Critical Commentary

to “Carcinoma Arising in Ectopic Hamartomatous Thymoma”

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Michal and co-authors describe another example of ectopic hamartomatous thymoma (EHT). This well-defined entity represents one of the group of peculiar soft tissue tumors of the neck that show partial microscopic similarity to immature, mature or even involuting thymus. Some of those tumors bear resemblance to mediastinal thymomas, some of them even bear resemblance to thymic lesion and by doing so avoid all unnecessary diagnostic procedures.

Although it is generally believed that the first description of EHT was presented by Rosai et al., this rare tumor was reported in 1982 in the English literature almost simultaneously by Smith and McClure as “an unusual subcutaneous mixed tumor exhibiting adipose, fibroblastic and epithelial components” \(^{10}\) and by Rosai et al. who named it first a “spindle cell thymic anlage tumor” \(^7\). The term ectopic hamartomatous thymoma was introduced by Rosai et al. two years later in 1984 \(^8\).

EHT is a benign, cellular lesion believed to show characteristics of both a hamartoma and a neoplasm. \(^4\) One can recognize these lesions at first glance if one is familiar with its appearance from personal diagnostic experience or from the literature. Otherwise one would hardly think about it and consider it e.g. sarcoma (with glandular formation as in malignant glandular schwannoma), metastatic adeno-or spindle cell carcinoma, biphasic synovial sarcoma, cutaneous adnexal carcinoma, syringoma, soft tissue adenomatoid tumor, (adeno-) myoepithelial tumor or mixed tumor of the salivary gland \(^2,8,10\). The list of look-alike tumors can be further extended and in the differential diagnosis the following neoplasms can be taken into account: thymolipoma (that can show epithelial proliferations with even oxyphilic cells \(^8,10\)), parathyroid lipoadenoma \(^10\), thyroid spindle cell tumor with mucous cyst \(^4\) and according to some authors, even dermatofibrosarcoma infiltrating fat tissue \(^2\). Of course pathologists should be aware of this unusual ectopic thymic lesion and by doing so avoid all unnecessary diagnostic procedures.

Helpful characteristics for the recognition of EHT are:
1) The classical superficial or deep location in the soft tissues of the neck (right or left side) and the supraclavicular or suprasternal area.
2) The marked (and unexplained) male predominance.
3) The size ranging from 2 up to 19 cm in diameter, probably related to a slow indolent growth even up to 30 years. Tumors are well circumscribed, but not encapsulated.
4) The microscopic findings: a haphazard mixture of epithelial elements including solid nests, trabeculae and (small) cysts with mature adipose tissue and to a minor degree small lymphocytes. Michal et al. do not mention if they found any preexistent Hassall bodies. Structures highly suggestive for Hassall corpuscles which we find most interesting pinpointing almost directly and convincingly to a thymic origin, were occasionally identified in the 15 previously published cases \(^8\), but residual thymus has not been found in the periphery of these tumors \(^1\). Lymphocytes are inconspicuous and only rarely arranged in nodular pattern being reminiscent of the thymic medulla. They are mostly not considered an integrant part of these tumors in contrast to the fat tissue that is recognized as their essential part \(^2\). It is therefore amazing that Michal et al. suggest the process of lipomatous metaplasia of granular spindle cells because until now, all authors recognized only mature fat tissue due to possible entrapment of fat cells during tumor growth \(^1,10\) or as an involutary phenomenon in atrophic thymus \(^8\). The most conspicuous component is represented by spindle cells. Their epithelial character is established on the basis of immunohistochemistry (positive cytokeratine) and electronmicroscopy (tonofilaments and desmosomes). Myoid cells have been described only by Saced et al. \(^9\). Psammoma bodies can be demonstrated as well.

5) Focal preexisting lymphoid tissue as can be expected in lymphnode homing metastasis is absent.
6) There are no signs of malignant invasive growth; the number of mitoses is nil or very low, there is no necrosis. A malignant variant of this lesion has virtually not been reported till now. However, other types of ectopic cervical thymomas can show malignant behaviour \(^1\). In general, thymoma is a tumor of which the histology may not reflect the biological behaviour and correlation between histology and prognosis appear controversial \(^5\). Well encapsulated thymomas with benign histology may show widespread metastases and even lack of invasive growth can not rule out malignancy \(^5,6\). The authors put strong emphasis in the lightmicroscopic as well as in the electronmicroscopic findings on the granular aspect of different cellular components. They even consider on that basis their case as a hitherto undescribed granular cell variant of EHT. In our opinion, the figures related to this granularity are not convincing and, if so, it remains doubtful if this granularity is really caused by the cup-shaped subcellular structures. One would rather expect a cytoplasmic packing with innumerable large and/or small mitochondria as e.g. in cells called oncocites. A close association of curved profiles of rough endoplasmic
reticulum particularly encircling mitochondria, as described in this case, is not a rare phenomenon, particularly in cells engaged in active protein synthesis. It remains to answer if this view holds true for EHT. Up to now the EM findings by Michal et al. are interesting and in a sense unique. They have not been described earlier in the literature on the ultrastructure of EHT which generally is limited and mostly made to prove the epithelial character of the epithelial islands and the spindle cell component.

We take no firm stand regarding the pathogenesis of EHT. Most authors agree on or propose its branchial pouch derivation, the ectopic or aberrant thymic origin, a vestige of thymopharyngeal duct or the cervical sinus of His. Nevertheless, should we still consider ectopic salivary gland tissue as the origin of EHT? Heterotopic salivary gland tissue in the lower neck can frequently be found in the vicinity of the sternoclavicular joint. Furthermore, epithelium of the oxyphilic type has been reported as a component of EHT and constitutes also a well known component of neoplastic and non-neoplastic lesions of the salivary gland. From histological studies of the normal thymus, it appears that mature appearing salivary gland tissue may also be present in this organ.

References