Case Report

Primary Pulmonary Paraganglioma

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We describe a 46-year-old man with a mass in the lower lobe of the right lung. The tumor was initially suspected to be a poorly differentiated adenocarcinoma after endobronchial biopsy. Subsequently, a right lower lobectomy was performed, and a paraganglioma was diagnosed histologically. Using whole-body CT scan and metaiodobenzylguanidine (MIBG) scintigraphy, we excluded the involvement of other organs. No evidence of recurrence or metastasis was found during the follow-up period of 3 years. Primary pulmonary paragangliomas are very uncommon tumors. Literature relevant to this disease entity is discussed.
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Paragangliomas are uncommon tumors arising from paraganglionic tissue dispersed from the base of skull to the pelvic diaphragm.[1] These tumors produce symptoms by secreting catecholamines or by local tumor expansion. They can be also part of several hereditary disorders.[2] These tumors have been reported in a variety of uncommon locations, including the lung parenchyma. Here, we report a case of primary pulmonary paraganglioma in a 46-year-old man. We also highlight the thorough evaluation for other occult tumors with emphasis on new methods of topographic diagnosis of paraganglioma.

Case Report

A 46-year-old man complained of cough and yellowish sputum for 2 months. A chest radiograph and computed tomography (CT) of the chest at a community hospital disclosed a mass, measuring $4.5 \times 4 \times 4.5$ cm^3, in the superior segment of the right lower lobe (RLL) of the lung near the hilum (Fig. 1). Bronchoscopic examination disclosed a polypoid mass obstructing the superior segmental bronchus of RLL. Endobronchial biopsy revealed poorly differentiated adenocarcinoma.

The patient was transferred to our chest clinic for further evaluation in June 1998. His past medical and family history were unremarkable. He was an engineer without smoking habit. On examination, his vital signs were stable. His chest expanded symmetrically with clear breathing sound. A hemogram and blood biochemistry values were all within normal limits. A whole-body bone scan revealed no abnormal focal area of increased uptake of radioactivity. There was no organic lesion in the brain CT scan. The patient underwent a RLL lobectomy with bronchoplasty and

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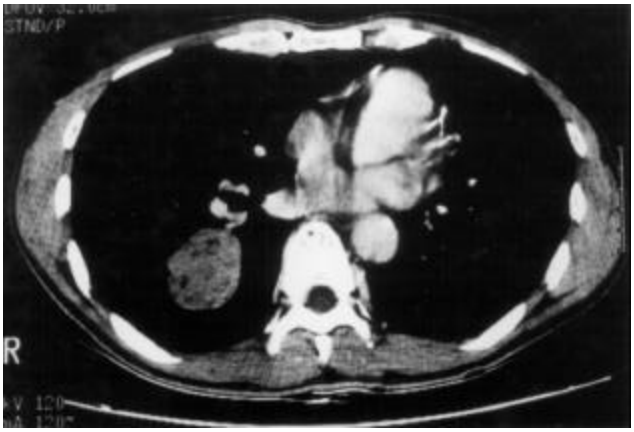

Fig. 1. Chest CT scan showing a well-circumscribed mass with inhomogenous density and relatively low vascularity.

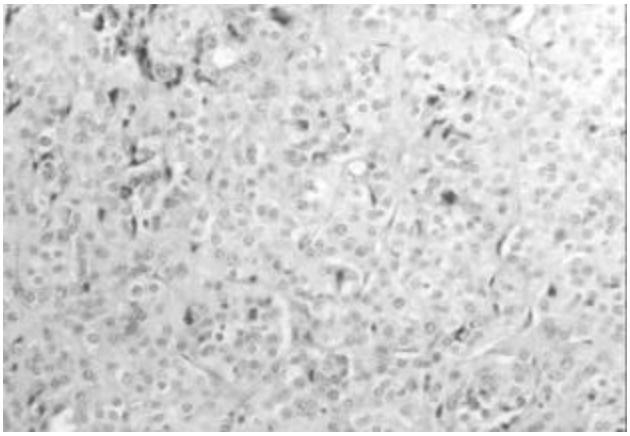

Fig. 2. Nesting ovoid cells separated by delicate fibrovascular septa are characteristic for paraganglioma. (H & E; original magnification, × 200).

radical lymph node dissection on July 3, 1998.

