AJNR Am J Neuroradiol 19:1417–1422, September 1998

Imaging of Perineural Tumor Spread from Palatal Carcinoma

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Summary: Carcinomas of the hard or soft palate are known to spread perineurally along palatine branches of the maxillary nerve. Imaging of perineural tumor spread from the palate has been underemphasized in the imaging literature. We report the findings from eight patients in whom spread from primary cancers of the palate was seen along the palatine nerves. Indications of perineural spread include enlargement or excessive enhancement of a nerve, or abnormal density/signal intensity, enhancement, or widening of the pterygopalatine fossa, cavernous sinus, or Meckel's cave.

Perineural extension of head and neck tumors is a well-known phenomenon that has been described in the literature (1–10). Squamous cell carcinomas of cutaneous or mucosal origin, and particularly adenoid cystic carcinoma of major or minor salivary gland origin, are the most common primary tumors to spread via the perineural mechanism (1, 3, 4, 8, 11, 12). The presence of perineural tumor spread has considerable implications for prognosis and treatment (12). Failure to recognize areas of perineural spread may contribute to treatment failure or recurrence.

Carcinomas of hard or soft palate origin are known to spread perineurally along the palatine branches of the maxillary nerve (11, 13–15). Imaging of perineural tumor spread from the palate has, however, been underemphasized in the literature (2). In fact, one of the largest imaging series on perineural tumor spread had no cases that originated in the palate (9). We review the anatomy of the innervation of the palate and describe the imaging features of perineural spread related to palatal carcinoma.

Methods

We identified eight cases of perineural spread along the course of the palatine nerves in patients with documented primary cancers of the palate. The histologic diagnosis was confirmed in all but one case (this patient had a lingual squamous cell carcinoma and was undergoing gene therapy; the palate lesion was presumed to be squamous cell carcinoma). CT and MR imaging examinations were each available in six patients, and both MR imaging and CT studies were available in four patients. All CT studies were performed on GE equipment. Scanning was performed with 3- or 5-mm-thick axial sections at 3- to 5-mm intervals after administration of intravenous contrast material. Soft-tissue and high-resolution bone windows were generated in all cases. MR imaging was performed on GE Signa units with standard spin-echo or fast spin-echo techniques, and fat-suppressed, postcontrast axial and coronal T1-weighted sequences. Parameters included a 16- to 18-cm field of view, 3- to 5-mm-thick sections, and 1- to 1.5-mm gaps. Some patients had initial imaging examinations performed at other institutions with different equipment/imaging parameters.

Findings taken to represent perineural tumor spread include enlargement or excessive enhancement of a nerve, or abnormal density/signal intensity, enhancement, or widening of the pterygopalatine fossa, cavernous sinus, or Meckel's cave.

Representative Case Reports

Case 1

A 66-year-old man was undergoing gene transfer therapy at our institution for advanced, recurrent squamous cell carcinoma of the tongue. During this treatment, a new primary mass was detected in the right side of the soft palate during CT scanning (Fig 1A). At this time, the pterygopalatine fossa (Fig 1B) and palatine foramen (Fig 1C) were normal. Owing to protocol considerations, the patient received no therapy for the new lesion in the palate. A scan obtained several months later showed abnormal attenuation/enhancement and widening of the right pterygopalatine fossa (Fig 1D); a high-resolution CT scan with bone windows showed destruction of the palatine foramen (Fig 1E), consistent with perineural spread along the palatine nerves.

Case 2

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. An MR imaging study performed at an outside institution showed masslike soft-tissue fullness in the right orbital apex and cavernous sinus (Fig 2A). This was initially interpreted as idiopathic inflammatory orbital pseudotumor. A biopsy of the cavernous sinus yielded a diagnosis of adenoid cystic carcinoma. A retrospective review of the initial MR imaging study performed near the time of biopsy showed a tumor in the right pterygopalatine fossa and a subtle mass in the right side of the hard palate (Fig 2B). The patient received

Received September 16, 1997; accepted after revision November 21.

