CASE REPORT

Acinic cell carcinoma with lymphoid stroma mistaken for a metastatic intraparotid lymph node at frozen section analysis

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Abstract

Acinic cell carcinoma is a rare salivary gland tumor. The variant with lymphoid stroma is even rarer and has distinct histological features. We describe the case of a forty three year-old woman who presented with a left retroauricular mass of 5 years duration; magnetic resonance imaging revealed a well-circumscribed mass of 1.5 cm suggestive of pleomorphic adenoma. The patient underwent inferior polar parotidectomy. Frozen section analysis was performed and the interpretation of the sample suggested a metastatic intraparotid lymph node. The definitive final diagnosis of acinic cell carcinoma with lymphoid stroma was made on the basis of histological and histochemical findings, after a review of the literature.

Key words: acinic cell carcinoma, parotid, salivary gland, lymphoid stroma, differential diagnosis

INTRODUCTION

Acinic cell carcinoma (ACC) is a distinct entity with few cases documented to date.[1] Marked lymphocytic infiltrate is a common feature in ACC[2] However, ACC with Lymphoid stroma represents a separate subgroup with a thin fibrous capsule, a microfollicular growth pattern and a prominent lymphoid infiltrate completely surrounding the epithelial component.[2]

Lack of familiarity with this entity may lead to misdiagnosis, especially at frozen section analysis. In fact, this neoplasm can be mistaken for other malignant, more aggressive and even benign neoplasms. Recognition of this rare histologic variant is also important because it behaves far less aggressively than the conventional ACC**.**

We present through this case an exceptional pattern of ACC mistaken for a metastatic intraparotid lymph node at frozen section analysis, and we discuss clinicopathologic features and differential diagnoses.

CASE REPORT

A forty three year-old woman presented with a five-year history of a left-sided, painless mass of the retroauricular region which was not enlarging. His medical history did not highlight any significant evidence. On examination, the mass was firm in consistency, mobile, well-circumscribed, without external signs of inflammation, measuring 1.5 cm in diameter. There was no evidence of clinical lymphadenopathy and the rest of physical examination was normal.

Magnetic resonance imaging showed a parotid mass with well-defined margins raising the possibility of pleomorphic adenoma. Inferior polar parotidectomy was performed and was sent for frozen section analysis. The excised specimen showed a well-demarcated mass of 1.5 cm surrounded by scant glandular parenchyma. Microscopically, the tumor was thought to develop in an intraglandular lymph node, it showed a solid and a microcystic pattern, tumor cells had acinar differentiation. A lymphoepithelial differentiation was also seen. In the absence of cytological atypia or mitotic activity and because of lack of fibrous stroma and invasive growth pattern, diagnosis was rendered difficult.The adjacent salivary gland tissue was tumor free. We suggested the possibility of a metastatic lymph node. The possibility of a benign tumor was not excluded. In order to avoid a serious misinterpretation, we recommended waiting for the final histology which showed an encapsulated tumor lacking features of intraparotid lymph node with no evidence of subcapsular sinuses. The tumor was composed of solid masses with glandular or duct-like lumens. (Fig 1).

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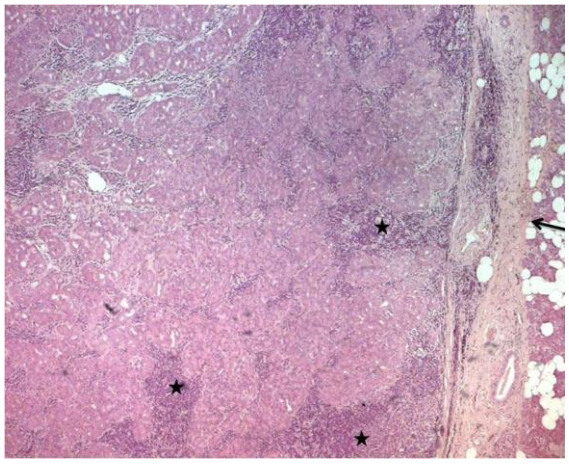

Figure 1 The epithelial component shows a microcystic growth pattern and is surrounded by a prominent lymphoïd strroma (stars). A fibrous thin capsule (arrow) without subcapsular sinuses is seen in the periphery of the mass separating the tumor from the normal parotid gland

The tumor cells showed serous acinar differentiation with granular basophilic cytoplasm. No cellular atypia were seen and mitoses were very rare. Rare vacuolated cell were observed. This epithelial component was completely surrounded by a reactive lymphocytic component with several secondary lymphoid follicles. No areas of necrosis or hemorrhage were identified. Salivary gland tissue outside the capsule was free of tumor. The tumor cells were positive for PAS staining (Fig. 2).

