



Case report of a ganglioneuroma with metaplasia by adipocytes: use of a multi-disciplinary team as a key aid in difficult diagnosis and combined surgery

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Abstract: Herein, we present a rare case of a dumb-bell ganglioneuroma (GN) with metaplasia by adipocytes that was surgically resected in a 24-year-old woman who was asymptomatic. Because of the difficult diagnosis with no consensus about the location of the tumor, diagnostic and surgical procedures were performed with the assistance of a multi-disciplinary team (MDT) and the use of video-assisted thoracoscopic surgery (VATS). After conventional thoracotomy, histopathological and immunohistochemical examinations revealed that the tumor consisted of spindle cells, ganglion cells, and adipose cells. The histopathological diagnosis was GN with metaplasia by adipocytes. The tumor was resected, and the patient had no postoperative complications during a 3-year follow-up. For tumors whose location cannot be confirmed in the posterior mediastinum or in the retroperitoneum, VATS is an effective confirmatory tool. The recruitment of a MDT can be invaluable for formulating and providing treatment options for the patient.

Keywords: Ganglioneuroma; adipocyte; multi-disciplinary team

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Introduction

Ganglioneuroma (GN) is a rare and well-differentiated benign tumor that arises from the sympathetic nervous system. It is slow-growing and occurs more commonly in children than in adults. GNs are most commonly found in the posterior mediastinum or the retroperitoneum. Most GNs have no symptoms and are found coincidentally on radiography during routine health examinations (1). GNs located in the posterior mediastinum and growing along the spine might penetrate the intervertebral foramen into the spinal canal. This modality is called a dumb-bell or sandglass tumor (2). The penetrating growth might cause damage to the vertebral body and the spinal cord. Although GNs are usually asymptomatic, complete resection is the optimal choice for a penetrating dumb-bell GN. Some

complicated cases might require a variety of surgical techniques, thus benefitting from the participation of surgeons with various specialties (3).

Herein, we present a case of dumb-bell GN with metaplasia by adipocytes. The highlights in this case included not only the rare fatty replacement within the tumor, but also the location of the tumor, which resulted in uncertainty in diagnosis and preoperative planning.

Case presentation

A 24-year-old woman (height: 165 cm; weight: 52 kg) visited our department for examination of a right-sided posterior mediastinal mass that was incidentally discovered on a chest radiograph obtained during a routine medical

