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Pathology in Focus

Ectopic cervical hamartomatous thymoma showing extensive myoid differentiation

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Abstract
Ectopic 'hamartomatous' thymoma is a rare benign neoplasm. These tumours are found in the neck and are thought to be part of a spectrum of ectopic cervical thymic neoplasia. The clinical and histological features are discussed and the literature is reviewed. An attempt is made to explain in embryological terms why such lesions appear to occur more commonly on the left side.

Key words: Hamartoma; Thymus neoplasms; Neck.

Introduction

Ectopic 'hamartomatous' thymoma is an exceptionally rare benign tumour arising in the neck (Rosai *et al.*, 1984). Fifteen cases have been reported in the literature (Chan and Rosai, 1991). Of these only one previously has described small areas of myoid differentiation (Saeed and Fletcher, 1990). These lesions behave in a benign fashion and are thought to be either hamartomatous in type or benign mixed neoplasms of thymic origin.

This case describes the histological appearances with characterization of cellular lineage by immunocytochemistry and electron microscopy. The unusual appearances, site and presentation may cause problems in histological interpretation and may lead to histological misdiagnosis as synovial sarcoma (Fetsch and Weiss, 1990), branchial cleft anomaly or hair germ tumour (Chan and Rosai, 1991).

Case report

A 47-year-old man presented with a soft mobile subcutaneous lower neck mass deep to the platysma and immediately posterior to the left sternocleidomastoid muscle. Clinically it was thought to be a lymph node. It had been present for several years with no increase in size detected recently. The specimen measured 3.8 × 3.5 × 2.0 cm. It appeared encapsulated, solid and had a white appearance on cut section.

Histologically there was a well circumscribed nodule composed of bland fibroblastic actin positive spindle-shaped cells with slightly blunted nuclei, a moderate amount of eosinophilic cytoplasm and inconspicuous nucleoli. These cells blended haphazardly with foci of mainly peripheral mature adipose tissue and randomly located epithelial islands (Fig. 1). Such epithelial islands varied from cystic spaces lined by cuboidal and flattened epithelial cells to more solid areas showing squamous differentiation. Tubular epithelial foci were also present with irregular microscopic cleft-like cystic spaces forming a smaller component. Throughout the lesion were scattered mature lymphocytes with a tendency to aggregate adjacent to epithelium with focal lymphocytic permeation of the epithelium. No capsule could be identified on microscopy.

Forming a conspicuous part of this tumour was an area composed of ovoid cells containing abundant brighter eosinophilic cytoplasm and elongated markedly hyperchromatic nuclei (Fig. 2). Such cells had the morphological appearance of fetal type skeletal muscle and upon immunostaining, were positive for myoglobin and negative for smooth muscle specific actin. They were also negative for desmin. These myoglobin positive cellular aggregates were also randomly located and not obviously related to any particular epithelial element.

Staining with the pan and high molecular weight anticytokeratins, K3350 and K3330 (Biogenesis), showed both the epithelial and spindle cell components to be strongly positive. With the low and intermediate molecular weight anticytokeratins, Cam 5.2 and K3340, epithelial areas stained strongly and spindle areas less intensely.

The lymphocytes were LCA (PD7/26, [CD45]) and T cell (MT1 and UCHL1) positive. They were negative for B cell markers (MB2 and L26). No staining was seen for vimentin or for S100 protein.

On electron microscopy numerous well formed intercellular desmosomal junctions were seen together with cytoplasmic tonofilaments in the spindle cell areas (Fig. 3).

Discussion

Benign spindle cell squamous tumours have been reported in the testis (Miettinen *et al.*, 1986), lower neck and supraclavicular fossa. Rare neck region tumours are thought to be of hamartomatous thymic origin on histological, immunocytochemical and electronmicroscopical appearances (Fetsch and Weiss, 1990). We have applied a wide range of antibodies to the epithelial, spindle, 'myoid' and lymphoid components. On immunohistochemical and electronmicroscopical grounds both the epithelial and spindle cell components are of epithelial origin. Admixed lymphocytes showed a thymic phenotype. Spindle cell areas were positive for epithelial antigens but with the exception of actin were negative for mesenchymal markers. Such a staining pattern could be compatible with myoepithelial differentiation (Fetsch and Weiss, 1990). Cytokeratin positivity for Cam 5.2 and K3340 in both the spindle and epithelial areas is a different pattern from that recorded in epidermal derived tissues which are

