A case of ganglioneuroma of the ureter and review of the literature

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Abstract
Ganglioneuroma is a rare tumor originating from neural crest tissue of the sympathetic nervous system. We report on an approximately 55-year-old woman who was admitted to hospital with abdominal pain. Surgery revealed a tumor in her right ureter, which was pathologically confirmed as a ganglioneuroma. The patient underwent transabdominal total hysterectomy, bilateral adnexal resection, release of pelvic and intestinal adhesions, right ureteroscopy, right ureteral lesion excision, and ureteral anastomosis. A literature review indicated that most ganglioneuromas are benign tumors. Clinicians may consider total or subtotal tumor resection, depending on the tumor location and patient's condition. The patient's clinical condition may improve after surgery combined with periodic long-term follow-up.

Keywords
Ganglioneuroma, ureter, immunohistochemistry, case report, tumor resection, hysterectomy

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Introduction
Ganglioneuroma is a rare benign tumor originating from sympathetic nerve cells, and represents a histological subtype of peripheral neuroblastoma. Ganglioneuroma can occur at any age, but is more common in children over 10 years of age. Tumors usually occur in the paraspinal sympathetic plexus,1 with the most common sites including the retroperitoneum, adrenal glands, and posterior mediastinum,2 with rare occurrences in the gastrointestinal region3 and even rarer cases in the urinary system, with only sporadic reports.4 We report a case of ganglioneuroma in the ureter, and review and analyze the clinical manifestations,

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imaging diagnoses, pathologic features, and clinical courses of similar cases in the literature, with the aim of improving the diagnosis and treatment of this disease.

Case presentation

The reporting of this study conforms to CARE guidelines.⁵ The patient’s personal details have been removed. The patient and their family were informed that the data and accompanying images would be submitted for publication, and they signed an informed consent form for treatment and for publication of this report (a copy can be provided to the journal as required). This case report was approved by the ethics committee of Maoming People’s Hospital (PJ2022MI-k004-01), Maoming, Guangdong Province, China.

An approximately 55-year-old woman was hospitalized in November 2020 with a history of abdominal pain with cessation of defecation and flatulence for more than 10 days. The abdominal pain was mainly located in the right lower abdomen, with persistent distension and lack of defecation and flatulence, without nausea, vomiting, dizziness, headache, chills, or fever. The patient had previously been seen at a local hospital, and abdominal plain film x-ray examination showed pneumatization of the intestine and dilatation of the right ureter. After receiving anti-infective and rehydration treatment, the patient’s abdominal pain was slightly relieved, but defecation and flatulence were still absent, and she was therefore transferred to our hospital for emergency treatment. Upper abdominal computed tomography (CT) combined with 3D reconstruction showed that the right ureteral pelvic segment was poorly visualized (poorly defined with the right part of the cervix), with mild hydronephrosis in the upper ureter and right kidney. CT urography showed a soft tissue nodule next to the right side of the uterine cervix, suggesting a tumor lesion with invasion or compression of the right ureteropelvic segment. The patient underwent transabdominal total hysterectomy, bilateral adnexal resection, release of pelvic and intestinal adhesions, right ureteroscopy, right ureter retrograde intubation, right ureteral lesion excision, and ureteral anastomosis.

Intraoperatively, a right ureteral mass measuring 4.0 × 3.0 cm was found. In section, the tumor was a yellowish-gray solid mass with no obvious envelope, invading the ureteral lumen, with no normal ureteral mucosa in the eroded part of the tumor. A tumor measuring about 1.0 × 0.5 cm was found in the right vaginal dome stump. Postoperative pathology revealed no obvious tumor cells in an ascites smear. The uterus showed proliferative endometrium, chronic inflammation of the cervix, and lymphocytes in the local muscular and plasma layers, considered to be associated with chronic inflammation, but no obvious abnormalities in the bilateral adnexa. There was chronic inflammation in the right vaginal stump. Immunohistochemistry of uterus samples showed cytokeratin (CK) (+) in the endometrium, CD56 (−), synaptophysin (syn) (−), Ki67 (focal +), and leukocyte common antigen (LCA) (focal +). Examination of the right ureter showed no abnormality in the ureter mucosa, but the wall of the ureter showed severe chronic inflammation with neurofibrillar tissue hyperplasia, lymphocytic infiltration, and localized nerve bundle hyperplasia with ganglion cells, suggesting ganglion cell neuma. Immunohistochemistry of the right ureter showed CD3 (focal +), CD20 (focal +), CK (−), Ki67 (10% +), S-100 (+), CD56 (+), syn (−), and chromogranin A (−) in one wax block (Figure 2), and CK (−), Ki67 (1% +), and LCA (+) in another wax block. The final pathological diagnosis was ganglioneuroma. The patient was satisfied with their treatment and was followed
up for 1 year after discharge, with no tumor recurrence.