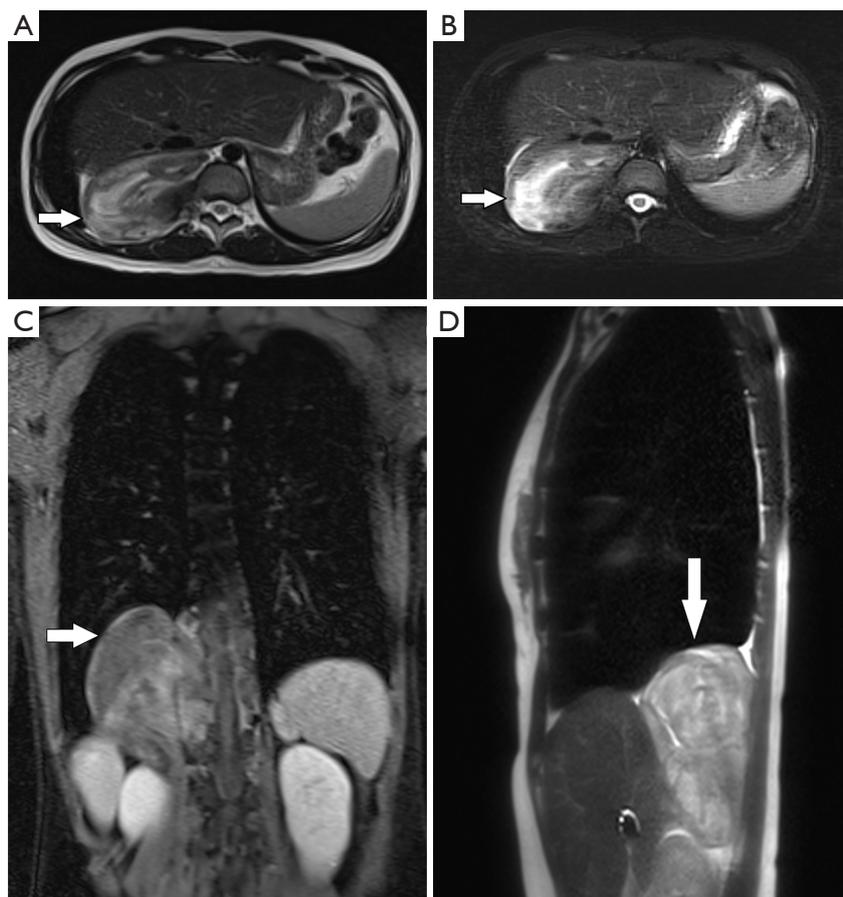


Figure 1 Magnetic resonance images of the tumor. (A) T2-weighted image showing a high signal intensity with mixed signals (arrow); (B) fat-suppressed image on T2-weighted images showing that the mass follows the prominent enhancement and heterogeneous signal intensity (arrow); (C) coronal scanning; (D) sagittal scanning.

examination. She was asymptomatic and had no significant past medical history. The results of a physical examination and laboratory tests were unremarkable, except for reduced air entry to her right lower chest.

Non-contrast-enhanced and contrast-enhanced magnetic resonance imaging (MRI) of the thoracic and upper abdomen demonstrated a right paravertebral mass that extended from T10 to L1. The tumor was adjacent to and extended into the T10/T11 intervertebral foramen. The right kidney and the liver were partially displaced by the huge tumor. There were areas of heterogeneous density within the mass (*Figure 1*). Based on these radiologic features, the primary diagnosis was a neurogenic tumor in the posterior mediastinum or retroperitoneum. Because of the suspicion of malignancy, uncertainty of the tumor location, and the need to guide the subsequent surgery, computed tomography angiography (CTA) of the abdominal

aorta was performed. The images revealed a mixed density tumor apparently adjacent to the thoracic vertebrae and the right posterior costophrenic angle. Non-contrast computed tomography (CT) images showed that the central portion of the tumor had an irregular strip of soft tissue density, with a CT value of -20 HU. Contrast-enhanced images confirmed the slightly heterogeneous tissue density observed on enhanced MRI. During the arterial phase, images showed blood vessels of the tumor originating from the posterior side of the abdominal aorta, the 11th intercostal artery, and the branches of the subcostal artery, thus nourishing the middle, upper, and lower parts of the tumor, respectively (*Figure 2*). In addition, the images showed that the 12th rib had been eroded owing to the infiltration and invasion by the tumor. Because the interior region of the tumor was rich in fatty tissues, an adipose tissue-derived tumor could not be excluded.



Figure 2 Computed tomography angiography of the tumor. (A) Coronal image showing blood vessels to the tumor originating from the back of the abdominal aorta, the 11th intercostal artery, and the branches of the subcostal artery; (B) three-dimensional reconstruction of the tumor's blood supply.

Multi-disciplinary team recruitment

After a brief discussion between thoracic surgeons and radiologists resulted in no clear consensus on the tumor location, general surgeons and neurosurgeons were called in for further discussion. Careful consideration was given to the planning of the surgical procedure. It was thought that the tumor was more likely to be located in the posterior mediastinum. However, the retroperitoneum could not be totally excluded as the tumor location. After discussion with the multi-disciplinary team (MDT), right-sided video-assisted thoracoscopic surgery (VATS) was considered as a first step. Next, if the tumor was located in the posterior mediastinum, thoracic surgeons and neurosurgeons would together complete the surgery. Otherwise, if the tumor was located in the retroperitoneum, general surgeons would cooperate with neurosurgeons to complete the surgery.

Resection

In preparation for surgery, the patient was placed in the left lateral decubitus position. A 1.5-cm long incision was made in the 8th intercostal space, along the anterior midaxillary line. Thoracoscopic exploration revealed that the tumor was located in the right posterior mediastinum and was close to the diaphragm. The diameter of the tumor was >10 cm. Sequential posterolateral thoracotomy was performed through the 10th intercostal space. The tumor was tightly adhered to the peripheral tissues and had a rich vascular supply. The main part of the rounded lesion was resected via careful blunt and sharp dissection. To expose the residual pedicles in the narrow foramen, neurosurgeons widened the T10/T11 foramen and carefully dissected and excised residual pedicles from the thoracic spine. Residual

tumor tissues and pedicles on the surface of the dura mater were delicately dissected and removed. The mass had caused erosion in the 12th rib, and the entire rib was also resected.

