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CASE REPORT

Mizuhiko Terasaki · Takashi Tokutomi · Hikaru Maruiwa
Yasuo Sugita · Hiroshi Harada · Minoru Shigemori

High-grade adenoid cystic carcinoma originating from the lacrimal gland

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Abstract Among primary lacrimal gland tumors, adenoid cystic carcinoma (ACC) is the most common malignant epithelial neoplasm; it is characterized by local intracranial invasion. A case with unusual dumbbell-type intracranial extension representing cavernous sinus syndrome is described. A 49-year-old woman was admitted to our hospital with right cavernous sinus syndrome. Computerized tomographic (CT) scans and magnetic resonance (MR) imaging demonstrated well-enhanced intraorbital and middle fossa tumors mimicking multifocal mass lesions. Operative findings revealed an ACC originating from the lacrimal gland and extending into the right cavernous sinus and middle fossa along the nerve sheath in the superior orbital fissure. Although MR image findings of intracranial ACC often resemble the image findings for meningiomas, intracranial ACC is very aggressive in comparison with meningioma. It is best treated surgically and aggressively.

Key words Adenoid cystic carcinoma · Cavernous sinus syndrome · Lacrimal gland

Adenoid cystic carcinomas (ACCs), known as cylindromas, arise from the salivary, lacrimal, or other exocrine glands. The tumors are slow growing, with local invasion and recurrence. The incidence of intracranial invasion has been reported as 4% to 22%,[1] but distant metastases are not uncommon.

ACCs represent 11% of epithelial neoplasms in the lacrimal gland.[2] However, ACCs originating in the lacrimal gland invade the intracranial cavity more frequently than do carcinomas of the salivary gland.[1]

M. Terasaki (✉) · T. Tokutomi · H. Maruiwa · M. Shigemori
Department of Neurosurgery, Kurume University School of Medicine, 67 Asahi-machi, Kurume 830-0011, Japan
Tel. +81-942-31-7570; Fax +81-942-38-8179

Y. Sugita · H. Harada
Department of Pathology, Kurume University School of Medicine, Fukuoka, Japan

We report here a patient with high-grade ACC originating in the lacrimal gland and invading the cavernous sinus, which was revealed by neuroimaging to have a multicentric formation. The unusual biological behavior and neuroimaging of this tumor are presented, with special reference to differential diagnosis.

Case report

History and examination

A 49-year-old Japanese woman admitted to our hospital on June 19, 1998, had a 9-month history of progressive headache with periorbital pain on the right side. Removal of the myoma uteri had occurred in April 1998. Neurological examination on admission revealed visual loss, oculomotor nerve palsy, abducens nerve palsy (double vision when she moved her eyes to the right side), and trigeminal nerve palsy (absence of the corneal reflex) on the right side.

Computerized tomographic (CT) scans demonstrated two well-enhanced mass lesions on the lateral wall of the right orbit and the medial side of the right middle fossa. Molecular resonance (MR) imaging of both lesions showed isointensity on T1 and T2 weighting (Fig. 1). These lesions had homogeneous enhancement with intravenous gadolinium diethylene triamine pentaacetic acid (Gd-DTPA) (Fig. 2). The dura mater adjacent to the tumor was also enhanced extensively. Neuroradiologically, there was no evidence of relevance for these tumors. Right cerebral angiography revealed a tumor stain via the ophthalmic artery. Under a presumptive diagnosis of meningioma, malignant lymphoma, or metastatic carcinoma, the patient underwent surgery on July 7, 1998, in which a right epi- and subdural combined (Dolenc's) approach was used.