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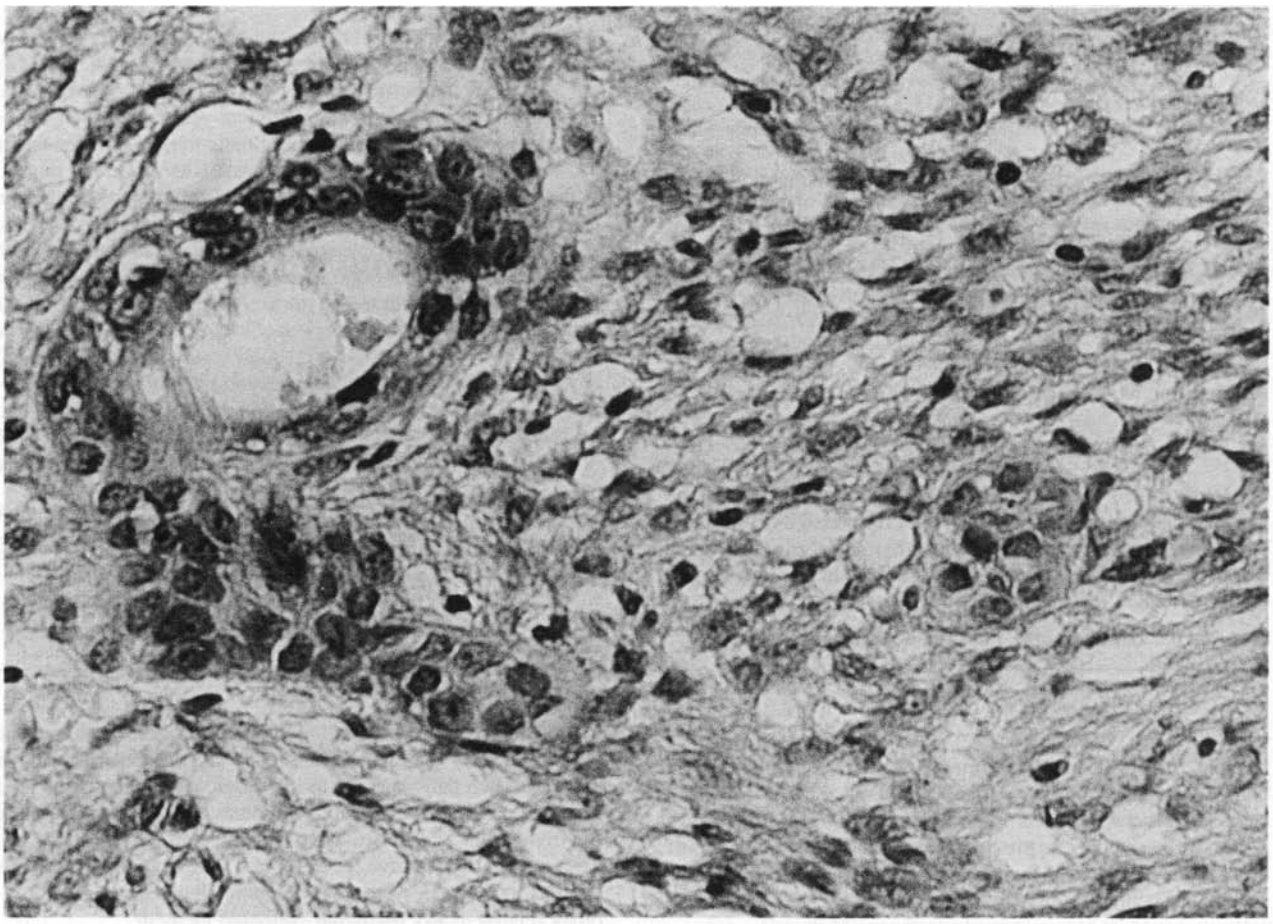

