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Case report

Carcinoma of the thyroid showing thymoma-like features

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Summary. A new case of thyroid carcinoma with thymoma-like features, occurring in a 45-year-old lady, is reported. In order to establish the incidence of residual thymic tissue, 2575 consecutive surgically removed thyroid glands were also examined. Thymic tissue was found to be present in up to 1.4% of the cases. The clinicopathological and immunohistochemical features of the case together with its possible relationship with the persistence of aberrant nodules of thymic tissue in the neck are discussed.

Key words: Thymoma – Thymic carcinoma – Thyroid

Introduction

Primary thyroid carcinomas showing thymoma-like features are rare, recently recognized neoplastic conditions (Asa et al. 1988; Chan and Rosai, in press; Kakudo et al. 1988; Miyauchi et al. 1985, 1989; Willis 1960), probably related to aberrant nodules of ectopic thymic tissue entrapped within the thyroid gland. Thymic tissue has been found in the neck along the path of thymic descent, in 20% of fetuses and stillbirths (Gilmur 1941), and in 1.8% of adult patients with Graves' disease (Yamashita et al. 1983). It has also been seen within the thyroid gland (Carpenter and Emery 1976; Lau et al. 1984; Rosai and Levine 1976).

The purpose of the present paper is to describe a new case of primary thyroid carcinoma with thymoma-like features, to discuss its possible histogenesis and to investigate the incidence of aberrant thymic tissue in a large series of consecutive thyroid surgical specimens.

Case history

A 47-year-old lady presented with increasing dyspnoea and difficulty in swallowing due to a large nodule in the anterior neck. The nodule was painless, had an irregular surface and was hard in consistency. It appeared to occupy the central portion of the thyroid extending to both lobes. It was cold on scintigraphy, and had enlarged during the past 18 months. At the time of admission, an ^{131}I scintigram revealed a decreased uptake in the whole thyroid gland. Bronchoscopy and tomography of the trachea showed a marked reduction of the tracheal calibre in the juxtalaryngeal tract. Nevertheless, no lesions of the mucosa were evident. Chest radiography showed no abnormalities. At the time of surgery the thyroid mass was adherent to the deep soft tissues and extended to the tracheal wall. It was deemed inoperable and a tracheostomy was performed. A portion of the tumour was obtained for histology.

Three years later, radiotherapy was administered in order to shrink the neoplasm. The mass decreased slightly in size and the patient developed hypothyroidism. The thyroid mass remained unaltered for the following 7 years. The patient then died of myocardial infarction. There was no post-mortem.

Materials and methods

The tissue obtained for histology measured 5 cm in greatest dimension and weighed 25 g. It was fixed in 10% buffered formalin, embedded in paraffin and stained with haematoxylin and eosin

Table 1. Antisera employed for immunohistochemistry

Antiserum	Clonality	Source	Dilution
EAB 902[a]	M	Ortho Diagnostic Systems (Milan, Italy)	1:1500
EAB 903b	M	Ortho Diagnostic Systems	1:1500
Vimentin	M	Dakopatts (Copenhagen, Denmark)	1:200
Thyroglobulin	P	Dakopatts	1:30000
Chromogranin-A	M	Dr. R.V. Lloyd, Michigan, USA	1:120
Calcitonin	P	Ortho Diagnostic Systems	1:1
T-cells (UCHL-1)	M	Dakopatts	1:1000
B-cells (L-26)	M	Dakopatts	1:800

M, monoclonal; P, polyclonal
[a] Low-molecular-weight keratins
[b] High-molecular-weight keratins

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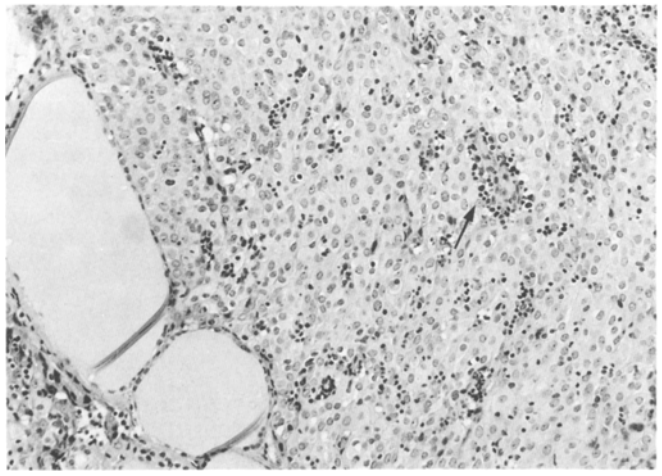