Operation

After complete resection of the right sphenoid wing and orbital roof, a round, lobulated intraorbital tumor was found

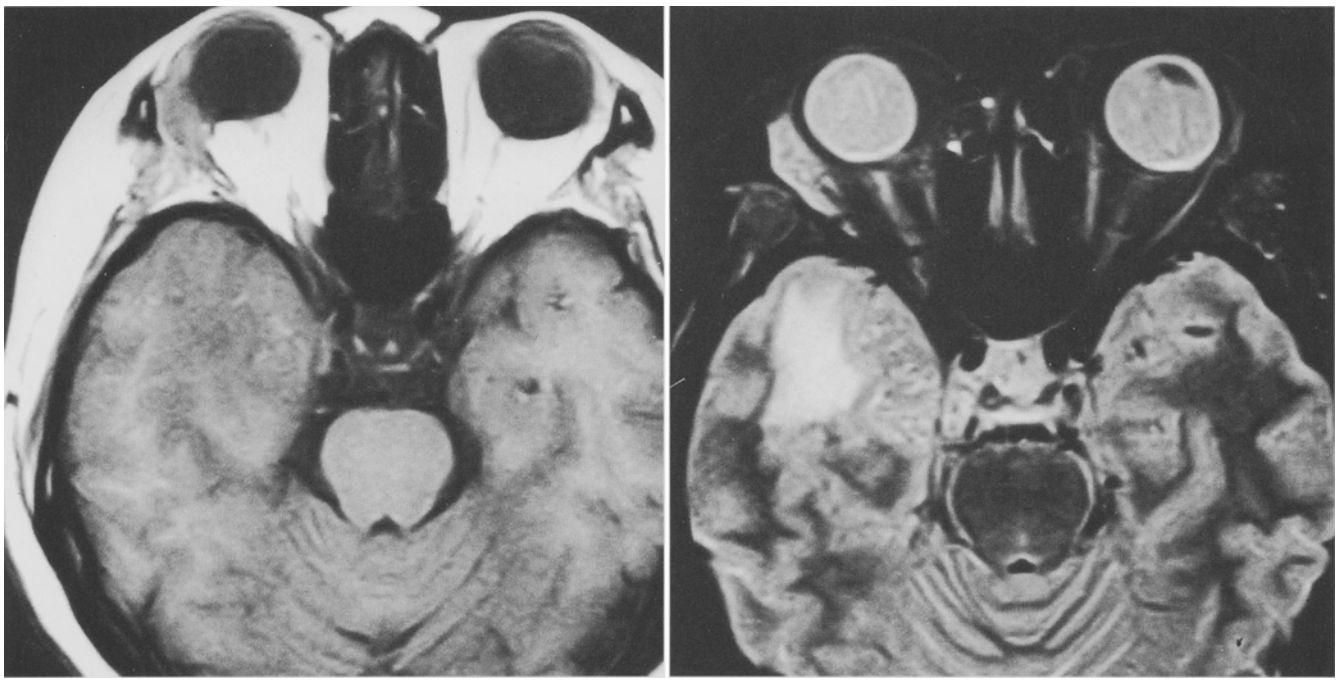

Fig. 1. Axial T1- (**a**) and T2- (**b**) weighted MR images showed isointense tumors in the right orbit (*arrow*) and middle fossa (*arrow*)