A well-circumscribed soft brownish tumor, measuring 5.5 × 3.5 × 3.5 cm^3, with 1 cm from the bronchial resection margin was found. Grossly, the tumor was friable and sharply demarcated from surrounding lung parenchyma without invasion of the visceral pleura. There were several enlarged lymph nodes, soft and black to gray-colored, over the right interlobar, hilar, subcarinal, and paratracheal regions. On pathological examination, the tumor was composed of ovoid cells with characteristically granular amphophilic to basophilic cytoplasm (Fig. 2). The nuclei were round to ovoid with salt and pepper-type chromatin pattern.

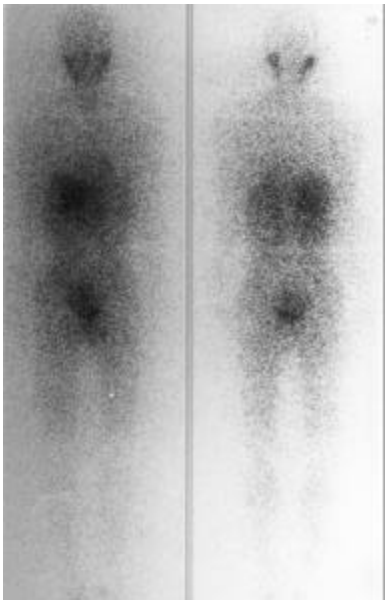

Fig. 3. The I^{131}-MIBG scintigraphy at 48 hr after injection of 1 mCi of agent revealed no abnormal focal area of uptake in the whole-body survey.

There were giant tumor cells with intranuclear inclusions. The tumor cells were arranged in characteristic nests separated by delicate fibrovascular septa. Characteristic neuroendocrine patterns with the apical granular cytoplasm towards the capillaries rather than into the glandular lumen were also noted. Some tumor cells showed brownish pigments suggestive of lipochrome pigments or neuromelanin pigments. All resected lymph nodes were free of tumor. Immunohistochemistry demonstrated an intense cytoplasmic staining reaction for synaptophysin and S-100 protein-reactive sustentacular cells. A staining pattern for neuron-specific enolase was also present. Stainings for mucicarmine, carcinoembryonic antigen (CEA) and cytokeratin were negative. The findings were consistent with paraganglioma.

In the following evaluation, there was no visible mass lesion in the whole-body CT scan imaging. The 24-hr urine vanillylmandelic acid was 6.54 mg (normal range: 1.0-7.5 mg). The patient had an uneventful recovery. There has been no recurrence or metastasis during the subsequent 3 years. In the interim, metaiodobenzylguanidine (MIBG) scintigraphy was done on May 14, 1999, which did not find any I^{131}-MIBG avid lesion in the whole-body survey (Fig. 3).

Discussion

Intrathoracic paragangliomas are infrequent tumors. Most of them are located in the mediastinum, originating from aorticopulmonary paraganglia or paravertebral sympathetic chains.[3] In the lung, the so-called "multiple minute chemodectomas" are more frequent than primary pulmonary paragangliomas. The former are found in approximately 3% of autopsies and occur frequently in association with chronic lung diseases. They are believed to originate from either muscle cells or cells strongly resembling meningoendothelial cells and be stimulated by ischemia. Primary pulmonary paragangliomas are very rare. The majority of them originate from the glomera in relation to the pulmonary vessels and nerves. Most are closely associated with the pulmonary arteries. Some authors have used this as criteria for diagnosis. According to the WHO classification, they are tumors belonging to the group of parasympathetic (non-chromaffin) branchiomeric paragangliomas, formerly also known as chemodectomas.[4]

Since the first case of primary pulmonary paraganglioma described by Heppleston in 1958, only 23 cases have been described.[5,6] It is female-predominated and usually presented as an asymptomatic, subpleural pulmonary nodule. Cytologically, it is difficult to differentiate from bronchial carcinoid by the morphological features. Endobronchial biopsy was done in our patient at the primary hospital. On microscopic examination, polygonal neoplastic cells organized into cords, nests, and sheets with occasional acinar configuration were found. He was first diagnosed to have poorly differentiated adenocarcinoma. Definitive diagnosis was made after surgical exploration. The characteristic cell nests surrounded by a delicate vascular stroma ("Zellballen" pattern) supported the diagnosis. In fact, from previous reports, it is very difficult, even impossible, to differentiate between paraganglioma and carcinoid tumor in the lung. The morphological features are not absolutely specific for paragangliomas as carcinoids, including bronchial carcinoids, may show a similar appearance. The demonstration of S-100 protein-reactive sustentacular cells, however, supports the diagnosis; although the presence of these cells has been demonstrated in some bronchial carcinoid tumors, they seem to have a more sporadic or inconstant distribution. There is also no consistent tendency for immunoreactivity of the chief cells helpful in the differentiation. Skodt *et al.* proposed that focally positive cytokeratin reactivity in the primary pulmonary paraganglioma was in accordance with the embryogenesis of paraganglionic cells.[6] On the contrary, we did not have similar finding in our patient. In fact, the negative finding was used by others to differentiate from the carcinoid tumors.[7]

