Middle mediastinal paraganglioma enclosing the left anterior descending artery
A case report

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Abstract

Rationale: Paragangliomas are extremely rare neuroendocrine tumors arising from ganglia. These tumors are barely found in the middle mediastinum.

Patient Concerns: A 31-year-old male patient was admitted to our hospital for treatment of an middle mediastinal tumor which was found incidentally on echocardiography during a medical checkup. Contrast-enhanced chest computed tomography (CT) demonstrated a well-defined hypervascularized heterogeneous mass located in the middle mediastinum. The tumor showed strong 18F-fluorodeoxyglucose (FDG) activity on positron emission tomography-computed tomography (PET-CT).

Diagnosis: Before the surgery, we presumed the mass was an angiogenic or neurogenic tumor. As a result, the histological features favored a diagnosis of paraganglioma.

Interventions: The tumor was completely removed by anterior thoracotomy, along with the proximal segment of the left anterior descending artery (LAD), and coronary artery bypass grafting (CABG) was performed immediately after the tumor excision.

Outcomes: The patient had an uneventful recovery. The patient did well in the postoperative follow-up without any complications and signs of recurrence at 3 months, 1 year, 2 year and 4 year.

Lessons: This report can increase the confidence in surgeries of mediastinal paragangliomas adhering tightly the adjacent structures.

Abbreviations: 18F-FDG = 18F-fluorodeoxyglucose, CABG = coronary artery bypass grafting, CCTA = coronary computed tomography angiography, CT = computed tomography, LAD = left anterior descending artery, MRI = magnetic resonance imaging, PET-CT = positron emission tomography-computed tomography.

Keywords: case report, computed tomography, coronary artery bypass, mediastinal tumor, neuroendocrine tumor

1. Introduction
Mediastinal paraganglioma is an extremely rare tumor derived from extraadrenal chromaffin cells, which accounts for no more than 0.3% of all mediastinal tumors and <2% of all paragangliomas.\textsuperscript{1,2} Mediastinal paraganglioma can be either functional with the ability to synthesize and release catecholamine or nonfunctional without the catecholamine secretion. Clinical symptoms may be caused by catecholamine excess (headache, tachycardia and sweating) or due to the mass effect (dyspnea, dysphagia and chest pain).\textsuperscript{3} However, most patients are asymptomatic and discovered accidentally.\textsuperscript{4} Here we present the first case of a nonfunctional middle mediastinal paraganglioma, which encloses the left anterior descending artery (LAD). The tumor was completely removed by anterior thoracotomy, along with the proximal segment of the LAD, and coronary artery bypass grafting (CABG) was performed immediately after the tumor excision.

2. Case report
A 31-year-old male patient was admitted to our hospital for treatment of an middle mediastinal tumor which was found incidentally on echocardiography during a medical checkup. He had no history of hypertension, headache or other specific symptoms. Electrocardiogram showed flat T-waves in lead I but no abnormalities in other leads. He was found to be positive for hepatitis B virus during the laboratory examination, but other laboratory data were within normal limits. Contrast-enhanced chest computed tomography (CT) demonstrated a well-defined hypervascularized heterogeneous mass measuring 7.7 × 7.2 × 6.3 cm located in the middle mediastinum (Fig. 1A–C), which followed a rapid peak and washout...
The tumor was adherent to the heart and the multiplanar curved reformat view showed it enclosed the proximal left anterior descending artery (LAD), but the lumen of the proximal LAD was absolutely patent without stenosis (Fig. 1D). The tumor showed strong $^{18}$F-fluorodeoxyglucose (FDG) activity on positron emission tomography-computed tomography (PET-CT), with a maximum standardized uptake value (SUV$_{\text{max}}$) of 31.3 (Fig. 2).

Based on the findings, we presumed the mass was an angio- or neurogenic tumor. The patient was scheduled for surgery due to its malignant potential. Surgical resection was going to be performed under cardiopulmonary bypass and cardiac arrest for the size and the location of the tumor. The pericardium was opened via a standard midline sternotomy. Intraoperatively, an encapsulated, highly vascularized, 8 × 8 × 7 cm mass was noted on the left side of the ascending aorta, between right ventricular outflow tract, pulmonary artery and left atrium. Several feeding vessels from aortic arch and pulmonary artery were identified and clipped. At first, the tumor was resected from the surrounding structures with relative ease. However, as the excision progressed caudally, the proximal LAD was found enclosed firmly by the tumor and cannot be separated completely. Thus, the proximal LAD was resected together with the mass and CABG was performed. The left greater saphenous vein was utilized as the coronary conduit. Perioperative blood loss was 460 ml. No obvious blood pressure fluctuations occurred during surgery. The duration of cardiopulmonary bypass and aortic cross-clamp was 297 min and 167 min respectively.

