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Original contribution

Sebaceous lymphadenoma of the thymus: A clinicopathologic and immunohistochemical study of 2 cases☆

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Summary Two cases of primary sebaceous lymphadenoma of the thymus are presented. The patients were a man and a woman 58 and 77 years old, respectively. The female patient had a history of breast carcinoma and on follow-up was identified to have an anterior mediastinal mass; the male patient did not have any history of malignancy, and the tumor was discovered during a chest radiographic evaluation when the patient presented with symptoms of fatigue, chest pain, and dyspnea. Histologically, both lesions were characterized by the presence of solid-cystic epithelial islands in a prominent lymphocytic background. The epithelial islands were haphazardly distributed in the form of small tubular structures with focal keratinization and groups of epithelial cells with clear cytoplasm, round nuclei and lack of mitotic activity in keeping with sebaceous cells. The presence of germinal centers in the lymphoid background was seen in both cases. Immunohistochemically, the epithelial component was positive for cytokeratin 8 (CAM5.2), cytokeratin 5/6, and for adipophilin in the sebaceous component. B- and T-cell markers were positive in the lymphoid component. Clinical follow-up in both patients showed that the 2 patients were well and alive 3 years after diagnosis. The cases herein presented expand the spectrum of salivary gland–type tumors in the mediastinum and raise awareness of lesions which are easily confused with other more common thymic tumors that have different prognosis and treatment implications.

1. Introduction

The existence of salivary gland–type neoplasms in the thoracic cavity is well documented in the literature. By far the most common location in this site is the lung where the vast majority of such cases have been described [1-7]. The mediastinum and the pleura only account for a small number of such tumors, which in turn can pose a challenge in their diagnosis [8-14]. The recognition of such neoplasms in the thoracic cavity is difficult not only due to their rarity but also because the possibility of a metastasis from an occult salivary gland tumor must be excluded before a diagnosis of a thoracic primary can be accepted.

More specifically, the occurrence of salivary gland–type tumors in the thymus—although rare—is well recognized. In the thymus, the most common variant is mucoepidermoid carcinoma, while other tumors in this group such as pleomorphic adenoma and adenoid cystic carcinoma are exceedingly rare [9-14].

To the best of our knowledge, the presence of sebaceous lymphadenoma in the thymic gland has never been reported. Thus, the current cases expand the spectrum of salivary

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gland–type tumors that can occur primarily in the thymus. Needless to say, the occurrence of such tumors can cause diagnostic difficulties, and awareness of their existence is essential in order to distinguish these tumors from other more common epithelial neoplasms of the thymic gland.

2. Material and methods

Two cases of thymic lesions with features reminiscent to those seen in sebaceous lymphadenomas of the parotid gland form the basis of this report. Four to 7 hematoxylin-eosin sections were available for evaluation in each case. Unstained paraffin sections were available for immunohistochemical analysis. Immunohistochemical studies using antibodies targeting cytokeratin (CK) 8 (CAM5.2) (1:50; BD Biosciences, San Jose, CA), CK5/6 (1:50; Dako, Carpinteria, CA), p40 (1:100; Biocare, Concord, CA), adipophilin (predilute; Fitzgerald, Acton, MA), CD45 (1:300; Dako, Carpinteria, CA), CD20 (1:1400; Dako, Carpinteria, CA), and CD3 (1:100; Dako, Carpinteria, CA) were performed in both cases. Adequate positive and negative controls were run, respectively. Clinical information was obtained by reviewing the respective clinical charts. The study was approved by the Institutional Review Board.

3. Results

3.1. Clinical features

The 2 patients were 1 female and 1 male patient, 77 and 58 years of age, respectively. The female patient had a history of breast carcinoma and was undergoing oncological follow-up on a routine basis. At chest imaging, an anterior mediastinal mass was discovered and clinically believed to represent metastatic disease. The male patient presented with symptoms of fatigue, dyspnea, and chest pain. Diagnostic chest imaging demonstrated the presence of an anterior mediastinal mass. The patient did not have any prior history of malignancy. Complete resection of the anterior mediastinal masses was performed in both cases in the form of thymectomy via median sternotomy. Clinical follow-up revealed that both patients were alive and well 3 years after diagnosis.

3.2. Pathological findings

The mediastinal tumors were described as circumscribed but unencapsulated masses with a nodular appearance. A rim of adipose tissue surrounded the lesions without any obvious tumor infiltration. The cut surface was tan to yellow and homogenous with focal small cystic changes. Areas of hemorrhage or extensive necrosis were not identified. The size of the tumors varied from 3.0 to 5.0 cm in greatest dimension.

The histological features of both tumors were similar. Low-power magnification revealed the presence of islands and nests of epithelial cells. These presented in the shape and form of small solid, tubular or cystic structures, some of which contained focal areas of central necrosis. These epithelial islands were embedded in a dense lymphoid-rich stroma, which in some areas included the presence of germinal centers (Fig. 1A). In other areas the lymphoid stroma was not as marked and was replaced by a fibrous or sclerotic background (Fig. 1B). On higher magnification, the epithelial nests were predominantly composed of cells with squamous differentiation and solid or cystic centers (Fig. 1C). Occasional larger cells with distinct cell borders and clear vacuolated cytoplasm in keeping with sebaceous cells could also be identified admixed with the squamous cells (Fig. 1D). In some areas the cystic centers contained necrotic-appearing debris, but cytologic atypia or mitotic activity were not present in any of the cases. Focal keratinization was noted in some tumor nests. In the periphery of the lesions, foci of residual thymic tissue with scattered Hassall's corpuscles were present; however, there were no histological changes to suggest thymoma elements.

3.3. Immunohistochemical findings

The epithelial component was diffusely and strongly positive for CK8 (CAM5.2), CK5/6, and p40 in keeping with squamous differentiation. Expression of adipophilin was restricted to the sebaceous component (Fig. 2). The lymphoid stroma was diffusely reactive for CD45 with CD20-positive B cells populating the germinal centers and CD3-positive T cells in the interfollicular areas in keeping with a reactive process.

4. Discussion

Lymphadenomas are benign tumoral lesions that occur most commonly in the salivary glands. Although commonly referred to as a benign salivary gland–type neoplasm, the notion that these lesions represent a hamartomatous process cannot be completely discounted. Even in the salivary glands the tumors are a rarity with only around 100 documented cases in the medical literature [15]. They typically affect adult patients, and the most common location is the parotid gland. Although the etiology is largely unknown, an altered immune status has been implicated in their development after a viral etiology including human herpesvirus (HHV)-8, papillomavirus, or Epstein–Barr virus could not be confirmed [15]. Histologically, the defining feature of lymphadenoma is its biphasic appearance with groups of epithelial cells—with or without sebaceous differentiation—set in a dense lymphoid background that is reactive in nature [15]. In the salivary glands, it has been speculated that the tumors likely arise from intranodal sebaceous inclusions [16]. Interestingly, not all of these tumors may show clear-cut sebaceous differentiation, and in the