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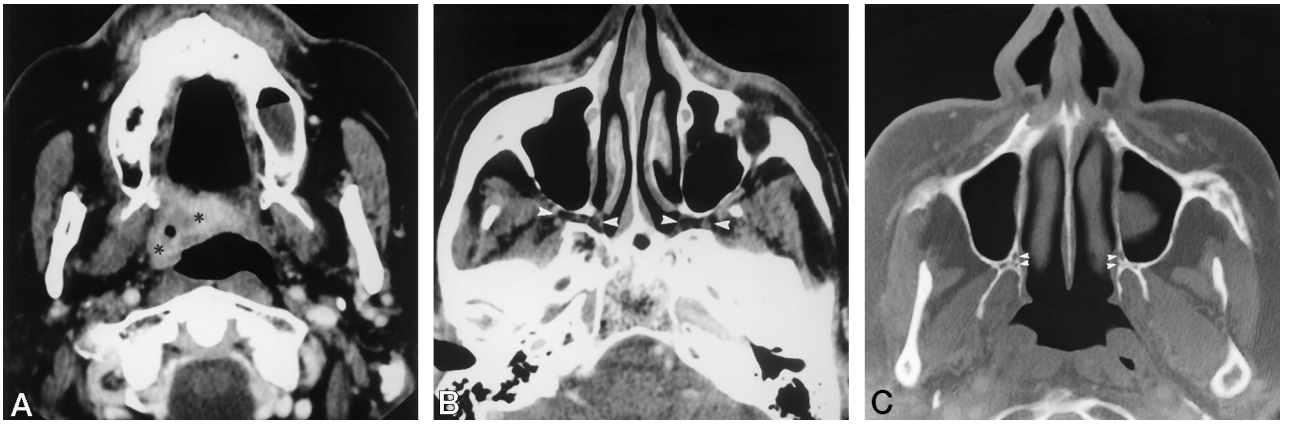

FIG 1. Case 1.

A, Axial contrast-enhanced CT scan shows enhancing, necrotic, midline/right-sided soft palate mass (*asterisks*).

B and *C*, Axial soft-tissue window through the pterygopalatine fossa (*B, arrowheads*) and bone window through the palatine foramen (*C, arrowheads*) performed at the same time as *A* show no abnormality.

D and E, Axial contrast-enhanced soft-tissue window through the pterygopalatine fossa (*D*) and bone window through the palatine foramen (*E*) obtained 4 months later show widening and abnormal enhancement within the right pterygopalatine fossa (*arrowheads*) and early extension through the posterior wall of the maxillary sinus (*arrow*). The bone window in *E* shows destruction of the right palatine foramen (*arrowhead*) (compare with *C*).

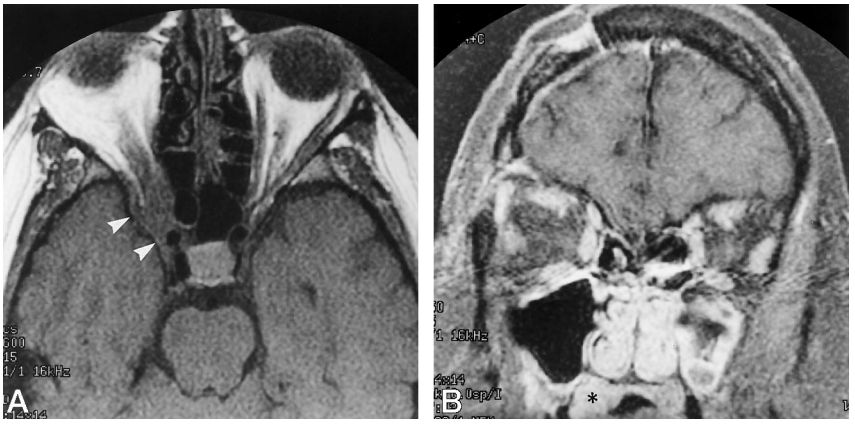

FIG 2. Case 2.

