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Clinical Study

Adenoid cystic carcinoma metastatic to the dura: report of two cases

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Comments

The report submitted by Kaur et al. describes two patients with extensive invasion of the dura by adenoid cystic carcinoma. Given the well-known propensity of this tumor type to invade in a perineural fashion, it is surprising that more cases such as these have not been reported, but the 'willingness' of these tumor cells to respect the dura, relatively-speaking, suggests that their mechanisms of invasion may be perhaps more controllable. In some fashion, their 'affinity' for the dura may provide a conceptual framework though which to study tumor spread. While the authors have mentioned the association between adenoid cystic carcinoma and neural cell adhesion molecules as being as potential area for future investigation, the mechanisms of tumor cell invasion are myriad.

Jack P. Rock

Summary

Adenoid cystic carcinoma (ACC) originating in the salivary and lacrimal glands usually spreads to the intracranial space by following cranial nerves into the cavernous sinus, temporal bone and cerebellopontine angle. We present two cases in which ACC metastasized extensively to the dura, suggesting that ACC has an affinity for the dura. Case 1, a 43-year-old man, was operated on 12 years earlier for invasive ACC of the right palate. He experienced recurrence of the tumor in the left cavernous sinus and sella, and extensive involvement of the dura of both right and left temporal fossae. Case 2, a 33-year-old woman, had spread of ACC to the right convexity dura and tentorium after undergoing a resection of a left-sided ACC tumor of the lacrimal gland two years earlier. Both patients underwent multiple resections and radiation treatment. Extensive, multifocal, bilateral spread of ACC to the dura in both cases indicates that ACC has an affinity for the dura.

Introduction

Adenoid cystic carcinoma(ACC), previously known as *cylindroma,* arises most often in the major or minor salivary glands, but can originate in the lacrimal gland, skin, breast, ear canal, lung, prostate and uterine cervix [1]. It is the most common malignant epithelial tumor of the lacrimal gland [2], and the second most common type of carcinoma arising in the salivary glands, following mucoepidermoid carcinoma [3]. Metastasis to lung, bone, liver and brain have been reported [4]. Local extension occurs between tissue planes and along nerves and blood vessels. The tumor often infiltrates and spreads through bone [5]. Perineural spread from the primary site is the most common mode of spread to the brain [6–11]. Hematogenous spread to the brain, although rare, has also been reported [1,12–15]. Intracranial spread is usually ipsilateral to the primary tumor, due to local extension or perineural spread to the cavernous sinus or temporal bone. We present two cases of metastasis of ACC to the ipsi- and contralateral dura without intraparenchymal tumor, suggesting that ACC may have an affinity for the dura.

Case reports

Case 1

A 32-year-old man initially presented with pain in the right maxilla and fullness in the right palate in

November, 1979. A biopsy of the right hard palate demonstrated ACC. In December, 1979 he underwent a right maxillectomy and resection of the tumor. He did well post-operatively for several years without evidence of tumor recurrence, until 1984, when he noticed numbness in the lower right face and tongue. A CT in January 1985 demonstrated increased soft tissue densities in the lateral and superior walls of the right maxillary sinus. In May 1985, he underwent exploration of the right maxillary space and orbit, which revealed recurrent ACC in the right maxillary area. He subsequently received radiotherapy to a total dose of 54 gray. Concomitantly, he experienced worsening right facial numbness and diplopia. A second recurrence was found in August, 1987 upon transoral biopsy of the right pterygopalatine space. He then underwent another course of radiation therapy totalling 45 gray. In March, 1991, CT showed tumor in the left cavernous sinus and sellar region, and a new mass in the lateral right temporal fossa (Figure 1(a)). He underwent a right temporal craniotomy for resection of the right temporal fossa mass. At surgery, an extensive sessile, dural-based ACC tumor was found extending from the cavernous sinus to the lateral Sylvian fissure. A second dural-based tumor was found extending anteriorly in a sulcus. The tumors did not appear to have originated in the brain or in the cranial bone, but appeared to be within the dura. Histologically, the tumors had a tubular morphology. Microscopically, solitary ducts were lined by predominantly cuboidal epithelium (Figure 2). Their lumens were variably expanded with mucin. They were surrounded by a few spindled cells and vascular fibrous connective tissue with bands of collagen. A partial resection of the tumors was performed, and post-operatively, he received a final, palliative course of radiation therapy consisting of 44 gray and three courses of chemotherapy utilizing Adriamycin, Cytoxan, and cis-platinum. Follow-up MRI in January, 1992 showed progression of the right-sided tumor into the right temporal

