Using imaging to diagnose lipomatous ganglioneuroma: a case report and literature review

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Abstract: We report a case of a well-defined lesion in an asymptomatic patient with lipomatous ganglioneuroma (LG) located close to the left thoracic spine. Its intensity was heterogeneous with adipocytes. The lesion extended into the spinal canal through the enlarged left intervertebral without bony erosion. The imaging, clinical, and pathological features of the tumor are analyzed. Contrast-enhanced magnetic resonance imaging (MRI) revealed that the lesion was moderate enhanced. 18-F-fluoro-2-deoxyglucose-positron emission tomography/computed tomography (18FDG-PET/CT) demonstrated high 18-F-fluoro-2-deoxyglucose (18FDG) uptake of the tumor lesion. The finial preoperative diagnosis from our radiologists was that the tumor may be a liposarcoma or neurogenic tumor, but pathology showed that this was incorrect. Some related literatures were reviewed for reference to summarize imaging characteristics of this disease and to assist radiologists in making more accurate diagnoses. All of the lesions had adipocytes in reviewed literature, and the fat-suppressed images showed that there was some low signal intensity within the lesions, some lesions had widened neural foramina and extended into the spinal canal, and some lesion had calcifications. LG is an extremely rare variant of ganglioneuroma. Using the correct measurement of the CT value, applying MRI for fat-suppressed images, using in phase, out phase and contrast-enhanced sequences, using FDG-PET/CT, mastering LG imaging diagnostics characteristics, and combining all of this with clinical, morphological characteristics and pathology results can help clinical workers decrease the misdiagnosis rate of LG.

Keywords: Lipomatous ganglioneuroma (LG); ganglioneuroma; adipocytes; imaging diagnosis; case report

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Introduction

Lipomatous ganglioneuroma (LG) is a rare subtype of ganglioneuroma. LG was first discovered by Hara *et al.* in 1999 but was named ganglioneuroma with fatty replacement (1). Adachi and other scholars first proposed to renamed LG in 2008 (2). It is easy to be misdiagnosed as an adipogenic tumor due to containing fat components, such as liposarcoma, which is a malignant tumor often occurred in elderly patient and prone to recurrence, during imaging diagnosis, it can also be misdiagnosed as a neurogenic tumor, because of its unique growth mode, but some scholars put forward a study that posterior mediastinal tumors with a broad base along the anterolateral aspect of the spine are more likely to be ganglioneuroma rather than schwannoma or neurofibroma (3).

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In this paper, we report on a case of a 57-year-old male patient with LG in the paraspinal sulcus of the posterior mediastinum is. And review some related literature. To summarize imaging features in CT, magnetic resonance imaging (MRI) and fluorodeoxyglucose-positron emission tomography (FDG-PET) of LG based on morphological, pathological and immunohistochemical characteristics.

At present, the precise pathogenesis of ganglioneuromas with abundant adipocytes remains unclear. To our knowledge, surgery is the best treatment for LG, no medication has been reported.

If we do not learn about LG and master its characteristics, it will easily lead to misdiagnosis, which should be avoided for doctors, especially for radiologists.

We present the following article in accordance with the CARE reporting checklist (available at https://dx.doi.org/10.21037/atm-21-6976).

Case presentation

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). 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 by the editorial office of this journal.

A 57-year-old male complained of he underwent a thorax computed tomography (CT) scan during a physical examination in a local hospital, and a thoracic paravertebral mass was diagnosed. There was no abnormality of his nervous system on admission, and he showed no related symptoms. He also did not have a history or a family history of thoracic paravertebral mass.

In our hospital, a FDG-PET examination showed a mass located in the left 10th to 12th thoracic vertebral (T10 to T12). The case demonstrated high 18FDG uptake, and the maximum standardized uptake value (SUVmax) was 2.4, suggesting the tumor lesion was more likely to be a liposarcoma (*Figure 1A*,*1B*). Further MRI of the thoracic vertebrae revealed an abnormal signal in the left side of T10 to T12 (*Figure 1C-1F*), suggesting an adipose-derived tumor that may have been a benign or a low-grade malignant tumor, or a differentiated liposarcoma. The CT scan of the thoracic vertebra showed a well-defined mass located in the left side of T10 to T12 (*Figure 1G*) that was 31 mm × 45 mm × 71 mm in size (horizontal × anteroposterior × vertical). The CT value was between −59 Hounsfield Unit (HU) and 21 HU. The left intervertebral foramen at the level of T11 to T12 seemed to be involved (*Figure 1F*,*G*), and there was no obvious bony erosion (*Figure 1H*), suggesting a low-grade malignant tumor such as a neurogenic tumor.