Fig. 1. Thyroid tissue is extensively replaced by the neoplastic proliferation. Lymphocytes are seen in a perivascular space (*arrow*). H&E, ×130

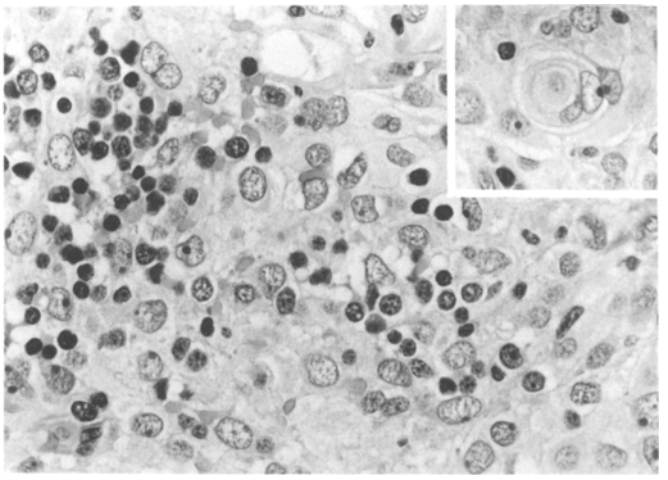

Fig. 2. The neoplastic cells have a round to ovoid nucleus and a prominent nucleolus; lymphoid elements are intermingled with these. In the inset there is a structure reminiscent of Hassal's corpuscle. H&E, ×375

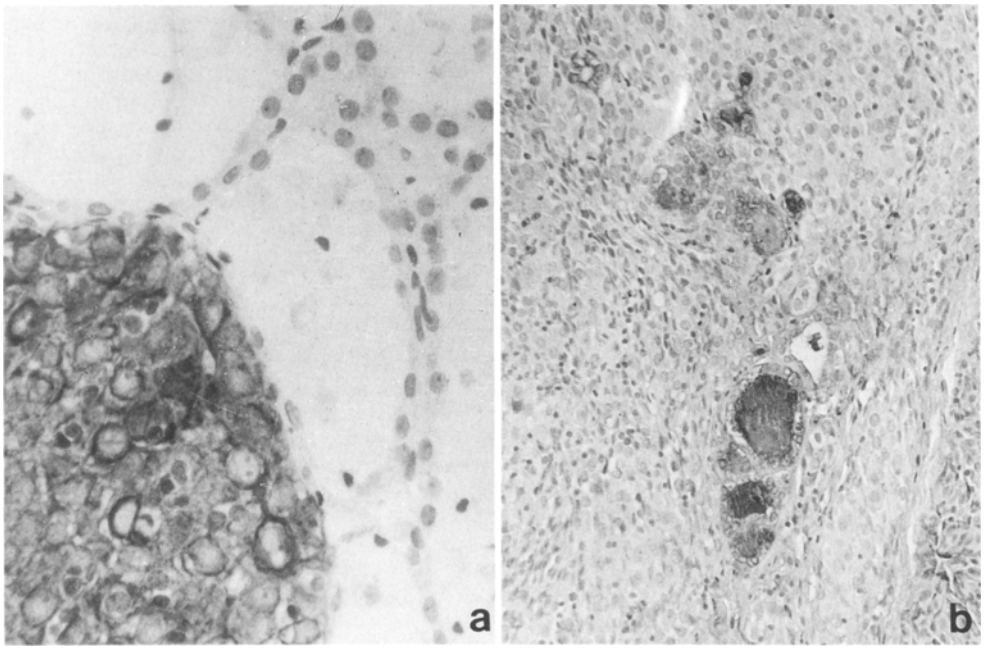

Fig. 3. The neoplastic cells are strongly immunoreactive with high-molecular-weight keratin antiserum (**a**). Thyroglobulin is seen within entrapped follicles (**b**). Strepto-avidin-biotin-immunoperoxidase: **a** ×250, **b** ×130

(H & E), periodic acid-Schiff (PAS) before and after diastase digestion and with alcian blue pH 2.5. For immunohistochemistry the strepto-avidin-biotin-peroxidase complex technique was used (Hsu et al. 1981). The antisera employed together with their respective dilutions are reported in Table 1.

