CASE REPORT

Palatal Adenoid Cystic Carcinoma Presenting as Perineural Spread to the Cavernous Sinus

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ABSTRACT—Adenoid cystic carcinoma of the hard or soft palate is a slow-growing, insidious disease with a tendency to spread via a perineural mechanism along the palatine branches of the maxillary division of the trigeminal nerve. Such spread may present first as a tumor in the pterygopalatine fossa or cavernous sinus. The purpose of this manuscript is to report three cases of palatal adenoid cystic carcinoma which presented as a mass in the cavernous sinus prior to discovery of the palate primary tumor. The imaging features of these cases are emphasized as is the need to search for a head and neck primary lesion when faced with a cavernous sinus mass.

Adenoid cystic carcinoma of salivary gland origin is an uncommon head and neck malignancy accounting for 4–15% of salivary gland tumors and 25–37% of minor salivary gland malignancies.^{1–3} The minor salivary glands are distributed widely throughout the upper aerodigestive tract mucosa but are concentrated in the posterior hard and soft palate.^{1,2,4} The palate is the most common site of both benign and malignant tumors of minor salivary gland origin. Adenoid cystic carcinomas are notorious for their tendency to spread along small cranial nerve branches, usually branches of the trigeminal nerve, a process known as perineural spread.^{2,5,6} In some cases, disease at the site to which the tumor spreads becomes clinically evident prior to detection of the primary carcinoma.^{7,8} In such instances, the true diagnosis may be obscure. Retrograde spread of adenoid cystic carcinoma along maxillary nerve (V_2) branches often involves the pterygopalatine fossa, orbit, or cavernous sinus.^{9–13} This pattern of neoplastic spread should be kept in mind when evaluating patients with cavernous sinus masses in order to avoid undertreatment or nontreatment of the primary disease. We describe three cases, one previously reported,⁸ in which a cavernous sinus mass represented perineural spread from a palatal adenoid cystic carcinoma. In all cases, the

primary tumor was not initially suspected or evident clinically, and in two cases, disease that may have led to the correct diagnosis was missed radiologically. In two cases, there was no evidence that the possibility of a head and neck primary tumor was ever considered or pursued.

CASE REPORTS

Patient 1, a 35-year-old woman, noticed right-sided numbness and a small lump in the roof of the mouth. Several months later, decreased visual acuity in the right eye prompted her to seek medical attention. After a several month work-up, a magnetic resonance imaging (MRI) and computed tomography (CT) study were obtained. These demonstrated mass-like soft-tissue thickening in the right orbital apex and cavernous sinus (Fig. 1). This was interpreted as idiopathic inflammatory orbital pseudotumor. Tumor in the right pterygopalatine fossa (Fig. 1) was not appreciated. A pterional craniotomy was performed, and biopsy of material from the right superior orbital fissure and parasellar/middle cranial fossa region was diagnostic for adenoid cystic carcinoma. According to the outside medical

Figure 1. Patient 1. Initial outside noncontrast axial T1-weighted MR images through the orbit and pterygopalatine fossa. Left: Soft-tissue infiltration is seen in the right orbital apex, superior orbital fissure, and anterior cavernous sinus (arrowheads). Right: There is tumor infiltrating the right pterygopalatine fossa (arrow) and extending posteriorly along the foramen rotundum (small arrowheads). Normal fat signal can be seen in the left pterygopalatine fossa (large arrowhead).

record, a head and neck primary tumor was never sought, and the patient reported that her oral complaints had been ignored. An MRI performed at the time of biopsy showed a subtle mass in the right hard palate and posterior maxillary alveolar ridge (Fig. 2) that was not appreciated. The patient received radiotherapy to her or-

Figure 2. Patient 1. Coronal postcontrast, fat-suppressed, T1-weighted MRI images through the posterior orbits and maxilla. Top: Image obtained at the time of cavernous sinus biopsy shows an enhancing mass in the right hard palate (*). Bottom: On image obtained 20 months after biopsy, the right-sided hard palate tumor is still evident and perhaps slightly larger (*). More tumor is now seen extending posterolaterally into the retromolar and lateral gingival region (arrows).

bital apex/cavernous sinus region. Twenty months after her initial surgery, the patient was evaluated at our institution. The palatal mass, which had not been included in the radiation field, had enlarged and become clinically evident (Fig. 2) and she had persistent disease in the orbital apex/cavernous sinus and pterygopalatine fossa. Other images (not shown) demonstrated perineural tumor spread along the vidian nerve.

