Case Report

Localized Multifocal Retroperitoneal Ganglioneuroma with an Infiltrative Appearance on Imaging: A Case Report

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Abstract

Multifocal ganglioneuromas are characterized by the presence of multiple benign neuro-epithelial tumor nodules and are less common than solitary tumors. A small percentage of ganglioneuromas present with a fatty appearance. Only a few cases of multifocal ganglio-neuromas have been reported, due to both their rarity and minimal symptomatic presentation; therefore, generalizations about risk factors and predictive markers are very difficult. Here, we report a case of multifocal retroperitoneal ganglioneuroma with an infiltrative appearance on computed tomography (CT). The tumor demonstrated slow growth on multiple imaging studies and was associated with abdominal and flank pain. The aggressive appearance eventually led to surgical resection 18 months after the initial incidental finding on CT. Postsurgical analysis of the tumor on imaging was crucial in revealing its nodularity and infiltration, as well as for clarifying its retroperitoneal location inseparable from the adrenal gland. Histology demonstrated Schwann cells and ganglion cells without atypia or increased cellularity, and with no mitosis or necrosis seen. Our case highlights the consideration of ganglioneuroma with fatty infiltration in the differential diagnosis of a fatty tumor in the mediastinum or retroperitoneum. Additionally, our report differentiates multifocal ganglioneuroma with fatty infiltration from lipomatous ganglioneuroma on radiology and histopathology.

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Introduction

Ganglioneuromas are slow-growing benign neoplasms that typically originate from the autonomic ganglion cells of the sympathetic nervous system. These neoplasms are most commonly found in the mediastinum and the retroperitoneum. In the retroperitoneum, they are most commonly associated with the adrenal gland. They usually affect middle-aged adults and have no known risk factors, although multiple ganglioneuromas can be seen with neurofibromatosis type 1, Cowden syndrome, and multiple endocrine neoplasia type 2. Although patients with these tumors are typically asymptomatic, they can occasionally present with pain or sequelae of abnormal hormone secretion, including vasoactive intestinal polypeptide, catecholamines, and testosterone [1]. They are very rare with a reported prevalence of 1 per million [2]. Most cases are discovered incidentally on cross-sectional imaging, with definitive diagnosis coming from the identification of ganglion cells and other neural components on pathology. Standard treatment is surgical resection, which yields an excellent prognosis with little to no complications.

A very small percentage of ganglioneuromas have a fatty appearance on cross-sectional imaging. This appearance may be related to either primary fatty changes that occur in the tumor (lipomatous ganglioneuromas) or infiltration of adjacent fat. Due to their fatty composition, these tumors may be mistaken for other fat-containing neoplasms on computed tomography (CT) and magnetic resonance imaging. Diagnosis of ganglioneuromas with a fatty component may require a combination of the fatty appearance on imaging in conjunction with characteristic findings on histologic examination.

Here, we present a 66-year-old woman with retroperitoneal multifocal ganglioneuroma with fatty infiltration. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000534060). Reporting more cases of this subtype of ganglioneuroma is necessary to better define its characteristics and help differentiate it from other lipomatous neoplasms in the retroperitoneum and mediastinum.

Case Report

A 66-year-old woman presented for further workup of a left renal mass which was discovered on ultrasound imaging 2 months prior to presentation. The left renal mass measured 3.3 cm and demonstrated contrast enhancement on CT, raising high suspicion for renal cell carcinoma (Fig. 1b).

Incidentally, a 4.5 cm ill-defined right retroperitoneal mass was also seen on imaging. This was inseparable from the right adrenal gland, had mild enhancement of several soft tissue nodules, and demonstrated possible infiltration of the retroperitoneal fat (Fig. 1). The central soft tissue component of the mass measured 4.1 × 3.0 × 4.5 cm, but the overall size of the mass, including the infiltrative portion extending into the pericaval fat, measured approximately 10 cm. There was a lobulated lateral margin and ill-defined medial and anterior margins. The mass was inseparable from the inferior vena cava (IVC) and displaced the IVC anteriorly (Fig. 1b). The ill-defined anterior border along the IVC is best seen in the sagittal plane (Fig. 1c). The left adrenal gland appeared normal.

