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Ex vivo excision of retroperitoneal soft tissue tumors: A case report

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Abstract. Ganglioneuromas are slow growing, clinically silent benign tumors for which surgery is considered to be the standard treatment. However, surgical excision in cases where surrounding structures are involved can be challenging. The present study reports a novel technique of *ex vivo* excision for the management of a retroperitoneal ganglioneuroma in a 21-year old patient, that appeared to be inoperable using standard surgical resection. Preoperative investigations revealed a large tumor with encasement of the origins of the superior mesenteric artery (SMA) and bilateral renal arteries. Initially, to prevent the need to explant the liver, the distal SMA (with takeoff of the replaced common hepatic artery) was anastomosed to the splenic artery. The bulk of the tumor along with the bilateral kidneys was mobilized from the retroperitoneum, and the aorta and inferior vena cava (IVC) were cross-clamped above and below the tumor and divided. The two kidneys were dissected free of the tumor at the back-table and were auto-transplanted in a standard technique following the reconstruction of the aorta and IVC. The patient tolerated surgery well and a one-year postoperative follow-up did not show any sign of tumor recurrence. Although technically demanding, *ex vivo* resection and auto-transplantation of the involved organs can be introduced as a final option for the treatment of tumors that are un-resectable using standard surgical techniques.

Introduction

Ganglioneuromas (GNs) are rare, slow-growing benign tumors arising from the sympatho-adrenal neuroendocrine system (1,2). GNs typically occur in children and adolescents, with up to 60% of patients <20 years old at the time of diagnosis. Additionally, females are more likely to be affected than males (3). GNs are the benign ends of a wide spectrum of peripheral neuroblastic tumors, which also include neuroblastoma, ganglioneuroblastoma and ganglioneuroblastoma intermixed (2,4). GN can be diagnosed *de novo* in healthy patients or in specific cases result from spontaneous or chemo- or radiotherapy induced maturation of less-differentiated neuroblastic tumors (neuroblastoma and ganglioneuroblastoma) (1,5). In addition, certain studies have presented an association between GNs and specific familial diseases including neurofibromatosis type 2 and multiple endocrine neoplasia type 2 (6,7). While GNs can occur anywhere along the sympathetic nervous system, the two most common locations of occurrence are the posterior mediastinum and retroperitoneum (6). Retroperitoneal tumors may originate from the adrenal glands or extra-adrenal tissues (6). There are a limited number of studies reporting tumor occurrence in uncommon locations, including the tongue, bladder, uterus and skin (8-10).

Although complete surgical excision is considered to be the treatment of choice in the management of these tumors, occasionally it can be challenging and in specific cases (such as when large tumors are involving the surrounding vital organs) it is not a feasible option. The current case report presents an innovative surgical approach to the management of a large retroperitoneal GN that was initially considered inoperable due to its encasement of major visceral vasculature. To the best of our knowledge, this is the first report of an abdominal cavity tumor managed by *ex vivo* tumor resection and bilateral renal auto-transplantation.

Case report

Patient. A previously healthy 21-year-old male was referred to the Columbia Presbyterian Hospital medical center (New York, NY, USA) with a large retroperitoneal tumor. The tumor was diagnosed almost a year prior to referral, following imaging studies, including computed tomography (CT) and magnetic resonance imaging (MRI), which were performed to investigate abdominal pain. Image-guided biopsy confirmed the diagnosis of GN; however, the date of surgical resection was deferred due to encasement of major visceral vessels. At the time of referral to the Columbian Presbyterian Hospital medical center, the patient was experiencing worsening epigastric pain accompanied by nausea. General laboratory work-up results were within normal limits (white blood cells, 7,000/l; hemoglobin, 11.1 g/dl; serum creatinine, 0.74 mg/dl). Contrast-enhanced CT scans revealed