Histologically, the tumor consisted of polygonal cells arranged compactly in nests (Zellballen) which were bordered by vascular stroma with rich fine capillaries. The cells had spindle nuclei, fine chromatin, inconspicuous nucleoli and abundant eosinophilic granular cytoplasm. Mitosis, foci of necrosis and invasion into adjacent structures were rarely present (Fig. 3A). Immunohistochemically, the tumor cells were positive for chromogranin (Fig. 3B), and S-100 protein (Fig. 3C) and had a low index of proliferation (Ki-67 index of 5%) (Fig. 3D). There were no signs of malignancy. These features favored a diagnosis of paraganglioma.

The patient did well in the postoperative follow-up without any complications and signs of recurrence on echocardiology and CT scans at 3 months, 1 year, 2 year and 4 year. Coronary computed tomography angiography (CCTA) was performed 4 year after surgery for evaluation of CABG patency and no stenosis or other vascular disorders with the graft was found (Fig. 4).

3. Discussion

Pheochromocytomas and paragangliomas are relatively rare neuroendocrine tumors which originate from chromaffin cells. The only difference between them is the anatomical location. The former is located in adrenal gland while the latter can be anywhere extraadrenal.[7] Paragangliomas are frequently located in the retroperitoneum, sometimes in the pelvis, the head and the neck and seldom in the mediastinum. Mediastinal paragangliomas located in the posterior mediastinum often arise from paravertebral ganglia and tend to be functional with catecholamine secretion. The most frequent complaints of functional paragangliomas secondary to hypercatecholamine are headache, tachycardia, arrhythmia and sweating.[8] Combined with clinical symptoms, elevated metanephrines in plasma and urine can strongly support the existence of those tumors. While mediastinal paragangliomas located in the anterior or middle
mediastinum often arise from para-aortic ganglia and tend to be nonfunctional.\cite{9-11} Those patients with nonfunctional tumors are generally noted occasionally during imaging studies or related symptoms of compression or invasion of adjacent structures, such as dysphagia, chest pain and dyspnea.\cite{10} As in our case, the patient didn’t show any complaints and the mass was first discovered by echocardiography during the medical check.

Imaging methods show great importance in diagnosis of mediastinal paragangliomas, which can provide the location and extension of the lesion and assess its invasiveness. Paragangliomas are usually highly vascular and demonstrate intense and heterogeneous enhancement on CT and magnetic resonance imaging (MRI). Although MRI was not performed in this case, it also plays an important role in the diagnosis. The intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images is a characteristic feature of this kind of tumor. Most paragangliomas are avid for $^{18}$F-FDG, which was also seen in our case. Although the highly uptake of $^{18}$F-FDG is nonspecific to paragangliomas, it is still of great value to determine whether there is metastasis.\cite{9}

The differential diagnosis for a middle mediastinal mass includes congenital cysts, lymphadenopathy and angiosarcoma. Congenital cysts, including pericardial cyst, esophageal cyst and bronchial cyst, usually appear as well-circumscribed water-like density/intensity with thin walls. They never show any enhancement on CT or MRI and thus can be excluded.\cite{12} Lymphadenopathy, like malignant lymphoma and metastasis, sometimes shows marked contrast enhancement on CT or MRI. However, metastatic tumors can be ruled out by revelation of the original lesion. Angiosarcoma usually demonstrates pronounced heterogeneous contrast enhancement resembling paraganglioma, which is the most controversial differential diagnosis.\cite{8,10} Thus, histological and immunohistochemical evaluation are necessary to make a definitive diagnosis. The microscopic pattern of paragangliomas are special. The tumor cells are arranged in a typical nesting pattern and separated by abundant microvasculature.

**Figure 2.** Positron emission tomography-computed tomographic scan demonstrated a marked accumulation of $^{18}$F-fluorodeoxyglucose in middle mediastinal mass.
The cells have round or oval nuclei and eosinophilic cytoplasm. We can occasionally identify a few mitoses or mild to moderate nuclear pleomorphism in the proliferative tumor cells. Paragangliomas are intensely immunoreactive to chromogranin, synaptophysin and S-100 protein but negative for cytokeratin and epithelial membrane antigen.