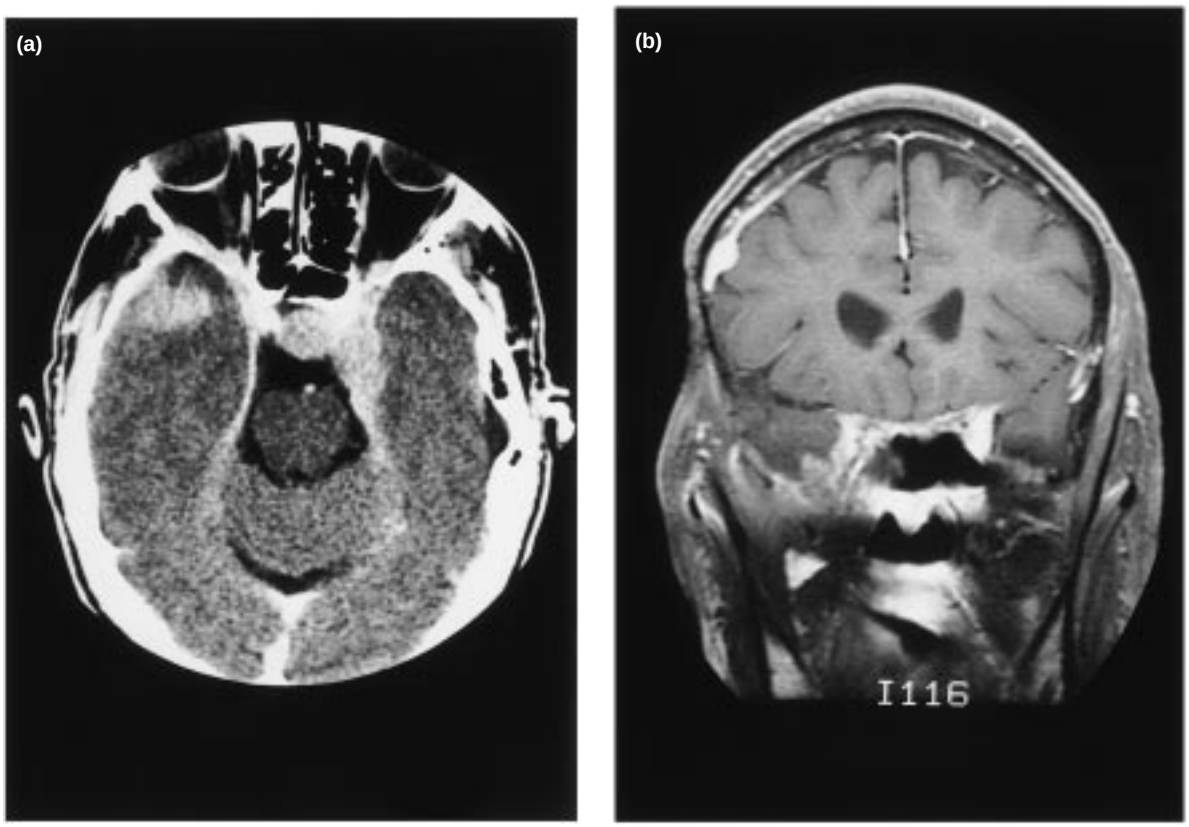

Figure 1. Case 1: (a) March, 1991 CT demonstrates contrast-enhancing masses in the anterior right temporal region and the left cavernous sinus; (b) January, 1992 TI-weighted MRI shows a contrast-enhancing dural-based mass in the right frontal area.