The patient was operated on with a thoracic paravertebral tumor resection surgery in prone position. During the operation, a longitudinal incision was made at the center of 3 cm to the left of the preoperative positioning point. The length of the incision was about 10 cm. The surgery exposed the transverse process of T10 to T12 and remove part of the 11th rib. The tissue has a yellow and white appearance, a tough texture, a clear boundary, and was 6 cm × 7 cm in size. When the tumor was dissected along the boundary, we found that the base of the tumor was wide, the medial part entered the intervertebral foramen, and the lateral part was close to the parietal pleura. During the resection process, we found that the tumor was hypervascular, especially the paravertebral part in the deep medial area. The operation was successful, and postoperative recovery went well.

Postoperative pathological analysis revealed the total size of the specimen was about 6.5 cm × 5 cm × 2 cm, it had a gray and yellow appearance in section, and the tissue was medium solid. The pathological results also showed that there was a mixture of mature lipomatous components and ganglioneuromas in the patient's thoracic paravertebral tumor (*Figure 2*). These findings were consistent with LG. Results of immunohistochemistry were as follows: Neuronal Nuclei (NeuN) (−), Synaptophysin (syn) (+), S-100 protein (+), Neurofilament (NF) (+), Ki-67 protein (+1%), and Smooth Muscle Actin (SMA) (−).

In the case we describe here, a CT scan showed that there was no calcification but there were fatty components, which caused the tumor shows heterogeneous low density. The MRI scan showed a heterogeneous high signal on T1 Weight Image (T1WI) and T2 Weight Image (T2WI), and an enhanced scan showed moderate enhancement. The tumor was located in the posterior mediastinum, and it expanded and extended the adjacent intervertebral foramen into a "dumbbell" shape. The SUVmax of 2.4 in the PET-CT in our case was slightly high compared with the cut-off value (SUVmax: 1.8). All these reasons contributed to the tumor being misdiagnosed as other benign or a low-grade malignant tumor, most likely a liposarcoma or neurogenic tumor, in the preoperative imaging examinations. Overall, this case of LG is worth