Although paraganglioma is typically benign, it still has malignant potential, including local invasiveness and distant metastasis. Surgical resection is the preferred therapeutic strategy for paraganglioma due to its resistance to chemotherapy and radiotherapy. As paraganglioma is highly vascular and adhere firmly to adjacent great vessels or heart, the operation can cause massive bleeding. Therefore, the vascular supply of the tumor should be evaluated by preoperative angiography and preventive embolization can be performed if necessary. In our case a preoperative embolization did not be performed because there were no apparent nourishing blood vessels arising from the adjacent great vessel. In addition, there was no massive bleeding during the
operation. Cardiopulmonary bypass is often adopted to ensure a safe and complete excision. Sometimes the adjacent tissues can be excised together with the tumor. As in our presented case, the proximal LAD was resected and revascularized with a great saphenous vein graft. For functional paragangliomas, catecholamine crisis is another concern. Thus, adrenergic blockers and calcium channel blockers can be used preoperatively to avoid perioperative hypertensive crisis. After surgery, a regular follow-up is needed to evaluate whether there is local recurrence or metastatic spread. Fortunately, majority parents who achieved successful resection have a favorable prognosis.

In conclusion, we experienced an extremely rare case of asymptomatic and nonfunctional paraganglioma arising from the middle mediastinum, which firmly enclosed the proximal LAD. To ensure a complete resection of the tumor, a portion of the LAD was excised and revascularized. The patient has a favorable prognosis without recurrence. As far as we know, such a case has not been reported before. This report can increase the confidence in surgeries of mediastinal paragangliomas adhering tightly the adjacent structures.

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References
[1] Wang JG, Han J, Jiang T, et al. Cardiac paragangliomas. J Card Surg. 2015;30:55–60.
[2] Buchanan SN, Radecki KM, Chambers LW. Mediastinal paraganglioma. Ann Thorac Surg. 2017;103:e413–4.
[3] Brown ML, Zayas GE, Abel MD, et al. Mediastinal paragangliomas: the mayo clinic experience. Ann Thorac Surg. 2008;86:946–51.
[4] Young WFJ. Paragangliomas: clinical overview. Ann N Y Acad Sci. 2006;1073:21–9.
[5] Suzawa K, Yamamoto H, Ichimura K, et al. Asymptomatic but functional paraganglioma of the posterior mediastium. Ann Thorac Surg. 2014;97:1077–80.
[6] Lin M, Chang Y, Lee Y, et al. Non-functional paraganglioma of the posterior mediastinum. Interact Cardiovasc Thorac Surg. 2009;9:540–2.
[7] Neumann HPH, Young WFJ, Eng C. Pheochromocytoma and paraganglioma. N Engl J Med. 2019;381:552–65.
[8] Takahashi Y, Kamitani T, Kawanami S, et al. Mediastinal paraganglioma. Jpn J Radiol. 2015;33:433–6.
[9] Taieb D, Hicks RJ, Hindie E, et al. European association of nuclear medicine practice guideline/society of nuclear medicine and molecular imaging procedure standard 2019 for radionuclide imaging of pheochromocytoma and paraganglioma. Eur J Nucl Med Mol Imaging. 2019;46:2112–37.
[10] Mehta CK, Gillespie CT, Lin X, et al. Rare middle mediastinal paraganglioma mimicking metastatic neuroendocrine tumor. Ann Thorac Surg. 2015;100:702–5.
[11] Balcombe J, Torigian DA, Kim W, et al. Cross-sectional imaging of paragangliomas of the aortic body and other thoracic branchiomeric paraganglia. AJR Am J Roentgenol. 2007;188:1054–8.
[12] Jeung MY, Gasser B, Gangi A, et al. Imaging of cystic masses of the mediastinum. Radiographics. 2002;22:79–93.
[13] Ortega PE, Sosa LA, Patel M, et al. Cystic paraganglioma of the anterior mediastinum. Ann Diagn Pathol. 2010;14:341–6.
[14] Fledner SMJ, Lehnert H, Pacak K. Metastatic paraganglioma. Semin Oncol. 2010;37:627–37.
[15] Matsumoto J, Nakajima J, Takeuchi E, et al. Successful peroperative management of a middle mediastinal paraganglioma. J Thorac Cardiovasc Surg. 2006;132:705–6.
[16] Wald O, Shapira OM, Murar A, et al. Paraganglioma of the mediastinum: Challenges in diagnosis and surgical management. J Cardiothorac Surg. 2010;5:2–4.
[17] Ma L, Mei J, Liu L. Thoracoscopic resection of functional posterior mediastinal paraganglioma: a case report. J Thorac Dis. 2014;6:1861–4.
[18] Yang Z, Shi Q, Bao F. A case of an unexpected posterior mediastinal functional paraganglioma: case report and literature review. BMC Anesthesiol. 2020;20:1–5.
[19] Takahashi T, Nogmura H, Kuriki K, et al. Superior mediastinal paraganglioma associated with von Hippel-Lindau syndrome: Report of a case. World J Surg Oncol. 2014;12:1–5.
[20] Shi G, Cui Y, He Y, et al. An unusual case of incomplete Carney triad: An 18-year-old girl suffering from multiple benign tumors. J Thorac Dis. 2016;8:E1202–6.