Patient 2, a 47-year-old woman, developed right-sided sixth cranial nerve paresis. She reported "double vision and a funny feeling in the right side of the face." MRI at an outside institution showed a mass in the right cavernous sinus (Fig. 3). This was believed to be a meningioma or trigeminal neuroma. Neoplastic involvement of the pterygopalatine fossa and foramen rotundum was, in retrospect, present but was not appreciated at that time (Fig. 4). A small mass in the right hard palate (Fig. 5) also was not appreciated. The cavernous sinus mass was resected and histologically confirmed to be adenoid cystic carcinoma, for which the patient received radiotherapy. A search for a primary cancer was fruitless because the palate primary was entirely submucosal and did not deform the oral surface of the palate (Fig. 5). Follow-up imaging showed regression of the cavernous sinus tumor, but again missed the disease in the hard palate and pterygopalatine fossa, although in retrospect, disease was present at those locations. Thereafter, the patient developed right eyelid pain, ptosis, right-sided blindness, and eventually right-sided facial paralysis. Upon evaluation at our institution, MRI revealed massive tumor involvement of the pterygopalatine fossa, V_2 within the foramen rotundum, cavernous sinus, middle cranial fossa, and Meckel's cave (Fig. 6). There was posterior perineural tumor spread along the greater superficial petrosal nerve into and including the geniculate ganglion, accounting for the facial nerve paresis (Fig. 6). There was also antegrade perineural tumor spread inferiorly along the mandibular nerve (V_3) through foramen ovale and anteriorly along the infraorbital nerve (Fig. 5). The original palatal lesion, never having received therapy, had enlarged considerably (Fig. 5).

Figure 3. Patient 2. Initial outside coronal T1-weighted MRI image showing a right-sided cavernous sinus/parasellar/Meckel's cave mass (arrow).

Patient 3 was the subject of a previous report.⁸ Briefly, the patient was a 49-year-old man who was initially believed to have trigeminal neuralgia. MRI revealed a cavernous sinus mass, with biopsy diagnostic for adenocarcinoma. The patient failed to respond to radiation and chemotherapy, developed multiple cranial neuropathies, and then failed to respond to gamma knife therapy. His condition progressed to complete ophthalmoplegia. Ultimately, a mass was detected in the ipsilateral hard palate; biopsy showed adenoid cystic carcinoma, histologically identical to the initial cavernous sinus specimen. By this time, the patient had a massive skull-base tumor with perineural tumor spread along multiple cranial nerves, including the greater superficial petrosal nerve. To our knowledge, the palate primary was radiologically and clinically silent at first presentation.

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DISCUSSION

Perineural tumor spread is common in head and neck malignancies, particularly squamous cell carcinomas of the skin and adenoid cystic carcinomas of the major or minor salivary glands.^{13,14} The second and third divisions of the trigeminal nerve are among the most common nerves affected by perineural tumor spread.¹¹ The descending portion of the seventh cranial nerve may also be affected,¹¹ as may smaller cranial nerve branches.^{8,15} Perineural tumor spread is a poor prognostic indicator.¹⁴ Perineural spread from palatal carcinoma has been described in the head and neck literature.^{1,9,12,16} Detection of the palatal primary tumor may be difficult because these lesions are often submucosal in origin¹ and, as in Patient 2, may not be palpable.

The neuroanatomy of the maxillary division of the trigeminal nerve facilitates perineural tumor spread from the palate as follows: from the hard and soft palate, sensory fibers of the greater and lesser palatine nerves, respectively, pass through the greater or lesser palatine foramen and course upward along the descending pterygoid canal to enter the pterygopalatine fossa. There, the fibers pass uninterrupted through the sphenopalatine (pterygopalatine) ganglion and join the main trunk of V₂. The fibers then course posteriorly through the foramen rotundum, cavernous sinus, and Meckel's cave and finally into the brainstem.¹⁷ Other ef-

Figure 4. Patient 2. Initial outside noncontrast axial, T1-weighted MR images. Left: Tumor can be seen widening the right pterygopalatine fossa (arrow). Right: A slightly more cephalad image shows tumor extending posteriorly through a grossly widened right foramen rotundum (arrows).