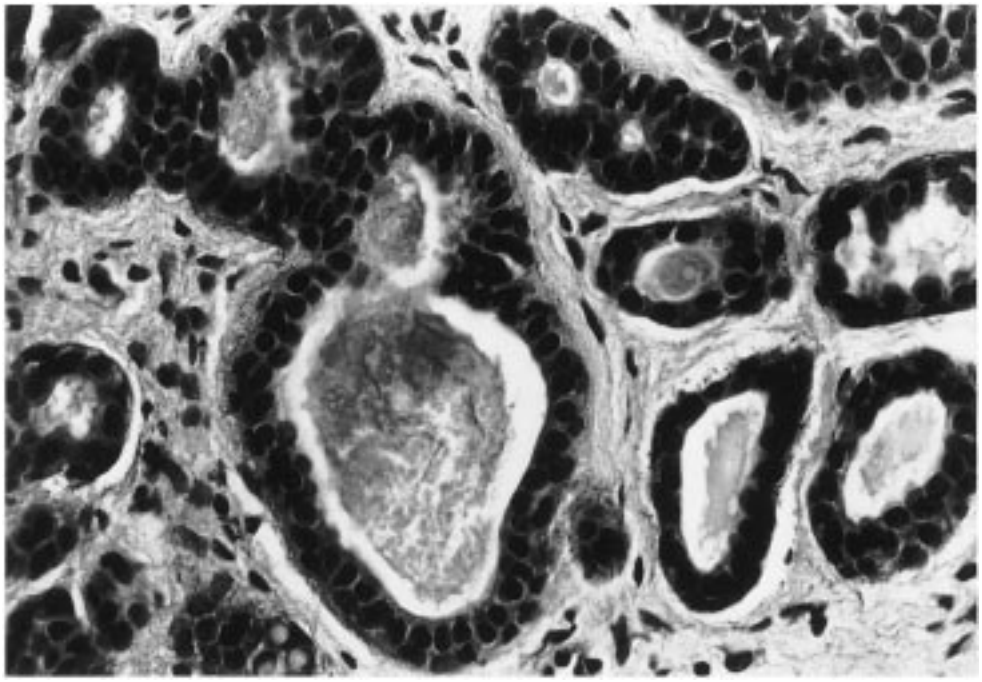

Figure 2. Case 1: Histologic section shows a tubular pattern of ducts with solitary lumens surrounded by less cellular fibrous connective tissue. Hematoxylin and eosin, 670×.

lobe, associated with meningeal and right frontal lobe enhancement (Figure 1 (b)). In July 1992, the patient expired.

Case 2

A 29-year-old woman developed drooping of the left eyelid in September 1994. MRI showed a left lacrimal gland mass. An excisional biopsy of the lesion in January, 1995, showed ACC with positive margins. In February, 1995 she underwent a radical resection of the lesion, including a left orbitofrontal craniectomy, orbital exenteration, and orbital reconstruction. At pathologic analysis, ACC was found involving the bone of the orbital roof. Post-operatively, she underwent fractionated radiation therapy, with a total dose of 64.4 gray. Follow-up surveillance MRI scans in 1995 and 1996 showed no evidence of recurrent tumor. In April 1997, she was found to have a nontender, nonmobile lumb over the skull in the right parietal area. MRI showed a multilobular dural-based enhancing mass involving the right parietal subgaleal space, the right parietal area, the right temporal pole, and the right infratemporal region (Figure 3 (a)). There was no evidence of left-sided tumor recurrence. Fine needle aspiration of the subgaleal mass confirmed ACC with both cribriform (Figure 4 (a)) and basaloid (Figure 4 (b)) patterns mixed together in a vast array of large and small lobules. The cribriform lumens contained mucin. These lobules were surrounded by vascular fibrous connective tissue with both thick bands of collagen and myxoid foci. In June, 1997 she underwent a right temporoparietal craniectomy and cranioplasty for resection of the tumors. The temporalis muscle and underlying calvarium were found to be infiltrated with tumor. The right parietal tumor had violated the pia and infiltrated the brain; this tumor was carefully dissected away from the brain. Multiple nodules of tumor appeared to be tracking along the dura in the distribution of the middle meningeal artery. The infratemporal tumor had not infiltrated the pia, and it was also dissected away from the temporal lobe. Post-operatively, she underwent another course of radiation therapy to a dose of 54 gray. In September, 1997 she became pancytopenic; a bone marrow biopsy showed extensive infiltration by metastatic ACC and a bone scan showed multiple areas of uptake in the skull, spine, the right