Right flank pain was the only reported symptom associated with the tumor. The patient had a clinical history of hypothyroidism and hyperlipidemia, both were managed medically with levothyroxine and atorvastatin, respectively. Surgical history consisted of laparoscopic cholecystectomy in 2010. Physical examination demonstrated right flank tenderness. The patient had no pertinent family history.
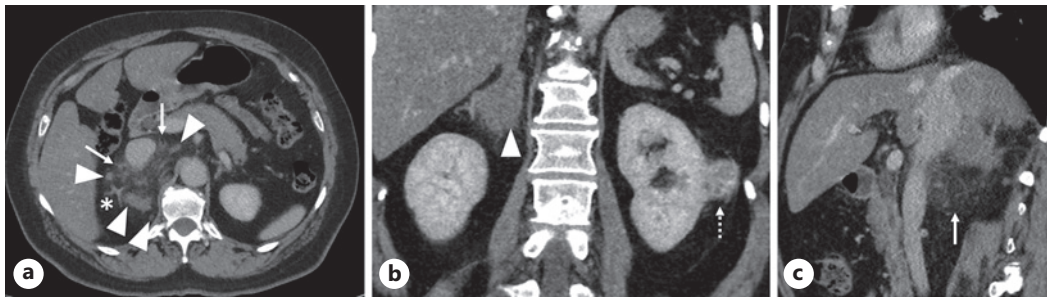
Case Reports in Oncology

Case Rep Oncol 2023;16:1142–1147

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Fig. 1. Axial (**a**), coronal (**b**), and sagittal (**c**) images on contrast-enhanced computed tomography (CT) scans before surgery. There is a lobulated heterogeneous mass with soft tissue components (**a**, **b**, arrowheads) near the right adrenal gland. The tumor demonstrates fat infiltration adjacent to the inferior vena cava (**a**, **c**, solid arrows). An exophytic mass can be seen arising from the left renal interpole (**b**, dotted arrow), which is of heterogeneous density consistent with an incidental renal cell carcinoma. The adrenal gland is marked by a white star (*).

The differential diagnosis of a retroperitoneal mass is broad. However, due to its proximity to the right adrenal gland and the appearance of fat within the tumor, considerations included ganglioneuroma, adrenal adenoma, myelolipoma, lipoma, liposarcoma, angiomyolipoma, collision tumor, metastasis, and myxoid pseudotumor of fat [3]. Adrenal adenoma is the most common benign adrenal mass with microscopic fat, and myelolipoma is the most common benign adrenal mass that contains macroscopic fat [4]. Pheochromocytoma and adrenocortical carcinoma are also considered in the workup of an adrenal mass, although they rarely possess fatty tissue [4].

CT-guided biopsy of the right adrenal mass was performed 3 months later, which demonstrated ganglion and Schwann cells (Fig. 2). No atypia, mitosis, or necrosis was seen. These biopsy findings, in combination with the heterogeneous fatty appearance on CT, suggested either a lipomatous or infiltrative ganglioneuroma. Chest CT showed no thoracic metastases.

For the left renal mass, the patient underwent uncomplicated robotic-assisted laparoscopic partial left nephrectomy. The histologic evaluation revealed a completely excised grade 2 T1a clear cell renal cell carcinoma, which was limited to the kidney.

Follow-up CT imaging 11 months after the initial CT demonstrated that the soft tissue component of the right retroperitoneal mass had grown to 4.7 × 3.3 × 4.6 cm (previously 4.1 × 3.0 × 4.5 cm) with persistent adjacent nodularity. Due to the interval growth, surgical resection of the mass was performed without complications. The tumor was resected in two portions, measuring 8.8 and 6.6 cm in greatest dimension. The largest soft tissue nodule of the tumor was adherent to the adrenal gland, measuring 4.5 cm. On histological examination, the tumor was not well-circumscribed, and fat was present (Fig. 3). The tumor contained ganglion and Schwann cells (Fig. 3). No increased cellularity, atypia, mitosis, or necrosis was seen. Immunostain for S100 was diffusely positive showing no areas of loss. These findings, in combination with the CT appearance, suggested multiple clustered ganglioneuromas with infiltration of retroperitoneal fat.