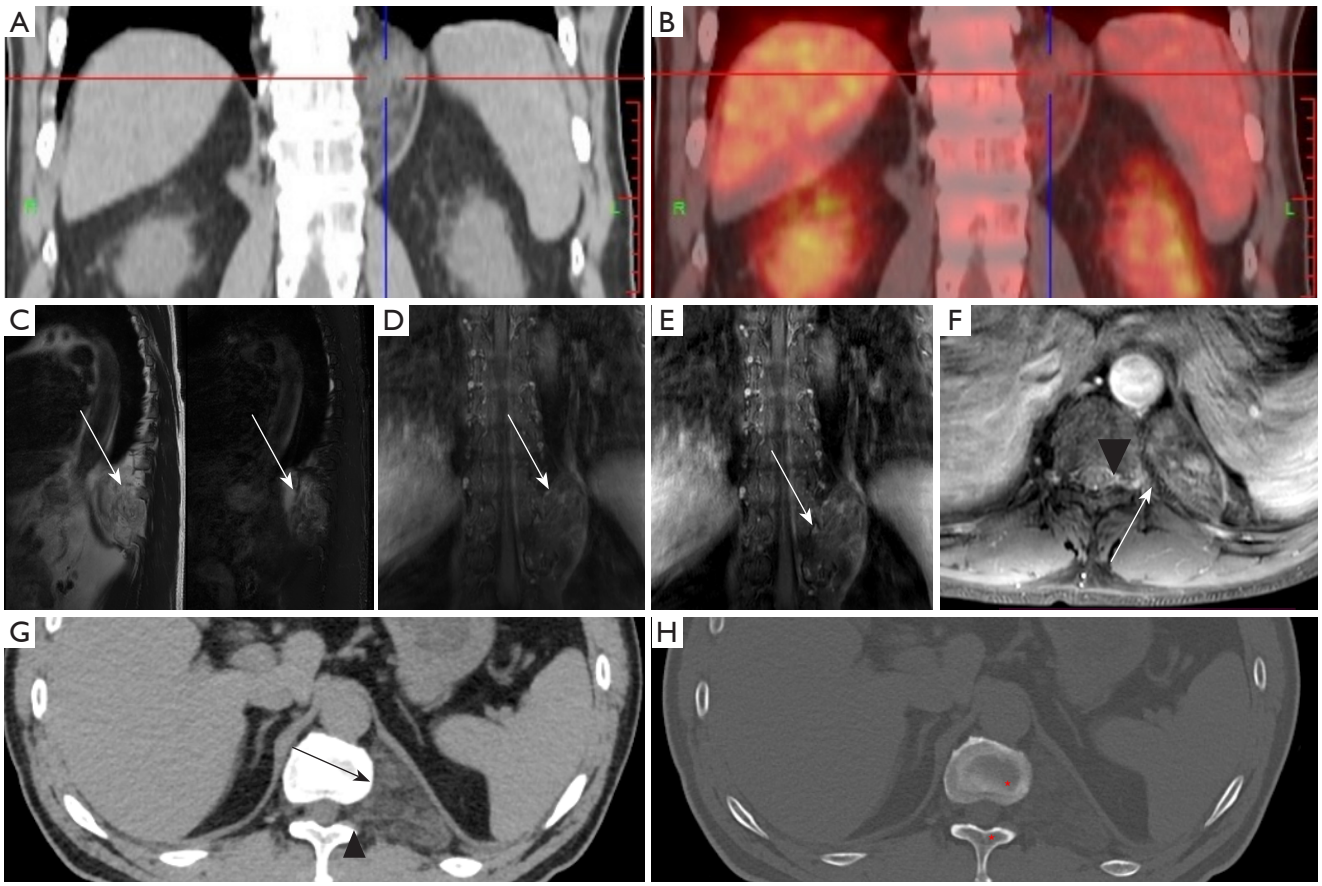

Figure 1 Imaging examinations of our case. (A) FDG-PET/CT scan at almost the same level as (B). (C) Sagittal T2WI shows a heterogeneous signal, and the inherent T2 hyperintensity of the fatty component of this lesion (white arrow) is suppressed on the fat suppression sequence. (D) T1 fat suppression. (E) Coronal T1 post-contrast fat suppression sequence. (F) Axial T1 post-contrast fat suppression sequence. the lesion grows in the oblong shape with craniocaudal orientation (white arrow), the vertical diameter is longer than the anteroposterior diameter, the signal was mixed, and the tumor tissue extends into the left intervertebral foramen (black triangle). The soft tissue component of the mass shows heterogeneous enhancement. (G,H) CT scan of the thoracic vertebrae. The mass in the left paravertebral (black arrow) demonstrates heterogeneous density with soft tissue and fatty tissue. The left intervertebral foramen is slightly enlarged (black triangle). No obvious bony erosion was found (red star). FDG-PET/CT, fluorodeoxyglucose-positron emission tomography/computed tomography; T2WI, T2 weighted images.

summarizing and learning.

Discussion

There are three kinds of tumors in the sympathetic nervous system: neuroblastoma, ganglioneuroblastoma, and ganglioneuroma. LG is a rare subtype of ganglioneuroma. Ganglioneuroma is the most common tumor in the sympathetic nervous system and can be seen in all the sites with undifferentiated neural crest cells. LG is generally well differentiated. Most LG tumors are benign and are commonly located in the posterior mediastinum and retroperitoneal. LG, previously known as ganglioneuroma with fatty replacement, is characterized by mature adipose components and ganglioneuroma and was thought to be caused by a tumor lesion that had degenerated by fatty replacement (1). After many pathological studies, most scholars believed that the component of adipocytes in the tumor derived from the abnormal differentiation of primitive nerve cells themselves, and that the tumor cells of ganglioneuroma originated from the neural crest, which may have the capacity for lipomatous differentiation (4). Finally,

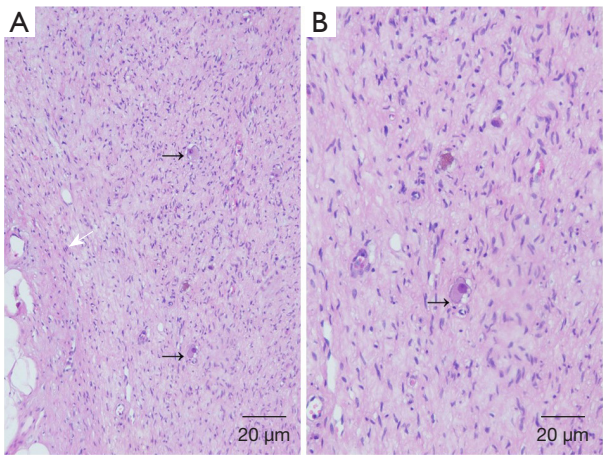

Figure 2 Pathological results showed that lipomatous ganglioneuroma was composed of mature adipocytes and ganglion cells. (A) Neural bundles (white arrow) encasing mature adipose tissue (hematoxylin-eosin, ×40). (B) The ganglion cells (black arrow) in the neural background were large, with nuclei that deviated apart from the center and prominent nucleoli (hematoxylin-eosin, ×100).

this theory overcame the original understanding that the adipose tissue in the tumor was degenerated and replaced by some cellular components of ganglioneuroma (5).