We also carried out a literature review by searching the PubMed and China Knowledge Network databases for studies published from 1980 to 2021 using the search terms: (gangliocytoma OR gangliomeuroma OR gangliocytoma OR gangliocytoma OR ganglion cell neuroma OR ganglioblastoma) AND (subject: kidney – ureter – bladder – urethra). Using this strategy, we identified 10 reported cases in 10 papers. The age, location, clinical features, and follow-up features of the patients are shown in Table 1.

**Discussion**

Ganglion cell neuromas consist of mature ganglion cells and nerve fibers. Based on the current literature review, the mean age of onset of urological ganglion cell neuroma was $25.9 \pm 12.2$ years, with a male to female ratio of 2:3 (4 men and 6 women), with a slightly higher incidence in women than men, consistent with the report by Liying et al.6 The mean age of onset in men was $24.3 \pm 19.3$ years (2–49 years) and the mean age of onset in women was $27.0 \pm 6.5$ years (19–34 years).

According to the International Neuroblastoma Pathology Classification, neuroblastoma, ganglioneuroblastoma, and ganglioneuroma represent a spectrum of maturation from neuroblastoma as the most primitive form to ganglioneuroma as the most mature form,7 with ganglioneuroblastoma maturation defined as the link between these two. Decarolis et al. found that the median age at diagnosis increased with increasing neuroblastoma differentiation.8 Taken together, these data suggest that age can be used as a prognostic factor.

Most ganglioneuromas are slow-growing benign tumors. The disease may be asymptomatic in the early stages, and is only detected during routine physical examinations in some patients. However, a few patients develop local pressure symptoms, such as abdominal pain, because of pressure on adjacent tissues. This report focused on ganglion cell neuromas occurring in the urinary tract. Ganglioneuromas at these sites can cause urinary tract obstruction with lower urinary tract symptoms and pelvic pain, as well as complications of secondary to local compression. There have been rare cases of ganglioneuromas associated with

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**Figure 1.** Histopathology of ganglioneuroma (original magnification 10×10; hematoxylin and eosin). Ganglion cells are present the in hyperplastic nerve fiber bundle.

**Figure 2.** Histopathology of the ovary (original magnification 10×10; hematoxylin and eosin). The green arrow indicates formation of white bodies in the ovary medulla after menopause, and the red arrow indicates thick-walled vessels in the medulla. No ganglioneuromas were found.
| Reference          | Sex  | Age (years) | Side and location | Size CM                     | Clinical symptoms                                                                 | Treatment       | Metastasis       | Complications                          | Follow-up |
|--------------------|------|-------------|-------------------|----------------------------|----------------------------------------------------------------------------------|-----------------|-----------------|----------------------------------------|-----------|
| Yue et al. 4       | F    | 23          | Bladder           | 23                         | None                                                                             | No surgery      | None            | None                                    | NR        |
| Le Ji'an et al. 9  | M    | 1           | Kidney/right      | 2, 6 (C2)                 | Diarrhea                                                                        | TR              | WDHA            | None                                    | 1 y NR    |
| Cooper et al. 10   | F    | 3           | Kidney/left       | 0, 3 (C2)                 | Abdominal pain                                                                  | TR              | Renal artery inflammation             | None                                    | 1 y NR    |
| Qi et al. 15       | F    | 33          | Bladder           | 3, 4 (diffuse polypoid protuberances) | Frequent micturition, and dysuria                                              | TR              | NM              | Symptom of local compression            | NM        |
| Shuangyue et al. 17| F    | 9           | Kidney/left       | 1, 9 (C2)                 | None                                                                             | TR              | None            | None                                    | None      |
| Minghao et al. 18  | M    | 25          | Kidney/right      | 25, 6 (C2)                | Abdominal pain                                                                  | TR              | None            | Mass complicated with severe hydronephrosis | 2 y NR    |
| Zhang et al. 19    | M    | 4           | Kidney/left       | 4, 6 (C2)                 | Abdominal pain                                                                  | TR              | None            | Clear cell carcinoma of 6 months distant metastasis | NR        |
| Cai et al. 20      | M    | 22          | Bladder           | 22, 3 (x 3.5)             | Frequent micturition, urgent urination, odynuria                                | TR              | None            | None                                    | NR        |
| Hua et al. 21      | M    | 21          | Hilus renalis/ left | 1.3 x 1.3 x 1.1           | Abdominal pain                                                                  | TR              | None            | None                                    | NR        |
| Ying et al. 22     | F    | 22          | Bladder           | 10, 8 x 4                 | None                                                                             | TR              | None            | None                                    | NR        |
watery diarrhea, hypokalemia, and achlorhydria syndrome, such as the case reported by Lejian et al., as well as renal ganglioneuroma presenting as an apparent renal artery aneurysm, and retroperitoneal ganglioneuroma presenting as obstructive pyelonephritis, all secondary to local compression and requiring a combination of imaging and pathology to achieve a differential diagnosis.