A, Axial T1-weighted (600/15/2) MR image at initial presentation shows an infiltrating soft-tissue mass in the right orbital apex and cavernous sinus (*arrowheads*). There was tumor in the pterygopalatine fossa as well (*not shown*).

B, Fat-suppressed postcontrast coronal T1-weighted (650/15/1) MR image performed shortly after biopsy suggests an enhancing mass in the right side of the hard palate (*asterisk*). This lesion had enlarged considerably by the time the patient was seen at our institution.

radiotherapy for the orbital apex/cavernous sinus lesion, and when she was examined at our institution 20 months later, not only had the cavernous sinus and pterygopalatine fossa disease progressed but the palate lesion had enlarged and become clinically evident. Other images (not shown) revealed perineural spread along the vidian nerve.

Case 4

A 47-year-old woman presented with right-sided sixth cranial nerve paralysis and reported "double vision and a funny feeling in the right side of the face." MR imaging at an outside institution showed a mass in the right cavernous sinus. This was believed to be a meningioma or trigeminal neuroma. Neoplastic involvement of the pterygopalatine fossa and foramen rotundum were, in retrospect, present (Fig 3A). A small mass in the right side of the hard palate was also present, in retrospect, on the initial MR imaging study (Fig 3B). 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 lesion was fruitless because the palate mass was entirely submucosal and did not deform the oral surface of the palate. Despite follow-up imaging that showed regression of the cavernous sinus disease, multiple right-sided cranial neuropathies developed, leading ultimately to blindness and right-sided facial paralysis. When the patient was examined at our institution, MR imaging revealed massive tumor involvement of the pterygopalatine fossa, the V_2 nerve within the foramen rotundum, the cavernous sinus, the middle cranial fossa, and Meckel's cave (Fig 3C). There was also presumed antegrade perineural spread inferiorly along the mandibular nerve through the foramen ovale (Fig 3C) and anteriorly along the infraorbital branch of V_2 (Fig 3D). In addition, there was posterior perineural spread along the greater superficial petro-