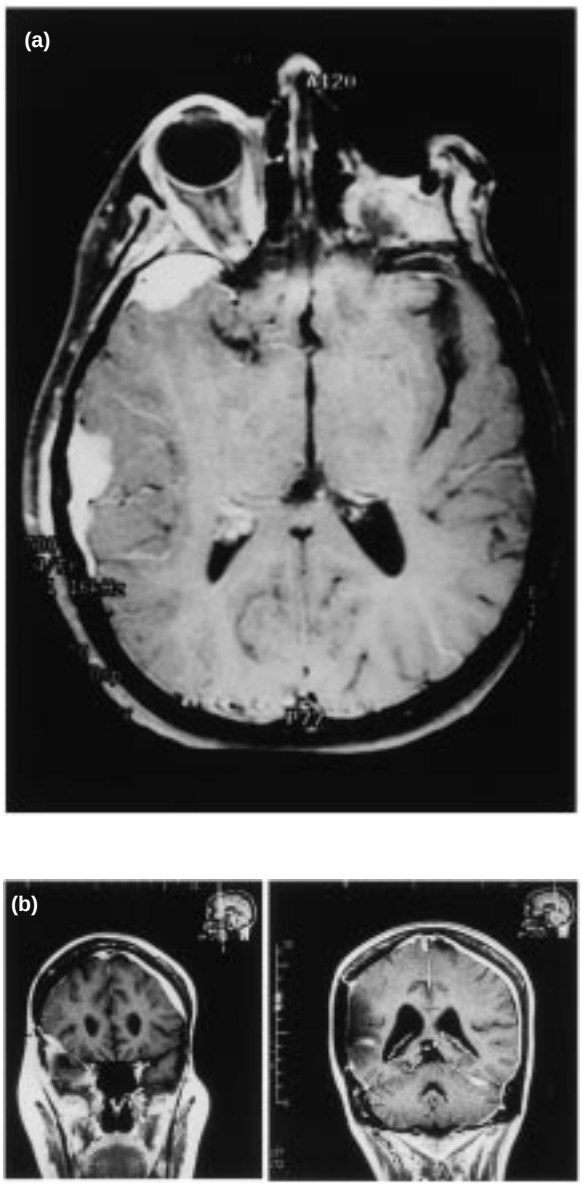

Figure 3. Case 2: (a) April, 1997 TI-weighted MRI demonstrates dural-based contrast-enhancing masses in the right anterior temporal and temporoparietal areas; (b) February, 1998 follow-up MRI shows extensive *en plaque* tumor involvement of the left convexity and tentorium.

humerus, several ribs, the scapulae, and both femurs. A follow-up MRI in February, 1998 showed extensive dural thickening involving the left convexity and tentorium (Figure 3(b)). The patient expired in May, 1998.

Discussion

Intracranial invasion (intraparenchymal or dural) by ACC occurs in 22% of patients [16–18]. A review of 53 cases of ACC with intracranial spread demonstrated involvement of the Gasserian ganglion in 35.8%, temporal lobe or middle fossa in 20.7%, cavernous sinus in 15.1%, chiasmal region in 7.5%, cerebellopontine angle in 5.7%, and posterior fossa in 5.7% of cases [6]. In a series of 16 patients with intracranial ACC, Gormley and colleagues found the most common sites of tumor involvement to be the infratemporal fossa (14 patients), cavernous sinus (13 patients), and middle fossa (13 patients) [19].