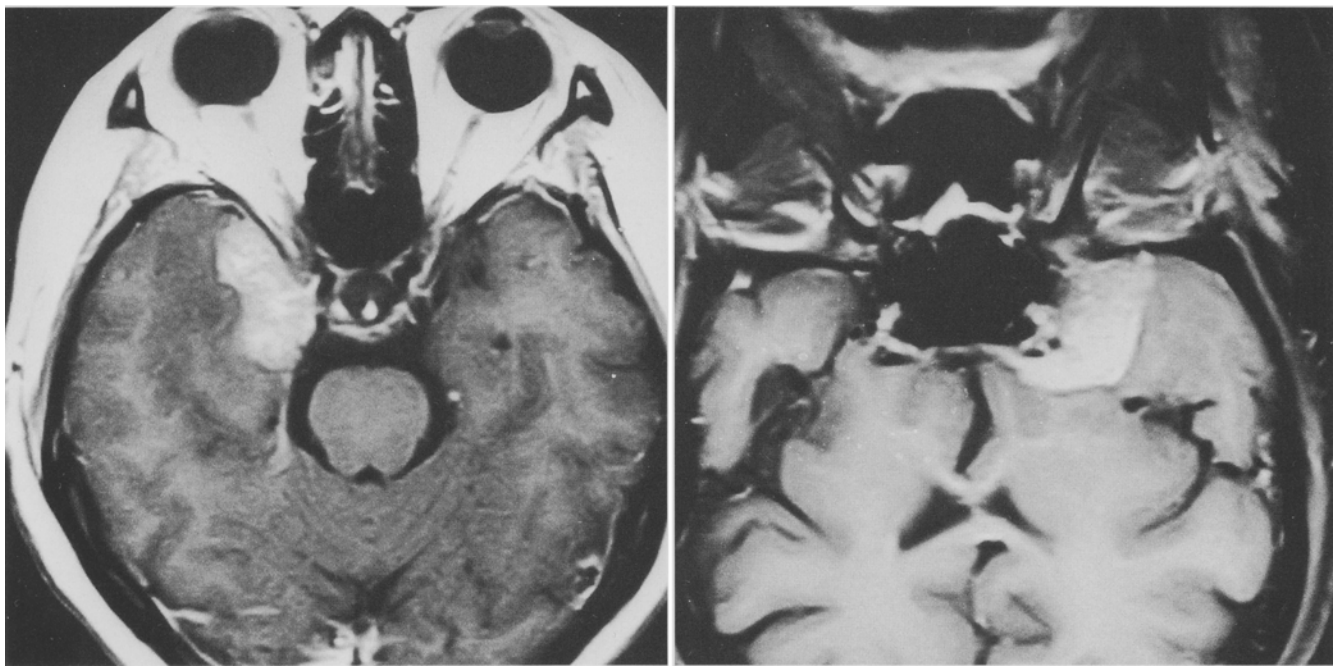

Fig. 2. Preoperative gadolinium-enhanced MR images showed well-demarcated, hyperdense, well-enhanced masses in the right orbit and middle fossa extending to the cavernous sinus (*arrow*) and cerebellopontine angle. No definable relation between these tumors was seen

in the superior part of the orbit. The tumor had invaded the superior orbital fissure along the nerve sheath and extended into the right cavernous sinus and middle fossa. The middle fossa mass partially adhered to the outer layer of the cavernous sinus. The intraorbital and middle fossa tumors were completely removed, and the outer layer of the dura of the cavernous sinus was coagulated. Gross inspection revealed that the resection of the lesion was complete. The patient was extubated postoperatively and awoke quickly without any new neurological deficits (Fig. 3).

