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Case report

Utility of immunohistochemical staining for the diagnosis of Extra-adrenal mediastinal paraganglioma

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ABSTRACT

Extra-adrenal, mediastinal paraganglioma are rare tumors that origin from sympathetic ganglia. Common diagnostic steps include CT, MRI and PET-Scan. We present a case where immunohistochemical staining was an essential step for final diagnosis in a patient without symptoms of endocrine activity and an uncommon location of this tumor entity. In combination with clinical particularities on the origin of the tumor and characteristic morphology, the immunohistochemical staining of tumor tissue is a necessary diagnostic tool for paraganglioma.

1. Introduction

Extra-adrenal, mediastinal paraganglioma are rare tumors that origin from sympathetic ganglia and often present with tachycardia or flush. Diagnosis in asymptomatic patients can be challenging and asks for a synopsis of CT, PET-CT, clinical information and immunohistochemical staining.

1.1. Case report

A 51-year old Caucasian woman was admitted to hospital after an incidental finding of a mediastinal tumor. Because of an uncertain paresthesia of both hands a CT was undertaken showing, beside a carpal tunnel syndrome, the tumor. She had no other symptoms, especially no flush, hypertension, globus sensation, tachycardia or B-symptoms. The tumor was bilocated caudal the aortic arch and the aortic bulbus. A diagnostic probe of the tumor via mediastinoscopy showed a well differentiated, low proliferative active neuroendocrine differentiated tumor. A high expression of synaptophysin, NSE and chromogranin could be seen but CK7-expression was missing. The proliferation activity was 2% with no mitoses. The origin was supposed to be the lung or the thymus. A DOTATOC-PET/CT scan showed an intensified somatostatin receptor expression of the tumor with a higher expression in the ventrocaudal part of the tumor. There was no other location of neuroendocrine tumor tissue found. The left main bronchus was compressed from outside with an unhindered passage possible by flexible bronchoscopy. Via median sternotomy and transpericardial preparation a tumor of 3 × 3 × 1.7 cm size impressed rough on palpation located directly ventral to the aortic bulb. A second tumor, sized 4 × 4.2 × 3.6 cm, was palpated caudal the aortic arch (see Fig. 1).

Both tumors were removed in healthy tissue. The histopathologic examination revealed nodular infiltrates composed of nests and trabeculae of polygonal cells (see Fig. 2).

Additional immunohistochemical staining was done showing high positivity of chromogranin and synaptophysin as well as high positivity of S-100 in sustentacular cells and low proliferative activity of <1% in staining for MIB-1 (see Figs. 3 and 4).

Staining for thyroglobulin and GFAP was negative. So, the histological diagnosis was consistent with a paraganglioma.

Patient recovered well from the operation and was discharged from ICU on first post-operative day. She is now in regular check-up.

2. Discussion

Paraganglioma (or glomus tumor) are rare neuroendocrine tumors of sympathetic or parasympathetic paraganglia that most frequently occur in the head and neck but can also be found in the abdomen, pelvis or thorax, often associated to the Zuckerkandl organ. Glomus tumor in the mediastinum are mostly located in the anterior mediastinum [1]. A case series of the Mayo Clinic indicated that most patients are female with a median age of 39 years [2]. Paraganglioma may have endocrine activity and lead to symptoms like tachycardia or flush. The only curative

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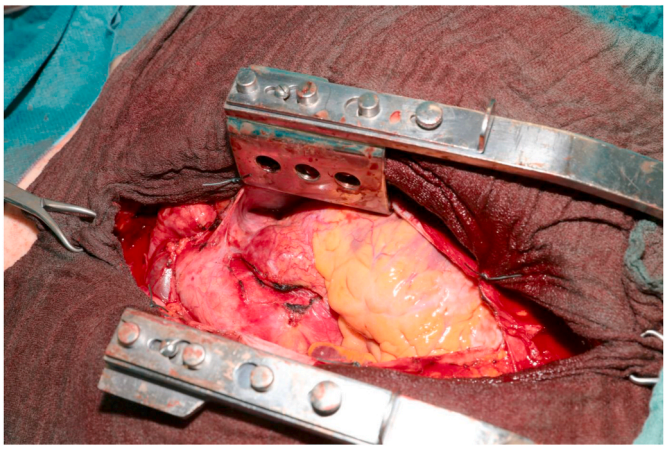