Pathological findings

The tumor measured 12 cm × 10 cm × 5 cm, with a pedicle measuring 6.5 cm × 1.5 cm. Tumor sections were grayish-white in color and had a whorled pattern. Histopathological examination of the tumor showed that it comprised three cell types: spindle cells, ganglion cells, and adipose cells. Immunohistochemically, tumor cells were positive for S-100 spindle protein, vimentin, synaptophysin, and neuron specific enolase in focal areas, and were negative for CD68, neurofilament, desmosine, chromogranin A, and cytokeratin (*Figure 3*). The histopathological diagnosis of GN with metaplasia by adipocytes was definitively made after the discussion took place between two specialists.

The patient has been undergoing regular follow-up examinations annually in our clinic. She shows no signs of recurrence 3 years since surgery (*Figure 4*).

Discussion

Nearly 75% of posterior mediastinal tumors originate from neurogenic tissues. GNs are tumors arising from the neural crest cells, and belong to a group that also includes peripheral nerve sheath tumors, melanomas, and neuroendocrine tumors (4). GNs are histologically different from schwannomas, neurofibromas, neurofibrosarcoma, pheochromocytomas, and other neurogenic tumors to some extent. These other tumors originate from sympathetic ganglion cells, peripheral nerves, and paraganglia (5). Separate mature ganglion cells in nests, Schwann cells in

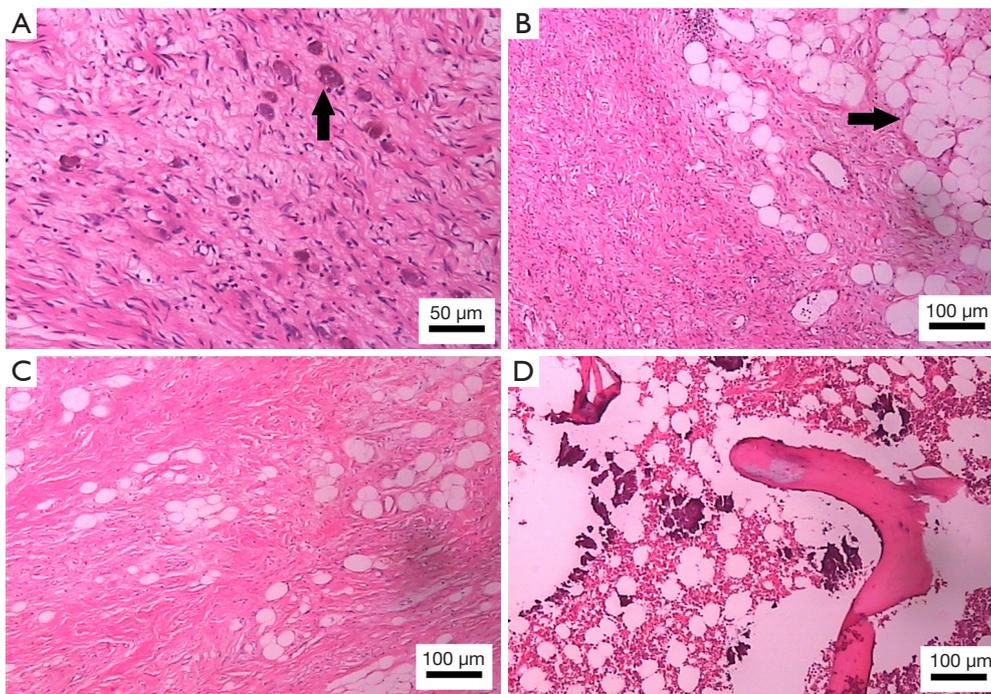


Figure 3 Histopathological examination of the tumor using hematoxylin and eosin staining showed (A) ganglion cells (arrow; 200× magnification); (B) adipose tissue (arrow; 100× magnification); (C) hyaline change, adipose tissue, and nerve fiber in pedicles of the tumor (100× magnification); (D) osseous tissue and necrotic osseous tissue in the resected 12th rib (100× magnification).