Most patients with LG accidentally found the tumor lesion in other examinations, and they were typically asymptomatic (1,2,5-7). *Table 1* shows that only 3 of 8 patients had related symptoms such as radiation-induced chest wall pain, left hypochondrium pain, and right shoulder back pain (4,8,9). Most patients reported on in existing literature were middle-aged, and there are 4 females and 4 males. The maximum diameter of the reported tumors was 12 cm. LG most commonly occurred in the posterior mediastinum and retroperitoneum, and less commonly in the adrenal medulla.

Under a microscope, LG is mainly composed of differentiated ganglion cells, Schwann cells, and nerve fibers. In the case in our report, the final pathological diagnosis of the postoperative specimen suggested a mixed lesion of mature fat and ganglioneuroma. Demir MK and other scholars also reported a case of immature ganglioneuroma with fatty components (9). In that case, the immunohistochemistry showed that immature ganglion cells were positive for synaptophysin (Syn protein) but negative for neurofilament protein (NF protein). In our case, the immunohistochemistry showed that S-100 protein in Schwann cells was positive, and syn protein and NF protein in ganglion cells were positive, which suggested that the component was a mature ganglioneuroma.

Although the final diagnosis of LG mainly depends on pathology, imaging examination also plays an important role in the diagnosis and differential diagnosis of LG. Ganglioneuroma grows slowly and is restricted by the surrounding organs. It often grows along the space of the surrounding organs in a drilling pattern. Most ganglioneuromas are oval shaped, round, and "D" or "dumbbell" shapes (7), most they grow beside the spine (3), and most are well-defined. Some tumors can be cystic or have punctate calcifications (5,7,8). CT scans show that LG typically has a uniform low-density that is lower than muscle density. With an enhanced scan, the enhancement was not obvious or could only slightly be seen in parts of the tumors (5,8). In contrast, a ganglioneuroma grows in an oblong shape with craniocaudal orientation, and the vertical diameter is longer than the anteroposterior and horizontal diameter, which is clue for the diagnosis of benign tumors and the differentiation from other neurogenic tumors (8). MRI scans show that LG has a moderate or high signal on T1WI, obvious heterogenous high signal on T2WI, and some of them have whorled appearance features, which corresponds to interlacing bundles of Schwann cells and collagen fibers (10). The enhancement degree of the tumor may be related to the varying proportions of the components, such as myxoid matrices, cell components, collagen fibrils, and vessels. The presence of abundant myxoid matrices has been attributed to the progressive accumulation of contrast medium in the extracellular space (11). From the findings of our case report and results in existing literature, we suggest that a multi-phase scan should be performed when CT or MRI contrast-enhanced scan is performed. The application of delayed phase is particularly important for accurate diagnosis of LG in patients.

After knowing the growth pattern and imaging characteristics of ganglioneuroma, the existence of the fatty component in the LG can be confirmed by measuring the CT value of different areas of the tumor, finding the high signal intensity both on T1WI and T2WI that can be suppressed on the fat suppression sequence, and examining if high signal in during the in-phase decreases in the out-phase.

According to the imaging features of the cases in the literature we reviewed (*Table 1*), CT scan showed the intensity was heterogeneous with lipomatous in the lesions, while MRI scan showed heterogeneous signal on T1WI and T2WI. Some of them had some special growth