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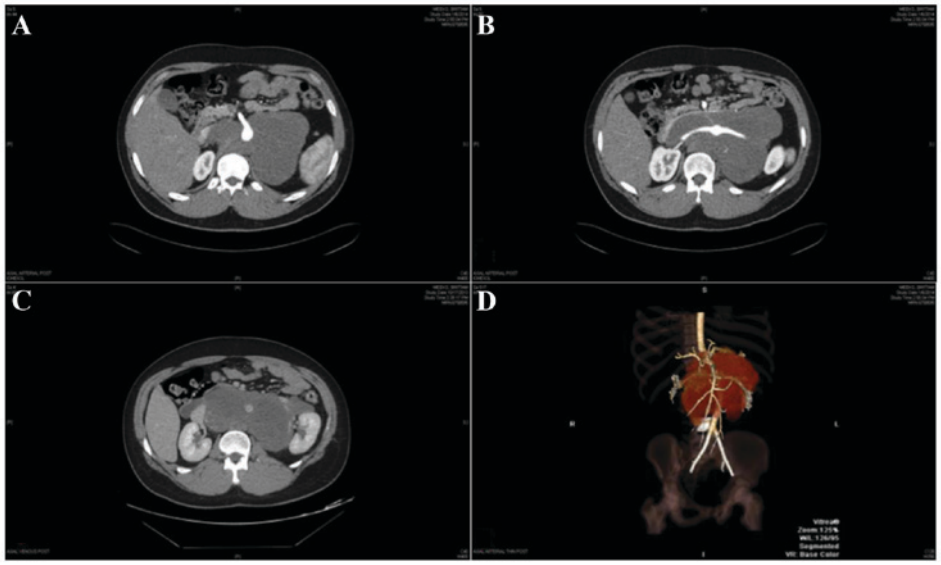

Figure 1. CT angiogram images of the tumor demonstrate (A) encasement of the origin of the superior mesenteric artery, (B) encasement of the origins of the bilateral renal arteries and (C) involvement of the inferior vena cava at the level of right renal vein. (D) Reconstructed CT angiogram image of the tumor showing encasement of the origin of superior mesenteric artery and bilateral renal arteries. CT, computed tomography.

a large (11.5x19.4x16.0 cm) homogeneously hypo-dense retroperitoneal mass, occupying almost the entire abdominal cavity, with a lateral displacement of the bilateral kidneys (Fig. 1). The tumor size was significantly larger compared with the patient's previous MRI scan, which was performed approximately a year earlier. CT angiography revealed that the aorta was encircled by the tumor without any obvious invasion, that the inferior vena cava (IVC) exhibited tumor involvement; the common hepatic artery was totally replaced at the origin from the superior mesenteric artery (SMA); there was a replaced left hepatic artery at the origin from the left gastric artery; and the origin of the SMA and both renal arteries were encased by the tumor (Fig. 1). A positron emission tomography-CT scan did not reveal any signs of metastasis. Considering the worsening clinical symptoms and growing size of the tumor, the patient underwent surgical resection.

Surgical technique. The abdominal cavity was accessed through a midline incision with bilateral subcostal extensions. The tumor was visible in the middle of abdomen. Subsequent to mobilizing the duodenum and right hemi-colon, the distal portion of the SMA was exposed and the splenic artery was isolated. The common hepatic artery was completely replaced with origin arising from the SMA. The SMA was dissected down to the aorta. Since the SMA origin was encased by the tumor, the distal section of the SMA (with a completely replaced common hepatic artery) was anastomosed to the splenic artery (a branch of the celiac artery) subsequent to ligating the distal splenic artery. Subsequently, the tumor and the bilateral kidneys were further mobilized from the retroperitoneum. The right adrenal gland was carefully preserved; however, the left adrenal gland was mostly removed with the tumor specimen. The aorta and IVC were then cross-clamped above and below the tumor and divided, as both structures were encased by the tumor. Following the dissection of the tumor from additional retroperitoneal attachments and division of the two ureters, the tumor and bilateral kidneys were removed to the back-table.