Based on the cases collected in this paper, most ganglioneuromas have a good prognosis, with no recurrence detected at 1 to 2 years of follow-up. Only one patient with combined renal clear cell carcinoma developed distant metastases 7 months after surgery and had a poor prognosis. A small number of ganglioneuromas can undergo malignant transformation, and reports in the literature demonstrate two differentiation tendencies: the development of neuroblastoma, and transformation to malignant nerve sheath tumor; however, very few spontaneously transform to malignant nerve sheath tumors. Pathology is the gold standard for confirming the diagnosis of ganglion cell neuroma, which demonstrates a large number of ganglion cells in microscope sections, against a Schwann cell interstitial background, with the most common characteristic being the presence of mature ganglion cells. In most cases, the ganglion cells were positive for S-100 protein, as in the present case report. Immunohistochemistry can be used as a reference to determine the origin of the tumor and for a differential diagnosis, especially in confusing cases.

CT is currently the imaging method of choice for ganglioneuroblastoma. CT has a high soft tissue-density resolution that can clearly show changes such as subtle calcification and necrotic liquefaction within the mass. In addition, enhanced scans can also provide insights into the lesion’s blood supply, the surrounding vessels and their relationship to the mass, tumor metastasis, and the extent of invasion, which can make a diagnosis of a typical ganglioneuroma and thus provide an accurate basis for surgical treatment.

Because ganglioneuromas are usually considered to be benign tumors, surgical resection is the main treatment and chemotherapy is generally not recommended. Depending on the location of the tumor and the quality of life requirements, some patients only underwent subtotal tumor resection, with no signs of tumor enlargement and no distant metastases after 7 months of postoperative follow-up. The current case confirmed the recommendation of Duhem-Tonnelle et al., who suggested that ganglioneuromas could be treated without radical resection, and subtotal resection, without endangering vital structures, was sufficient. Decaroli et al. found that patients with partially resected masses who underwent incomplete resection did not experience tumor progression if the tumor remnant was less than 2 cm. In conclusion, surgical treatment alone may be sufficient for patients diagnosed with ganglioneuroma, including total or subtotal resection depending on the situation, while regular long-term follow-up is essential.

Conclusions
The current patient was admitted to hospital with abdominal pain and cessation of defecation. A ureteral mass was found on CT examination, and the final pathological diagnosis after surgery was a nodular neuroma arising in the ureter. A literature review and case reports indicated that age could be a prognostic factor. The clinical presentation of ganglioneuroma is relatively insidious, and pathological examination together with imaging techniques provide the gold standard for its diagnosis. Given that most ganglioneuromas are benign, clinicians can consider performing total or subtotal resection, depending on tumor location.
location and the general condition of the patient, with regular long-term follow-up, generally leading to favorable outcomes.

**Author contributions**
KL performed the case report and wrote the manuscript; CX and YX contributed to the pathological specimens.

**Declaration of conflicting interests**
The authors declare that there is no conflict of interest.

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