Table 1 Characteristics of LG patients in the surveyed literature

Reference	Sex/age (year)	Location	Size (cm)	Clinical symptoms	Special imaging findings	Enhancement
Adachi *et al.*	Male/73	Retroperitoneum	2×2×1.5	Asymptomatic	Rich in fat elements on CT scan; mixed density both on T1WI and T2WI	–
Meng *et al.*	Male/44	Retroperitoneum	9.5×9.5×2.5	Intermittent pain in the left hypochondrium	Iso- and hypointense on T1WI; heterogeneously iso- and hyperintense on T2WI	Heterogeneously avid enhancement
Duffy *et al.*	Female/27	Posterior mediastinum	–	Asymptomatic	The tumor appeared to enter and widen the right intervertebral foramina; intermediate and high signal intensity on T1WI and T2WI	Some enhancement in the areas of intermediate T1 signal intensity
Ko *et al.*	Female/53	Posterior mediastinum	9×4.5×10	Asymptomatic	The tumor crossed into the left posterior mediastinum; mixed signal intensity on T1WI.	The soft tissue component enhanced minimally
Yorita *et al.*	Female/66	Posterior mediastinum	12×6×4	Asymptomatic	Low signal intensity was seen on T1WI with intermediate to high signal intensity on T2WI. grow through the adjacent intervertebral foramen and extend into the spinal canal with a “dumbbell” or “hourglass” configuration.	Slight to mild heterogeneous enhancement
Abdelazim *et al.*	Male/48	Posterior mediastinum	3.3×5.6×9.2	Constant sharp left axillary pain radiating to the anterior chest wall	Punctate calcifications; the mass had an oblong shape with craniocaudal orientation; whorled appearance on both T1WI and T2WI	The peripheral soft tissue components of the mass showed heterogeneous enhancement
Demir *et al.*	Male/33	Posterior mediastinum	–	Scoliosis	Scattered fatty areas; calcifications and vertebral scalloping; heterogeneous low-signal intensity on T1WI with high-signal intensity lipomatous component.	Intense enhancement
Hara *et al.*	Female/54	Posterior mediastinum	11×3×6.5	Asymptomatic	Whorled appearance on CT scan	–

LG, lipomatous ganglioneuroma; CT, computed tomography; T1WI, T1 weight image; T2WI, T2 weight image.

patterns, some cases showed that the lesions expanded into the adjacent intervertebral foramen or extended into the spinal canal, and some of them were accompanied by “dumbbell” or “hourglass” signs. Two cases showed that the lesion had whorled appearance features. Calcifications were reported in two cases. Most of the enhancement was mild to moderate and inhomogeneous.

The SUVmax value of the PET-CT is also helpful for diagnosing LG. According to existing literature, the SUVmax value of a well-differentiated liposarcoma is about 2.3±1.7 (mean ± standard deviation), and the cut-off value is taken to be 1.8 to differentiate a benign neurogenic tumor from a malignant tumor. A ganglioneuroma may have a high uptake that is similar to the pattern of a low-grade malignant tumor as shown by PET imaging because the presence of brown adipose tissue may lead to a false-positive

result in FDG-PET (7).

As for differential diagnoses, other neurogenic tumors with a "dumbbell" shape or a craniocaudal orientated growth feature include schwannoma, ganglioneuroblastoma, and neurofibroma, while other fat-containing tumors include, but are not limited to, lipoma, liposarcoma, angiomyolipoma, and teratoma. It is also important to master the imaging features of above tumors to distinguish LG from them.

In general, this article combines the case we reported with the related literature we reviewed, to summarizes the imaging features in CT/MRI/FDG-PET of LG based on morphological, pathological and immunohistochemical characteristics. Most patients with LG are asymptomatic cases and often find the tumor accidentally, so the misdiagnosis rate of preoperative diagnosis is very high. We would suggest that CT and MRI scans, even PET-CT, should be correctly combined for an accurate imaging diagnosis. Calcification and bony erosion can be better observed on a CT scan than other imaging techniques. MRI can further clarify the components of the tumor, especially the application of the fat-suppression sequence, in-phase and out-phase sequence, and multi-phase contrast-enhanced scan, which are conducive to the qualitative diagnosis for radiologists. A coronal view can also be more convenient for doctors to observe the morphological characteristics of the tumor and the tumor's relationship with adjacent intervertebral foramen. As for the treatment, surgical resection should be considered first. In addition to regular review, the patient does not need any adjuvant therapy and has favourable prognosis, what's more, there is no report of postoperative recurrence or metastasis.

Although our report is a rare case of ganglioneuroma containing adipocytes, the imaging features of this case did not have all the typical imaging characteristics that were found in existing literature. The relevant English literature reviewed only contained 8 cases of LG. Only 3 reported cases were from Asia. Therefore, we appeal to more clinicians can report related cases and summarize LG's characteristics.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/atm-21-6976). All authors report that they receive payment from the Military Medical Science and Technology Youth Training Program and National Key Research and Development Program of China. The authors have no other 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 this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). 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 by the editorial office of this journal.

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