

## Case Report

# Well-differentiated acinic cell carcinoma with lymphoid stroma associated with osteoclast-like giant cells of the parotid gland in children: a case report and literature review

Zhengjin Liu\*, Chao Pan\*, Ping Yin, Hongfeng Liao

Department of Pathology, Zhongshan Hospital, Xiamen University, Xiamen, Fujian, P. R. China. \*Equal contributors.

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**Abstract:** Acinic cell carcinoma of the parotid gland in children rarely occurs. Well-differentiated acinic cell carcinoma with lymphoid stroma is a subtype hardly seen but has a better prognosis than conventional acinic cell carcinoma. We hereby report a previously unreported case of a 9-year-old Chinese girl with well-differentiated acinic cell carcinoma with lymphoid stroma associated with osteoclast-like giant cells of the parotid gland. The pathology, diagnosis, presentation, management, and the clinical outcome are discussed and the literature is reviewed.

**Keywords:** Well-differentiated acinic cell carcinoma with lymphoid stroma, osteoclast-like giant cell, parotid gland, children, superficial parotidectomy

## Introduction

Although acinic cell carcinoma (ACC) is rare, it is the second most common salivary malignancy in children [1-4]. The recently separated well-differentiated ACC with lymphoid stroma is rare but has a better prognosis than conventional ACC [5, 6]. It is defined as a well-circumscribed to encapsulated tumor with a solid or microcystic pattern in which the tumor cells are all surrounded by and intermingled with a prominent lymphoid response [5]. Here we report that it has a more unusual morphological feature, whereby the tumor cells are interspersed with osteoclast-like giant cells. Both components share the same nuclear, immunophenotyping, and special staining features, which have never been reported to our knowledge. Due to its rarity and specific clinical manifestations, a high degree of suspicion is required for diagnosis, and experience in individual surgeons remains limited. We present and discuss a case and review the literature.

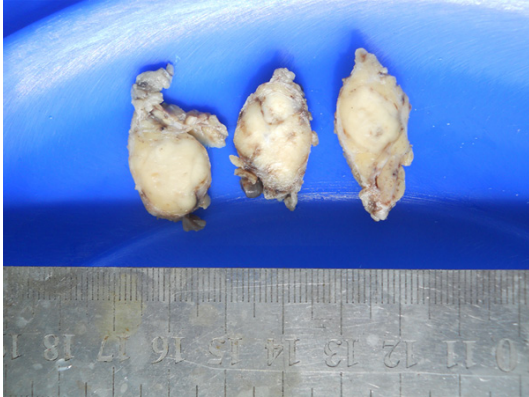
## Case report

A 9-year-old Chinese girl was referred to our head and neck department for the manage-

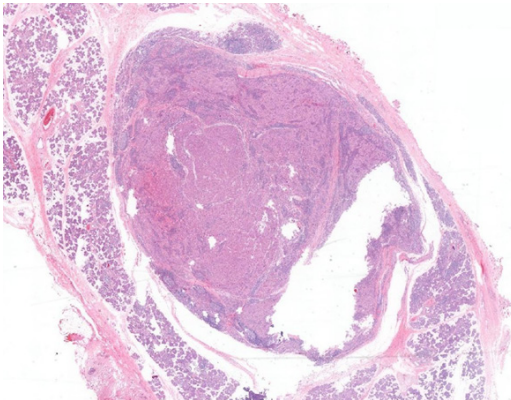
ment of a parotid region lesion. She complained of a painless swelling under the left of the ear lobe that had been gradually enlarging upon the course of 6 months. Physical examination found a mass measuring about 1×2 cm in size, located in the left parotid region, which was well-defined, movable, and not tender, solid in consistency and painless to palpation. Gums and mucous membranes in the mouth, pharynx were normal. Right parotid and double submandibular gland were without palpable abnormalities. Facial nerve functions appeared normal. Other systemic symptoms were unremarkable, with normal vital signs and no evidence of lymphadenopathy. Ultrasonography of the left parotid region of the head and neck revealed a solid oval mass measuring 16×12 mm within the left parotid gland. On imaging, the mass was quite sharply demarcated from the surrounding normal parotid tissue. No lymphadenopathy was seen.