FIG. 1
Spindle cell areas blend smoothly with central epithelial islands (×160)

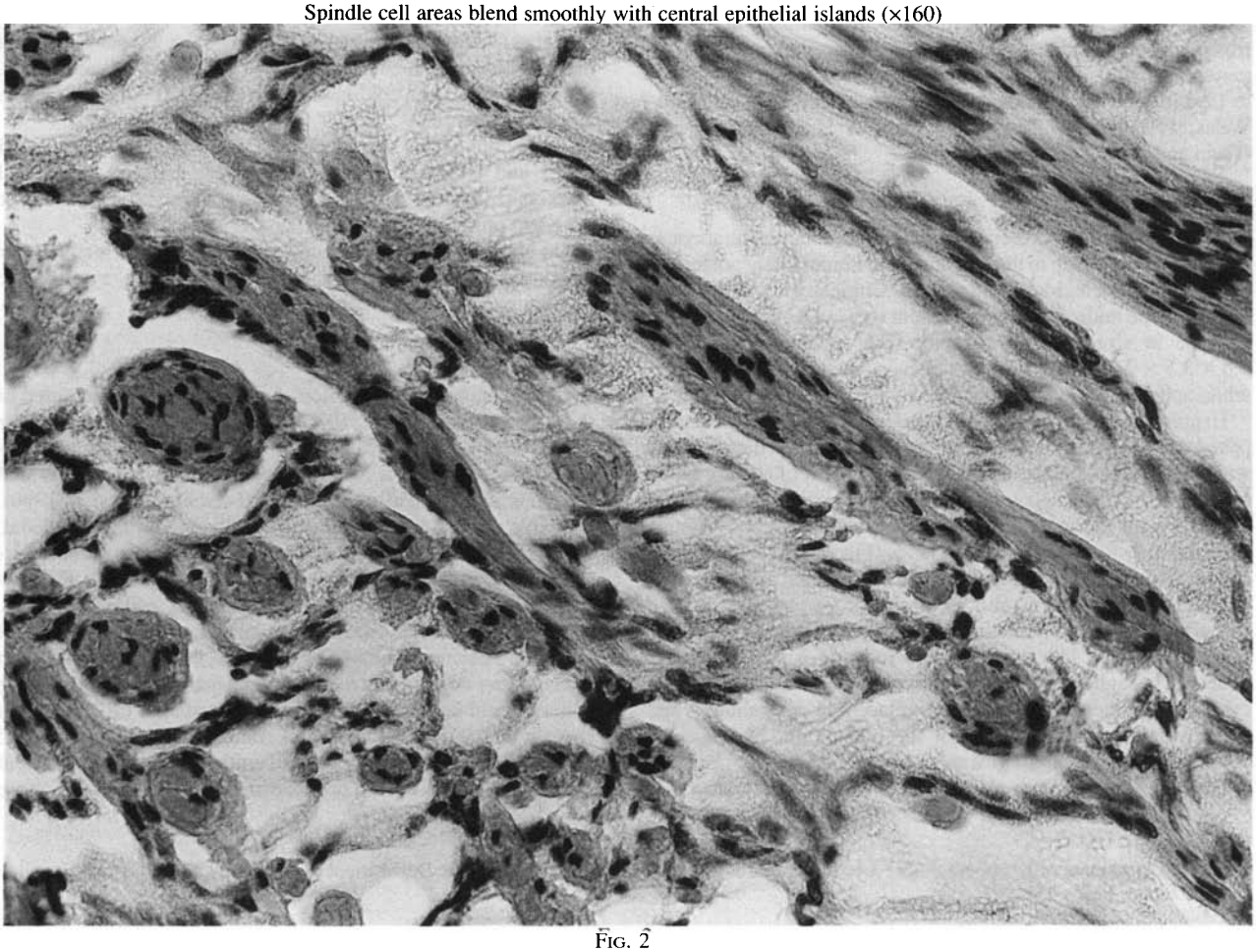

FIG. 2
Markedly hyperchromatic nuclei in sheets of eosinophil myoid cells (×350)

