CASE REPORT

Paraganglioma of the thyroid gland: cytologists' enigma

Kafil Akhtar, Prasenjit Sen Ray, S Shamhsad Ahmad, Rana K Sherwani

Department of Pathology,
Jawaharlal Nehru Medical
College, AMU, Aligarh,
Uttar Pradesh, India

Correspondence to
Dr Prasenjit Sen Ray,
psenray@gmail.com

SUMMARY

Paraganglioma is a neuroendocrine tumour derived from extra-adrenal cells of the neural crest paraganglia of the autonomic nervous system. These rare neoplasms comprise of around 0.012% of head and neck tumours. Paraganglioma arising in the thyroid gland is exceptionally uncommon and can present as a diagnostic challenge on fine-needle aspiration cytology (FNAC). We report a case of primary thyroid paraganglioma in a 19-year-old woman who presented with a solitary thyroid nodule without palpable cervical lymphadenopathy. FNAC from the lesion caused diagnostic dilemma by mimicking follicular neoplasm and C-cell-derived thyroid tumours; final diagnosis was established by histopathology and immunohistochemistry. The main purpose of this case report is to discuss the differential diagnosis and emphasise on the need of immune markers in the diagnosis of thyroid paraganglioma. In view of the uncertain malignant potential of these tumours, a long-term follow-up is recommended.

BACKGROUND

Paraganglioma is a neuroendocrine tumour derived from extra-adrenal cells of the neural crest paraganglia of the autonomic nervous system. In the head and neck region, paraganglia associated with the parasympathetic system are normally located in the jugulo-tympanic, laryngeal, vagal and carotid bodies.¹ Paraganglioma can arise from any of these structures, carotid body being the commonest site (~80% cases). Overall, this rare neoplasm accounts for around 0.012% of all head and neck tumours.²

De novo paraganglioma arising in the thyroid gland is exceptionally rare and only a few cases have been reported in the literature. Most likely, they represent a subset of laryngeal paraganglioma. The pre-operative diagnosis of these tumours can be challenging because the cytological and histological features overlap with more common primary thyroid neoplasms. This report describes a case of paraganglioma of the thyroid gland in a 19-year-old woman who presented with a solitary thyroid nodule without palpable cervical lymphadenopathy.

The main purpose of this case report is to discuss the differential diagnosis and pitfalls that can be encountered in the evaluation of thyroid paraganglioma, especially on fine-needle aspirate smears, and emphasise on the need of immune markers in diagnosing this condition.

CASE PRESENTATION

A 19-year-old Indian woman presented in the surgery clinic with a solitary, firm, non-tender anterior neck mass measuring 4.5×3.5 cm and extending from the midline towards the left side. The swelling appeared about a year ago, was gradually increasing in size and moved with deglutition. There was no previous history of swelling in the same region, difficulty in respiration, change of body weight or appetite. The family history was unremarkable, particularly regarding thyroid diseases. Cervical lymph nodes were not palpable. A provisional diagnosis of solitary thyroid nodule was made.

INVESTIGATIONS

Ultrasonography of the neck showed a 4.2×3.4 cm, hyperechoic, non-homogeneous nodule with no cervical lymph node enlargement. Serum thyroid hormone profile was within normal limits. Fine-needle aspiration cytology (FNAC) of the nodule revealed good cellularity smears consisting of nests of round to oval cells with fine granular chromatin, without prominent nucleoli and delicate cytoplasm (figure 1). These cells showed a vague follicular arrangement and the background was haemorrhagic. Colloid was not observed in the smears examined. While the quantity of cellularity and the pattern of arrangement pointed towards a follicular neoplasm, the chromatin pattern favoured neuroendocrine tumour. However, the age of the patient and the clinical history were not in favour of a malignant lesion. Based on these findings, a differential diagnosis between primary thyroid

Figure 1 Fine-needle aspirate smear showing small nests of round to oval tumour cells with fine nuclear chromatin, without prominent nucleoli and delicate cytoplasm. Vague follicular arrangement is present (H&E, ×400).

To cite: Akhtar K, Sen Ray P, Ahmad SS, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009518

Figure 2 CT scan of the neck showing an enhancing non-calcific soft tissue lesion in the left lobe of thyroid gland (orange arrow). The lesion is totally separate from the adjacent carotid vessels (yellow arrow).

neoplasm (medullary carcinoma vs follicular neoplasm) was offered and the patient was taken up for further investigations.

