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Correspondence

Lymphadenoma of the parotid gland: cytological findings, tissue correlation and differential diagnosis

Dear Editor, Lymphadenomas are uncommon benign circumscribed parotid gland neoplasms composed of epithelial nests, trabeculae and glands surrounded by conspicuous lymphoid tissue.[1] The tumour cells are cytologically bland and of two types: abluminal and luminal,[1] which are not easily distinguishable from each other cytologically on aspirate smears. They are better appreciated on tissue sections by immunohistochemistry: abluminal cells are positive for p63 and high-molecular-weight cytokeratin and luminal cells are positive for epithelial membrane antigen (EMA) and CAM 5.2.

A 41-year-old female presented with a 1-year history of a slow growing painless left upper neck mass. The patient was a non-smoker, with unremarkable past medical history. Physical examination revealed a palpable 2-cm firm, non-tender, mobile nodule below the left mandibular angle. No facial nerve involvement or enlarged cervical nodes were noted. A computed tomography (CT) scan revealed a 3-cm solid, well-demarcated, nodular tumour within the superficial lobe of the left parotid gland. There was no evidence of haemorrhage, necrosis, calcification, or infiltration of adjacent soft tissue. A fine needle aspiration (FNA) was performed. Two months later the patient underwent a left superficial parotidectomy. No clinical or radiological evidence of tumour recurrence has been found in a 2-year follow-up period.

The FNA was performed using a 25-gauge short needle. Air-dried smears were stained with Diff-Quik® (Fisher Scientific, Pittsburgh, PA) for immediate evaluation, and smears fixed in 95% ethanol were Papanicolaou-stained for subsequent examination. No cell block preparation was obtained. Aspirate smears revealed a cellular specimen composed of cohesive conspicuous three-dimensional epithelial aggregates in a lymphoid background. The epithelial aggregates were composed of approximately 10–20 relatively small cells displaying occasional gland-like arrangements and variable nuclear overlapping. Tumour cells had round nuclei, bland chromatin and scanty cytoplasm (Figure 1a,b). Only a few cells displayed small nucleoli, and no mitotic activity or cytological atypia was seen. There was no sebaceous or oncocytic differentiation. The background was composed of a polymorphic population of lymphoid cells, mostly small mature-appearing lymphocytes, a few germinal centre fragments, tingible-body macrophages and rare plasma cells. The FNA specimen was signed out as a low-grade basaloid neoplasm, with a differential diagnosis of basal cell adenoma, cellular pleomorphic adenoma and lymphadenoma.

The subsequent parotidectomy specimen showed a well-circumscribed 3-cm pink-tan fleshy nodule surrounded by unremarkable salivary gland tissue. The entire gland was embedded after fixation and routine sections were stained with haematoxylin and eosin (H&E). Immunohistochemical staining was performed with the labelled streptavidin-biotin-peroxidase detection system using the Ventana automated immunostainer (Tucson, AZ, USA). Epithelial membrane antigen EMA (dilution 1 : 10; Ventana) and p63 (dilution 1 : 100; Ventana) were used. Histological examination revealed an encapsulated neoplasm composed of randomly distributed epithelial nests and glands surrounded by abundant lymphoid stroma with scattered germinal centres. No sebaceous or oncocytic differentiation was present. The epithelial nests were composed of cytologically bland cuboidal and basaloid cells with scant cytoplasm and round slightly enlarged nuclei (Figure 1c). Nucleoli were small and conspicuous in only a few cells. The lymphoid stroma consisted mostly of small mature appearing lymphocytes admixed with a few intermediate size lymphoid cells and histiocytes. No vascular sinuses or defined cortical and medullary regions were present. Ductal (luminal) and basal cell (abluminal)

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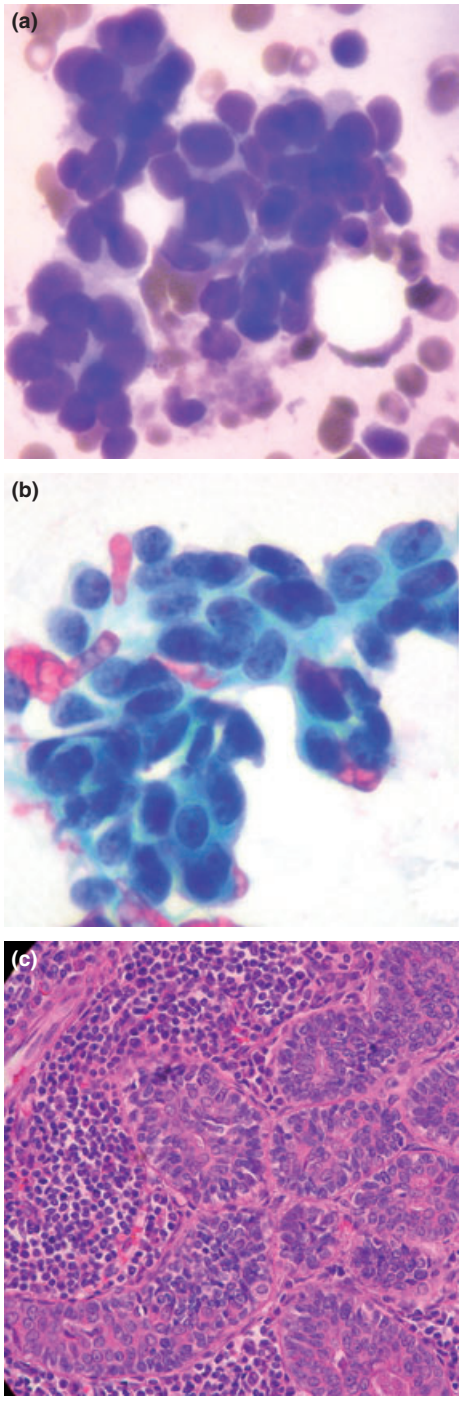

Figure 1. (a) Aggregates of medium-size basaloid tumour cells displaying gland-like arrangements (Diff-Quik × 600). (b) Tumour cells showing rounded nuclei, bland chromatin, small nucleoli and scanty cytoplasm (Papanicolaou × 600). (c) Epithelial nests with focal gland-like arrangements composed of cuboidal and basaloid cells surrounded by lymphoid stroma (haematoxylin and eosin × 400).