The girl otherwise enjoyed good health, with no history of fever, weight loss, decreased appetite, or other systemic symptoms. There was no history of facial droop or other symptoms relating to the head and neck. No chronic or heritable illnesses were apparent in the family histo-

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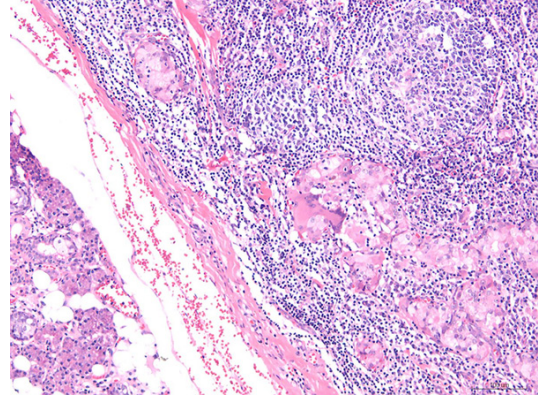
**Figure 1.** Gross specimen shows a well-encapsulated mass in the lobe of parotid gland with well-circumscribed, gray, homogeneous cut surface. The mass is measured 1.5 cm×1.2 cm×1.2 cm.



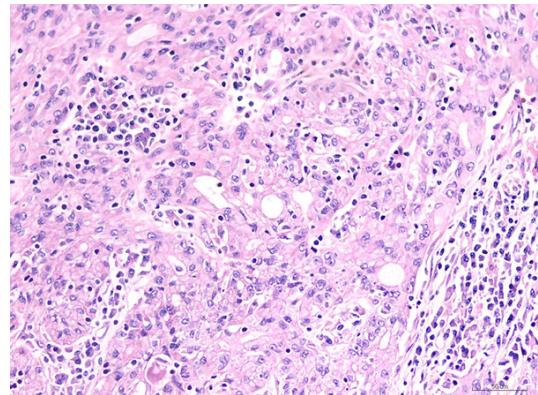
**Figure 2.** Scanning magnification showing a single, sharply circumscribed nodule is surrounded by a thin fibrous capsule. The stroma comprises a diffuse heavy infiltrate of lymphocytes, particularly dense at the margins. The immediate appearance suggests an intraparotid lymph node. (Hematoxylin and eosin stain).

ry. Provisionally it was diagnosed as a benign salivary gland tumor. One week later a superficial parotidectomy was performed. The tumor was completely encapsulated by fibrous tissue and the facial nerve was preserved.

The extirpated specimen was a superficial lobe of the left parotid gland, in which an oval and complete fibrous capsule mass was located. Grossly, the mass showed a 1.5×1.2×1.2 cm, firm, well-encapsulated, with well-circumscribed, gray, homogeneous cut surface (**Figure 1**). It adhered to the surrounding normal parenchyma of the parotid gland. Microscopically, the low-power view showed a single, well-circum-



**Figure 3.** The tumor is enveloped by a thin fibrous capsule and entirely surrounded by diffuse heavy lymphoid stroma with numerous well-developed germinal centers. No marginal sinuses can be observed. (Hematoxylin and eosin stain, Magnification, 100×).

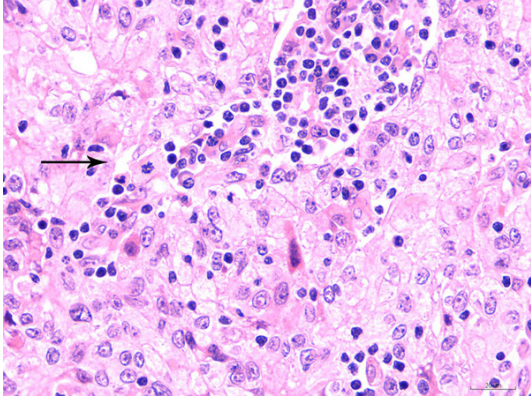


**Figure 4.** Tumor cells grow in solid and microcystic pattern. (Hematoxylin and eosin stain, Magnification, 200×).

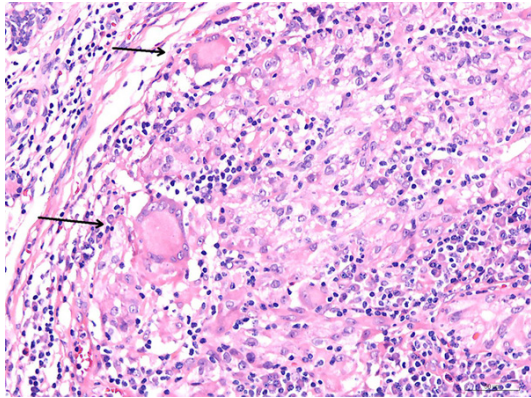
scribed nodule surrounded by a thin fibrous capsule. The stroma comprised a diffuse heavy infiltrate of mature lymphocytes within which numerous well-formed germinal centers were particularly dense at the margins (**Figure 2**). The immediate appearance suggested an intraparotid lymph node, but careful examination failed to show any marginal sinuses (**Figure 3**). The tumor cells were large, polygonal with lightly basophilic, granular and vacuoles cytoplasm and round, eccentric small nuclei, which were arranged in solid sheets and microcystic patterns (**Figure 4**). The cellular morphology was uniform. There was no significant pleomorphism, and mitotic figures were extremely scant (**Figure 5**). Among tumor cells scattered osteoclast-like giant cells (**Figure 6**). The tumor cells



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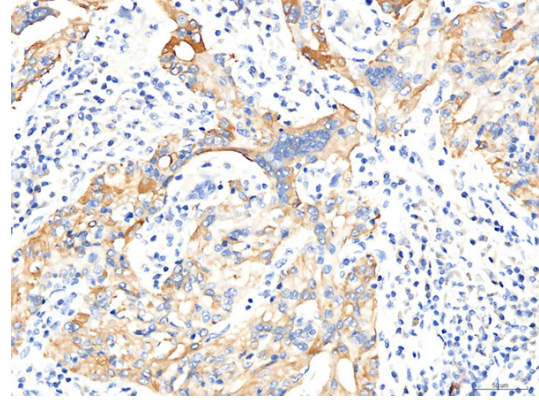


**Figure 5.** Most of the tumor cells are large, polygonal cells with lightly basophilic, granular cytoplasm and round, eccentric nuclei. The cellular morphology was uniform. No significant pleomorphism and mitotic figures (thick arrow) are extremely scant. (Hematoxylin and eosin stain, Magnification, 400×).

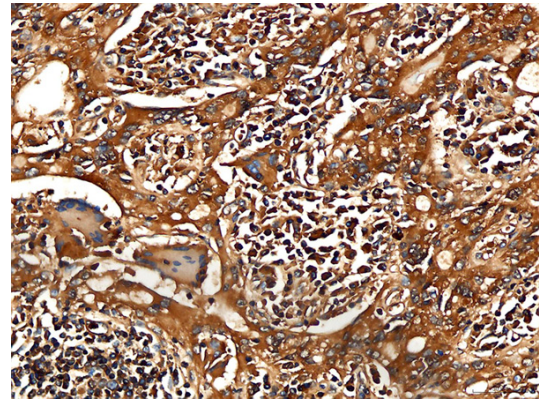


**Figure 6.** Tumor cells are scattered osteoclast-like giant cells (thick arrow). Tumor cells and osteoclast-like giant cells have a common nuclear morphology. (Hematoxylin and eosin stain, Magnification, 200×).

and the osteoclast-like giant cells had a common nuclear morphology. Within the tumor uneven thickness of the fiber separation could also be seen. Salivary gland tissue outside the tumor showed chronic inflammatory changes. Immunohistochemistry of the tumor cells showed that they are reactive for cytokeratin (**Figure 7**), alpha 1-antitrypsin (**Figure 8**), alpha 1-antichymotrypsin, carcinoembryonic antigen, Leu M1 antigen. The tumor was nonreactive with cytokeratin 14 and the Ki-67 labeling index about 2.5%. CD3, CD20, and Ki-67 staining showed normal lymphoid tissue structure. The cytoplasmic zymogen-like granules were PAS positive and resistant to diastase digestion. However, PAS positivity was very patchy



**Figure 7.** Both the cytoplasm of the tumor cells and the osteoclast-like giant cells are positive for cytokeratin. (Immunohistochemical stain, Magnification, 200×).



**Figure 8.** Both the cytoplasm of the tumor cells and the osteoclast-like giant cells are positive for alpha 1-antitrypsin. (Immunohistochemical stain, Magnification, 200×).

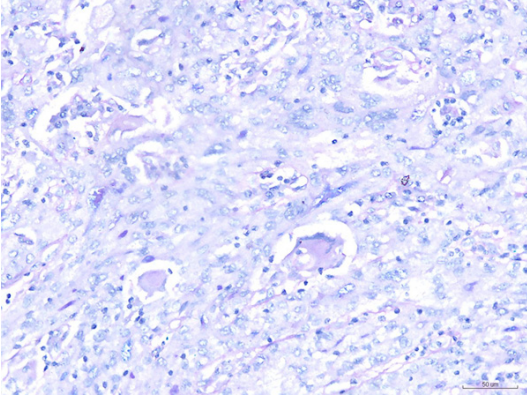
and not immediately obvious (**Figure 9**). Osteoclast-like giant cells immunohistochemistry and PAS staining results were consistent with the tumor cells.

Based on histology, special staining, and immunohistochemistry, the pathologist diagnosed well-differentiated ACC with lymphoid stroma of the parotid gland. Without further treatment, the patient's postoperative course was uneventful and she remained in good health 56 months later with no evidence of residual or recurrent disease.

### Discussion

Less than 5% of all salivary gland tumors occur to children and young adults and salivary neo-

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**Figure 9.** Both the cytoplasmic granules of the tumor cells and the osteoclast-like giant cells are stained with PAS and are resistant to diastase digestion. (Periodic Acid-Schiff stain, Magnification, 200×).

plasms account for less than 10% of all pediatric head and neck tumors [1-4]. ACC is “a malignant epithelial neoplasm of salivary glands in which at least some of the neoplastic cells demonstrate serous acinar differentiation, which is characterized by cytoplasmic zymogen secretory granules” [6] and accounts for about 3% to 6% of all salivary gland tumors and between 7% and 17.5% of malignant salivary neoplasms in major series [7, 8]. After mucoepidermoid carcinoma, ACC is the second most common malignant salivary gland neoplasm occurring in childhood [9]. There is a slight female predominance in most published series, and tumors are seen over a wide age range (3-91 years) with a fairly uniform age distribution from the third to seventh decades. The mean age in the largest series is 44 years. Four percent of the patients are under 20 years old [6-8]. There is no predilection for any ethnic group. The overwhelming majority, almost 80%, of ACC occurs in the parotid gland, and about 17% involve the intraoral minor salivary glands. Only about 4% develop in the submandibular gland, and less than 1% arise in the sublingual gland [6]. Occasional cases are reported in the lacrimal gland [10] and seromucous glands of the upper and lower respiratory tract [11, 12].

Most investigators consider that these tumors arise from neoplastic transformation of the terminal (intercalated) duct cells with histological differentiation toward serous acinar cells [13]. No well-established clinical associations for ACC exist, although single reports have docu-

mented ACC in patients with ataxia telangiectasia [14, 15], Sjögren’s syndrome [16], oculocerebrorenal syndrome [9], and coexistent with pituitary adenoma [17].

The typical ACC manifest as a slow enlarging, solitary, unfixed mass, but a few are multinodular and/or fixed to skin or muscle. A third of patients also experienced pain, which is often vague and intermittent, and 5-10% develop some facial paralysis. While the duration of symptoms in most patients is less than a year, it can be up to several decades in some cases [6]. The typical ACC is intraparenchymal, circumscribed, tan-gray, rubbery, and solitary nodule, but some are ill-defined with irregular peripheries and/or multinodularity. The cut surface appears lobular and varies from white to yellow to tan and red. They may be varying from firm to soft and can be homogeneous or show extensive cystic change. Recurrent tumors form multifocal and often poorly defined nodules. Although generally less than 3 cm, diameters as large as 22 cm have been recorded [18]. Neoplasms with marked lymphocytic infiltration may resemble a lymph node, and gross cystic change may be present. Dedifferentiated ACCs, a rare high-grade variant, is grossly bosselated tumors exhibiting ill-defined borders that typically infiltrate adjacent soft tissue and/or bone [19].

While serous acinar cell differentiation defines ACC, several cell types and histomorphologic growth patterns are recognized. These are acinar, intercalated ductal, vacuolated, clear, and non-specific glandular and solid/lobular, microcystic, papillary-cystic, and follicular growth patterns [6]. It is not uncommon for a given tumor to exhibit a mixture of cell types and architectural patterns. This morphologic diversity, together with the heterogeneity of the cellular component, contributes to the widely variable histologic appearances of this tumor.

The recently separated well-differentiated ACC with lymphoid stroma constitutes a rare subgroup that behaves far less aggressively than other ACCs. At low-power view, they form single, well-circumscribed nodules surrounded by a thin fibrous capsule. The stroma comprises a diffuse heavy infiltrate of mature lymphocytes within which are numerous well-formed germinal centers that are particularly dense at the



margins. The immediate appearance suggested an intraparotid lymph node, but failed to show any marginal sinuses. The tumor cells were arranged in solid sheets and microcystic patterns. The cellular morphology was uniform as there was no significant pleomorphism, and mitotic figures were extremely scant.

The well-differentiated ACC with lymphoid stroma has a low proliferative activity with MIB1 indices between 0.5% and 3.7% (mean, 1.7%). In contrast, the conventional ACC revealed higher proliferative activity with MIB1 indices between 3.4% and 45% (mean, 17%) [5]. Other immunohistochemical profiles are the same as conventional ACC that are nonspecific and are rarely of diagnostic value. Although the zymogen granules of normal salivary glands stain consistently for anti-alpha amylase, those in ACC show very variable reactivity [20]. It has been reported immunoreactive for cytokeratins, transferrin, lactoferrin, alpha 1-antitrypsin, alpha 1-antichymotrypsin, IgA, carcinoembryonic antigen, Leu M1 antigen [21-24], vasoactive intestinal polypeptide [25], cyclooxygenase-2 [26], amylase and bone morphogenic protein 6 [27]. Some tumors are positive for estrogen and progesterone receptors [28], and prostate-specific antigen [29]. Although about 10% of ACCs are positive for S-100 protein [21], there appears to be no evidence of basal cell or myoepithelial differentiation [30, 31]. In a recent study, cytokeratin 14 and P63, which has been used as myoepithelial marker, is detected in a wide range of salivary tumors but was not a feature of ACC [32, 33].

Scattering among the tumor cells and containing 2 to more than 30 nuclear, the osteoclast-like giant cells may be very large. It is unrelated to necrosis, hemorrhage, and has a common nuclear morphology with the tumor cells. It is with more eosinophilic cytoplasm, lack of proliferation activity, no mitotic figures or Ki-67 nuclear expression. It has the same immunophenotype and PAS staining characteristics with the tumor cells. The above has shown that the osteoclast-like giant cells may be fused tumor epithelial cells or may be dying cells. Its significance remains to be further elaborated.

Uncommon occurrence of the well-differentiated ACC with lymphoid stroma brings about the diagnostic difficulty. The important differential diagnosis is from a lymph node metastasis of

an adenocarcinoma arising from the parotid or elsewhere. Residual nodal architecture with subcapsular and medullary sinusoids would indicate a secondary tumor and also the rare cases of true ectopic ACC arising in intraparotid lymph nodes [34-36]. It may also be confused with mucoepidermoid carcinoma. The absence of goblet cells, squamous elements, and being negative for cytokeratin 14, P63 immunoreactivity distinguish it from mucoepidermoid carcinoma [32, 33]. Furthermore, in ACC, mucicarmophilic material is frequently extracellular and nuclei tend to be more bland, uniform, and peripherally located. While many conventional ACCs are surrounded by a heavy lymphoid stroma, but with only partial or areas entirely devoid of lymphocytes. Most important, the morphological growth pattern of these ACCs in the areas devoid of lymphoid stroma was always other than microcystic. Proliferative activity was also high. The fibrous capsule was incomplete or missing. The clinical outcome of these ACCs was significantly worse, with high rates of recurrences or metastases. A heavy lymphoid infiltrate by itself seems to have no prognostic significance [37].

### Conclusion

Well-differentiated ACC with lymphoid stroma of the parotid gland in childhood is rare and sometimes associated with osteoclast-like giant cells. It requires a high index for clinical suspicion, accurate diagnosis, and appropriate surgical treatment. If the condition is appropriately dealt with from the beginning, its morbidity is extremely low and permanent to cure is highly probable.

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### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Chao Pan, Department of Pathology, Zhongshan Hospital, Xiamen University, 201 Hubin South Road, Xiamen 361004, Fujian, China. Tel: +86 592 2993341; Fax: +86 592 2993344; E-mail: Panchao@xmu.edu.cn

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