Fig. 1. Intraoperative view of bilocated paraganglioma aorticopulmonale

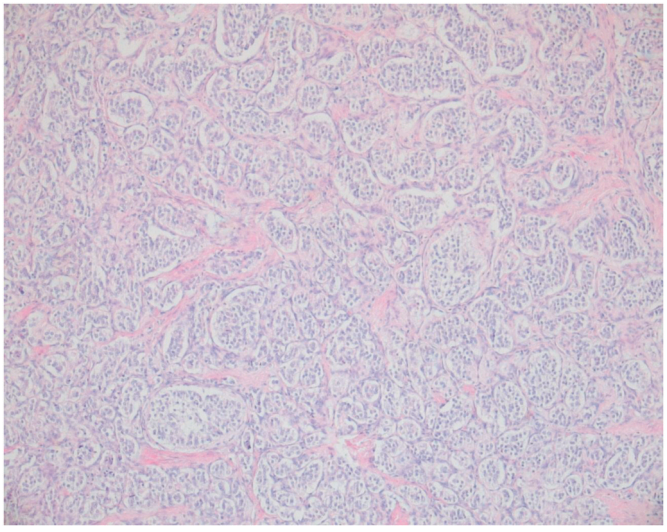

Fig. 2. Characteristic Zellballen morphology (100x).

therapy option is the complete resection of the tumor. Diagnostic steps often include blood test, urinary testing, CT or MRI and DOTATOC-PET [3]. Herein, we present a case where immunohistochemic examination represents the crucial diagnostic tool. Immunohistochemical staining is essential in the diagnosis of neuroendocrine tumors. Differentiation of morphological similar neuroendocrine tumors needs to be confirmed by immunohistochemistry including at least chromogranin A and synaptophysin. It is well known that most paraganglioma express chromogranin and synaptophysin. However, distinction between paraganglioma and typical carcinoid tumors can be achieved by immunoreactivity for S-100. High positivity for S-100 is seen in the sustentacular cells of paragangliomas [4]. Because of the histomorphological pattern the pathologists thought about other tumor entities. The paraganglioma has to be distinguished from medullary thyroid carcinoma and because of the positivity of some neuroendocrine neoplasia, TTF-1 was not recommended. Otherwise a neoplasia associated to the vertebral column must be ruled out due to the localization of the tumor. Hence, negative IHC Stain thyroglobulin and GFAP were useful in differential diagnosis.

Still, conclusive differentiation between neuroendocrine tumors is not possible without clinical information on surgical site. The histomorphological as well as the immunohistochemical patterns are very similar. The initial histopathological examination revealed a neuroendocrine differentiated tumor with low rate of mitosis. In combination