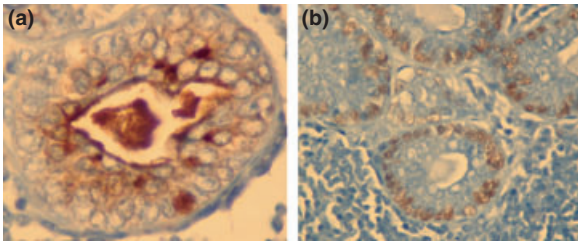

Figure 2. (a) Ductal cells highlighted by luminal stains (epithelial membrane antigen immunostain; × 400). (b) Basal cells displaying nuclear immunoreactivity for abluminal markers (p63 immunostain; × 400).

differentiation of epithelial nests was supported by epithelial membrane antigen (EMA) and p63 stains, respectively (Figure 2a,b). The histopathological findings were those of a parotid gland non-sebaceous lymphadenoma.

The presence of a conspicuous lymphoid background associated with an epithelial component in cytological preparations of the rare lymphadenoma cases creates a potential pitfall for misidentifying them as one of the various primary and metastatic tumours discussed below. To the best of our knowledge only one cytology study of fine needle aspiration biopsy findings from non-sebaceaous lymphadenomas has been previously published in the English medical literature.[2] The term 'basaloid neoplasm' is sometimes used in salivary gland cytopathology to categorize epithelial tumours composed of relatively small cells with scant cytoplasm, generally narrowing the differential diagnosis to basal cell adenoma, cellular pleomorphic adenoma, basal cell carcinoma, adenoid cystic carcinoma, and small cell carcinoma. In our case, the cytology smears do not display the marked cytological atypia, mitotic activity and tumour cell necrosis generally seen on basal cell carcinoma, adenoid cystic carcinoma and small cell carcinomas. In addition, cytological preparations from basal cell adenomas and cellular pleomorphic adenomas generally lack the conspicuous polymorphic lymphoid component present in lymphadenomas. Although our initial interpretation was basaloid neoplasm, on retrospective review it was noted that the tumour is better classified as a biphasic neoplasm in view of the dual population of lymphoid and epithelial cells.

The main cytological differential diagnosis of aspirate smears from a parotid gland tumour with a dual population of lymphoid and epithelial cells includes sebaceous lymphadenoma, Warthin tumour, acinic cell carcinoma, lymphoepithelial carcinoma, and a

metastatic neoplasm. FNAs from sebaceous lymphadenomas show lymphoid and bland epithelial cell clusters being only distinguishable from non-sebaceous lymphadenomas by the conspicuous sebaceous differentiation of their epithelial cells.[3] Warthin tumours generally show monolayered sheets of cytologically bland oncocytic cells in a background of small lymphocytes, granular debris and squamous metaplasia.[4,5] The epithelial cells seen in cytological preparations from lymphadenomas lack the characteristic granular cytoplasm, rounded nuclei and conspicuous nucleoli characteristic of oncocytes.[2]

Acinic cell carcinomas are characterized by the presence of serous acinar cells, at least focally.[6] In about one-third of cases a prominent lymphoid background is present, corresponding to an associated dense lymphoid stroma.[7] Aspirates are often hypercellular, comprised of large and small irregular aggregates of bland-appearing acinar cells with finely granular cytoplasm.[7] Lymphadenomas do not show lesional cells with the characteristic cytoplasmic granularity of serous acinar cells and generally the lymphoid background present on smears is more conspicuous than in acinic cell carcinoma cases. Lymphoepithelial carcinoma may present as a circumscribed mass, but most lesions are infiltrative and ill defined.[8] FNAs are characterized by cohesive clusters of pleomorphic tumour cells with enlarged nuclei, coarse chromatin and conspicuous nucleoli admixed with a polymorphic lymphocytic background.[9] The degree of pleomorphism seen in cases of lymphoepithelial carcinoma is not seen in lymphadenoma cases.

Metastatic squamous cell carcinomas and melanomas are the most common head and neck metastases involving major salivary glands,[10] while carcinomas of the lung, breast and kidneys are the most frequent source of more distant tumours.[9] The cytological features often mimic the primary neoplasm, and are different from the cytologically bland epithelial cohesive tumour cells seen in lymphadenoma cases. However, certain malignancies have a well-differentiated phenotype and review of previous slides from the primary malignancy and rational use of immunohistochemical stains are the best approach to distinguish metastatic disease from a second neoplasm.

Parotid gland lymphadenoma is a benign biphasic tumour with a basaloid epithelial phenotype and a polymorphic lymphoid component in FNA smears, but because it is a very uncommon tumour, it is not usually considered under the basaloid neoplasm category in most cytopathology textbooks. In the appropriate clinical setting and using radiological correlation, the FNA findings of bland basaloid cell clusters focally displaying small gland-like formations amidst a polymorphic lymphoid background can be diagnostic of parotid gland lymphadenoma, prompting simple excision and preventing more radical unnecessary surgical procedures.

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