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Case report

Unclear retroperitoneal tumors, an interdisciplinary challenge – A case report and review of the literature☆

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ABSTRACT

Introduction and importance: Unclear retroperitoneal tumors impose major challenges for clinicians. Tumors can originate primarily from retroperitoneal tissue or secondarily invade into the retroperitoneum. While benign lesions also occur, malignant tumors are far more common. Clinical presentation depends on replacement or invasion of other organs and is therefore highly variable. The heterogeneous tumor composition makes a definitive preoperative diagnosis difficult. Surgical resection is the gold standard for treatment but often proves challenging due to frequent involvement of large retroperitoneal vessels.

Case presentation: We present the case of a 70-year old woman diagnosed with a large, unclear retroperitoneal tumor. Initial clinical symptoms were increasing dyspnea and dysphagia in our clinic. Gastroenterologic and cardiologic workup was unremarkable. Computed Tomography (CT) revealed a large retroperitoneal mass in the right upper abdomen with severe displacement of the inferior vena cava and renal veins. The patient was scheduled for primary tumor resection. The procedure was challenging due to the vessel involvement and large blood pressure alterations during tumor mobilization. The post-op pathologic workup then revealed the rare finding of a completely resected paraganglioma. The post-surgical course was uneventful. One year after diagnosis, the patient is relapse-free.

Clinical discussion: Among retroperitoneal tumors, paragangliomas and pheochromocytomas are rare tumor entities. Asymptomatic, sporadic disease is hard to identify preoperatively and can cause unexpected complications in the OR. An experienced team is crucial in achieving best short- and long-term outcomes.

Conclusion: This case impressively shows the challenges of retroperitoneal tumors and the importance of interdisciplinary work in these cases.

1. Introduction

The unclear retroperitoneal tumor remains a major diagnostic and therapeutic challenge for clinicians of multiple disciplines. The majority of these lesions are malignant tumors and their clinical presentation is dependent on involvement of surrounding organs. Paraganglioma and Pheochromocytoma are rare tumors of the sympathetic nervous system that can occur in the retroperitoneum. They can be silent or endocrinologically active. Preoperatively asymptomatic tumors can prove challenging for the OR team of surgeons and anesthesiologists due to intraoperative catecholamine release. The prognosis is dependent on complete tumor resection and the presence or absence of metastases. This report offers a complete clinical workup at a German university hospital of a large paraganglioma including a review of the literature. This case report is compliant with the SCARE guidelines 2020 [1].

2. Case presentation

A 70-year old female (BMI 23 kg/m^2) was admitted to our surgical clinic with the diagnosis of an unclear right-sided retroperitoneal tumor.

Abbreviations: IVC, inferior vena cava; PGL, paraganglioma; PCC, pheochromocytoma; PPGL, paraganglioma and pheochromocytoma combined.

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The patient initially presented to her general physician with exercise-related dyspnea, retrosternal pain, and dysphagia.

Initial cardiologic (ECG, long-term blood pressure (BP) measurement, echocardiography) and gastroenterologic workup was without pathologic finding. Contrast-enhanced Computed Tomography (CT) of the abdomen revealed an unclear subhepatic retroperitoneal tumor of $15 \times 12 \times 14$ cm. The tumor showed displacing growth without signs of infiltration into adjacent organs or metastatic spread. Importantly, the inferior vena cava (IVC) and left renal vein were stretched by the tumor.

At the time of presentation in our clinic, the patient was in good physical shape (WHO performance status 0). Medical history only included a hemithyroidectomy in 2013 for thyroid follicular carcinoma in 2013 with regular follow-up. Echinococcus serology was negative. Permanent medication only included thyroid hormone substitution. The family history was empty.

2.1. Radiologic workup

In the given scan the origin of the mass remained unclear. However, it showed expansive growth from between the aorta and the IVC while displacing the IVC, suggesting that the lesion likely arose from this location. It could not be clearly separated from the right adrenal gland, so an adrenal tumor was unlikely but not excluded. The mass appeared predominantly cystic with arterial hyperenhancing septa and solid components, non-typical for hematoma or infectious diseases. Lacking highly invasive growth patterns, the leading differential diagnosis were sarcoma, retroperitoneal paraganglioma, retroperitoneal mucinous cystadenoma/cystadenocarcinoma, and retroperitoneal cystic teratoma (Fig. 1A–D) [2,3].

