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Case report

Paraganglioma of the middle mediastinum

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ABSTRACT

A 60-year-old female was evaluated for significant weight loss, nausea, vomiting, and dysphagia. A computed tomography (CT) of the chest showed a 3 cm mass in the middle mediastinum. CT scan of the abdomen and pelvis revealed no abnormality. Positron emission tomography (PET) of the whole body revealed tracer uptake in the pre-carinal nodal mass. There were no other suspicious foci of tracer uptake. Mediastinoscopy and biopsy revealed a well-differentiated low-grade neuroendocrine tumor. She underwent sternotomy, and after careful mobilization of the great vessels, the middle mediastinal mass was successfully resected. Final pathology revealed a paraganglioma with no morphological signs to suggest malignancy. The right lower paratracheal lymph node did not show any tumor cells. She did well postoperatively.

1. Introduction

Paragangliomas are rare tumors arising from extra-adrenal autonomic paraganglia and sometimes referred to as extra-adrenal pheochromocytomas. Paragangliomas can histologically mimic neuroendocrine tumors and can occur at similar locations. The majority are found incidentally, but some can secrete catecholamines or cause local mass effect. Thoracic paragangliomas are rare and commonly occur in the posterior mediastinum. Paragangliomas have malignant potential and respond poorly to chemotherapy and radiation. Surgical resection is the standard of care. Patients without evidence of metastatic disease have the best prognosis.

2. Case presentation

A 60-year-old female with a past medical history of asthma, hypertension, hyperlipidemia, and chronic dysphagia presented to our emergency department for evaluation of significant weight loss (18 kg in 2 months), nausea, vomiting, and worsening dysphagia. She had a long-standing history of difficulty swallowing pills for which she did not seek medical attention and now had increasing difficulty with swallowing solids. She denied any cough, shortness of breath, fever, or headaches. Her blood pressure was 128/77 mm Hg, the temperature was 36.7° Celsius, heart rate was 68 beats/minute, respiratory rate was 18 breaths/minute, and oxygen saturation was 97% while breathing ambient air. On physical exam, she was sitting comfortably without any distress. Lung sounds were clear bilaterally, and no stridor or wheezing was heard. A systolic murmur was heard on auscultation.

The necessary laboratory workup was unremarkable. CT chest with intravenous contrast was performed for evaluation of weight loss, which revealed a 2.8 × 2.7 × 3.4 cm necrotic mass in the aortopulmonary window without surrounding lymphadenopathy (Fig. 1). Initial differentials were an enlarged lymph node due to lymphoma or granulomatous disease, metastatic disease, a bronchogenic cyst. CT abdomen and pelvis was performed to exclude an intra-abdominal pathology, which showed no neoplastic process. QuantiFERON-Gold was negative. Mediastinoscopy for tissue sampling was planned. PET scan of the whole body was performed to examine any heterogeneity of the activity in the mass to help target the sampling during mediastinoscopy and exclude any other active lesions. It revealed ^{18}Fluorodeoxyglucose (18-FDG) uptake in the pre-carinal nodal mass, mostly inferiorly (SUV max 4), and no other foci of tracer uptake. She underwent mediastinoscopy, and biopsy revealed a well-differentiated low-grade neuroendocrine tumor. The whole-body octreotide scan revealed tracer uptake in the midline of the thoracic region consistent with the known mediastinal neuroendocrine tumor and no other suspicious foci of tracer uptake to suggest distant metastasis. Evaluation of dysphagia with an esophagogastroduodenoscopy showed a stricture, which was dilated.