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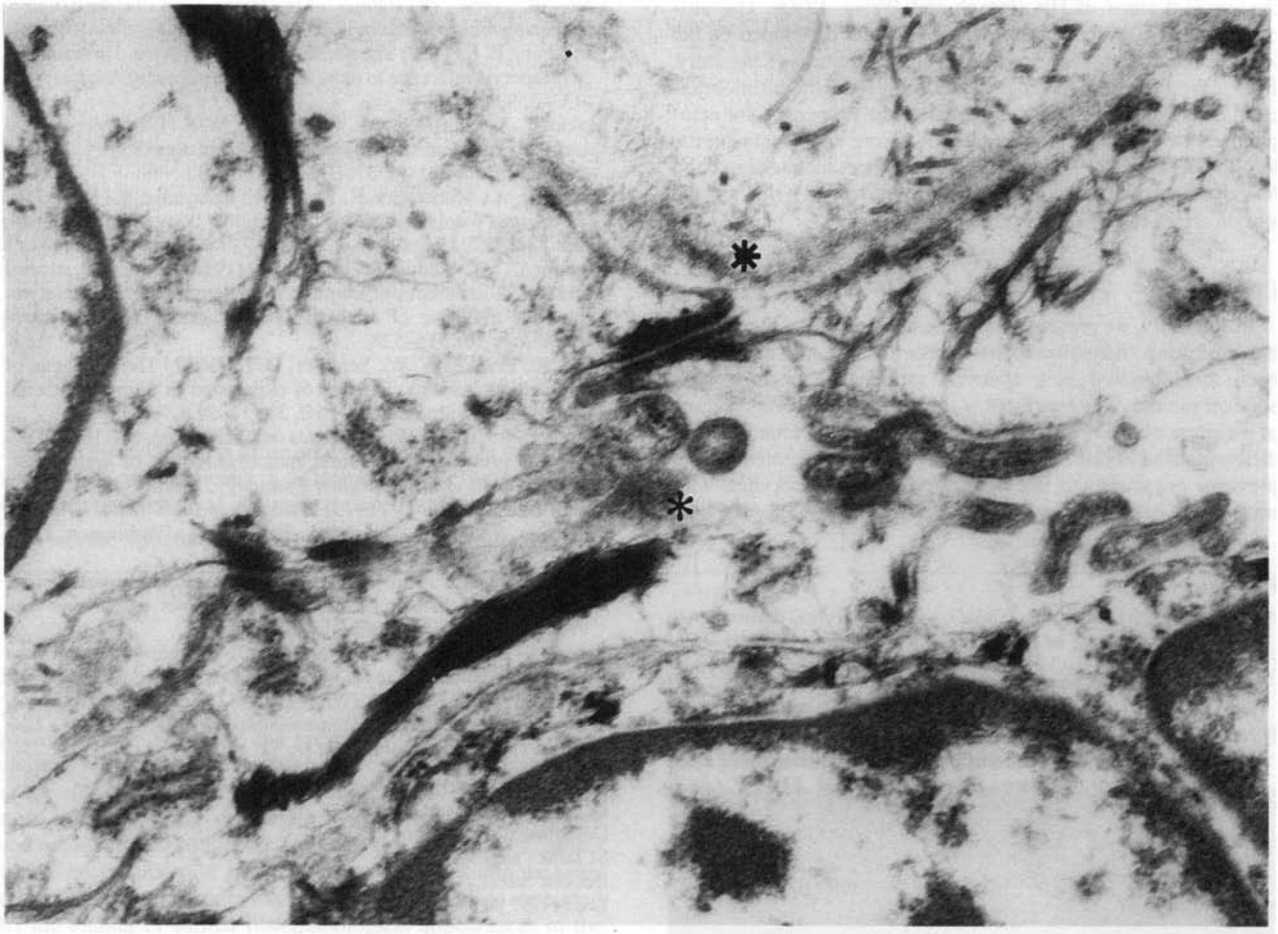

FIG. 3

(EM) Intracellular well formed desmosomes,* cytoplasmic tonofilaments* and close membrane contact indicate epithelial differentiation (×7600)

often Cam 5.2 negative (Makin *et al.*, 1984). The high molecular weight cytokeratin staining patterns are fully compatible with pharyngeal/branchial pouch origin (Moll *et al.*, 1982). There was also a scattered population of lymphocytes throughout the tissues with aggregation of lymphocytes around epithelial structures. This pattern resembled that seen in stress involuting thymus where lymphocytes may permeate the epithelium (Chan and Rosai, 1991) and in which epithelioid cells show spindle-shape metamorphosis.

