Salivary gland acinic cell carcinoma.

by Lester D. R. Thompson, MD

Figure 1. This low-magnification view shows a number of lobules, or balls of blue cells. There is infiltration into the surrounding parotid gland parenchyma.

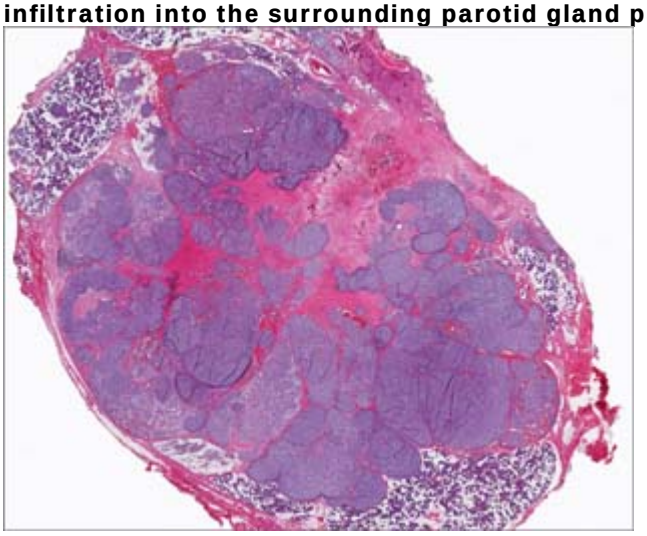
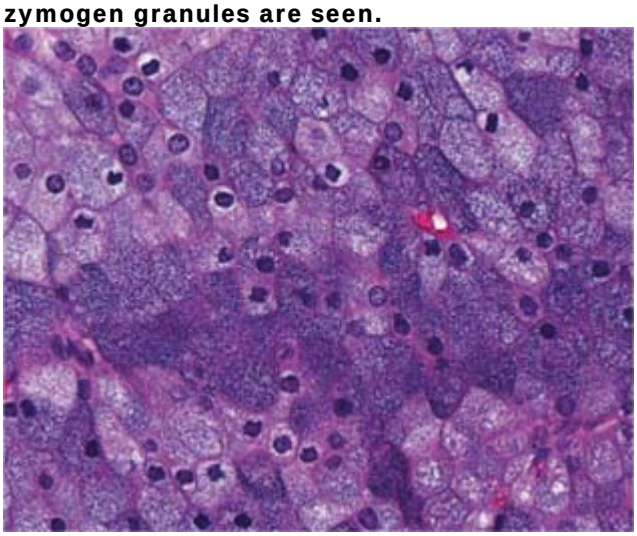


Figure 2. Serous acinar cells, which are most characteristic of AcCC, are large, polygonal cells with abundant and lightly basophilic and granular cytoplasm. Dense, blue-purple, fine to coarse zymogen granules are seen.



Acinic cell carcinoma (AcCC) is a malignant epithelial salivary gland neoplasm that demonstrates serous acinar cell differentiation with cytoplasmic zymogen secretory granules. While serous-type cells tend to predominate, ductal cells are also part of this neoplasm. There are a few cases that are thought to be related to radiation exposure. AcCC accounts for about 6% of all salivary gland tumors and 10 to 12% of all malignant salivary gland tumors. Patients present at a wide range of ages (mean: 40s). Children are also affected, as AcCC is the second most common neoplasm in the pediatric age group after mucoepidermoid carcinoma. Overall, females are more affected than males by a ratio of 3:2.

The parotid gland is composed almost exclusively of serous-type acini, and it is the most common site of AcCC (˜80% of cases); other reported sites are the palate (up to 15%), submandibular gland (4%), and sublingual gland (1%). It is interesting that this tumor is the most common bilateral malignant salivary gland neoplasm, although its bilateral presentation is not nearly as common as the bilateral presentations of benign tumors: Warthin and pleomorphic adenoma.

Most patients present clinically with a slowly enlarging solitary mass. Pain or tenderness is present in as many as 50% of cases. The tumors are usually circumscribed to irregular, and their mean greatest size is about 3 cm. On microscopic examination, they extend into the adjacent parenchyma, and they display a wide variety of different patterns of growth, even though one is dominant (figure 1). The cells are arranged in sheets, nodules, or aggregates in a solid/lobular pattern. Small spaces in the microcystic pattern create a lattice-like or sieve-like appearance. Papillary structures are not uncommon. A follicular pattern contains proteinaceous fluid.

Figure 3. Higher-grade tumors are frequently associated with areas of necrosis and degeneration. In this view, multiple areas within the tumor exhibit the characteristic acinar cell appearance.

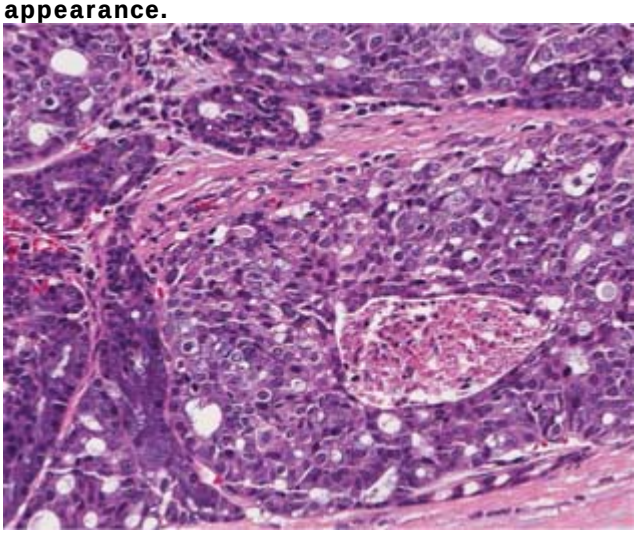
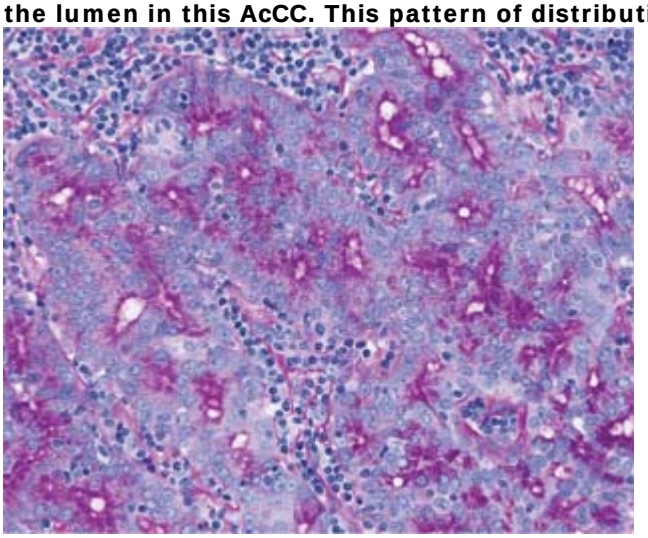


Figure 4. Periodic acid-Schiff-positive diastase-resistant zymogen granules are accentuated at the lumen in this AcCC. This pattern of distribution is quite common.



AcCCs are referred to as *blue dot tumors* because of their basophilic, granular cytoplasm and round, basophilic nuclei. Many different cell types can be seen, but the serous acinar cells are most easily identified. These are large, polygonal cells with abundant and lightly basophilic and granular cytoplasm that contains dense, blue-purple, fine to coarse zymogen granules (**figure 2**). Intercalated duct-type cells tend to be smaller and may have cytoplasmic vacuoles. Glandular cells and clear cells make up the remaining cell types. In a few cases, psammoma bodies can be seen. A lymphoid infiltrate, sometimes quite prominent, including germinal center formation, can be seen; it represents part of the concept of tumor-associated lymphoid proliferation (TALP). Histologically, it may simulate a lymph node.

Dedifferentiation into a high-grade carcinoma, which is rare, heralds a poor prognosis (**figure 3**). A number of variants are recognized, including solid, microcystic, papillary-cystic, and follicular. Periodic acid-Schiff-positive, diastase-resistant zymogen granules can usually be identified, although they may be patchy and limited (**figure 4**). No mucin is present. The pathologic differential diagnosis includes a normal salivary gland, papillary cystadenocarcinoma, mucoepidermoid carcinoma (specifically for the microcystic pattern of AcCC), metastatic thyroid carcinoma (for the follicular pattern), and a number of clear cell primary salivary gland tumors, as well as metastatic renal cell carcinoma.

Complete surgical excision is the treatment of choice, with radiation employed for incompletely excised or advanced-stage tumors. The prognosis is generally good (5-year survival: 80 to 90%). The clinical stage is the most reliable predictor of outcome. Recurrences develop locally in about 35% of cases, most within 5 years of diagnosis. A poor prognosis is associated with regional lymph node and distant metastases, multiple recurrences, incomplete resection, submandibular gland or parotid deep lobe involvement, age beyond 30 years, and large tumor size.

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Suggested reading

1. Al-Zaher N, Obeid A, Al-Salam S, Al-Kayyali BS. Acinic cell carcinoma of the salivary glands: A literature review. Hematol Oncol Stem Cell Ther 2009; 2 (1) 259-64.
2. Hoffman HT, Karnell LH, Robinson RA, et al. National Cancer Data Base report on cancer of the head and neck: Acinic cell carcinoma. Head Neck 1999; 21 (4): 297-309.
3. Michal M, Skálová A, Simpson RH, et al. Well-differentiated acinic cell carcinoma of salivary glands associated with lymphoid stroma. Hum Pathol 1997; 28 (5): 595-600.
4. Slater LJ. Acinic cell carcinoma and PAS-positive granules. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998; 86 (5): 507-8.

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