Intracranial extension of ACC most commonly occurs by spread through the skull base or extension along cranial nerves [6,9,11,12,16,21,22]. It has been postulated that cranial base invasion is along three routes: the eustachian tube (peritubal space), the mandibular and maxillary nerves, and the internal carotid artery [23]. Although the usual sites of hematogenous metastases are lungs (70%), bones, and liver [16,21,24–26] some reports of brain metastasis have been made [1,3,15,24,27,28]. Although a case of contralateral spread of adenoid cystic carcinoma with a primary in the parotid gland has been described [1], such a finding has never been described for a primary tumor arising in the lacrimal gland.

Widespread involvement of the dura was seen in both of our cases. In Case 1, ACC extended from the lateral cavernous sinus dura to the lateral temporal dura and to the dura of the contralateral cavernous sinus. In Case 2, the patient had a multilobular dural-based enhancing mass invading the right parietal bone, subgaleal space, the right parietal lobe, and the area of the right temporal region. The extensive involvement of the dura, and the presence of dural-based metastatic lesions contralateral to the primary lesion, suggests that the ACC has an affinity for the dura. This observation is supported by a previous report of two cases of dural-based ACC mimicking menigioma on CT [20].

Dissemination of the tumor to the contralateral side of the dura in both cases raises questions about the mode of spread of ACC. The ultimate spread of the tumor in Case 1 to the right temporal dura and the left cavernous sinus from a primary site in the right palate may have occurred via direct extension, hematogenous spread, or both. Upon reaching the right temporal dura, perhaps by direct extension through the base of the skull, the tumor may have extended along the