In order to ascertain the real incidence of the intrathyroid ectopic thymic tissue, 2575 consecutive thyroid biopsies were examined. Of these, 2066 were retrieved from the files of the Institute of Pathology of the University of Bologna, while 509 were obtained from the Histology Unit of the Institute of Otorhinolaryngology. These cases were collected over a 3-year period (1986–1988).

Results

Histological examination shows that the thyroid tissue from this patient appears extensively replaced by a neoplastic proliferation with an infiltrative growing front extending into the perithyroid soft tissues (Fig. 1). The neoplastic cells coalesce into large lobules irregularly surrounded by thick fibrous septa. The neoplastic elements are polygonal or spindle-shaped with abundant eosinophilic cytoplasm and well-defined borders. The nuclei vary from round to oval, have dispersed chromatin and show prominent nucleoli (Fig. 2). The mitotic count is low (3/10 high-power fields; ×400 on average). Microcystic spaces are frequently seen among the tumour cells. No mucin was localized in these. Focally, the neoplastic elements form small, whorled clusters which are reminiscent of Hassall's corpuscles (Fig. 2, inset). Numerous mature lymphocytes are present throughout the tumour, intermingled with the neoplastic

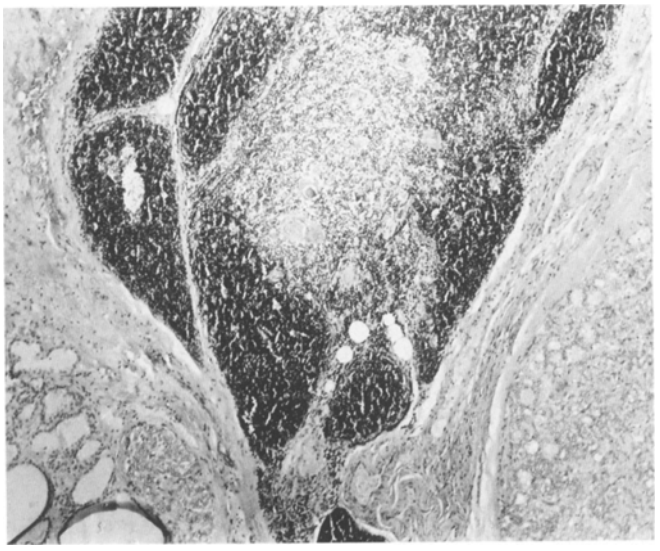

Fig. 4. Well-formed thymic tissue is seen among thyroid follicles. H&E, ×100

cells. Numerous lymphocytic elements are also seen in occasional perivascular spaces.

The PAS stain reveals small intracytoplasmatic, diastase-labile glycogen droplets in numerous neoplastic cells, but no alcianophilic material is present.

Immunohistochemically, most of the neoplastic elements show a strong reactivity with high-molecular-weight keratin antiserum (Fig. 3a), whereas low-molecular-weight keratin antiserum, although immunologically evident in most of the cells, gives a weak reaction. Most of the mature lymphocytes are immunoreactive with T-cell antiserum (UCHL-1), while the B-cell antiserum (L-26) stains about 30% of lymphocytes. The vimentin antiserum stains blood vessels, and the thyroglobulin antiserum gives positive results only in the residual normal thyroid tissue (Fig. 3b). All other antisera employed give negative results.

Ectopic nodules of thymic tissue were found in 18 out of the 2066 (0.8%) cases retrieved from the Institute of Pathology, and in 7 of the 509 (1.4%) cases obtained from the Institute of Otorhinolaryngology. The age of the patients with aberrant thymus ranges from 5 to 65 years (mean 36.8). In 1 case the residual thymic tissue appears entrapped within the thyroid tissue (Fig. 4). One other case has a perithyroid fibrous cyst, 4 cm in greatest dimension, showing thymic tissue scattered in its wall. The remaining 23 cases represent nodules of thymic tissue, measuring from 2 to 30 mm in greatest dimension, located in the perithyroid soft tissues.

