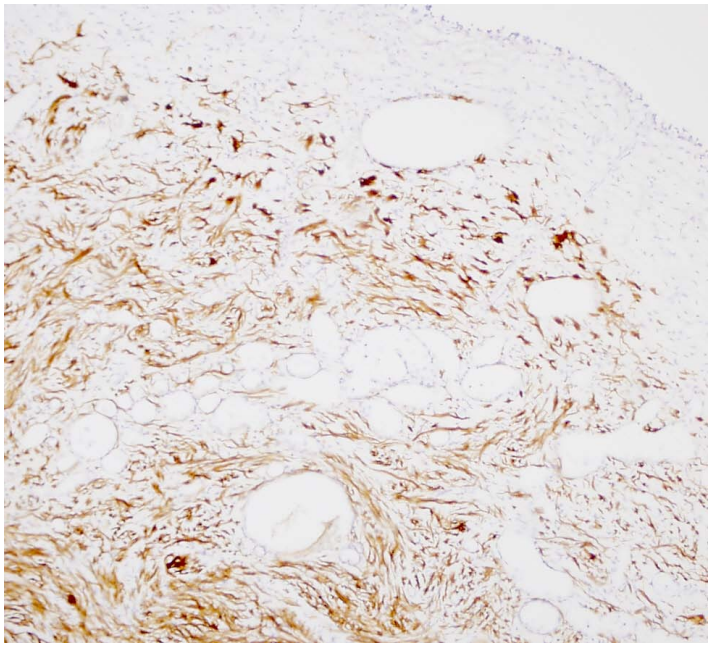


DISCUSSION

Peripheral neuroblastic tumors are categorized as NBs, GNBs and GNs in a spectrum that starts from NBs, which are the most primitive form, and extends to GNs, which are the most mature form. GNs contain a predominantly ganglioneuromatous component, whereas GNBs contain a predominantly ganglioneuromatous component with a minor neuroblastomatous component. Unlike these 2 tumors, NBs predominantly contain a neuroblastomatous component. Disease prognosis is worsened by an increase in the neuroblastomatous component [12].

GN is a neurogenic tumor that is seen very rarely in the bladder, and it has a benign clinical prognosis. Five case reports exist in the current literature in which bladder-located, composite paraganlioneuroma-ganglioneuromas are documented [5-9]. However, there have been 2 previously documented cases of bladder-located, pure GN. Previously reported GN-related

Figure 4. Strong end diffuse expression of S-100 protein in neuromatous portion of the tumor beneath the urothelium (x 10, H & E).



lesions are generally in the posterior mediastinum, which is the most common location, and in the retroperitoneum [7,13,14]. GN at these locations present either as an asymptomatic, slow-growing mass that is identified incidentally, or as a massive form that presents with pressure symptoms. Treatment for these cases is surgical removal of the lesion. So far, there have not been reports of recurrence or metastasis after surgery. One parameter that indicates that the tumor tends to show a benign progress is a low Ki-67 proliferation index. As in the other 5 composite paraganglioma-GN cases, the Ki-67 proliferation index in our patient is less than 1% as well, and it is stated that the lesion does not have malignant potential. The tumor is comprised of ganglion cells that are histologically on varying differentiation grades and of Schwann cells. While ganglion cells stain positive on neuronal-specific enolase staining, the spindle cell component stains strongly with the S-100 protein [15]. In our case, the tumor was composed of mature and immature ganglion cells and Schwann cells. Since the neuroblasts did not consist of an evident bundle structure, they were diagnosed as GNs.

In the literature, another case report documenting a bladder GN has been published in Japan. The tumor was identified in an adult dog, which had developed recurrent oliguria. A 2.5 cm x 1.0 cm solid mass located at the trigone of the bladder has not recurred or metastasized after open surgical resection [16].

In clinical practice, urologists mainly follow the same algoritm for commonly seen bladder tumors. Nevertheless, rare bladder neoplasms cause ambiguity for practicians. Another rare neoplasm of the bladder, which is not familiar for urologists, is perivascular epithelioid cell tumors (PEComas). PEComas co-express smooth muscle and melanocytic immunohistochemical markers [17]. As there are just a few malignant cases, PEComas are considered of unknown malignant potential. Similar to GNs, a few cases of PEComas have been reported previously in the urinary system.

In a multicenter study, prognostic subgroups of 552 patients in whom GN and GNB were identified by histopathological analysis were defined in detail for the first time [1]. In this study, of 43 patients diagnosed with GN, 40 patients underwent complete resection and 3 patients underwent incomplete resection. None of these patients have had a recurrence or died from tumor burden, thus showing that the prognosis in this group has been perfect.

Neurogenic tumors do not have a distinguishing appearance on conventional scanning methods. Therefore, when any lesion that is localized to the retroperitoneum or mediastinum is identified, neurogenic tumors are considered in the differential diagnosis. However, a neurogenic tumor that is localized in the bladder can be diagnosed only histopathologically. On cystoscopy, the macroscopic appearance of a dirty gray-colored, hard, dense, lobulated lesion might lead to consideration of a diagnosis other than that of a bladder tumor. When such a lesion is encountered on cystoscopy, GN should be considered in the differential, and required histopathological analysis should be performed to obtain a diagnosis.

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