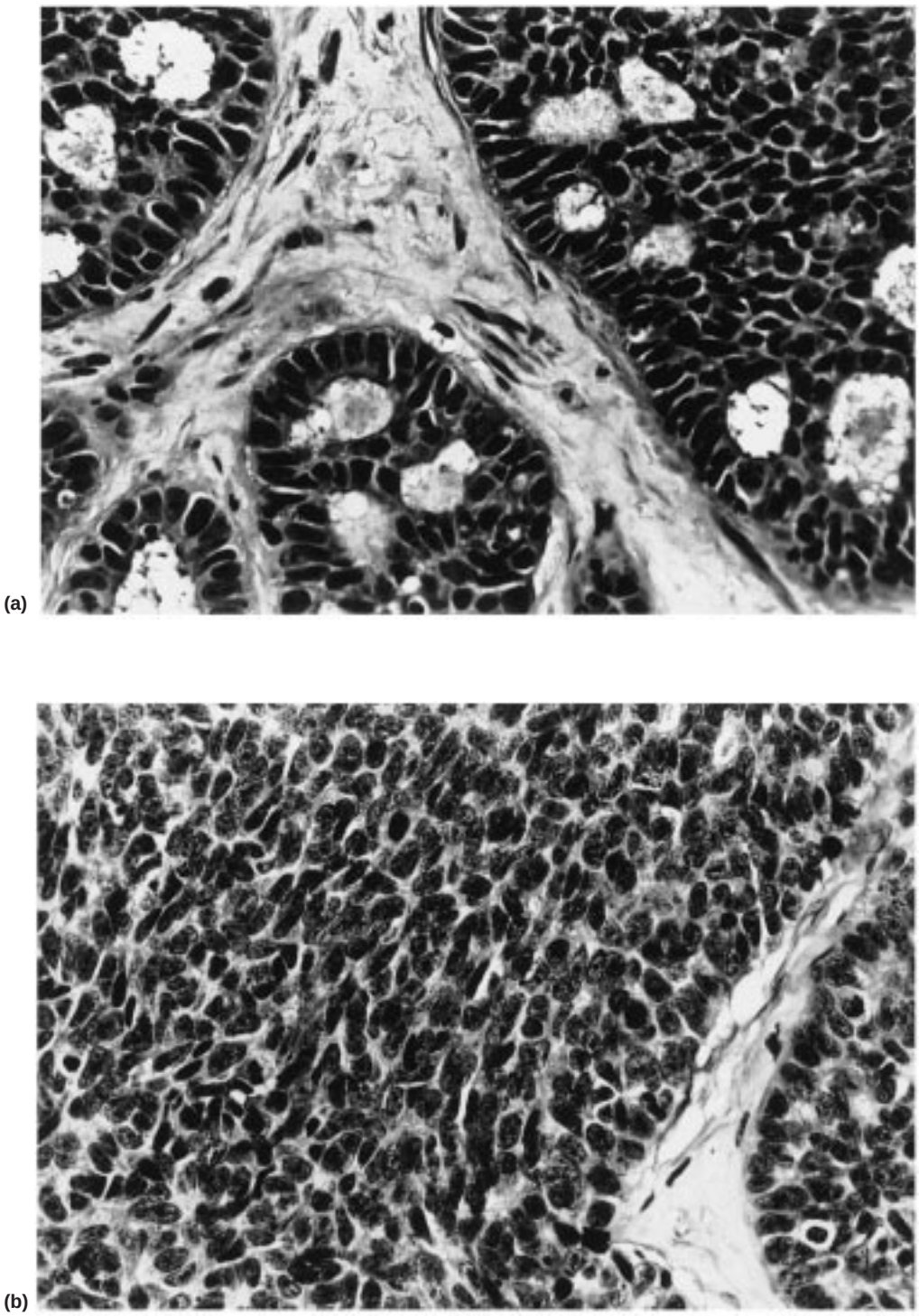

Figure 4. Case 2: (a) Portions of the pathologic specimen demonstrate cribriform elements in multiple epithelial lobules surrounded by less cellular fibrous connective tissue; (b) Other areas show a basaloid pattern of solid epithelial lobules. Hematoxylin and eosin, 670×.

dura to the contralateral cavernous sinus. Alternatively, the tumor may have spread hematogenously via the sphenoparietal sinus, circular sinus, or superior petrosal sinus to the cavernous sinus. In Case 2, hematogenous spread is the most likely route of metastasis to the right temporal and parietal dura from a primary tumor in the left lacrimal gland. A direct venous passage is possible. Tumor cells may have traveled from the primary site in the left orbit to the cavernous sinus via the superior ophthalmic vein. A network of emissary veins, the venous plexus of the foramen ovale, unites the cavernous sinus with the pterygoid plexus. The parietal trunk of the middle meningeal vein, draining the parietal dura, passes through the foramen spinosum into the pterygoid plexus [29]. Retrograde flow of tumor cells may have occurred from the pterygoid plexus to the parietal dura via the parietal trunk of the middle meningeal vein. Alternatively, contralateral spread may have occurred simply because of widespread metastatic disease, demonstrated by extensive bone marrow involvement, combined with an affinity of ACC for the dura.

The mechanism of the affinity of ACC for dura may be related to neural cell adhesion molecules (NCAMs). Gandour-Edwards and colleagues found a strong association between ACC-NCAM expression and perineural spread in patients with ACC infiltration of the skull base [30]. The role of other cell adhesion molecules, and their relationship to ACC and the dura, is an area for future investigation.