Figure 5. Patient 2. Noncontrast coronal, T1-weighted MR images. Left: Initial outside study obtained at the same time as Figures 3 and 4 shows a small mass in the right side of the hard palate (arrow). Note that the oral surface of the palate is not deformed. This lesion would not have been palpable. Right: Image obtained upon referral to M. D. Anderson Cancer Center shows considerable enlargement of the palate mass. Notice the enlargement of the right infraorbital canal/nerve indicating antegrade perineural tumor spread (arrow).

ferent, postganglionic parasympathetic secretomotor fibers (branches of the seventh cranial nerve) also course within the palatine nerves as follows: seventh nerve fibers originating in the nervus intermedius leave

the seventh nerve at the geniculate ganglion as the greater superficial petrosal nerve.^{8,17,18} Exiting the superior surface of the temporal bone through the facial hiatus, the greater superficial petrosal nerve courses medially and anteroinferiorly to the foramen lacerum and joins the deep petrosal nerve of the sympathetic plexus to enter the vidian or pterygoid canal as the vidian nerve or nerve of the pterygoid canal.^{8,17,18} Arriving in the pterygopalatine fossa, these fibers synapse in the sphenopalatine ganglion, and some of the postganglionic fibers join the palatine nerves to course inferiorly into the hard and soft palate. Other postganglionic parasympathetic fibers from the sphenopalatine ganglion supply secretomotor innervation to the nasal cavity and lacrimal gland via other branches of V₂.^{8,17,18} Clearly, access to this neural pathway by carcinoma can result in widespread extension and a variety of neurologic signs and symptoms.

Imaging evidence of perineural spread includes any of the following: widening and/or destruction of neural foramina (in this case, the greater and lesser palatine foramen or foramen rotundum),^{2,6,13} replacement of normal fat density (CT) or signal intensity (T1-weighted MRI) with abnormal enhancement or widening of the pterygopalatine fossa, widening or excessive enhancement within the foramen rotundum (or foramen ovale), or expansion or abnormal enhancement of the cavernous sinus or Meckel's cave.^{10,11,19} CT is more sensitive in the detection of bone destruction, and high-resolution, fat-suppressed, contrast-enhanced MRI is better for detection of abnormal perineural enhancement.^{8,20} Adenoid cystic carcinoma may also spread perineurally with "skip" areas of normal-appearing intervening tissue.^{21,22} There is relatively little in the imaging literature specifically addressing perineural spread from the palate.⁴

When a cavernous sinus mass is detected, the diagnostic possibilities are many and include meningioma, trigeminal neuroma, granulomatous/inflammatory diseases, and hematogenous metastases. It is important to ascertain that a cavernous sinus mass is truly limited to

Figure 6. Patient 2. Contrast-enhanced, fat-suppressed, axial T1-weighted MRI images through the skull base. Top: Enhancing tumor can be seen in the right pterygopalatine fossa (*), foramen rotundum (arrow), and cavernous sinus/Meckel's cave (arrowheads). Bottom: Image slightly more caudal shows tumor infiltrating posterolaterally along the course of the greater superficial petrosal nerve (small arrowheads). Abnormal enhancement and thickening indicate tumor involvement of the geniculate ganglion (black dot), and the labyrinthine (large arrowhead) and proximal tympanic (arrows) segments of the right facial nerve.

or has arisen primarily within the cavernous sinus, for not to do so, as in the cases presented here, may have adverse consequences. Careful radiologic and clinical scrutiny of adjacent anatomic structures such as the orbit, skull base foramina, and pterygopalatine fossa is mandatory. If disease is found or suspected at these sites, the search for a head and neck primary tumor, such as palatal adenoid cystic carcinoma, should be exhaustive. The entire head and neck region must be carefully evaluated clinically and with dedicated imaging because of the possibility that tumor could have spread perineurally to the cavernous sinus from a wide variety of primary sites anywhere along the course of the three trigeminal nerve divisions.

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