Subsequently, a CT scan of the neck mass demonstrated an enhancing non-calcific soft tissue lesion of $4.1 \times 3.4 \times 2.5$ cm inside the left lobe of the thyroid gland (figure 2). The patient was taken up for lobectomy followed by excision biopsy. On gross examination, the tumour measured $4.1 \times 3.3 \times 2.5$ cm and the cut surface was solid, vascular with multiple areas of haemorrhage and necrosis (figure 3). Upon microscopic examination, H&E-stained sections revealed a poorly circumscribed neoplasm with a nesting pattern ('Zellballen'), composed of large cells, with moderately pleomorphic nuclei containing variably sized nucleoli and eosinophilic granular cytoplasm (figure 4). The stroma had numerous blood vessels. Immunohistochemical studies showed that tumour cells were diffusely positive for chromogranin (figure 5) and synaptophysin, while negative for cytokeratin and calcitonin stains. Focal S-100 positivity was present in the peripheral sustentacular cells. Thus, a final diagnosis of paraganglioma of thyroid was made.

DIFFERENTIAL DIAGNOSIS

The first-line investigation in solitary thyroid nodule is FNAC. On cytology, paraganglioma shows loose clusters of cells having delicate cytoplasm, round to oval nuclei with mild anisonucleosis and evenly distributed granular chromatin. The cells often

Figure 3 Gross photograph: cut section of the tumour was solid, vascular with areas of haemorrhage.

Figure 4 Microphotograph showing nesting pattern ('Zellballen') composed of large cells, with moderately pleomorphic nuclei containing variably sized nucleoli and eosinophilic granular cytoplasm (H&E, $\times 100$).

form a vague follicular pattern in a bloody background owing to the rich vascularity of these neoplasms.³

The commonest primary thyroid lesion that closely overlaps these cytological features of thyroid-associated paraganglioma is medullary carcinoma. The presence of mild anisokaryosis and spindled cells further potentiate the probability of the latter. Again, the haemorrhagic background of paragangliomas along with the follicular pattern of the cell arrangement can be confused with follicular neoplasm of thyroid. Because the tumours included in this differential diagnosis are morphologically similar, immune markers are essential in distinguishing them.³⁻⁵ This immunoreactivity is best studied on cell block preparation.^{4,5}

On histopathology sections, medullary carcinoma of the thyroid can be confused with paraganglioma, especially when the former exhibits a nesting (paraganglioma-like) pattern of growth. Another disorder that may be confused with paraganglioma is hyalinising trabecular adenoma, a benign thyroid neoplasm that shows a prominent nesting pattern with prominent hyaline deposits, resembling a paraganglioma.^{2,6} Here again, immunohistochemistry serves as a handy tool.

Differential expression of a panel of immunohistochemical markers, including chromogranin A, synaptophysin, cytokeratin, S-100, thyroglobulin and carcinoembryonic antigen (CEA) can

Figure 5 Microphotograph showing diffuse immunohistochemical cytoplasmic positivity of tumour cells with chromogranin ($\times 400$).

be used to distinguish thyroid-associated paraganglioma from primary thyroid tumours. In contrast to medullary carcinoma of the thyroid, thyroid paraganglioma tends to exhibit S-100 protein staining in sustentacular cells compressed at the periphery of the cell nests, but they lack staining for cytokeratin, CEA and calcitonin. Paragangliomas are negative for thyroglobulin—a feature that distinguishes it from follicular lesions. Hyalinising trabecular adenoma is usually negative for chromogranin and positive for thyroglobulin and cytokeratin, unlike paraganglioma. Thus, the role of immunohistochemistry in distinguishing thyroid-associated paraganglioma from its common differential diagnoses are most important.^{2 4–7}

TREATMENT

The patient underwent left lobectomy of thyroid followed by histopathological examination.

OUTCOME AND FOLLOW-UP

The patient is currently doing well without any evidence of recurrent disease at the time of the last follow-up (6 months after the surgery).

DISCUSSION

In 1964, Van Miert⁸ described the first reported case of primary thyroid paraganglioma. Since then, less than 30 cases have been reported in literature. The age of patients spanned from 9 to 73 years with a clear cut female preponderance.² Most thyroid paragangliomas are confined within the thyroid capsule, but in few cases the neoplasm was reported to be locally invasive with infiltration through the tracheal wall.^{9 10}

Paraganglioma may arise at any site where normal paraganglionic tissue exists. Usually, they occur at highly predictable sites and the carotid body has been cited as the most common site of occurrence in the head and neck region (accounting for around 80% cases).² The thyroid gland is an unusual site of primary paraganglioma. Most of these lesions present as slowly enlarging thyroid nodules of several years duration. Usually they are non-functional, that is, do not secrete catecholamines. Clinically, most cases are dismissed as nodular goitre, thyroglossal cyst or follicular adenoma.^{7 11–13}

Radiology plays an important role in confirming the exact location of paragangliomas: whether they are truly of the thyroid origin or are extending from a primary focus in proximal organs like carotid body, larynx, etc. Paragangliomas have rich blood supply. As such, this rare neoplasm should be considered in the differential diagnosis of any hypervascular thyroid nodule. Like their counterparts in other parts of the body, thyroid paraganglioma appears as homogeneous or heterogeneous hyperenhancing soft-tissue mass at CT scan, multiple areas of signal void interspersed with hyperintense foci (salt-and-pepper appearance) within tumour mass at MRI and an intense tumour blush with enlarged feeding arteries on angiography.^{2 14}