References

1. Gelber ND, Ragland RL, Knorr JR et al.: Intracranial metastatic adenoid cystic carcinoma: presumed hematogenous spread from a primary tumor in the parotid gland. Am J Roentgenol 158: 1163–1164, 1992
2. Henderson JW: Orbital Tumors. New York: Raven Press, 1994
3. Conley J, Casler JD: Adenoid Cystic Cancer of the Head and Neck. Thieme Medical Publishers, Inc., 1991
4. Fu KK, Leibel SA, Levine ML et al.: Carcinoma of the major and minor salivary glands. Cancer 40: 2882–2890, 1977
5. Naugle T Jr, Tepper DJ, Haik BC: Adenoid cystic carcinoma of the lacrimal gland: a case report. Ophthal Plast Reconstr Surg 10: 45– 48, 1994
6. Alleyne CH, Bakay RA, Costigan D et al.: Intracranial adenoid cystic carcinoma: case report and review of the literature. Surg Neurol 45: 265–271, 1996
7. Vrielinck U, Ostyn F, van Damme B et al.: The significance of perineural spread in adenoid cystic carcinoma of the major and minor salivary glands. Int J Oral Maxillofac Surg 17: 190–193, 1988
8. Parker GD, Hansberger HR: Clinical and radiographic issues in perineural tumor spread of malignant disease of the extracranial head and neck. Radiographics 11: 383–399, 1991
9. Lee Y, Castillo M, Nauert C: Intracranial perineural metastasis of adenoid cystic carcinoma of head and neck. The Journal of Computed Tomography 9: 219–223, 1985
10. Ginsberg LE, De Monte F, Gillenwater AM: Greater superficial petrosal nerve: anatomy and MR findings in perineural tumor spread. Am J Neuroradiol 17: 389–393, 1996
11. Swash M: Invasion of cranial nerves by salivary cylindroma: four cases treated by radiotherapy. J Neurol Neurosurg Psychiat 34: 475– 480, 1971
12. Wakisaka S, Nonaka A, Morita Y et al.: Adenoid cystic carcinoma with intracranial extension: report of three cases. Neurosurgery 26: 1060–1065, 1990
13. Hara H, Tanaka Y, Tsuji T et al.: Intracranial adenoid cystic carcinoma: a case report. Acta Neurochir (Wien) 69, 1983
14. Hammond MA, Hassenbusch SJ, Fuller ON et al.: Multiple brain metastases: a rare manifestation of adenoid cystic carcinoma of the parotid gland. J Neurooncol 27: 61–64, 1996
15. Matsumura A, Kuwahara O, Dohi H et al.: A case report of adenoid cystic carcinoma of the lung with brain metastasis. Kyobu Geka 41: 72–75, 1988
16. Vincentelli F, Grisoli F, Leclercq TA et al.: Cylindromas of the base of the skull: report of four cases. Journal of Neurosurgery 65: 856–859, 1986
17. Conley J, Dingman DL: Adenoid cystic carcinoma in the head and neck (cylindroma). Arch Otolaryngol 100: 81–90, 1974
18. Gonzalez C, Zuich KJ: Uber die zylindromatosen epitheliome der schadelbasis (‘Zylindrome’). Zbl Neurochir 25: 111–125, 1964
19. Gormley WB, Sekhar LN, Wright DC et al.: Management and long-term outcome of adenoid cystic carcinoma with intracranial extension: a neurosurgical perspective. Neurosurgery 38: 1105–1112, 1996
20. Morioka T, Matsushima T, Ikezaki K et al.: Intracranial adenoid cystic carcinoma mimicking meningioma: report of two cases. Neuroradiology 35: 462– 465, 1993
21. Dodd GD, Jing BS: Radiographic findings in adenoid cystic carcinoma of the head and neck. Ann Otol 81: 591–598, 1972
22. Marsh JL, Wise DM, Smith M, Schwartz H: Lacrimal gland adenoid cystic carcinoma: intracranial and extracranial en bloc resection. Plast Reconstr Surg 68: 577–585, 1981
23. Shotton JC, Schmid S, Fisch U: The infratemporal fossa approach for adenoid cystic carcinoma of the skull base and nasopharynx. Otol Clin North America 24: 1445–1464, 1991
24. Eby LS, Johnson DS, Baker MW: Adenoid cystic carcinoma of the head and neck. Cancer 29: 1160–1168, 1972
25. Koka VN, Tiwari RM, Van der Waal I et al.: Adenoid cystic carcinoma of the salivary glands: clinicopathological survey of 51 patients. J Laryngol Otol 103: 675–679, 1989
26. Witt R: Adenoid cystic carcinoma of the minor salivary glands. Ear Nose Throat Journal 70: 218–222, 1991
27. Koller M, Ram Z, Findler G, Lipshitz M: Brain metastasis: a rare manifestation of adenoid cystic carcinoma of the breast. Surg Neurol 26: 470– 472, 1986

28. Spiro RH, Huvos AG, Strong EW: Adenoid cystic carcinoma: factors influencing survival. Am J Surg 138: 579–583, 1979
29. Gabella C: Cardiovascular. Gray's Anatomy. New York: Churchill Livingstone, 1995
30. Gandour-Edwards R, Kapadia SB, Barnes L et al.: Neural cell adhesion molecule in adenoid cystic carcinoma invading the skull base. Otolaryngology – Head and Neck Surgery 117: 453–458, 1997

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