Pulmonary paragangliomas are mostly benign. Only 3 malignant cases have been reported. Distinction between benign and malignant paragangliomas is difficult on a purely morphologic basis. It has been made by examining the behavior of metastasis to regional lymph nodes.[8] By contrast with mediastinal paragangliomas, pulmonary paragangliomas have a better prognosis. The former usually preclude a complete excision due to their intimate relation to the great vessels, their rich vascular supply, and the neoplastic invasion of vital organs in the mediastinum.

Recently, the introduction of MIBG scintigraphy and magnetic resonance (MR) imaging has provided new insights into paragangliomas and has tremendously changed the topographic diagnosis of paragangliomas.[9,10] The former has been found to be accurate in the localization of functioning paragangliomas, especially at extra-adrenal sites. Consideration was even given to the therapeutic potential of I^{131}-MIBG-targeted radiotherapy in neural crest tumors.[11] No abnormal MIBG uptake site was found in our patient postoperatively using this technique. We did cheaper whole-body CT scan imaging rather than MR imaging to seek other tumors that did not take up MIBG. The result was also negative. Adrian *et al*. proposed that the latter has the advantages of a higher spatial resolution, not involving ionizing radiation and not being hampered by medication as in the case of MIBG scintigraphy.[9]

Primary pulmonary paraganglioma usually presents as a solitary, peripheral asymptomatic nonfunctioning mass in the lung parenchyma. Our patient had a much more uncommon disease process comprising parenchymal and airway components.[12]

The endobronchial lesion with obstruction accounts for his initial manifestation of cough with purulent sputum. The prognosis was determined by the tendency of neighboring lymph node invasion. Complete resection predicted a favorable outcome.

References

1. Fonseca V, Bouloux PM. Pheochromocytoma and paraganglioma. *Baillieres Clin Endocrinol Metab* 1993;7:509-44.
2. Carney JA. The triad of gastric epitheloid leiomyosarcoma, pulmonary chondroma and functioning extra-adrenal paraganglioma: a five-year review. *Medicine* 1983;62: 159-69.
3. Odze R, Begin LR. Malignant paraganglioma of the posterior mediastinum: a case report and review of the literature. *Cancer* 1990;65:564-9.
4. Williams ED, Siebenmann RE, Sobin LH. Histological typing of endocrine tumors. In: *WHO international histological classification of tumors.* Geneva: World Health Organization, 1980:33-9.
5. Heppleston AG. A carotid-body-like tumor of the lung. *J Path Bact* 1958;75:461-4.
6. Skodt V, Jacobsen GK, Helsted M. Primary paraganglioma of the lung: report of 2 cases and review of the literature. *APMIS* 1995;103:597-603.
7. Hasleton PS. Benign lung tumors and their malignant counterparts. In: Hasleton PS, ed. *Spencer's Pathology of the Lung.* 5th ed. New York: McGraw-Hill, 1996:895-917.
8. Lemonick DM, Pai PB, Hines GL. Malignant primary pulmonary paraganglioma with hilar metastasis [letter]. *J Thorac Cardiovasc Surg* 1990;99:563-4.
9. van Gils AP, van Erkel AR, Falke TH, Pauwels EK. Magnetic resonance imaging or metaiodobenzylguanidine scintigraphy for the demonstration of paraganglioma? Correlation and disparities. *Eur J Nucl Med* 1994;21:239-53.
10. Shapiro B, Sisson JC, Shulkin BL, Gross MD, Zempel S. The current status of metaiodobenzylguanidine and related agents for the diagnosis of neuro-endocrine tumors. *Q J Nucl Med* 1995;39:3-8.
11. Troncone L, Rufini V. I^{131}-MIBG therapy of neural crest tumors. *Anticancer Res* 1997;17:1823-31.
12. Simoff MJ. Endobronchial paraganglioma. *J Bronchol* 2001;8:203-6.