The kidneys were flushed with Ringer's lactate solution at the back table and the two kidneys were removed from the tumor. While the kidneys were being prepared for auto-transplantation, the aorta and IVC were replaced by a 19 mm Dacron IMPRA® F3519 graft (BARD Peripheral Vascular, Inc., Tempe, AZ, USA) and a 20 mm ringed-Gortex MAQUET 095220 graft (Boston Scientific, Marlborough, MA, USA), respectively. Following the restoration of flow through the aorta and the vena cava, the right kidney was auto-transplanted to the right groin in a standard manner and successfully reperfused (cold ischemia time, 3 h 33 min) (11). The left kidney was subsequently implanted to the left groin and reperfused uneventfully (cold ischemia time, 4 h 57 min). The blood flow to the two kidneys was examined using Doppler ultrasound, which revealed arterial and venous flows and waveforms to be normal. Subsequent to the completion of hemostasis, ureteroureterostomy anastomosis was performed over double J stents in both sides. The surgery was uneventful and the patient was transferred to surgical intensive care unit for monitoring. Continuous veno-venous hemodialysis was continued until post-operative day five and subsequently stopped as the serum creatinine level normalized. The post-operative course was complicated by prolonged ileus possibly attributed to narcotic use. The patient was discharged home 19 days after surgery. At the one-year follow-up appointment, the patient was doing well and a follow-up CT scan did not reveal any signs of recurrence.

Specimen. The tumor presented as a semi-firm multi-lobulated tan-white mass measuring 21.5x18.1x7.8 cm. Samples (4 μm thickness) were fixed with 10% neutral-buffered formalin solution for 6 h at room temperature, stained for S-100 protein and examined with a light microscope [for staining, Rabbit anti-S100 (cat. no. 760-2523) was used as primary and iVIEW DAB Detection kit (cat. no. 760-091) as secondary antibody (both Ventana Medical Systems, Inc., Tucson, AZ, USA) incubated for 30 min at 37˚C]. Upon histopathological

examination, the tumor was observed to be composed of interwoven bundles of neurofilaments (stained strongly positive for the S-100 protein) and Schwannian-like spindle cells on a loose and edematous background without signs of nuclear atypia or mitoses. This was consistent with the diagnosis of ganglioneuroma. Surgical margins were free of the tumor.

Discussion

GNs originate from neural crest cells (12). GNs are clinically silent tumors and are usually identified incidentally during routine imaging studies. When GNs become symptomatic, it is mainly due to the effect of the tumor mass on neighboring organs (12). Furthermore, these tumors are capable of excreting a wide variety of neuropeptides, and clinical presentation with signs and symptoms owing to hormone excess including hypertension, diarrhea and sweating is infrequent (2,13). Despite the availability of different non-invasive radiologic modalities e.g., CT scans and MRI scans, a definitive pathological diagnosis of these tumors is dependent on the post-operative histopathological findings and in certain instances pre-operative image-guided biopsies (6,14,15).

The prognosis of patients following complete surgical removal of the tumor is excellent, without any need for adjuvant or neoadjuvant radio- or chemotherapy (2,6). However, surgical excision in the case of the tumors involving surrounding anatomic structures, particularly visceral vessels, can be demanding and occasionally not feasible. Besides a high rate of reported surgery-related complications (including neurological dysfunctions) in the literature, in a number of studies patients underwent elective nephrectomy to make the tumor resectable (16-18). In the presented case, surgical resection was initially deferred due to encasement of the aorta, IVC, origins of the superior mesenteric artery and bilateral renal arteries. Previously, complete resection of the tumor with reconstruction of major vascular structures was shown to be a safe method with acceptable outcome for complete resection of large retroperitoneal tumors including sarcoma (19-22). However, even in these studies, nephrectomy appeared to be inevitable in order to meet the oncological standards of complete resection (20,22). In the case of the present study, considering the bilateral involvement of the origin of renal arteries, nephrectomy would have left the patient requiring lifetime dialysis. The shorter cold ischemia time may result in a faster post-implantation renal function recovery. Wan *et al* introduced fractionated resection as a novel method for completing the resection of retroperitoneal tumors surrounding major vessels (23). Considering the slow-growth pattern of the tumor and the possibility of late recurrence, long-term follow-up of the patients including vigilant physical examination and repeated imaging studies is an important part of the post-operative management (23).

In conclusion, although routine surgical excision is the treatment of choice in the management of retroperitoneal GNs, occasionally complete *in vivo* resection is deemed to be impossible due to extent of involvement of surrounding vital structures. In such cases, *ex vivo* resection with auto-transplantation of the explanted organs may offer the most effective method for improving patient prognosis.

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