A skeletal muscle component which was present in our case is rarely found in these tumours. Only one previous case report demonstrated a minor myoid component (Saeed and Fletcher, 1990). They also found it to be myoglobin positive and desmin negative. In the case we now report obvious myoid differentiation was present (Fig. 2). Such a feature would be in keeping with derivation from pharyngeal pouch or associated muscular tissue of the pharynx (Rosai and Levine, 1976). It is known that the third pharyngeal pouch gives rise to pharyngeal and laryngeal musculature. The myoid component in the thymus is thought to be indirectly related to the immune reaction which causes the associated condition of myasthenia gravis (van der Geld *et al.*, 1964). No such clinical association has been found in this case after a six year follow up and there is no report so far of myasthenia, immune deficit or red cell aplasia complicating any benign spindle cell squamous tumour of the neck. Such ectopic hamartomatous thymomas may however reach appreciable size (up to 19 cm) and could, like thymic cysts, compress a vital structure in the neck (Al-Shihabi and Jackson, 1982). Most ectopic hamartomatous thymomas present well into adult life in contrast to thymic cysts which occur predominantly in the under 21 age group. It is conceivable that hamartomatous thymoma represents the adult counterpart of the involuted thymic cyst even though, unlike the thymic cyst, residual thymic tissue is not recorded without the capsule. It is of interest that cystic dilatation of epithelial lined spaces is common to both lesions as is their site of location in the lower neck. Elongated cystic spaces lined by squamous epithelium are also seen in involuted thymus and are thought to be derived from Hassall's corpuscles (Henry, 1968).

On embryological considerations it is to be expected that hamartomatous thymomas will also be described in the superior and anterior mediastinum and, ectopically, even in the pleura where thymomas are recorded (Moran *et al.*, 1992). Some authors regard hamartomatous thymomas as the benign end of a spectrum of ectopic thymoma which includes intrathyroid spindle cell thymoma and carcinomas showing spindle-like thymic differentiation (Chan and Rosai, 1991). A single case of osteosarcoma arising in ectopic pleural cavity non-spindle cell squamous hamartomatous thymic tissue has been described (Valderrama *et al.*, 1983).

Of eight cases in the literature in which the side in which the ectopic hamartomatous thymoma was located is mentioned, six were found on the left, excluding the case we now describe, and only two on the right. While, in view of the small numbers, such left sided dominance may be a chance finding, it could also indicate a trend and point to an alternative histogenesis. The balance of opinion favours origin of such tumours from the third branchial/pharyngeal pouch which gives rise during embryogenesis to the thymus (Fetsch and Weiss, 1990; Chan and Rosai, 1991). However, thymic tissue is also thought to take origin from fourth pharyngeal pouch (thymus IV) and the region of the ultimobranchial body which in turn is derived from the fifth pharyngeal pouch (Miyauchi *et al.*, 1992) and some authors have conceded the possibility of origin of this tumour from thymus IV or even

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the cervical sinus of His (Fetsch and Weiss, 1990). The ultimobranchial body is well known to be better developed on the left side than the right during human embryogenesis (Kingsbury, 1939). We therefore speculate that origin from the ultimobranchial body for some cases could explain the propensity for ectopic hamartomatous thymoma to occur more commonly on the left side of the neck. We would however expect such lesions to be found close to or even attached to the thyroid gland if this was the site of origin for all of the cases.

Conclusion

In summary, we present a case of a rare and under recognized but intriguing 'hamartomatous tumour' which has in the past been misdiagnosed as a synovial sarcoma or peculiar skin adnexal tumour. The treatment is surgical removal and no cases of recurrence have been reported with this benign variant. Myoid differentiation in this tumour has only been documented on one previous occasion and does not appear to be associated with myasthenia gravis or any immune deficit.

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