Figure 4 Chest radiography performed during a follow-up examination. The radiograph showed no obvious abnormalities.

the stroma, neuroma, and fibrous tissue can be detected through microscopic examination of these tumors (6). GNs, as the rarest of neural crest tumors, are mainly found in adolescents or young adults (7). Schulman et al. reported that the mean age of presentation was 7 years (8). Patients with GNs are usually asymptomatic. However, patients might experience discomfort or pain in the chest, or have symptoms caused by intrusion into or compression of the spinal cord or other organs and tissues.

The extremely rare case presented here was that of a GN localized at the junction of the posterior mediastinum and the retroperitoneum in a young woman. The location led to a lack of consensus between the thoracic surgeons, general surgeons, neurosurgeons, and radiologists regarding the appropriate surgical treatment. The difficulty in surgical design was further complicated by the formation of a pedicle that extended from the tumor to the neural foramen. The appearance of fat cells within the GN was another unique feature in this case. GNs are typically composed of more benign and well-differentiated cells. It is unusual for GNs to have adipocyte metaplasia. Only a few such cases have been reported previously in English and Japanese (9-15). While

the exact pathogenesis of a GN with adipocyte metaplasia is still unclear, we speculated that the atrophied tumor might be replaced gradually by mature adipocytes and adipose tissue (10). Alternatively, during metaplasia of the tumor, cells might be converted into adipocytes (14). In the current case, GN was not suspected until the surgical specimen was analyzed.

Radical resection of a dumb-bell GN is the optimal treatment choice. However, it is necessary to confirm and pinpoint the tumor location by CT and MRI. Evaluation of the tumor's intraspinal invasiveness and extension based on CT and MRI are equally important in order to guide the surgical approach (16). On CT imaging, GNs might be identified as homogeneous or heterogeneous masses, with low to intermediate attenuation. Calcification can be detected in nearly 20% of cases. After contrast administration, the tumors demonstrate mild to moderate enhancement (17). On MRI, T1-weighted images display a hypointense lesion and T2-weighted images present a hyperintense lesion (18). In our case, MRI showed a homogeneous uniform signal on T1-weighted images and a heterogeneous hyperintense signal on T2-weighted images. Owing to the possibility of malignancy, CT and CTA of the tumor blood supply were performed to help guide the surgery. As in previous cases, our case showed a well-defined, heterogeneous lesion with an irregular strip of soft tissue (non-contrast CT value of -20 HU). Contrast-enhanced images demonstrated a slight heterogeneous enhancement. However, calcification in the tumor was not found. Blood supply to the tumor was confirmed in the arterial phase of a CTA scan and multiplanar reconstruction (MPR) of three-dimensional images from MRI and CTA scans. Additionally, erosion of the 12th rib by the tumor was detected.

The MPR images were analyzed by several radiologists to determine whether the tumor was located in the retroperitoneum or the posterior mediastinum, and to identify the exact blood supply to the mass. Unfortunately, there was no consensus about the precise location of the tumor. To facilitate decision-making for a surgical approach, a MDT was introduced. The MDT included experts from the departments of thoracic surgery, neurosurgery, general surgery, radiology, and pathology. The resulting agreement was to first confirm the location of the tumor by performing right-sided exploratory VATS through a 1.5-cm single port to minimize trauma. If the mass was determined to be located in the pleural cavity, the surgery would be completed by thoracic surgeons and neurosurgeons. General

surgeons and neurosurgeons would finish the surgery if the tumor was located in the retroperitoneum. In this case, the tumor was in the pleural cavity. A MDT can facilitate the consensus opinion of all of the relevant specialists and other healthcare professionals before a management plan is undertaken (19).

Conclusions

GNs are tumors that arise from neural crest cells. A rare case of a GN with metaplasia by adipocytes has been presented. This type of dumb-bell tumor requires radical resection because it can cause chest pain and severe compression symptoms as the disease progresses. MPR can be used to observe the tumor in axial, sagittal, and coronal planes, so that the location of the tumor and its relationship with adjacent organs and tissues can be determined. VATS exploration is an effective way to intraoperatively evaluate the precise location of the tumor before resection. During the perioperative period, the recruitment of MDT resources is invaluable for assessing and formulating individual surgical plans.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tcr.2017.03.67>). The authors have no conflicts of interest to declare.

Ethical statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written

informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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