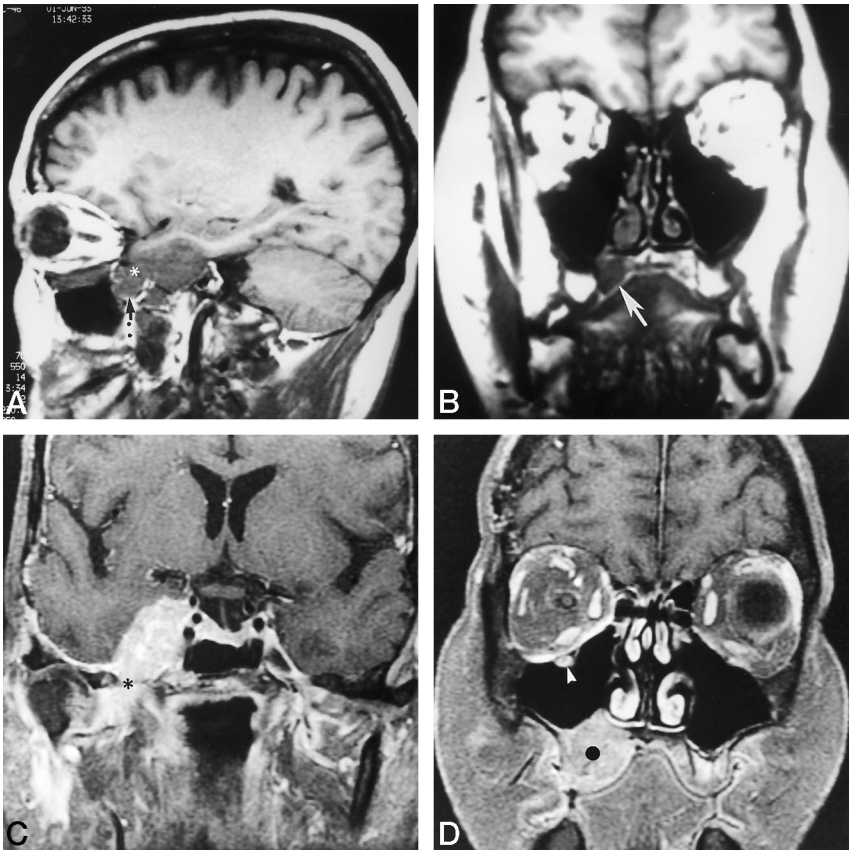

FIG 3. Case 4.

A, Sagittal T1-weighted (550/14/2) MR image of a cavernous sinus mass at the time of initial outside presentation shows tumor extending anteriorly through a widened foramen rotundum (*asterisk*) into the upper pterygopalatine fossa (*arrow*). Fat in the lower pterygopalatine fossa (*black dots*) appears normal, suggesting a skip lesion.

B, Coronal T1-weighted (640/14/2) MR image at the same time as *A* shows a subtle submucosal mass in the right side of the hard palate (*arrow*). This lesion would not have been palpable.

C, Coronal fat-suppressed, contrast-enhanced T1-weighted (500/12/2) MR image obtained at presentation to our institution shows a large right-sided cavernous sinus, parasellar, and Meckel's cave mass. Tumor is spreading inferiorly along V_3 in an antegrade fashion (presumably) through a widened foramen ovale (*asterisk*).

D, Coronal fat-suppressed, contrast-enhanced, T1-weighted (500/12/2) MR image obtained at a position anterior to *C* shows that the lesion in the right side of the palate has enlarged (*black dot*). There is enlargement and abnormal enhancement of the right infraorbital nerve (*arrowhead*), representing presumed antegrade perineural spread along this branch of V_2.

TABLE 1: Clinical summary of patients with perineural spread of palatal carcinoma

Case	Age (y)/Sex	Tumor Type	Clinical Presentation of Palate	Symptoms Related to Perineural Spread
1	66/M	SCCa (presumed)	Asymptomatic palate lesion	None
2	35/F	ACCa	Numbness, lump, roof of mouth	Decrease in visual acuity (tumor in orbital apex)*†
3	66/M	ACCa	Palate mass	Facial pain/paresthesia
4	47/F	ACCa	Asymptomatic	6th cranial nerve paresis, ipsilateral facial paresthesia.† Cavernous sinus mass on MRI
5	49/M	ACCa	Asymptomatic	Trigeminal neuralgia.† Cavernous sinus mass on MRI
6	69/F	ACCa	Previously resected soft-palate tumor, with recurrence	Facial pain/paresthesia
7	69/F	ACCa	Palate mass	None
8	72/F	ACCa	Palate ulcer	2 yr. history of cheek numbness and ipsilateral facial paralysis

Note.—SCCa indicates squamous cell carcinoma; ACCa, adenoid cystic carcinoma.

* Tumor in pterygopalatine fossa was asymptomatic.

† Site of perineural spread was first evidence of disease; palate lesion became evident only later.

sal nerve into and including the geniculate ganglion, accounting for the facial nerve paresis. The original palate lesion, having been outside the radiation field, had enlarged considerably and was evident clinically (Fig 3D).