2.2. Treatment

As there were no signs for irresectability, the patient was scheduled for primary resection one month after the first presentation in our clinic. The procedure was performed by Prof. Dr. D. Henne-Bruns, chief of surgery, PD Dr. Mathias Wittau, attending surgeon, and Dr. Benno Traub, surgical resident. Exploratory laparotomy showed the large tumor in the lesser sac, compressing the pylorus, pushing the liver upwards, and with extended compression of the IVC and hepatoduodenal ligament. The surgical situs after exploration is shown in Fig. 2A. First, the hepatoduodenal ligament was secured with a vessel loop. Next, the liver was completely mobilized with exposure of the hepatic veins and the IVC subdiaphragmatically in order to achieve control over venous backflow. Both renal veins were exposed and secured with vessel loops, as was the IVC distal of the renal vein confluence. Following this, the IVC was dissected from the tumor. The tumor was freed from attachments on the left side of the IVC with the upper margin of the pancreas and the retroperitoneum under careful preparation of the left renal artery and the celiac axis. After complete mobilization, the tumor could be removed *in toto*. Since no clear macroscopic margins were achievable towards the right adrenal gland, it was removed together with the specimen. The situs after tumor resection is shown in Fig. 2B, the tumor itself in Fig. 2C.

Due to the tumor location, control over hemostasis was crucial and all involved vessels were exposed and secured with vessel loops.

Macroscopically, the tumor had a benign appearance. Given the long attachment of the IVC to the tumor, a safety margin as required for malignant lesions was not achievable and a microscopically positive resection margin (R1) could not be ruled out during surgery.

During the operation, the patient showed extensive alterations in systolic BP ranging from 220 mm Hg to 60 mm Hg, requiring extensive pharmacological BP management. There were no bleeding complications during the surgery to explain the BP alterations. Additional compression of the IVC was avoided by lifting the liver upwards during preparation of the IVC. Due to this clinical presentation, the right adrenal gland was removed together with the tumor despite the absence of clinical signs for a pheochromocytoma preoperatively. After tumor removal and repositioning of the IVC in the anatomically correct position, no more BP alterations occurred.

The surgery took 270 min, blood loss was estimated to be 1500 ml.

Postoperatively, the patient was placed in the ICU as was moved to

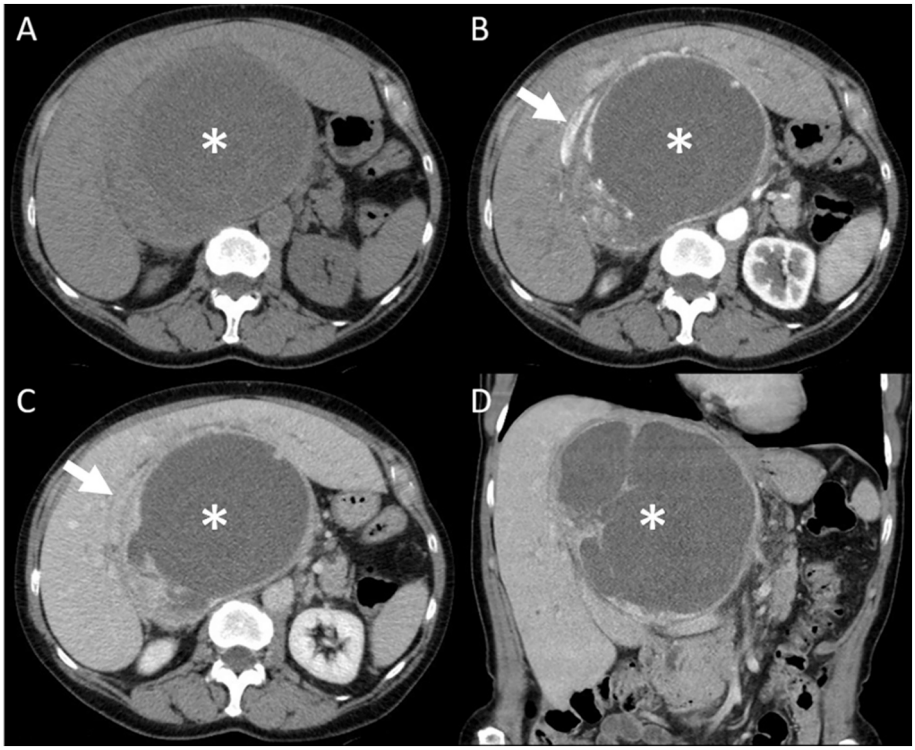

Fig. 1. Pre-operative CT-scan. Native (A) and contrast-enhanced scans (B–D) in transversal (A–C) and coronar (D) sections. Asterix marks the predominantly cystic tumor, the white arrow marks the severely displaced IVC.