She eventually underwent sternotomy with successful resection of the middle mediastinal mass, after mobilization of the great vessels. Final pathology revealed uniform cells with well-differentiated neuroendocrine nuclear features surrounded by spindle cells. These cells were

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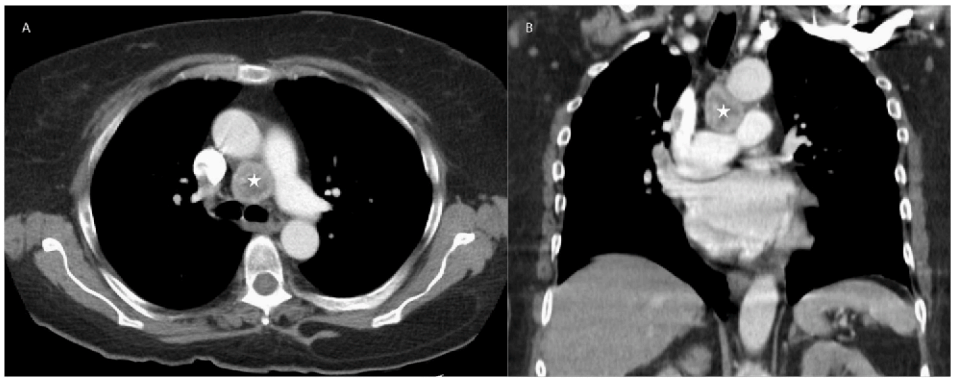

Fig. 1. Computed tomography of the chest shows a round heterogeneous lesion (denoted by a star) in the middle mediastinum (A) axial view (B) coronal view.

strongly positive for S-100 immunostaining and GATA3 with negative pan-cytokeratin consistent with a paraganglioma. The lower right paratracheal lymph node was negative. She had an uneventful recovery and was discharged six days post-surgery. She will be followed closely as an out-patient with surveillance imaging.

3. Discussion

Paragangliomas are rare neuroendocrine tumors derived from embryonic neural crest cells. They can arise from either parasympathetic or sympathetic paraganglia; two types occur with similar frequency. Parasympathetic ganglia-derived paragangliomas are mainly located in the head and skull base along the branches of the glossopharyngeal and vagus nerves. Sympathetic ganglia-derived paragangliomas arise outside of the adrenal gland anywhere along the sympathetic chain, with the majority occurring in the abdomen (75%). Paragangliomas account for less than 0.3% of mediastinal masses [1]. These tumors arise from the paravertebral aortosympathetic paraganglia in the posterior or from the aortopulmonary paraganglia in the middle mediastinum. Paragangliomas of the aortopulmonary paraganglia are exceptionally rare and make up less than 1% of mediastinal tumors [2]. The aortopulmonary paraganglia are typically found in one of the five locations: between the ascending aorta and pulmonary trunk, between the ductus arteriosus and the pulmonary artery, between the right subclavian and right common carotid arteries, between the left subclavian and left common carotid arteries, or caudad to the left subclavian artery adjacent to the aortic arch [2].

Most paragangliomas are diagnosed in the third to fifth decade of life. The majority are found incidentally, but some may also present with local symptoms depending on the location and proximity to the nearby structures. These can be cough, hoarseness, dyspnea, chest, or back pain. Some paragangliomas can secrete catecholamines and may present with symptoms of hypertension, headache, and diaphoresis. In a case series from Brown et al., 13 out of 14 patients were found to have catecholamine secreting mediastinal paragangliomas [3]. CT scan is usually the initial modality of imagining revealing a mass in a characteristic location in the para-aortic region of the middle mediastinum or paravertebral region of the posterior mediastinum. Typical imaging characteristics are also seen in magnetic resonance imaging. Radioisotope imaging using metaiodobenzylguanidine (MIBG) scintigraphy and PET/CT with 18-FDG is used for localization and staging of these tumors when appropriate. Plasma and urine levels of metanephrine and normetanephrine are commonly measured in cases of suspected secretory paragangliomas. Differential diagnosis includes lymphadenopathy, thymic carcinoid, bronchogenic cyst, or aortic arch aneurysm.