Results

Patient and clinical data are listed in Table 1. Data pertaining to the sites of tumor involvement are given in Table 2. In three cases, the initial presentation related to a cavernous sinus mass and the primary palate lesion was either not initially known or suspected and detected only later. In two of those patients (cases 2 and 4), a review of previous imaging studies revealed a visible primary tumor in the palate that was not observed initially. The palatine foramen showed destruction in five cases (Fig 4) and probable destruction in one other case. In all cases, the pterygopalatine fossa had abnormal attenuation on CT scans or abnormal signal intensity/enhancement on MR images. Presumed perineural spread along other

cranial nerve branches was common, including antegrade spread (Table 2). Perineural spread into the greater superficial petrosal nerve (either from the pterygopalatine fossa via the vidian canal/nerve or from Meckel's cave) was seen in three cases, and in two of these cases there was further involvement of more posterior aspects of the facial nerve.

Discussion

The neuroanatomy of the palate as it pertains to perineural tumor spread is shown in Figure 5. The palate is innervated by both the maxillary division (V_2) of the trigeminal nerve and the facial nerve (5, 16). The bulk of neural supply to the palate is via the palatine nerves, the branches of V_2, which supply sensory innervation. The lesser and greater palatine nerves, from the soft and hard palate, respectively, enter the lesser and greater palatine foramina and course upward through the pterygopalatine canal to enter the pterygopalatine fossa (16). There, the sensory fibers pass uninterrupted through the sphenopalatine (pterygopalatine) ganglion and join the main trunk of V_2. The fibers then course posteriorly through the foramen rotundum, enter the cavernous sinus, and proceed through Meckel's cave and finally into the brain stem. The facial nerve provides parasympathetic vasomotor and secretomotor innervation to the palate as follows: facial nerve fibers originating in the nervus intermedius leave the geniculate ganglion and exit the temporal bone via the facial hiatus to enter the middle cranial fossa as the greater superficial petrosal nerve (GSPN) (5, 16, 17). The GSPN courses anteroinferiorly and medially to the foramen lacerum, where it is joined by the deep petrosal nerve of the carotid sympathetic plexus to form the vidian nerve or nerve of the pterygoid canal (5, 16, 17). The vidian nerve courses anteriorly through the vidian canal and enters the pterygopalatine fossa. The fibers synapse in the spheno(pterygo)palatine ganglion. Some of the postganglionic fibers join the palatine nerves and course inferiorly to the palate. Other postganglionic parasympathetic fibers from the sphenopalatine ganglion supply secretomotor innervation to the nasal cavity and lacrimal gland via other branches of V_2 (5, 16, 17).

Primary tumors of the palate are not common, but several tumor types do occur here. The palate has the highest concentration of minor salivary glands of any site in the upper aerodigestive tract (11, 18). Tumors of minor salivary gland origin are most prevalent in the palate, and of these tumors, the majority are adenoid cystic carcinomas (4, 11). Other minor salivary gland cancers of the palate include mucoepidermoid carcinoma, adenocarcinoma, myoepithelioma, and malignant mixed tumor (11). Squamous cell carcinoma also arises in the palate, especially the hard palate (13, 15). Squamous cell carcinomas of palatal origin are generally discovered relatively early in their course. However, palatal tumors of minor salivary gland origin are often submucosal (11) and may, as in several of our cases, lack symptoms, thus preventing diagnosis until after perineural tumor spread occurs.

TABLE 2. Summary of imaging findings, n = 8

Site of Involvement	No. of Cases
Pterygopalatine fossa	8
Palatine foraminal destruction	5
Foramen rotundum (V_2 perineural spread)	5
Cavernous sinus	4
Intraorbital	4
Masticator space	4
Greater superficial petrosal nerve perineural spread	3
Meckel's cave	3
Foramen ovale (V_3 perineural spread)	2
Vidian nerve perineural spread	2
Bulky intracranial disease	2
Infraorbital nerve perineural spread	1