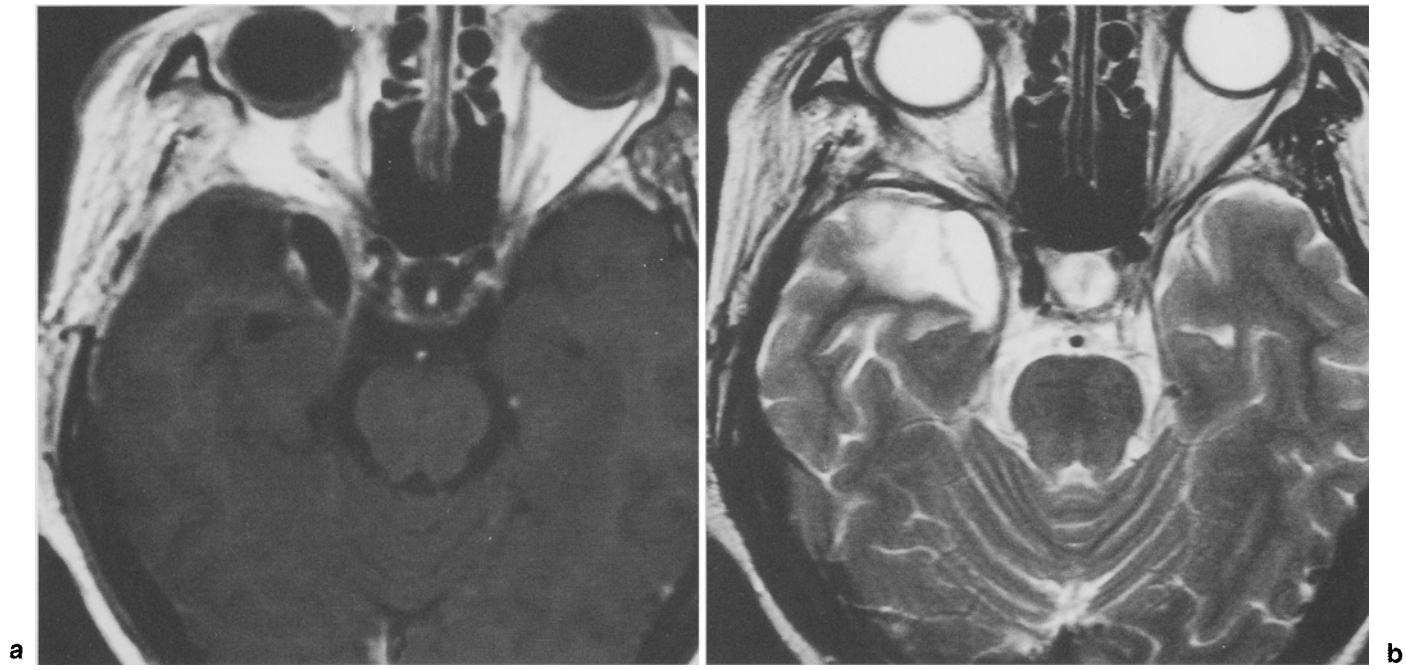

Fig. 3. Postoperative MR images on T1 (**a**) and T2 (**b**) weighting showed the extent of tumor removal from the middle fossa and the orbital exenteration. Part of the tumor was seen in the cavernous sinus