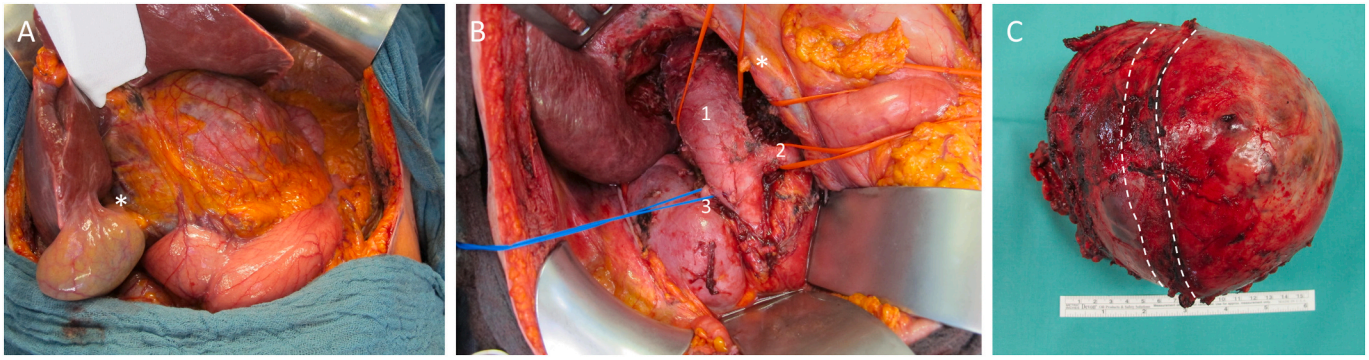

Fig. 2. Surgical tumor resection. A: Situs after explorative laparotomy reveals a large tumor in the lesser sac with displacement of liver, stomach and duodenum, hepatoduodenal ligament, and IVC (*). B: Situs after tumor resection with the IVC repositioned in its original position. IVC (1) and renal veins (2, 3) are secured with vessel loops. C: Tumor after resection, contact with IVC is marked with white dashed line.

the general ward on POD 5.

2.3. Pathologic workup

The surgical specimen was intact and consisted of a unifocal, well-circumscribed tumor measuring 15 × 14.5 × 9.5 cm that adhered firmly to the right adrenal gland. The tumor's cut surface demonstrated extensive hemorrhagic and cystic degeneration. Microscopic examination revealed a slowly proliferating, pseudo-encapsulated, non-invasive neuroendocrine neoplasm with small to pleomorphic chief cells that were surround by sustentacular cells and arranged in sclerotic, trabecular, and organoid patterns (Fig. 3). This led to the diagnosis of a completely excised extra-adrenal sympathetic paraganglioma. Histological grading and risk stratification according to the Grading System for Adrenal Pheochromocytoma and Paraganglioma (GAPP) [4] revealed a low metastatic risk.

2.4. Outcome

The postoperative course was uneventful and the patient was discharged on day 11. Follow-up over one year was without complications and a control MRI was without signs of recurrence. Give the complete tumor resection, no signs of metastatic disease, and the questionable efficiency of systemic treatment [5], adjuvant chemotherapy was not scheduled.