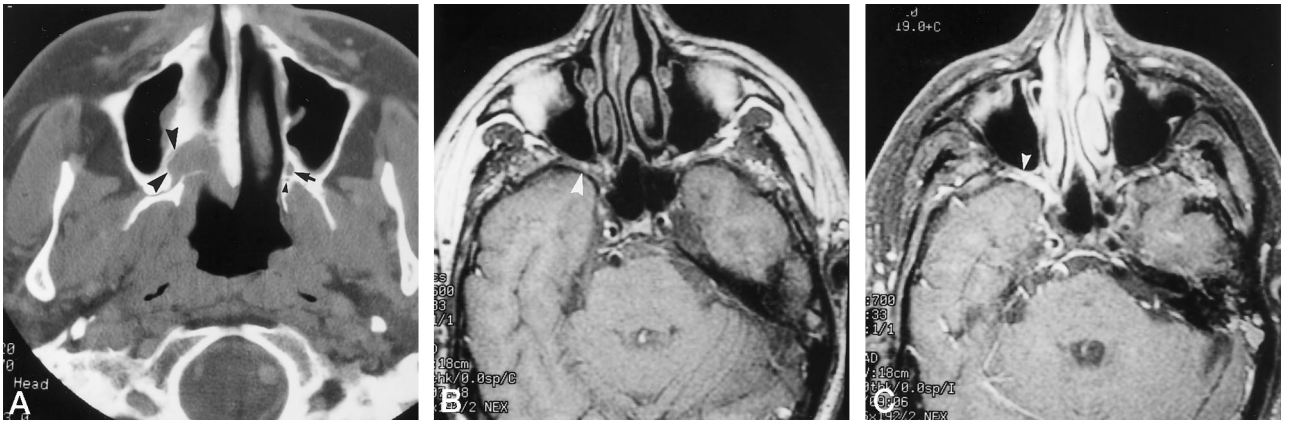

FIG 4. Case 3.

A, Axial CT scan with bone windows shows destruction of both right-sided palatine foramina (*large arrowheads*). The greater (*arrow*) and lesser (*small arrowhead*) palatine foramina on the left side are normal.

B, Axial T1-weighted (600/33/2) MR image shows subtle but definite loss of the normal fat signal hyperintensity in the right pterygopalatine fossa (*arrowhead*), representing tumor.

C, Axial postcontrast, fat-suppressed, T1-weighted (700/33/2) MR image shows excessive, abnormal enhancement in the right pterygopalatine fossa (*arrowhead*), representing tumor.