Discussion

The accurate preoperative imaging diagnosis in this case was difficult. Histologic examination following the initial CT biopsy suggested ganglioneuroma; however, the infiltrative appearance and multifocal nodularity seen on CT were unusual for ganglioneuroma. In
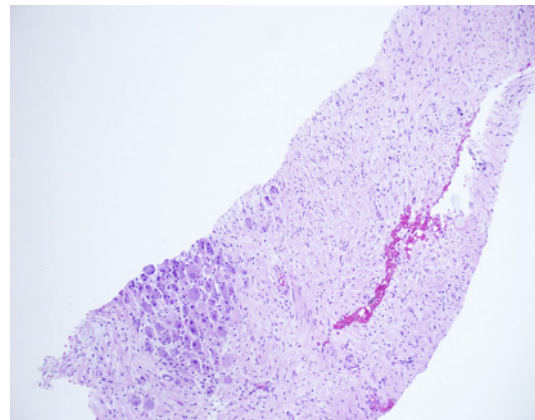
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Fig. 2. Hematoxylin and eosin stained biopsy section showing ganglion cells and spindled neural component in the background.
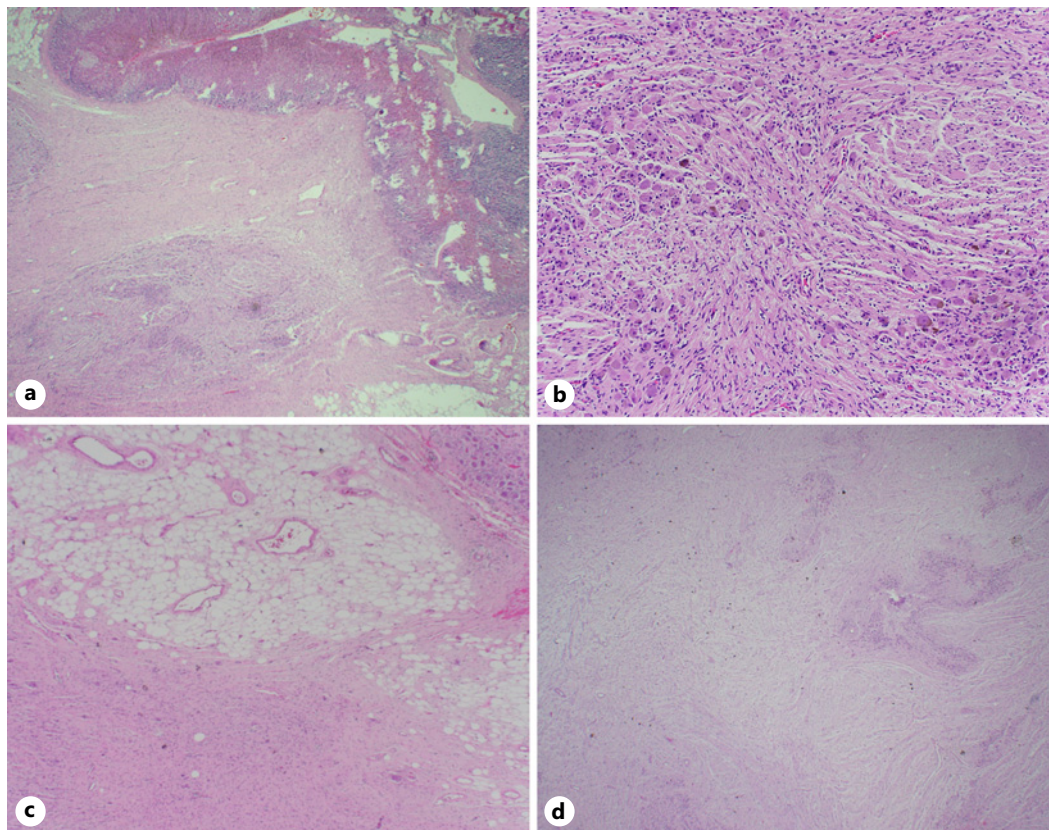

