Adenoid cystic carcinoma: Evaluation of perineural spread, prognosis and radiological characteristics

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Learning objectives

Adenoid cystic carcinomas (ACCs) are malignant tumors that originate in the major and minor salivary glands.

The aim of this work is to review our series of patients with ACC proved at histologic examination and describe clinical and epidemiological characteristics, the imaging findings and behaviour of these tumors, the modalities of treatment, the histologic patterns and prognosis, with emphasis on perineural tumor infiltration.

Background

ACC is a relatively rare tumor that constitutes 4%-15% of all salivary gland tumors. It is usually found in the minor salivary glands, where it constitutes 25%-30% of malignant neoplasms and is the most common malignant tumor. ACC constitutes 15% of tumors of the submandibular gland but only 2%-6% of tumors of the parotid gland.

It occurs between the 3rd and the 9th decades of life, with a maximum incidence between ages 40 and 70 years. Clinical features at presentation (nasal obstruction, swelling, and facial pain) are nonspecific, and more than 50% of patients have had symptoms for 1-5 years before presentation. Paresthesia of the trigeminal nerve, particularly V3 signals the onset of perineural extension.

Three main histologic patterns have been described: tubular, cribriform, and solid. The degree of cellularity increases from the tubular to the solid form. However, every specimen has mixed patterns and histologic grades.

The natural history of this carcinoma is characterized by a slow relentlessly malignant course. Repeat recurrences and distant metastases (to the lungs, cervical lymph nodes, bones, and liver) occur over many years, finally killing the patient.
Repeat surgical excision and radiation therapy are the treatment of choice. The mean survival rate is 60%-69% at 5 years and approximately 40% at 10 years.

Different factors have been reported to influence the prognosis: primary site of the tumor, size of the neoplasm, bone and nerve invasion, quality of surgical margins, and clinical stage of disease. However, the factor that appears to be most closely correlated with the prognosis of ACC is its predominant histologic pattern (tubular, cribriform, or solid) and its degree of cellularity, which increases from the tubular to the solid form. The greater the cellularity, the worse the prognosis.

We designed a retrospective analysis of 36 patients (20 male and 16 female patients) diagnosed of ACC between 2001 and 2009.

**Imaging findings OR Procedure details**

The most frequent location of the primary tumor was the maxillary sinus-nasal cavity complex (n=16) (Fig. 1 and 2), followed by submaxilar (n=6) (Fig. 3) and parotid glands (n=4). Less common locations were: Lingual glands, cavum (Fig. 4) etc.

On MR images, ACCs appeared as poorly defined neoplasms with infiltrative margins in the majority of the cases (Fig. 5 and 6).

Eleven patients underwent surgery and external radiation therapy. Six patients underwent surgery, external radiation therapy, and chemotherapy. Four patients underwent surgery and chemotherapy, whereas two patients underwent radiation therapy only. Thirteen patients underwent surgery only.

Ten patients developed two or more locoregional recurrences (Fig. 7 and 8), fifteen developed distant metastases, and only six developed ganglionar metastases.

Histologic specimens were classified as tubular, cribriform, or solid. In our series the results were: solid (n=7), cribriform (n=3), tubular (n=4), mixed (n=4) and nonspecific (n=17). The degree of cellularity increases from the tubular to the solid form. Several studies suggest that the best prognosis is associated with the greater number of glandlike spaces, whereas the worst prognosis is attributed to lesions with dense cellularity. However, our results are not in agreement with those of the literature.
One typical characteristic of adenoid cystic carcinoma is its capacity of dissemination by perineural infiltration. (Fig 5 and 9). Actually has been the malignant tumor most widely reported but other tumors have been shown to exhibit this phenomenon.

The second and third divisions of the trigeminal nerve and the facial nerve were most commonly involved with perineural tumor. Both antegrade and retrograde perineural tumor spread were seen, although retrograde spread was significantly more common. Perineural tumor infiltration is a form of direct primary spread of neoplasia. The areas of infiltration are microscopically continuous with the main focus of a tumor, although they may be macroscopically discontinuous. Perineural tumor spread has been demonstrated to occur wholly on principally in perineural or endoneural tissue planes along a path of least resistance. Nerve function can be preserved until later in the course of the disease.

The principal pathway of perineural spread was correlated with the tumor site and histologic type. Tumors of the lower lip, chin, and floor of the mouth can follow the inferior alveolar nerve (Fig. 12), and tumors of the tongue can extend along the lingual nerve to reach the cavernous sinus. The mandibular nerve is an important route of spread to the cavernous sinus for tumors of the nasopharynx, masticator space, and parapharyngeal space. The maxillary nerve can carry tumor from the palate, maxilla, midface, nose, and nasopharynx. Tumors of the forehead, eye, ethmoid and frontal sinuses, or lacrimal gland may extend along V1. Tumors of the parotid gland can follow the facial nerve or the auriculotemporal branch of V3.

Radiologic findings in perineural tumor spread include: foraminal enlargement (Fig. 12), foraminal destruction, obliteration of fat planes, nerve enlargement (Fig. 11), nerve enhancement, marked high intensity signal of the muscle on T2- weighted MR images at the initial stages of denervation due to edema (Fig. 10), neuropathic atrophy, convexity of the lateral cavernous sinus wall, and replacement of the trigeminal subarachnoid cistern with soft tissue (Fig. 11).

Perineural infiltration with nerve enlargement, contrast enhancement, or both was demonstrated in fifteen patients (In ten of them with MR and in five with CT). In 9 patients, perineural infiltration was noted at initial diagnosis of the primary tumor; in 6 patients, perineural infiltration was diagnosed on follow-up studies. The nerves most often affected were the maxillary division (V2) (Fig. 9) and the mandibular division (V3) (Fig. 10) of the trigeminal nerve.

Respect to the imaging techniques, MR images defined the tumor and its extension and enabled effective therapeutic planning (palliative versus curative surgery, and selection of margins of the tumors for the radiation therapy ports) and follow-up evaluation.
However MR images were not specific in differentiation of ACCs from other types of tumors; this result underscores the need for biopsy to ensure correct diagnosis.

Both CT and MR imaging can help detect perineural spread, but MR imaging is the modality of choice because of its multiplanar capability, its superior soft-tissue contrast, and the decreased amount of artifact from dental hardware. Thin-section axial and coronal T1-weighted MR imaging performed before and after the administration of gadopentetate dimeglumine is recommended as the optimal radiologic tool and technique for the investigation of perineural tumor spread.

As tumor accumulates along the nerve, the diameter of the nerve increases, which may cause foraminal enlargement and, eventually, foraminal destruction. This is well seen at cross-sectional CT (Fig. 12). Tumor extension through the foramen ovale and involvement of the Meckel cave is best seen on coronal T1-weighted MR images (Fig. 13). Enhancement of the nerve is best seen on fat-suppressed T1-weighted MR images because the enhancing nerve may be obscured by adjacent high-signal-intensity fat or chemical shift artifact on routine T1-weighted MR images.

Images for this section:
**Fig. 1:** Coronal T1-weighted pre and postcontrast MR images show a primary tumor located in the left maxillary sinus, with destruction of the hard palate.
Fig. 2: Axial contrast enhanced CT scan shows a posterior nasal cavity mass.
Fig. 3: Hyperintense mass on T2-weighted MR image in the right submaxillary gland.
**Fig. 4:** T1- weighted MR image obtained before and after administration of contrast, shows infiltrating tumor in the right side of the cavum.
Fig. 5: Coronal T1-weighted "fat-sat" enhanced MR image obtained at level of foramen ovale shows an infiltrating lesion at the middle cranial fossa which involves the cavernous sinus, destroys the skull base, and extends along the V3, branch of the trigeminal nerve.
**Fig. 6:** Sagittal T1-weighted pre and postcontrast MR image shows a tumor infiltrating both the soft and hard palate.

**Fig. 7:** Coronal T1 and T2-weighted MR images show postsurgical changes at the maxillary sinus. Note the locoregional recurrence involving the right orbital muscles.
Fig. 8: Axial T1-weighted enhanced MR image shows locoregional recurrence involving the cavernous sinus and orbital vertex, in a primitive orbitary ACC.
Fig. 9: Axial T1-weighted enhanced fat-suppressed MR image shows an infiltrating tumor at the middle cranial fossa that involves the Meckel's cave, with perineural spread into the foramen rotundum and the pterygopalatine fossa.
**Fig. 10:** Coronal T1-weighted enhanced fat-suppressed MR image shows marked enhancement of the left masticatory muscles at the initial stages of denervation, due to tumoral infiltration of V3.
Fig. 11: Coronal T2-weighted MR image shows signs of tumoral infiltration of a markedly enlarged left trigeminal nerve.
**Fig. 12:** Axial and coronal contrast-enhanced CT scans show signs of foramen ovale destruction and inferior alveolar canal enlargement.
Fig. 13: Coronal T1- weighted MR image obtained before and after administration of contrast shows tumor extension through the foramen ovale, and also involvement of the Meckel cave and cavernous sinus.
Conclusion

The most common means of extension of these neoplasms is by local and intracranial infiltration, particularly along nerve sheaths.

Both CT and MR imaging can help detect perineural spread, but MR imaging is the modality of choice.

Although, several studies suggest that the worse prognosis is associated with dense cellularity, our results are not in agreement with those of the literature.

Personal Information

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