CASE REPORT

Ganglioneuroma of the retropharyngeal space in a patient with glottic cancer

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SUMMARY

We describe the case of a 71-year-old man with a ganglioneuroma of the retropharyngeal space. The patient presented with a submucosal bulge of the left oropharyngeal wall during follow-up examination of a treated vocal cord carcinoma. CT and MRI revealed a non-specific, well-defined retropharyngeal soft tissue lesion. Positron emission tomography-CT did not show relevant metabolic activity, excluding the hypothesis of metastatic nodal disease. Surgical biopsy of the lesion was compatible with ganglioneuroma. Ganglioneuromas are well-differentiated tumours composed of mature sympathetic ganglion cells that account for approximately 1% of spinal and paraspinal tumours. Peripherally, ganglioneuromas are predominantly found in the posterior mediastinum and retroperitoneal space. Only nine ganglioneuromas of the retropharyngeal space have been reported in the English literature since the early 1980s.

BACKGROUND

Ganglioneuromas are rare, benign neurogenic tumours composed of mature ganglion and Schwann cells. Their anatomical distribution reflects the migration pattern of neural crest precursors to the sympathetic trunks, favouring the posterior mediastinum and retroperitoneal space. Fewer occur in the head and neck compartment. Among these, retropharyngeal ganglioneuromas pose additional diagnostic challenges by presenting at a variable age with non-specific symptoms (or as an incidental finding) and lacking distinguishing features in cross-sectional imaging studies. Complementary investigation is thus mandatory to exclude other lesions affecting this space, namely metastatic/lymphoproliferative adenopathy (the main differential diagnosis), retropharyngeal abscesses, other neurogenic tumours, salivary gland tumours, fibrosarcomas and rhabdomyosarcomas. Correct diagnosis is essential to guide appropriate therapeutic management.

CASE PRESENTATION

A 71-year-old man, followed in our institution for a treated squamous cell carcinoma (SCC) of the right vocal cord (stage T1N0), presented with a smooth submucosal bulge of the left oropharyngeal wall during a follow-up examination. His medical records included non-quantified smoking and drinking habits and an episode of laryngeal tuberculosis, successfully treated with tuberculostatics.

Figure 1 CT scan. Axial (A) and coronal (B) contrast-enhanced CT scans in soft tissue window show a well-demarcated space-occupying lesion (arrows) in the retropharyngeal space, pushing the pharyngeal wall anterior and medially and the longus colli muscle posteriorly. Laterally, there is no cleavage plane between the lesion and the poststyloid parapharyngeal space (carotid space). The lesion is hypodense to muscle and shows well-defined borders without infiltration of adjacent structures.

There were no accompanying symptoms, such as pain, dysphagia, foreign body sensation or neck stiffness.

INVESTIGATIONS

Laryngoscopy showed no evidence of local recurrence of the primary vocal cord tumour. Laboratory assessments were also unremarkable. Contrast-enhanced CT of the head and neck revealed a well-defined left retropharyngeal soft tissue mass, measuring 27×10×27 mm, hypodense relative to normal muscle. It bulged the pharyngeal wall anteromedially and the prevertebral muscles posteriorly, without displacing the carotid artery or the internal jugular vein ([figure 1](#)). MRI was performed for further characterisation. The lesion showed hypointense signal on T1-weighted (T1W) images and hyperintense signal on T2-weighted (T2W) images. There was also moderate and homogeneous enhancement after gadolinium administration ([figure 2](#)).

From a clinical perspective, the early stage of the original vocal cord tumour, as well as the paucity of lymph nodes draining the true vocal folds, made the hypothesis of retropharyngeal lymph node metastasis unlikely. Moreover, there were also no signs of local or cervical lymph node recurrence. An additional 18F-fludeoxyglucose (FDG) positron emission tomography (PET)-CT found neither evidence of increased metabolic activity in the

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Figure 2 MRI scan. Axial T1W (A) and axial (B) and coronal (C) T2W images depict a well-defined ovoid mass (arrows), clearly separated from the pharyngeal wall and prevertebral muscles by a fat plane, isointense to muscle on T1W images and homogeneously hyperintense on T2W images with a hypointense peripheral rim. Gadolinium-enhanced T1W axial images without (D) and with fat suppression (E) show moderate homogeneous enhancement. T1W, T1-weighted; T2W, T2-weighted.

retropharyngeal mass, nor elsewhere in the body ([figure 3](#)). Further characterisation by surgical biopsy revealed a fasciculated lesion of neural origin containing ganglion cells, compatible with ganglioneuroma ([figure 4](#)).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of a lesion in the retropharyngeal space should include primary lesions (from retropharyngeal space structures or persisting embryonic remnants) as well as lesions arising from neighbouring spaces (pharyngeal mucosal space, prevertebral space and parapharyngeal space). In the case we herein report, both the well-defined borders and the preserved cleavage planes with the neighbouring spaces suggested a primary origin in the retropharyngeal space.