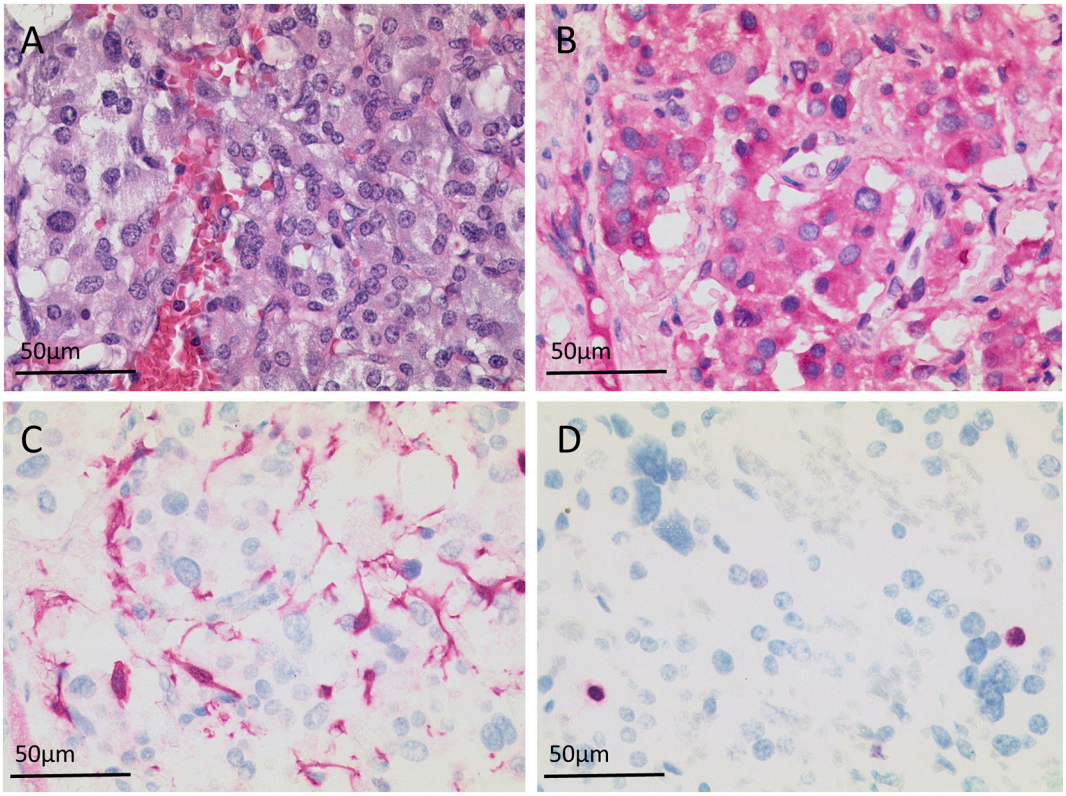

Fig. 3. Pathological workup. Hematoxylin-eosin staining (A) and immunohistochemical staining (B–D) of the excised extra-adrenal sympathetic paraganglioma (magnification 400×). Polygonal medium sized and larger pleomorphic chief cells arrange in an organoid pattern (A). Chief cells stain for the neuroendocrine marker chromogranin-A (B). Sustentacular cells surrounding the chief cells stain for S100 protein (C). Tumor cells show a low proliferative activity in the Ki-67 staining (D).

3. Discussion

3.1. Differential diagnosis and management of unclear retroperitoneal tumors

Solid neoplastic masses in the retroperitoneum must be distinguished between primary retroperitoneal tumors and neoplasms originating in retroperitoneal organs or secondarily invading the retroperitoneal space [6]. The latter include tumors arising in the adrenal glands, kidneys, and excretory system, secondary retroperitoneal organs (pancreas, colon), and systemic dissemination of neoplasms (metastases, lymphomas). These account for the majority of soft tissue retroperitoneal masses [7]. Diagnosis and treatment are based on the guidelines for the respective disease.

Soft tissue tumors, benign and more commonly malignant, are classified by their tissue of origin: Lipomatous, fibrous, smooth and skeletal muscle, vascular and perivascular, chondro-osseous, and tumors of uncertain differentiation [8]. Symptoms are usually nonspecific and patients often present late due to compression of the gastrointestinal or urinary tract [7].

Cross-section imaging is key in the diagnostic workup. CT of the thorax, abdomen, and pelvis is usually preferred for retroperitoneal masses and can offer an estimate of tumor differentiation [9].

Suspected resectable soft tissue sarcomas should undergo upfront surgery due to the risk of track implantation [9,10]. In this case, a soft tissue sarcoma could not be ruled out so primary resection was scheduled.

3.2. Paraganglioma and pheochromocytoma

Paraganglioma (PGL) and the closely related pheochromocytoma (PCC) (described together as PPGL) arise from chromaffin cells in neural ganglia [6,11]. As they are histologically indistinguishable, the WHO uses the anatomical location for classification: While pheochromocytomas arise from the adrenal medulla, paragangliomas arise from extra-adrenal paraganglia [12]. Both tumors are rare with an incidence of about 0.6 cases per 100,000 person-years and pheochromocytomas are at least 4 times more common [13]. Both entities are endocrinologically active tumors that commonly secrete a variation of catecholamines [11].