In all cases the aberrant thymus shows a lobular architecture and appears to be composed of mature lymphoid tissue with numerous Hassall's corpuscles. The latter appear well developed and frequently show central cavitation. The presence of adipose tissue within the gland is variable: it ranges from 5% to 30% of the whole lymphoid structure in patients under 30 years of age and from 40% to 80% in patients over 30 years of age. Parathyroid tissue intermingled with the ectopic thymus is observed in 7 out the 25 cases.

Immunohistochemically, the lymphoid tissue shows a strong reactivity with T-cell antiserum in most of the cortical cells, and in 60% of the medullary cells. B-cell antiserum stains about 40% of the medullary cells.

Discussion

The present tumour exhibits morphological features recalling those of thymomas: there is lobulated architecture, whorled clusters of cells reminiscent of Hassall's corpuscles, occasional perivascular spaces and intimal association with mature lymphocytes. In addition, the neoplastic cells show vesicular nuclei with prominent nucleoli and a relatively low mitotic count (3/10 high-power fields; ×400 on average). These are all features reported as characteristic of lymphoepithelioma-like thymomas (Rosai 1989). The mediastinum, lungs and oropharynx were clear of any neoplastic involvement at the time of the admission, as were tumours present in other organs 3 years later, when the patient was last seen. Therefore it appears that the thyroid was the primary site of origin of the lesion.

Six cases of thyroid carcinomas showing thymoma-like features were reported by Miyauchi et al. (1985, 1989). These were considered to be intrathyroid epithelial thymoma mimicking squamous cell carcinoma, from which they have to be distinguished. Kakudo et al. (1988) reported one case of thyroid carcinoma that they considered to be of probable thymic origin. Asa et al. (1988) described a case of thyroid thymoma which was very extensive and which was initially diagnosed as anaplastic thyroid carcinoma. Recently, Chan and Rosai (1991) reported two additional cases and reviewed the histology of five, previously reported as thyroid thymoma or thyroid carcinoma of thymic origin. They stated that the features of all these cases were very similar and suggested that the histology of these thyroid tumours is superimposable on that of lymphoepithelioma-like carcinomas seen in the thymus.

These tumours may be difficult to differentiate from squamous cell carcinoma (Kakudo et al. 1988; Miyauchi et al. 1985, 1989), anaplastic thyroid carcinoma [the case of Asa et al. (1988), and the present case] and medullary carcinoma (Asa et al. 1988). The lobulated pattern, the lymphocytic infiltration and the presence of structures reminiscent of Hassall's corpuscles are all features favouring the diagnosis of thymoma. In addition, the absence of immunoreactivity with anti-thyroglobulin, chromogranin-A and calcitonin antisera does not support a diagnosis of follicular or medullary carcinoma. Anaplastic carcinoma of the thyroid frequently do not show immunoreactivity with thyroglobulin antiserum (Ryff-de Leche et al. 1986). However, the low mitotic count of the present tumour, the absence of areas of necrosis together with the indolent course are not consistent with a highly malignant tumour such as the anaplastic thyroid carcinoma. Several cases of ectopic cervical thymomas have been reported in the neck, some of which involve the lower pole of the thyroid (Chan and Rosai 1991). These tumours have histological features identical to those of mediastinal thymomas (Chan and

Rosai 1991), and do not show nuclear atypia, prominent nucleoli and mitoses as seen here. The present tumour is also different from the case reported by Harach et al. (1985), as no mucinous cysts or glandular spaces were seen.

Cervical tumours of thymic derivation appear as a result of incomplete thymus descent (Rosai and Levine 1976). In our study, ectopic thymic tissue is found in up to 1.4% of cases. This incidence, although slightly lower, is in the same range as that reported by Yamashita et al. (1983) (1.8%). Gilmur (1941) found ectopic thymus in the neck of 20% of fetuses and stillbirths, but in view of physiological involution of thymic tissue, the discrepancy is probably related to the different age of the subjects examined. Thymic tissue is present either around or within the thyroid gland, as seen in one instance in our series. The occurrence of thymomas in the thyroid seems a distinct possibility. Nevertheless, as at the present no immunohistochemical or ultrastructural markers exist which can prove the thymic nature of this tumour, it seems appropriate (Chan and Rosai 1991) to designate it as "carcinoma with thymoma-like features".

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