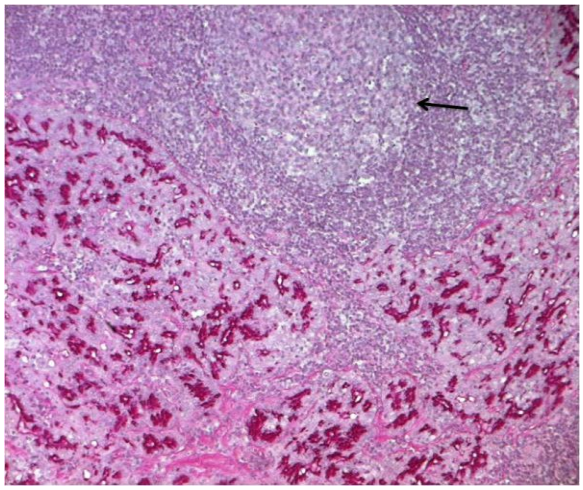

Figure 2 PAS staining. Note the well-developed germinal center in the lymphoid stroma (arrow)

Immunohistochemical stains showed strong membranous reactivity of most of tumor cells and acinar cells of the adjacent parotid parenchyma with Cytokeratins 7 and 18 whereas cells were completely negative for cytokeratins 8 and 20, for basal cell markers (34βE12, PS100, CK5/6) and myoepithelial markers (vimentin, PS100, smooth muscle actin). The surrounding cellular infiltrate was a mixture of CD20 and CD3 positive B and T lymphocytes and intraepithelial B and T lymphocytes were noted. Proliferation marker ki67 showed appropriate intense expression in the germinal centers and only a small number (less than 5%) of ki-67 labeled tumor cells (Fig. 3).

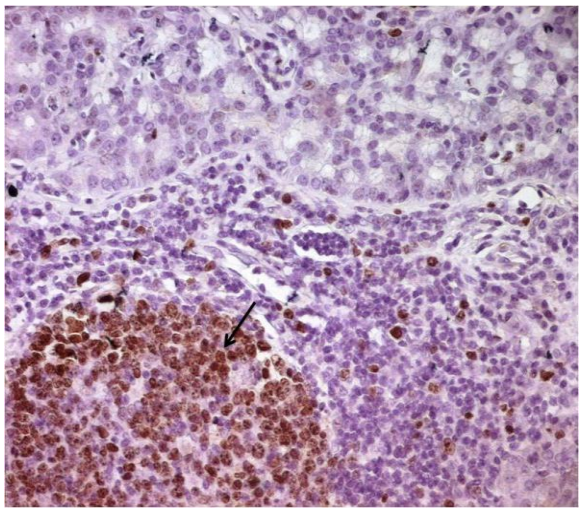

Figure 3 Ki67 staining. The proliferative activity of the tumor is very low. Note the Mib1 positive cells in the germinal centers (arrow)

Definitive histological result was ACC with lymphoid stroma. Recovery was uneventful and the patient did not receive any further treatment. The patient remains disease free two months later.

DISCUSSION

Marked lymphocytic infiltrate is a common feature in ACC.[2,3] A separate subgroup of ACC with a thin fibrous capsule, a micro follicular growth pattern and a prominent lymphoid infiltrate completely surrounding the epithelial component was first documented in 1997 by Michal *et al.*[1] who reported a series of 12 cases. Two additional anterior cases[4,5] published as ACC arising in intraparotid lymph nodes were thought to belong to this subgroup by the authors of this series but we believe that one of these two cases[4] did not meet the criteria of ACC with lymphoid stroma as it showed poorly-differentiated ACC in a hyperplastic intraparotid lymph node with extranodal involvement. We did not found in the English and French literature any further documentation of such cases, although some series of ACC included cases of ACC with prominent lymphoid stroma, without detailing their histological features.[3,6] In this proposed entity by Michal et al.[1] only a microcystic growth pattern was reported in