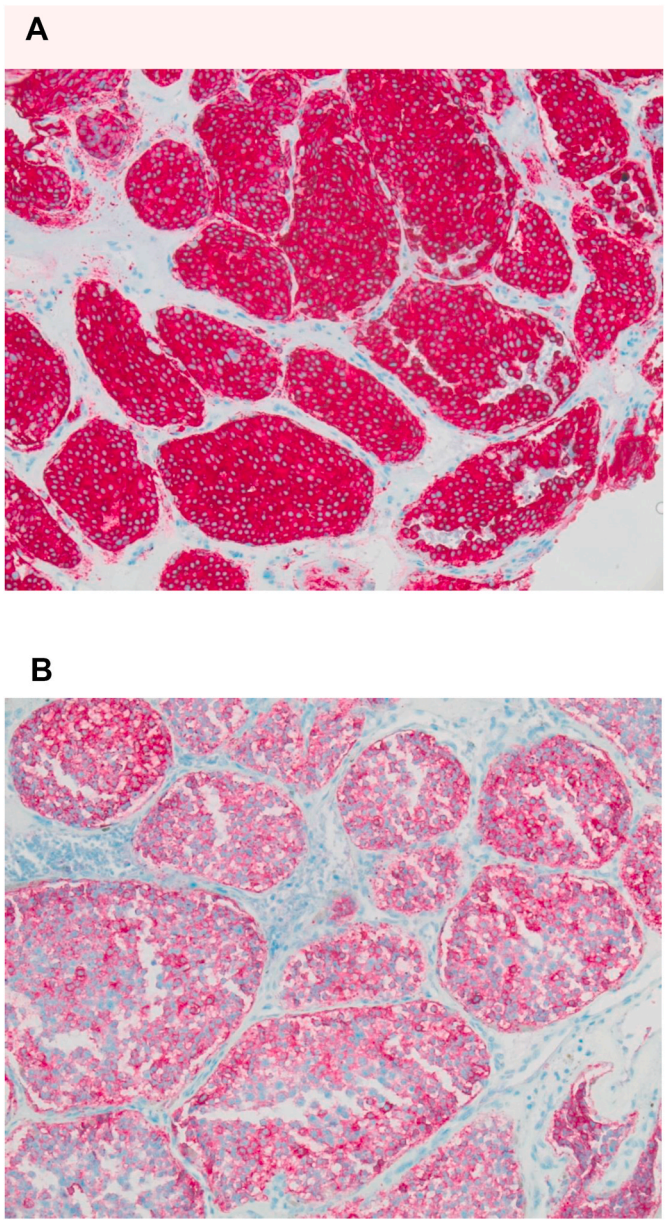

Fig. 3. a: Immunohistochemical staining for synaptophysin (200x), Fig. 3b: Immunohistochemical staining for chromogranin A (200x).

with pre-surgical presumption of pulmonary tissue this was consistent with a typical carcinoid. However, intraoperative finding of a mediastinal tumor along with the immunohistochemical pattern of paraganglioma led to the final diagnosis.

In the case outlined above, immunohistochemic staining was mandatory for diagnosis. However, final diagnosis was only possible by synopsis of DOTATOC-PET-Scan, clinical particulars of tumor origin, histomorphological pattern and immunhistochemic expression of chromogranin, synaptophysin and S-100.

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Declaration of competing interest

None.

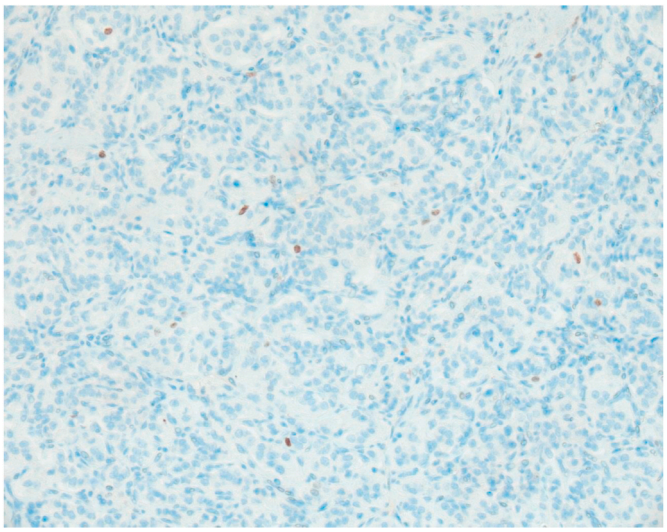

Fig. 4. MIB-1 index in the highest proliferative area (hot spot) is less than 1% (200x).

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