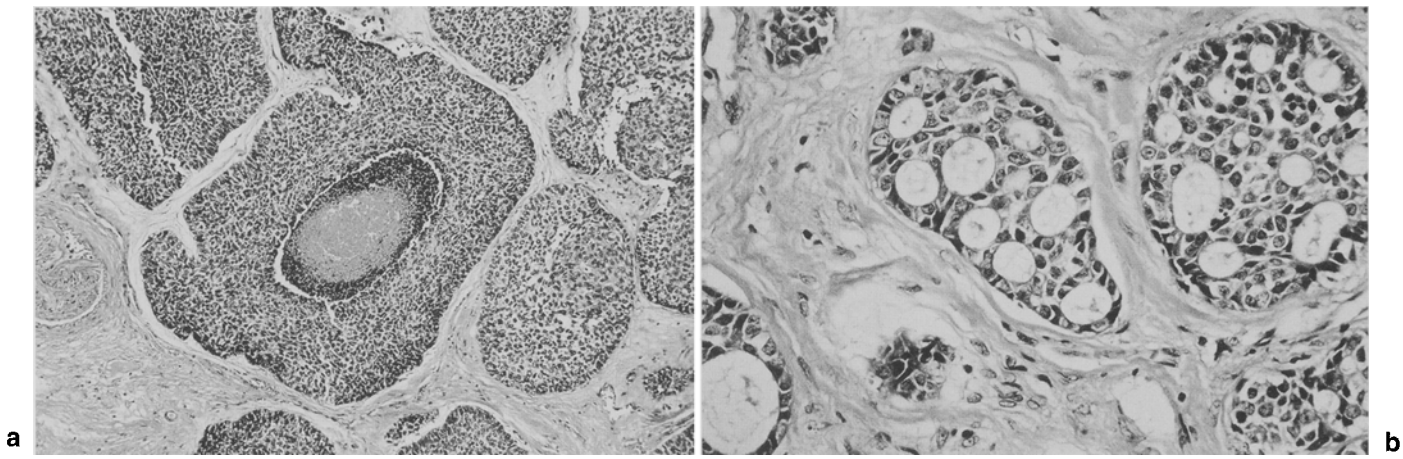

Fig. 4. **a** Histopathological microphotographs of adenoid cystic carcinoma. The tumor showed a solid pattern with central necrosis (original magnification, ×100). **b** In part, the tumor had a typical cribriform pattern (original magnification, ×200)

Histopathological examination

Both tumor masses had solid patterns and partially cribriform patterns that were typical for this type of tumor. The tumor cells had an abnormally low amount of cytoplasm and exhibited a basaloid appearance with focal necrosis. In these cells, the cytoplasm showed immunoreactivity for epithelial membrane antigen (EMA) and smooth muscle actin (SMA) and were positive for S-100 protein coinciding with the inside of the tubule. These findings confirmed the diagnosis of ACC (Fig. 4).

Postoperative course and treatment

Postoperatively, the patient did well and had no complications. The IIIrd, Vth, and VIth nerve palsy on the right side remained. The patient underwent irradiation (a total of 60 Gy) because of a residual tumor of the cavernous sinus, beginning on July 30, 1998. During 8 months of follow-up, the patient experienced no further progression of her symptoms.

Discussion

ACC is a well-recognized cancer originating in the exocrine glands from the major and minor salivary glands. It can also arise from the lacrimal gland, the upper respiratory tract, the lungs, the breasts, and the genital tract.[3] Although tumors that arise from the salivary gland typically have only a 1% chance of intracranial invasion,[4] 15% of lacrimal gland ACCs invade the intracranial cavity via perineural spread.[1] In addition to their local invasion and perineural extension characteristics, these tumors have a tendency toward local recurrence and distant metastasis. For these reasons, adjuvant therapies for these tumors are limited. Neurosurgeons need especially to be familiar with the tendency of ACCs to extend intracranially.

Three routes of intracranial invasion of salivary gland ACC were reported by Shotton et al.[5]: the eustachian tube (in the peritubal space), the mandibular and maxillary nerves, and the internal carotid artery. ACC in the Gasserian ganglion lesion arises from the glandular epithelia of the eustachian tube. Gonzalez and Zulch[6] reported ACC arising from the nasal fossa or paranasal sinus and invading the skull base via the mandibular and maxillary nerves. On the other hand, lacrimal gland ACC has a greater chance of invading intracranially for the following reasons: more neural and vascular structures exist in the orbit; the bones of the orbit are connected directly to the intracranial cavity; and the periorbit and the nerve sheath are closely connected. These factors increase the chance that a lacrimal gland ACC will invade intracranially via perineural, vascular, intraosseous, and leptomeningeal routes and the nerve sheath. In our case, although no clear evidence of the origin of the tumor could be identified radiologically, operative findings showed ACC of the lacrimal gland extending into the right cavernous sinus and middle fossa along the nerve sheath.

The histological appearance of ACC has been known to vary in microscopic patterns. The typical morphologic patterns are cribriform, tubular, and solid. Parzin and colleagues[7] showed a relation between recurrence and these morphological patterns. They reported recurrences in 59% of patients whose tumor had a tubular pattern, 89% of those with a cribriform pattern, and 100% of those with a solid pattern. Matsuba and colleagues[8] speculated that those patients with a cribriform pattern had the longest survival time, followed by those with tubular and solid patterns. In a study lasting more than 20 years, the longest period of survival for a patient with a solid pattern was 8 years, whereas 4 patients with the cribriform pattern survived for over 20 years.[9] The solid type of ACC seems to have the worst prognosis, characterized by numerous early recurrences, early metastasis, and frequent fatal evolution.