Head and neck paragangliomas usually develop slowly and exhibit a low proliferative activity. Although cases with malignant change have been reported, the clinical course of thyroid paraganglioma is generally known to be benign.⁹ The preferred treatment options are lobectomy or total thyroidectomy; an elective radical neck dissection is not indicated. Intraoperatively, thyroid-associated paraganglioma may result in significant intraoperative bleeding and is often densely adherent to the surrounding tissues, including the recurrent laryngeal nerve. Interestingly, the aggressive local behaviour of this tumour does not correspond to be potential for malignancy.¹¹

Careful histopathological examination of the resected specimen supplemented by judicious use of immunohistochemistry is critical in confirming the diagnosis. In view of an uncertain malignant potential, long-term follow-up is recommended for every case. The prognosis of thyroid paraganglioma appears to be favourable, provided that surgical excision is complete.^{6 11}

Learning points

- ▶ Paraganglioma arising in the thyroid gland de novo is a rare slow-growing neoplasm that can clinically present as solitary thyroid nodule.
- ▶ Its cytological features have a considerable overlap with primary neoplasms of the thyroid, and hence pose a diagnostic challenge on fine-needle aspiration cytology.
- ▶ A high index of suspicion, knowledge of the differential diagnoses and careful study of morphology combined with judicious use of immunohistochemistry are the key to an accurate diagnosis of thyroid paraganglioma.
- ▶ These lesions can be treated by surgical excision alone. However, in view of the uncertain malignant potential, a careful long-term follow-up is recommended.

Contributors KA and SSA jointly diagnosed the case on cytology. PSR undertook the literature search and the manuscript preparation. RKS and KA jointly examined the case on histopathology and immunohistochemistry. They also took part in the manuscript editing.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Barnes L, Tse LLY, Hunt JL, et al. Tumour of the paraganglionic system: introduction. In: Barnes L, Eveson JW, Reichart P, Sidransky D, eds. *World Health Organization classification of tumours: pathology and genetics of head and neck tumours*. Lyon: IARC Press, 2005:362–3.
- 2 Ferri E, Manconi R, Armato E, et al. Primary paraganglioma of thyroid gland: a clinicopathologic and immunohistochemical study with review of the literature. *Acta Otorhinolaryngol Ital* 2009;29:97–102.
- 3 Orell SR, Kljanić J. Head and neck; salivary glands. In: Orell SR, Sterrett GF, eds. *Orell & Sterrett's fine needle aspiration cytology*. 5th edn. New Delhi: Churchill Livingstone Elsevier, 2012:45.
- 4 Vodovnik A. Fine needle aspiration cytology of primary thyroid paraganglioma. Report of a case with cytologic, histologic and immunohistochemical features and differential diagnostic considerations. *Acta Cytol* 2002;46:1133–7.
- 5 Jayaram G, Orell SR. Thyroid. In: Orell SR, Sterrett GF, eds. *Orell & Sterrett's fine needle aspiration cytology*. 5th edn. New Delhi: Churchill Livingstone Elsevier, 2012:145.
- 6 Yano Y, Nagahama M, Sugino K, et al. Paraganglioma of the thyroid: report of a male case with ultrasonographic imaging, cytologic, histologic and immunohistochemical features. *Thyroid* 2007;17:575–8.
- 7 Hodge KM, Byers RM, Peters LJ. Paragangliomas of the head and neck. *Arch Otolaryngol Head Neck Surg* 1988;114:872–7.
- 8 Van Miert PJ. The treatment of chemodectomas by radiotherapy. *Proc R Soc Med* 1964;57:946–51.
- 9 Mitsudo SM, Grajower MD, Balbi H, et al. Malignant paraganglioma of the thyroid gland. *Arch Pathol Lab Med* 1987;111:378–80.
- 10 Brownlee RE, Shockley WW. Thyroid paraganglioma. *Ann Otol Rhino Laryngol* 1992;101:293–9.
- 11 Phitayakorn R, Faquin W, Wei N, et al. Thyroid-associated paragangliomas. *Thyroid* 2011;21:725–33.
- 12 Basu S, Viswanathan S. Primary paraganglioma of thyroid presenting as solitary thyroid mass. *J Can Res Ther* 2011;7:385–7.
- 13 Erem C, Kocak M, Nuhoglu I, et al. Primary thyroid paraganglioma presenting with double thyroid nodule: a case report. *Endocrine* 2009;36:368–71.
- 14 Lee KI, Oh YW, Noh HJ, et al. Extraadrenal paragangliomas of the body: imaging features. *Am J Radiol* 2006;187:492–504.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow