date, of the seven cases of intravascular adenomyomatosis (including ours), five show spatial juxtaposition to ordinary adenomyosis and only two do not. Similar molecular changes shared between leiomyomas and intravascular leiomyomatosis might be recapitulated with deep adenomyosis and endometrial stromal sarcoma; for example, the characteristic translocation t (7; 17) (p15; q21) that produces the JAZF1-JJAZ1 gene fusion product and is commonly seen in the latter. In our admittedly single case (FISH analysis performed in the IGENZ laboratory using the ZytoLight SPEC JAZF1 Dual Colour Break apart probe; ZytoVision, Germany), neither deep adenomyosis nor adenomyomatosis showed JAZF1-JJAZ1 gene fusion, implying that such gene rearrangement, frequently required for the multipotential perivascular stromal cells to acquire malignant potential, has not accrued in adenomyosis or adenomyomatosis. Further molecular studies in a well-funded molecular genetics laboratory will undoubtedly shed light on this problem in time.

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Ectopic cervical well differentiated thymic carcinoma: report of a diagnostically challenging rare case

Sir,

Ectopic thymic neoplasms are uncommon and are, with very few exceptions, thymomas of various types.[1] Only rare cases of thymic carcinomas have been reported in the literature.[2–8] The theory behind the origins of ectopic thymic neoplasms is based on the assumption of defective migration of embryonic thymus leading to the formation of ectopic thymic tissue.[1] This concept explains the presence of thymic tissue in the submandibular region, lateral neck, thyroid, paratracheal region and pericardial location but it does not easily explain the presence of ectopic thymic rests in the lung and pleural surfaces where ectopic thymic neoplasms also have been reported. The cervical region is the most common site for ectopic thymic neoplasms and these frequently pose diagnostic challenges. Analogous to the thymus proper, a spectrum of non-neoplastic lesions such as ectopic unilocular/multilocular thymic cysts to neoplastic lesions such as ectopic thymomas or thymic carcinomas can arise.

In this paper, we detail the clinicopathological features of an ectopic cervical well-differentiated thymic squamous cell carcinoma.

The patient first presented at 9 years old with a left submandibular well-circumscribed cystic lesion of 3 × 3 cm. It was a painless, cystic and mobile lump, with no overlying skin changes. A computed tomography (CT) scan performed showed a 3 cm lesion at level I. He underwent excision biopsy of the lesion and microscopic examination showed an encapsulated and partly cystic lesion composed of anastomosing trabeculae of mildly atypical squamous cells with whorl-like structures vaguely reminiscent of Hassall's corpuscles (Fig. 1A,B). No increased mitotic activity was seen. The lesion also contained a lymphoid stroma featuring CD3+ T cells and some TdT positive lymphocytes (Fig. 1C). No lymphoid follicles or subcapsular sinus was seen. At that time, the rendered diagnosis was ectopic thymic cyst. Three months later, the patient presented with another 2.5 cm painless, solid and mobile lesion in the same location. This lesion showed very similar histopathological features as the original excision (Fig. 1D). The diagnosis this time was ectopic thymic tissue with hyperplastic changes. No further treatment was given.

Eight years later, at age 17, the patient presented with two well-circumscribed left sided neck lesions: 5 cm over level IV and 3 cm over level II. Thorough clinical examination on

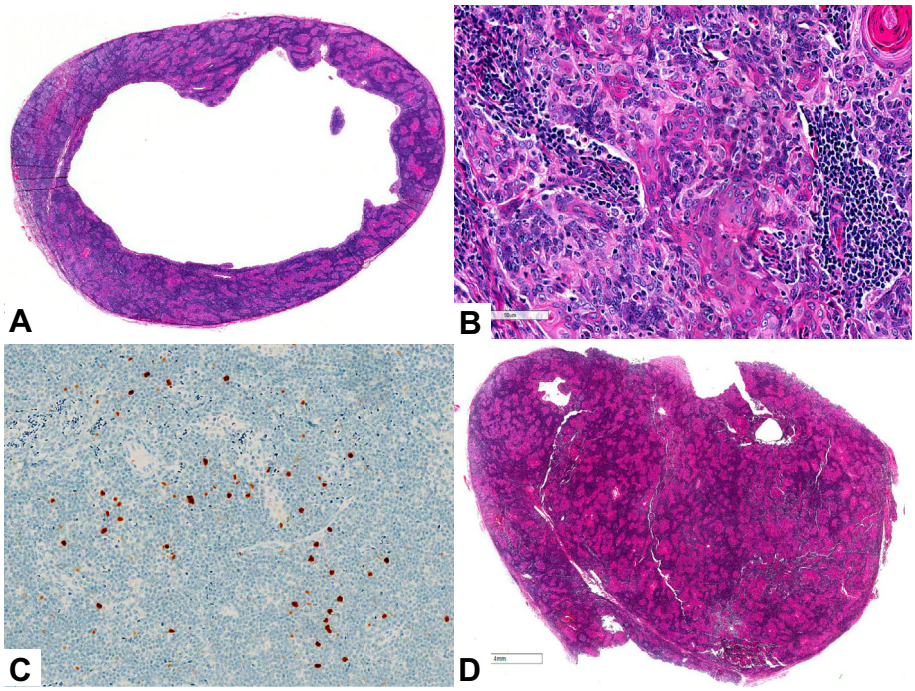

Fig. 1 (A,B) Initial resection specimen demonstrating an encapsulated and partly cystic lesion composed of anastomosing trabeculae of mildly atypical squamous cells with whorl-like structures vaguely reminiscent of Hassall's corpuscles (H&E). (C) TdT-positive lymphocytes are present. (D) Left neck lesion with similar features to the left submandibular specimen (H&E).

several occasions showed no neck lesions other than the above. Imaging with computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) scan did not detect any other pathological lesions within the neck, upper aerodigestive tract or thoracic cavity including the mediastinum. Excision biopsy of the two left level IV and level II neck lesions showed similar findings. Both lesions were encapsulated and composed of islands and anastomosing cords of epithelial cells along with closely associated lymphoid cells (Fig. 2A,B). The subcapsular region contained lymph node sinuses along with focal presence of lymphoid follicles with germinal centres corresponding to the cortical

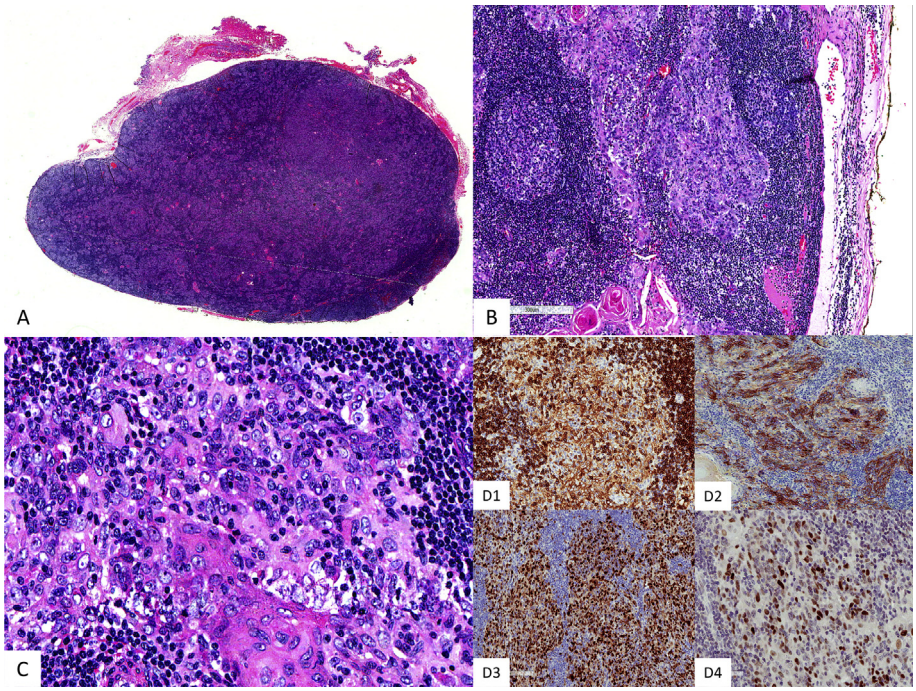

Fig. 2 (A) Metastatic tumour resection 8 years after initial resection showing similar appearing encapsulated left level IV and II neck lesions composed of islands and anastomosing cords of epithelial cells along with closely associated lymphoid cells (H&E). (B) The subcapsular region contained subcapsular lymph node sinuses along with focal presence of lymphoid follicles with germinal centres corresponding to the cortical region of a lymph node (H&E). (C) The epithelial cells exhibited an epithelioid morphology with nuclear pleomorphism and prominent nucleoli (H&E). (D1) Positive CD5 staining in the epithelial cells. (D2) Positive CD117 staining in the epithelial cells. (D3) Positive cyclin D1 staining in the epithelial cells. (D4) Moderately positive p53 staining in the epithelial cells.

region of a lymph node (Fig. 2B). The epithelial cells exhibited an epithelioid morphology and micro-cyst formation with keratin material present. Mild nuclear pleomorphism was evident in the epithelial cells with some prominent nucleoli seen (Fig. 2C). The mitotic activity was low [5 per 10 high power fields (HPFs)]. On immunohistochemistry, the neoplastic squamous epithelial cells were positive for p63, CD117, CD5, cyclin D1, and moderate to strong nuclear expression of p53 in approximately 30−40% of tumour cells was seen (Fig. 2D). The lymphoid cells were composed of mixed CD3 T lymphocytes and CD20 B lymphocytes with no TdT positivity. Subsequently, a left modified radical neck dissection (levels I to V) was also performed. This revealed four lymph nodes in level I and one lymph node in level III that were involved by metastatic carcinoma.

Adjuvant therapy included radiotherapy to the left neck (levels I to VI) and chemotherapy (5 cycles of cisplatin) after the neck dissection. He received a total of 200 cGy of IMRT over 30 fractions. Apart from radiation dermatitis, mucositis and neck stiffness, he did not experience any other significant complications related to the treatment. Routine blood tests have all been normal. Since the completion of chemo-radiation therapy, three imaging scans have been performed. Post-chemoradiation 6th month MRI, 13th month PET scan, 22nd month MRI and 23rd month chest X-ray were negative for tumour recurrence.

Over a period of 10 years, the patient presented with several neck lumps and the final neck dissection of cervical lymph nodes revealed presence of well differentiated metastatic squamous cell carcinoma. The latter finding raised pertinent questions regarding the origin of the metastatic squamous cell carcinoma and the true nature of the initially resected neck lumps. These questions are difficult to answer based on histological findings alone and require clinico-pathological correlation to resolve. Given the site, a secondary tumour from the upper aerodigestive tract has to be excluded. Our patient is young and extensive clinical workup did not reveal any other tumours. The retrospective analysis of all the histological samples provided clues to support our interpretation that the origin of the tumour was from the neck. Careful scrutiny of the histological features of the first level I and recurrent level I neck lumps revealed similar histological features to the later resected lesions in level II and IV. In our opinion, the architectural and cytological atypia in the squamous epithelial cells was beyond the commonly acceptable range of reactive atypia and, together with the presence of TdT positive lymphocytes in the earlier level I lesions, these findings were consistent with those of well differentiated ectopic thymic carcinoma. The lesions were adequately sampled and thorough microscopic assessment did not reveal any histologically distinct components to suggest a combined thymic epithelial neoplasm. The presence of subcapsular sinuses in the later (level II and IV) resected lumps which were absent in the earlier two resections confirms that these represent lymph nodes involved by metastatic carcinoma. The immunoexpression of CD117 and CD5 in the tumour cells further support thymic origin. Expression of CD117 is detected in approximately 80% of thymic carcinomas while that of CD5 is approximately 70%. The strong nuclear expression of cyclin D1 and p53 also support the neoplastic nature of these cells.

Ectopic thymic carcinoma is a difficult diagnosis to establish given the wide histological spectrum that it is associated with and the absence of specific markers. It is also a rare diagnosis with only seven reports documented previously in the literature; in the cervical region, parietal pleura, posterior mediastinum, intrapericardial and intrathoracic regions.[2−8] The finding of residual thymic tissue in the carcinoma with expression of CD5 and CD117 would aid the diagnostic process, as in the case reported by Yao *et al.*,[3] but these features are usually not readily present as can be seen in the rest of the cases. The basis on which the diagnosis of ectopic thymic carcinoma was made in the previously reported seven cases is summarised in Table 1. These cases were largely diagnosed based on close clinicoradiological correlation and positive immunomarkers, which were similar to our case.

Given its rarity, to date there is no standardised therapy for ectopic thymic carcinoma. Complete surgical resection remains the mainstay of treatment, followed by chemotherapy and radiotherapy. Some authors have documented concomitant thymectomies performed to exclude the possibility of a metastasis. The prognosis of thymic tumours is significantly associated with completeness of resection, tumour size and lymph node status.[9] The natural course of the tumour at an ectopic site is difficult to predict due to the low incidence, although it is likely to be analogous to the primary thymic tumour if completely resected. Based on the accounts of several authors, tumour grade appears to play a pertinent role in terms of prognosis. Suster and Rosai showed that well-differentiated primary thymic squamous cell carcinomas had a better prognosis than tumours with high-grade

Table 1 Previously reported cases of ectopic thymic carcinomas

Reference	Age/Gender	Site	Basis on which the diagnosis was established
Hsu *et al.*[2]	49/M	Neck (cervical region)	Immunoexpression of CD5 in tumour cells
Calderon *et al.*[4]	73/M	Intrapericardial	Correlation with imaging findings
Yao *et al.*[3]	24/F	Neck (cervical region)	Immunoexpression of CD5 and CD117 in tumour cells; focal thymic tissue near tumour
Zhu *et al.*[7]	73/M	Parietal pleura	Immunoexpression of CD5 in tumour cells; negative imaging findings of a mediastinal mass
Tan *et al.*[5]	31/F	Posterior mediastinum	Negative imaging findings of thymic tissue in the predominant location of the normal thymus
Matsuoka *et al.*[6]	83/M	Intrathoracic (tumour adherent to diaphgram and right lung)	Negative imaging findings of a mediastinal mass and no continuity with thymus
Jung *et al.*[8]	65/M	Neck (left jugulodigastric chain)	Correlation with clinicopathological and imaging findings; histological diagnosis of a thymoma in the neck lesion. Subsequently developed a tumour in the tongue base consistent with metastatic thymic carcinoma

histological features.[10] Patients with ectopic tumours following complete surgical resection were reportedly free of recurrence for a period of 6–24 months. In April 2018, our patient was disease free, 26 months after neck dissection and 23 months after chemoradiation treatment.

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Parasitic nodules of thyroid: some insights into the origin and early evolution

Sir,
Parasitic nodule (PN) of the thyroid, also known as sequestered, detached or accessory thyroid nodule, is a peripheral nodule of goitre that is anatomically separate from the main thyroid gland. Spontaneous detachment of thyroid tissue may occur in nodular goitre, Hashimoto's thyroiditis (HT), and Graves' disease. Alternatively, PN may represent concurrent hyperplastic changes in accessory thyroid tissue, i.e., portions of thyroid which did not fuse with the main gland during embryological development. Less than 100 cases of PN have been described in the literature, with the largest series reported by Rodriguez and Rosai.[1] Most PNs are single, located separate but close to the thyroid gland (<1 cm). Size can vary from a few millimeters to 6.5 cm.[1] Sometimes a fibrovascular pedicle connecting to the main thyroid can be discovered after careful dissection at surgery. The main practical significance is that PN needs to be differentiated from nodal metastasis of thyroid cancer.

It is believed that the main mechanism of PN formation is the mechanical action of neck muscles, which may separate the portion of goitrous thyroid extending through the fascia.[2] As a result, histological appearance of PN usually mirrors that of the main thyroid, frequently showing changes compatible with nodular goitre, HT or Graves' disease. The variable size of PNs suggests that in some cases large-sized nodules can separate from the thyroid, while in other situations subcentimetre nodules may detach early and undergo further growth in size supported by autonomous vascularisation. PNs can obtain blood supply from the thyroid via a thin fibrovascular pedicle, or from the surrounding soft tissues.

Recently, we reviewed a large series of neoplastic and non-neoplastic thyroid surgical specimens enrolled in the biomarkers project[3] and could identify 10 PNs sized 3–20 mm. This series of detached nodules along with the corresponding main thyroid gland was analysed in order to determine common histological features associated with the formation of PNs. Diagnostic criteria were as per recommendations of

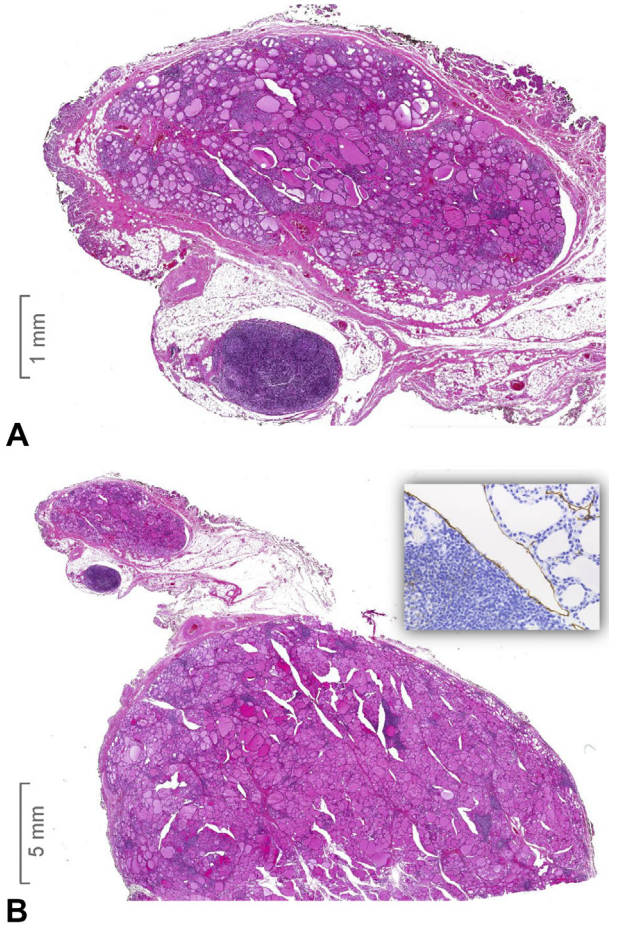

Fig. 1 Representative microscopic appearance of thyroid parasitic nodule. (A) A nodule of thyroid tissue enclosed by a thin capsule (H&E); note the perivascular location and intranodular vessel providing blood supply. (B) Parasitic nodule is located at a distance from the main thyroid (H&E); the latter shows signs of Hashimoto's thyroiditis, stromal septation by thin fibrous bands, and tissue clefting. Note that essentially similar features are found in the nodule in A. Inset: Cracking space lined by endothelium decorated by D2-40 immunostaining.