High-grade-type ACC, such as the present case, representing predominantly solid growth with central necrosis, should be distinguished from salivary duct carcinoma (SDC) and basaloid squamous cell carcinoma (BSCC). SDC rarely arises from the lacrimal gland and should be described as a primary ductal carcinoma of the lacrimal gland. It resembles invasive ductal carcinoma of the breast, especially comedo-carcinoma, and is known as one of the highest-grade carcinomas among salivary gland-type neoplasms. It also resembles high-grade ACC in its solid growth with central necrosis, but it differs in an important cytological feature: the large neoplastic cells occasionally have an apocrine-like appearance, whereas ACC is basically composed of basaloid/myoepithelial cells with scant cytoplasm.[2]

BSCC is known as a highly malignant neoplasm, with a predilection for the head and neck, which arises from the mucosal epithelium of various organs. It resembles ACC in its solid growth and also the trabecular or glandular structures with hyaline or mucoid stroma, but in a BSCC focal keratinization, a relation to the overlying mucosa and cytological atypia of the mucosal epithelium itself can occasionally be found.[10]

Neither tumor shows myoepithelial differentiation; therefore, in immunohistochemical tests of these tumors, SMA is not reactive, although S-100 protein is often immunoreactive.

CT findings in intracranial ACC commonly describe a well-demarcated, hyperdense, well-enhanced mass.[11] Morioka et al.[12] speculated that CT and angiography revealed no specific findings for ACC that distinguished those tumors from meningioma. Indeed, the CT findings in our patient demonstrated an isodense and well-enhanced mass resembling a meningioma.

There are no reports of MR image findings in intracranial ACC. In our case, MR demonstrated isointensity on T1- and T2-weighted images. This lesion was well enhanced with Gd-DTPA. Additionally, the dura mater adjacent to the tumor was extensively enhanced, showing the dural tail sign resembling meningioma. Morioka et al.[12] reported the tail was a confirmation of extensive invasion of the dura mater by ACC. These unique MR image findings suggest that if the neuroradiological features are those of a well-enhanced extra-axial tumor extending into the orbit and closely resembling the features of meningioma, intracranial ACC should be considered.

It has been most commonly reported in the literature that the best treatment of ACC is radical surgical resection.[5,9,13–17] Because of the character of these tumors, however, total resection is almost impossible. Most of these tumors recur within the first 3 years. Conley and Dingman[13] reported a 42% rate of recurrence in their series of 134 patients. Radiation therapy has been used successfully to reduce tumor volume upon the appearance of these recurrent tumors and symptoms. However, whether radiation therapy is essential for treatment of ACC is controversial. Even when local treatment has been achieved, distant metastasis can occur in as much as 39% of patients. Metastasis most often occurs in the liver, bone, and lung.[15,17,18]

It is quite apparent that local control and distant metastasis are major problems in the management of ACC. The development of neoadjuvant therapy for treatment of these tumors can be expected on the basis of the ongoing accumulation of clinical and histopathological data.[19]

The slow biologic growth of ACC, coupled with the likelihood of metastasis late in the course of the disease, results in relatively favorable 5-year survival rates; however, the long-term outlook for survival and cure has been far less favorable. In our case, gross total excision and irradiation were effectual for reduction of tumor volume, but the follow-up study has lasted only 8 months, and clearly a much longer term will be needed for a full assessment of the success of treatment.

In conclusion, the present case supports the previous finding that MR image findings of intracranial ACC are characterized by isointensity on T1- and T2-weighted images and by a dural tail sign on a Gd-DTPA-enhanced image, resembling the image findings for meningiomas. Additionally, in ACC originating from the lacrimal gland, neuroimaging study cannot always confirm a definable relation between intraorbital and intracranial masses, especially if the tumor has invaded along the nerve sheath.

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