Lymph node metastasis should always be considered in patients with a known primary malignancy of the head and neck, particularly one arising from the posterior pharyngeal wall or from the thyroid gland. In the present case, the patient actually had a history of SCC of the vocal cord. Nonetheless, the location of the primary lesion, the early stage of disease at diagnosis and the absence of local recurrence or cervical lymph node involvement made this hypothesis unlikely. Moreover, the absence of FDG uptake on PET-CT excluded the hypothesis of metastatic disease.

Lymphoproliferative disease is another important differential diagnosis of a retropharyngeal mass. Often, lymphoma shows low signal intensity on T2W images and restricted diffusion. These features reflect the hypercellular nature of the lesion and a high nuclear/cytoplasmic ratio (blue round cell tumour). Moreover, lymphoma should also be FDG avid, which was not the case.

Despite the lack of symptoms and normal laboratory findings, a retropharyngeal abscess due to recurrent tuberculosis was another possible diagnosis, given the prior medical history of the

patient. On CT/MRI, tuberculous lymphadenitis is most often non-homogeneous, containing cystic/necrotic areas and occasional calcifications. A suppurative lymphadenitis/abscess tends to course with pain and neck stiffness and a history of recent pharyngitis. Central necrosis, a peripheral ill-defined enhancing rim and restricted diffusion on MRI are expected imaging features in a mature abscess.

Vascular and lymphatic malformations should also be considered in the differential diagnosis of a retropharyngeal mass. High flow vascular lesions tend to show vascular flow voids and vivid enhancement. On the other hand, low flow vascular malformations show high signal intensity on T2W images with some thin internal architecture and a cotton-like centripetal pattern of contrast uptake. They may also contain phleboliths. Lymphatic malformations are highly hyperintense on T2W images and do not enhance after contrast administration unless they have

Figure 3 FDG-PET-CT. (A) FDG-PET-CT (18F-fludeoxyglucose positron emission tomography-CT) shows no appreciable increase in metabolic activity at the level of the lesion (B), thus making the possibilities of metastatic disease, lymphoma and other aggressive lesions less likely.

Figure 4 Pathology. (A) Fragments of the excised ganglioneuroma, with Schwann cells arranged in intersecting fascicles and scattered ganglion cells (low-power H&E stain/40 $\times$). (B) Detail of the boxed region in (A) shows scattered ganglion cells with vast eosinophilic cytoplasm and distinct cell borders, sometimes with finely granular gold-brown pigment, and single eccentric nuclei with prominent nucleolus (high-power H&E/200 $\times$).

mixed lymphangiohemangiomatous components. These vasculo-lymphatic lesions typically have well-defined lobulated margins, which were not present in this case.

Other neurogenic tumours, such as schwannomas and neurofibromas, though typically found in the poststyloid parapharyngeal space along the course of lower cranial nerves, may also affect the retropharyngeal space and the cervical sympathetic chain. Retropharyngeal space neurofibromas have been described in the literature,^{1–3} particularly in the context of neurofibromatosis,^{1,2} with imaging features resembling those presented here.

Ectopic salivary gland tumours can potentially occur in the retropharyngeal space but they are most often seen in the prestyloid parapharyngeal space. Whartin's tumours tend to be cystic with an enhancing mural nodule. High protein content can render them spontaneously hyperintense on T1W images. In contrast, pleomorphic adenomas or benign mixed tumours show no distinctive features, particularly when they are small.

Cystic lesions, such as ectopic branchial cleft and foregut duplication cysts, are rarely seen in the retropharyngeal space. These are purely cystic lesions that occasionally show some internal debris and enhancing septa after recurrent episodes of infection.

A retropharyngeal lipoma could be excluded on the basis of imaging features alone, since the lesion did not show fat density/signal intensity. Its malignant counterpart, liposarcoma, presents as an invasive soft tissue mass with variable metabolic activity on FDG-PET, depending on tumour grade. Other sarcomas, such as synovial sarcoma and rhabdomyosarcoma, are also aggressive lesions that originate from the prevertebral space and longus coli muscle, respectively.

Figure 5 Follow-up CT 2 years from the initial diagnosis. Axial (A) and coronal (B) contrast-enhanced neck CT images in soft tissue window showed stable disease compared with the initial scan (arrows).

Ganglioneuroblastoma and neuroblastoma, the malignant counterparts of neural crest sympathogonia-derived tumours, present as large, ill-defined, non-homogeneous masses that are FDG avid on PET-CT.

TREATMENT

Surgical resection of ganglioneuromas is curative. Retropharyngeal ganglioneuromas can be excised by transcervical or transoral approach.^{4,5} Iatrogenic ipsilateral Horner syndrome is an almost invariable complication that is frequently transient,^{5,6} although it may occasionally persist.⁷ However, since ganglioneuromas are benign lesions, a more conservative approach is also possible, delaying surgical intervention until lesion growth or malignant transformation is detected on serial imaging follow-up examinations.

OUTCOME AND FOLLOW-UP

Thus far, the patient has undergone over 2 years of clinical and imaging follow-up. The tumour has kept stable dimensions on subsequent follow-up CT scans (figure 5) and the patient remains asymptomatic.

Table 1 Retropharyngeal ganglioneuromas previously reported in the literature

Study reference	Patient gender/age	Presenting symptoms
5	Young boy (age not specified)	Incidental finding during routine tonsillectomy
14	67-year-old woman	Gradually worsening hoarseness, followed by dysphagia and difficulty sleeping
19	18-year-old man	Right-sided neck mass
4	42-year-old woman	Incapacitating neck pain, neck stiffness, dysphagia and right upper extremity weakness
20	2-year-old girl	Feeding difficulty with failure to thrive; intermittent obstructive sleep symptoms
12	35-year-old woman	Retroauricular pain and migraine
11	57-year-old man	Dysphagia and dyspnoea
21	2 and 12-year-old boys	2 years old—face swelling; 12 years old—mass noted during physical exam

Figure 6 Structure displacement by a retropharyngeal space-occupying lesion. As depicted in the scheme, a mass of the retropharyngeal space will typically displace the neurovascular bundle laterally, the prestyloid parapharyngeal space anteriorly and the prevertebral muscles posteriorly, while also causing a bulging of the oropharyngeal wall that can be incidentally detected on physical examination.

DISCUSSION

Ganglioneuromas are rare, benign tumours composed of mature sympathetic ganglion cells that originate from the neural crest, accounting for approximately 1% of spinal and paraspinal tumours.⁸ They are most commonly seen in the posterior mediastinum and in the retroperitoneum, with a minority of cases occurring in the cervical region.^{9–10} Despite being more prevalent in paediatric ages, ganglioneuromas can also present later in life.^{4,11–14} In a series of 234 ganglioneuromas, these tumours were further found to be more prevalent in women.^{15,16} Retropharyngeal ganglioneuromas show neither age nor gender preference, since five out of nine cases occurred in male patients, with four out of nine tumours having been diagnosed in adults (table 1).

In the head and neck, ganglioneuromas usually present as single masses with slow growth. They can be found incidentally (particularly in paediatric age) or present with dysphagia, dyspnoea, dysphonia, sleep disturbance or neck/retroauricular pain (due to mass effect). Among these symptoms, the most prevalent is dysphagia. Occasionally, tumour cells produce catecholamines or other neuropeptides leading to sympathomimetic symptoms. Retropharyngeal ganglioneuromas can also cause IX–XII cranial nerve symptoms due to extrinsic compression (figure 6).

CT imaging depicts ganglioneuromas as well-defined hypodense masses with moderate enhancement, at times showing a heterogeneous pattern that reflects the myxoid matrix of the tumour.^{6,9} Up to 20% may have calcifications.¹⁷ On MRI, these lesions are predominantly hypointense on T1W images and hyperintense on T2W images, showing variable and progressive enhancement. Increased signal intensity on T2W images is thought to reflect high cellularity and large interstitial volume.¹¹ Linear hypointense striations within the lesion likely correspond to interlacing bundles of Schwann cells and collagen fibres.¹⁴ Apart from the calcifications, the imaging features of our case correlate well with those described in the literature. However,

the absence of distinguishing imaging features implies that the diagnosis of these tumours is made histologically. In our case, histological characterisation was performed by surgical biopsy, which revealed the hallmark features of a ganglioneuroma: mature ganglion cells with voluminous cytoplasm dispersed in a schwannian background.¹²

Malignant transformation of these well-differentiated tumours is exceedingly rare but may occur particularly in ganglioneuromas that originate from more primitive neuroectodermal cells.¹⁸ Surgical excision is regarded as the treatment of choice for symptom-producing cervical ganglioneuromas.⁴ Despite being curative, resection will invariably cause iatrogenic Horner's syndrome, as the sympathetic origin of these tumours would predict. For this reason, the benefit of surgical resection must be weighed against the risk of damaging neighbouring vascular and neural structures. The multidisciplinary head and neck oncological group at our institution decided to carefully monitor this small retropharyngeal ganglioneuroma. To date, there has been no evidence of lesion growth and/or malignant transformation.

Learning points

- Detection of retropharyngeal ganglioneuromas predominantly relies on imaging techniques but the ultimate diagnosis is histological.
- In the absence of distinguishing imaging features, their differential diagnosis includes lymphadenopathies (metastatic or lymphoproliferative), other neurogenic tumours, vasculolymphatic malformations and fibromyxomatous lesions.
- Despite their rarity, this case report reinforces the need to consider ganglioneuromas in the differential diagnosis of a retropharyngeal mass, irrespective of age criteria and medical history.
- When symptoms are absent, a conservative approach with serial imaging studies represents a valid alternative to surgical excision.

Contributors AB was one of the consulting radiologists involved in the diagnosis of the present case report, having also planned the manuscript organisation. As senior author, she was responsible for revising it through its several stages of preparation. RBD wrote the manuscript and prepared the figures. DR compiled the patient's clinical data and selected illustrative CT and MR images. MR processed the surgical biopsy specimen and assembled the corresponding figure 4. All authors read the final version of the manuscript and agreed on its contents.

Competing interests None declared.

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