Fig. 3. Hematoxylin and eosin (HE) stained resection specimen. **a** Ganglioneuroma attached to the adrenal gland, HE ×20. **b** Ganglion and Schwann cells, HE ×100. **c** Tumor with entrapped fat, HE ×20. **d** Largest nodule, HE ×20.

particular, the presence of macroscopic fat suggested the possibility of a lipomatous tumor arising from the right adrenal gland. Histologic evaluation of the resected tumor suggested multifocal ganglioneuroma with fat infiltration rather than primary lipomatous ganglioneuroma (Fig. 3). The tumor appeared to be adherent to the adrenal gland as opposed to being of adrenal origin.

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There are additional characteristics that differentiate the tumor in this case from other reported cases of lipomatous ganglioneuromas or (non-lipomatous) multifocal ganglioneuromas. Lipomatous ganglioneuromas are typically unifocal, well-circumscribed, and non-infiltrative [5–10]. In contrast, this case demonstrated multiple nodules with apparent infiltration of surrounding fat. The pathogenesis of fat in lipomatous ganglioneuroma is unknown, but two proposed mechanisms are fatty replacement of degenerating tumor and adipocyte differentiation/metaplasia of tumor neural crest cells [6, 8, 9]. Some characteristics shared between this case and lipomatous ganglioneuromas include lack of encapsulation, adherence to nearby tissue, and heterogeneous enhancement.

Lipomatous ganglioneuromas are exceedingly rare, with only a handful of reported cases. It is possible, however, that these tumors are underreported, potentially making up around 12% of ganglioneuromas [11]. Their asymptomatic nature and slow growth suggest that nonurgent surgical intervention is reasonable.

Multifocal ganglioneuromas are also very rare and have been described in the posterior mediastinum, retroperitoneum, and adrenal gland [12–14]. Multiple ganglioneuromas in the gastrointestinal tract can be seen with Cowden syndrome. Our patient is less likely to possess a genetic condition predisposing to multifocal ganglioneuromas due to the late presentation of the tumor, the localized nature of the multifocal nodules, and the lack of other presenting signs and symptoms seen with these conditions, including abnormal hormone production.

The strengths of this report include the complete pertinent documentation from discovery to surgery and a thorough literature review of both multifocal and lipomatous ganglioneuromas. The limitations of the report include the small number of similar reported cases, which makes mechanistic explanations and correlations difficult.

Multifocal ganglioneuromas with infiltration of adjacent fat are exceedingly rare benign tumors that require unified findings from imaging and pathology for accurate diagnosis. We present a case of a 66-year-old female with multifocal retroperitoneal ganglioneuroma with infiltration of adjacent fat in the setting of a concurrent contralateral renal cell carcinoma. This case highlights the importance of careful analysis of data from multiple sources, including radiology, histology, and surgical pathology for an accurate diagnosis and stratification.

Acknowledgments

Statement of Ethics

Written informed consent was obtained from the patient for this publication and all accompanying images. There is no identifying information revealed in this publication. This retrospective review of patient data did not require ethical approval in accordance with local or national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

The manuscript was written by Joseph Rich. The manuscript was overseen and edited by Vinay Duddalwar, Phillip Cheng, Ramon Ter-Oganesyan, Shefali Chopra, and Peter Hu. Radiologic images were acquired and annotated by Vinay Duddalwar and Phillip Cheng. Pathology findings from the resection specimen were documented by Shefali Chopra. Pathologic images were acquired and annotated by Shefali Chopra and Manju Aron.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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