contrast to conventional ACC which usually display a mixture of two or more patterns including solid/lobular, microcystic, follicular and papillary-cystic.[6.7] In our case too, only a microcystic pattern was encountered. ACC is typically composed of acinic cells which are the diagnostic clue cells, other types of neoplastic cells including vacuolated cells, clear cells, non-specific glandular cells and intercalated ductal cells are encountered.[7] In the microcystic pattern, there are numerous small spaces within a solid neoplastic proliferation usually outlined by acinar cells and rarely by vacuolated and intercalated duct type cells[6] .Acinar cells were prevailing in our case too.

Special stains for PAS and immunohistochemistry for amylase identify the neoplastic acinar cells in tumors where acinar differentiation is not obvious[6]

There is no specific immunohistochemical profile specifically associated with ACC[3] In our case, tumor cells did not express CK8 and expressed CK7 in contrast to previous reports[8,9] and a characteristic membranous staining pattern was seen with CK18 as it was previously described.[9] The immunohistochemical analysis of proliferation markers provides additional prognostic information for this tumor[10]

ACC with lymphoid stroma has to be distinguished from ACC arising in an intraparotid lymph node. Except for the frequently occurring Warthin tumors, primary salivary gland tumors, which develop in lymph nodes of the parotid gland, are rare. These tumors arise from heterotopic intranodal salivary inclusions with acinar and ductal formations. [11] Hilus structure with salivary inclusions and marginal sinuses support origin within intraparotid lymph node.[12] Absence of an occult carcinoma in the salivary gland tissue is mandatory for the diagnosis of primary salivary gland tumor within a lymph node.[11]

ACC with lymphoid stroma may be confused with lymph node metastasis from low grade adenocarcinoma. However, nodal metastasis is not the primary presentation in low-grade adenocarcinoma. The lack of subcapsular sinuses may be helpful in ruling out nodal metastasis.[13]

We think that the main differential diagnosis here is non sebaceous lymphadenoma especially as ACC with lymphoid stroma does not show cellular atypia and other overt histological features of malignancy. Lymphadenoma is a rare and benign salivary gland neoplasm with 37 cases reported to date [12], it is composed of epithelial component in a dense lymphoid background. The epithelial component displays a wide spectrum of histological differentiation, with solid/lobular, cystic, glandular growth patterns and basoloid, ductal cells and/or polygonal cells with slightly basophilic non granular PAS negative cytoplasm. Myoepithelial cell participation, highlighted by immunohistochemistry, may be seen. A lymphoepithelial differentiation is possible. Acinar cell differentiation in ACC is the key differential criteria eliminating non sebaceous lymphadenoma[12,13] In our case, the clinical course is likely to be that of a benign tumor and we wonder if it can be designated as lymphadenoma with acinar cell differentiation.

ACC of the salivary glands is a low grade malignancy and has a favourable outcome with a tendency to both local recurrence and distant metastases. Recurrences and metastases may occur after variable lengths of time, sometimes after several years[10,14] However, ACC with lymphoid stroma behaves far less aggressively than the conventional ACC[1] with no evidence of disease within the follow-up period ranging from 19 months to 14 years. In the case of ACC arising in intraparotid lymph node and thought to be an ACC with lymphoid stroma,[5] the patient was free of disease 20 months after superficial parotidectomy. Features associated with poor outcome including positive surgical margins, histologic extracapsular extension, frequent mitoses, atypical mitoses, vascular and perineural invasion, nuclear pleomorphism and necrosis[3] are not seen in ACC with lymphoid stroma which explains its favourable outcome.

Management of ACC consists of wide local excision with clear surgical margins and long-term follow-up.[14]

CONCLUSION

ACC with lymphoid stroma is an unusual tumor, rarely encountered by pathologists and probably underdiagnosed as ACC arising in intraparotid lymph node. Recognition of this rare histological variant is important because it can be mistaken for other malignant, more aggressive and even benign neoplasms. This tumor has an excellent prognosis but adequate and long term follow-up after surgery appears to be the most appropriate management, seeing the limited number of cases. Further studies are needed to better define the diagnosis criteria of this entity.

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