What is your diagnosis?

A strange form of dysphonia... 

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1. Clinical history

A 40-year-old man, with no medical and surgical history apart from smoking, estimated at 15 pack-years, consulted for dysphonia associated with disabling snoring. The dysphonia had been present for 6 months and first occurred after “straining his voice”. Nasolaryngeal fibroscopy (or fiber-optic endoscopy) revealed a left supraglottic submucosal swelling, displacing the ventricular band associated with immobile vocal cords. No mucosal lesion was detected. Computed tomography of the neck and chest, performed elsewhere, was not contributive. Panendoscopy revealed normal mucosa with a firm submucosal mass that was not accessible to biopsy. Complementary MRI and transcervical microbiopsies were then performed (Fig. 1A–D).

2. Questions

• Interpret the MRI?
• Interpret histological sections?
• What is the most likely diagnosis?
• How would you complete the diagnostic and therapeutic management?

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Fig. 1. A. MRI of the neck, axial T1, FAT-SAT sequence. B. MRI of the neck, axial gadolinium-enhanced T1 sequence. C. Histological section of microbiopsies with protein P100 immunolabelling ×100. D. Histological section of microbiopsies with synaptophysin immunolabelling ×40.

What is your diagnosis?
3. Responses

3.1. Question 1

Head and neck MRI, axial section, T1 FAT-SAT sequence (Fig. 1A) and gadolinium-enhanced T1 sequence (Fig. 1B). An endolaryngeal mass was visualized, isointense on T1-weighted sequences, with transient but intense gadolinium enhancement.

Round or polyhedral chief cells (type I), arranged in cell nests with finely granular eosinophilic cytoplasm, were observed. They contained neurosecretory granules demonstrated by the presence of chromogranin and synaptophysin (indicating catecholamine synthesis). Sustentacular cells (type II) were also observed, related to Schwann cells in view of their positive labelling with protein P100 on immunolabelling (Fig. 1C and D). A rich neuroendocrine type of blood supply was observed between these clumps of cells.

The most likely diagnosis based on imaging and histological examination is that of laryngeal paraganglioma.

4. Discussion

On CT scan, paragangliomas present homogeneous, moderately intense tissue density with clearly demarcated contours. These tumours show rapid, intense and transient contrast enhancement and may consequently pass unnoticed on insufficiently documented CT imaging, as in the present case. MRI allows a more accurate diagnosis by visualizing the tumour blood supply, as paragangliomas often present an isointense T1 signal and an isointense or hyperintense T2 signal. Gadolinium enhancement is also intense and transient. Zones with a hyperintense T2 signal forming “pepper and salt” images are highly suggestive of the diagnosis. MR angiography is even more sensitive and specific by revealing an arterial blush over the lesion.

Paragangliomas arise at the expense of cells derived from the amine precursor uptake decarboxylation (APUD) system, which share histochemical and ultrastructural characteristics in common and which are able to decarboxylate amine precursors. The APUD system has now been integrated into the broader concept of the diffuse neuroendocrine system (DNES). DNES cells are disseminated throughout the body. They have a variable embryological origin and exert a control function on other cell types via the amines and peptides that they produce (neurotransmitters, hormones, local paracrine action). Embryologically, paraganglia are tissues derived from migration of neural crest cells. In the head and neck, migration of these cells follows branches of the IXth and Xth cranial nerves to form paraganglia along major arteries from the aortic arch to the base of the skull. They are highly functional satellites of the parasympathetic nervous system. Paraganglia function as chemoreceptors, sensitive to variations in the partial pressures of oxygen, carbon dioxide and arterial pH. Paragangliomas are endocrine tumours arising from these paraganglia. These tumours are most commonly located at the carotid or tympanojugular bifurcation. Laryngeal forms are much rarer, as only slightly more than 70 cases have been reported in the literature [1,2]. The most common laryngeal site is the superior larynx.

4.1. Question 2

4.1.1. Diagnostic work-up of paragangliomas

The diagnostic work-up of paraganglioma [3] must be completed by:

- urinary catecholamine assay to exclude rare cases of secreting tumours;
- systematic search for other paragangliomas by MIBG or 111indium-pentetreotide scintigraphy;

Fig. 2. A. Operative view of the tumour after lateral thyrotomy. B. Operative view after tumour resection, 1: superior laryngeal nerve. C. Operative specimen.
arteriography is now reserved for therapeutic management when preoperative embolization is necessary;

• endoscopic biopsies must not be performed when there is the slightest doubt about the diagnosis;

• subsequently, genetic screening should be proposed, especially to exclude specific syndromes and familial forms, as 30% of paragangliomas are genetically determined. Several mutations have been associated with the formation of these tumours, especially succinate dehydrogenase gene mutations [4]: SHDA, SHDB, SHDC, SHDD and SDHAF2. SDHB mutations are more frequently associated with malignant forms. Paragangliomas may be part of certain syndromes, such as Von Hippel-Lindau disease (VHL gene), multiple endocrine neoplasia type 2 (RET pro-oncogene), and neurofibromatosis type 1 (NF1 gene).

4.1.2. Therapeutic management

Standard treatment consists of surgery: either open surgery, as in our case, or, according to some teams, endoscopic surgery for small tumours [2,5]. In the present case, surgical resection was performed via a neck incision (Fig. 2) over the thyroid notch. Strap muscles were retracted and sectioned laterally. Resection of the upper third of the thyroid cartilage provided access to the tumour and allowed visualization of the superior laryngeal nerve. The lesion appeared to be in contact with branches of the superior laryngeal nerve (internal branch and Galen’s Anastomosis). En bloc resection of the tumour without effraction of the laryngeal mucosa was performed. Strap muscles were sutured at the end of operation. Tracheotomy was not required.

Radiotherapy can be considered in patients with a major surgical contraindication presenting signs of progressive disease or functionally threatening tumour. Rare cases of metastatic paraganglioma have been reported.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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