Paragangliomas are highly vascular tumors that are typically associated with blood vessels and neural structures. Pathologically paragangliomas are challenging to distinguish from other neuroendocrine tumors without immunohistochemical staining [4]. Paragangliomas are generally low-grade indolent neoplasms, but over time, about 15–35% display malignant behavior. Histologic features like mitotic index cannot state whether a paraganglioma is benign or malignant. Paragangliomas can be assessed as malignant only when there is metastasis to a site where paragangliomas are not known to occur [4]. In a retrospective review of 272 patients with metastatic paraganglioma by Hamidi et al., 35% had synchronous metastases, and 65% developed metachronous metastases [5].

Complete resection of the middle mediastinal paraganglioma provides the best long-term outcomes since these tumors are relatively resistant to chemotherapy and radiation therapy [3,6]. Due to close proximation of the mass with great vessels and cardiac structures, surgery can be complicated and best accomplished at experienced centers. Median sternotomy is usually performed with cardiac bypass and reconstruction if the left atrium or great vessels are involved. Two significant concerns include intraoperative bleeding and the catecholamine crisis in patients with metabolically active tumors.

Prognosis is generally favorable in patients with single solitary paraganglioma amenable to complete resection. Lamy et al. reviewed a cohort of 79 patients with middle mediastinal paraganglioma over 180 months. Survival was 84.6% with a mean survival time of 125.7±18.7 months (mean±standard error) in patients who underwent complete resection. Survival was 50% with a mean survival time of 71.5±13.8 months (mean±standard error) in patients who underwent partial resection and adjuvant therapy [6]. Prognosis in malignant paragangliomas is impacted by tumor burden, location of metastases, and rate of progression. In one review of patients with metastatic paraganglioma, the overall and disease-specific survivals were 24.6 and 33.7 years, respectively [5]. In one series of 192 patients, the five-year probability of recurrence was 20% in secretory extra-adrenal paraganglioma [7]. Given the risk of local recurrence and metastases, lifelong surveillance with imaging or biochemical testing in cases of secretory paraganglioma is warranted.

Declaration of competing interest

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

[1] Y. Takashima, T. Kamitani, S. Kawanami, M. Nagao, M. Yonezawa, Y. Yamasaki, S. Baba, H. Yabuuchi, T. Hida, K. Kohashi, K. Nakamura, H. Sonoda, Y. Oda, H. Honda, Mediastinal paraganglioma, Jpn. J. Radiol. 33 (7) (2015) 433–436.

[2] J. Balcombe, D.A. Torigian, W. Kim, W.T. Miller Jr., Cross-sectional imaging of paragangliomas of the aortic body and other thoracic branchiomeric paraganglia, AJR Am. J. Roentgenol. 188 (4) (2007) 1054–1058.
[3] M.L. Brown, G.E. Zayas, M.D. Abel, W.F. Young Jr., H.V. Schaff, Mediastinal paragangliomas: the mayo clinic experience, Ann. Thorac. Surg. 86 (3) (2008) 946–951.
[4] C.K. Mehta, C.T. Gillespie, X. Lin, A. Yeldandi, M. DeCamp, A. Bharat, Rare middle mediastinal paraganglioma mimicking metastatic neuroendocrine tumor, Ann. Thorac. Surg. 100 (2) (2015) 702–705.
[5] O. Hamidi, W.F. Young Jr., N.M. Iñiguez-Ariza, N.E. Kittah, L. Gruber, C. Bancos, S. Tamhane, I. Bancos, Malignant pheochromocytoma and paraganglioma: 272 patients over 55 years, J. Clin. Endocrinol. Metab. 102 (9) (2017) 3296–3305.
[6] A.L. Lamy, G.J. Fradet, A. Luoma, B. Nelems, Anterior and middle mediastinum paraganglioma: complete resection is the treatment of choice, Ann. Thorac. Surg. 57 (1) (1994) 249–252.
[7] L. Amar, A. Servais, A.P. Gimenez-Roqueplo, F. Zinzindohoue, G. Chatellier, P. F. Plouin, Year of diagnosis, features at presentation, and risk of recurrence in patients with pheochromocytoma or secreting paraganglioma, J. Clin. Endocrinol. Metab. 90 (4) (2005) 2110–2116.