Genetic susceptibility is a major component of PPGL pathogenesis. More than 20 genes are known to be associated with PPGL development [14]. Over 40% of all tumors are hereditary, making PPGL the most common human hereditary tumor [15].

Clinical presentation is dependent on endocrine activity. The classical symptom triad due to catecholamine release consists of headaches, palpitations, and sweating [16]. Alternatively, PGL and PCC are commonly diagnosed as incidental findings in cross-section imaging and in screenings of genetically susceptible individuals [13]. PPGL-related symptoms, incidental findings, and screens due to past history or genetic risk were each responsible for about a third of PPGL diagnoses [17].

Free plasma levels of metanephrines had the highest sensitivity of 99% of biochemical tests for PCC [18]. In CT diagnostics, chromaffin tumors present as tumors with low lipid content. Functional imaging can be useful, especially in the metastatic setting or with expected multiple neoplasms with ^{68}Ga-DOTA-conjugated somatostatin receptor-targeting peptide PET-CT showing superiority over other functional imaging methods [19].

Biopsies of PPGLs can be associated with a high risk of complications and are not included in current recommendations of clinical practice [15,20].

The only curative approach for PPGL is surgical resection [13]. Excessive intraoperative catecholamine release can cause severe hemodynamic instabilities and associated complications [21]. The Endocrine Society Guidelines therefore recommend premedication with α-adrenergic receptor blockade for patients with hormone-active PPGLs [22]. However, some groups propagated upfront surgery in order not to delay treatment with similar outcomes with and without premedication [23] so upfront surgery may be an option in asymptomatic patients.

A patient's prognosis after PPGL resection is dependent on a number of variables and syndromic diseases and PGL were identified as risk factors for recurrence [24]. The biological aggressiveness of a single tumor cannot be determined by histologic parameters and only the presence of metastases serves as proof for malignant behavior [13]. *In toto* tumor resection without capsule rupture is important for reducing risk of metastatic spread [25]. Management of metastatic disease is based on surgical metastasectomy, local ablation techniques, systemic chemotherapy, and irradiation techniques [13].

Our case combines the rare combination of a retroperitoneal paraganglioma that is not endocrinologically active. This allowed the tumor to reach an impressive size and only became symptomatic after displacement of adjacent organs. Definite preoperative diagnosis by cross-section imaging was not possible and histologic confirmation was avoided due to the risk of track metastasis in case of a sarcoma. Nevertheless, tumor mobilization intraoperatively triggered catecholamine release and resulted in severe blood pressure alterations. The successful complication-free treatment of the patient was only possible in the hands of experienced clinicians in their fields of surgery and anesthesiology in addition to diagnostic workup in radiology and pathology.

Paragangliomas in the literature are often disguised as other, more common masses. Visceral paragangliomas are often misinterpreted as gastrointestinal stroma tumors [26–28], or as tumors originating from the organ where the mass was found originally [29,30]. Our case presentation represents by far one of the largest paragangliomas reported in the literature. Like others, we initially misinterpreted the tumor as a potential retroperitoneal sarcoma due to its sheer size, but the experience in handling large abdominal masses resulted in successful treatment of the patient. This case impressively demonstrates the necessity of a complete differential diagnostic workup.

4. Conclusion

Management of retroperitoneal tumors is challenging and involves a multidisciplinary approach. Paragangliomas and Pheochromocytomas are rare tumor entities. Asymptomatic, sporadic disease is hard to identify preoperatively and can cause unexpected complications in the OR. An experienced team is crucial in achieving best short- and long-term outcomes.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Consent

Written informed consent was obtained from the patient regarding the planned surgery beforehand.

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review on request.

Ethical approval

Not applicable

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CRediT authorship contribution statement

Benno Traub, Johannes Lemke, Doris Henne-Bruns, and Mathias Wittau were responsible for the clinical management of the case. Doris Henne-Bruns, Mathias Wittau, and Benno Traub performed the surgery. Benno Traub and Johannes Lemke and Mathias Wittau wrote the manuscript.

Benedikt Haggenmüller was responsible for the pathologic workup.

Lisa Baumann was responsible for the pathologic workup.

Declaration of competing interest

The authors declare no conflicts of interest.

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