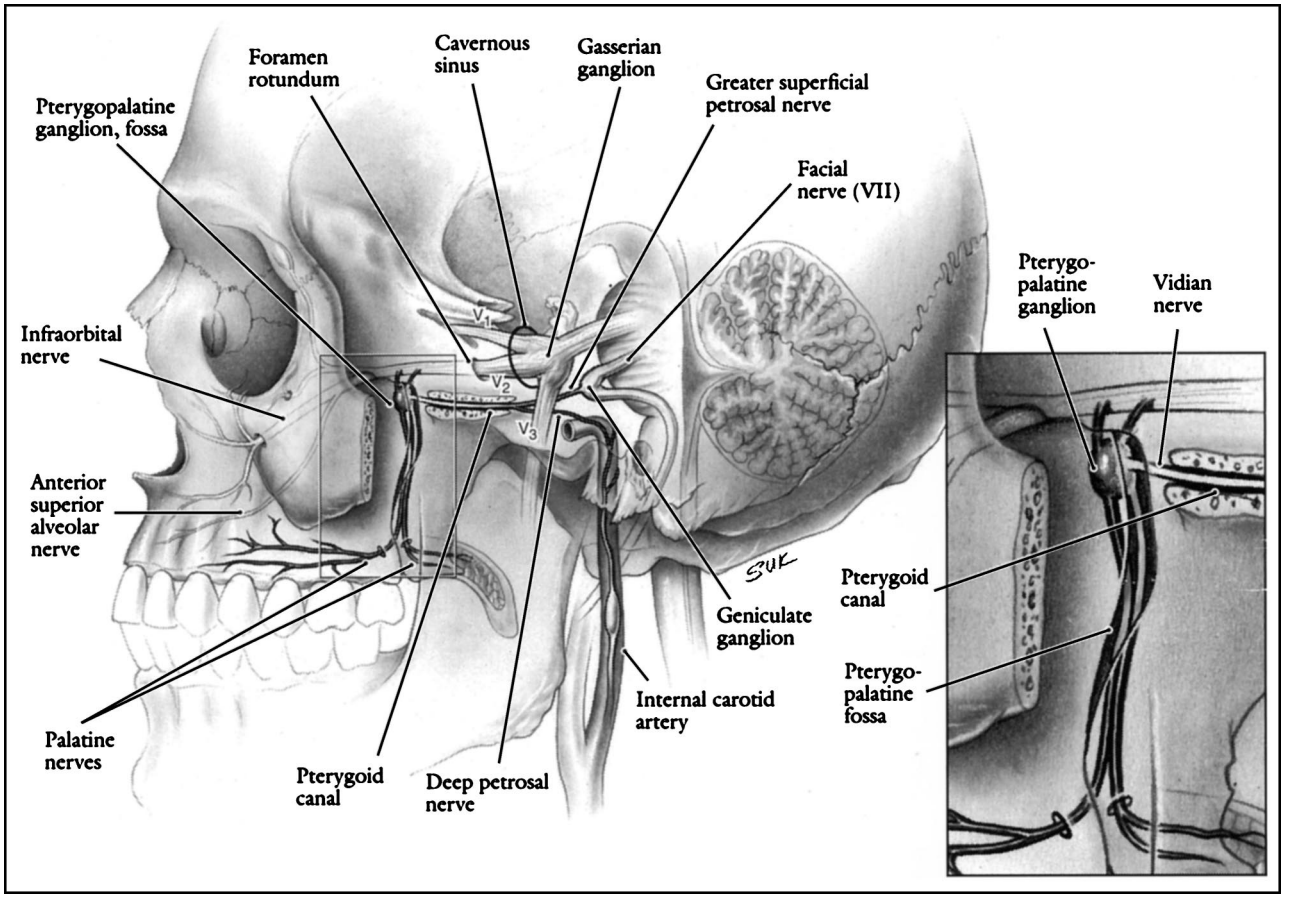

FIG 5. Diagrammatic representation of innervation of the palate.

Symptoms of perineural tumor spread from the palate include facial pain/paresthesias and other neuropathies related to branches of V_2. In two of our patients (cases 1 and 7), however, perineural tumor was asymptomatic. Intraorbital tumor involvement (which may spread from the inferior orbital fissure in the setting of pterygopalatine fossa disease) may affect visual acuity. Antegrade spread along V_2 or V_3 may result in neuropathies of those nerves, and involvement of the cavernous sinus may lead to multiple cranial neuropathies. Finally, posterior spread along the GSPN may result in facial neuropathy and have considerable implications for therapy, including unresectability (5). These symptoms may represent spread from a primary head and neck cancer and can occur before presentation or detection of the primary lesion. In case 4, for instance, the initial palate lesion was asymptomatic, and because the lesion was entirely submucosal, it was not palpable. Imaging would have been crucial for detecting such a primary lesion.

Conclusion

In the examination of patients with a known palatal carcinoma, it is imperative to evaluate those areas to which tumor may spread perineurally and to remember that such spread may be discontinuous, with skip areas (8, 19). The palatine foramina should be carefully examined on high-resolution CT scans with bone windows for signs of widening or destruction. However, just as perineural tumor spread along the palatine nerves can occur in the absence of detectable palatine foraminal destruction, the presence of such destruction need not indicate perineural spread but merely the direct destructive effect of the tumor. Abnormal attenuation within the pterygopalatine fossa on soft-tissue CT windows, or abnormal signal intensity/enhancement on postcontrast T1-weighted fat-suppressed MR images is strong evidence of perineural tumor spread (2, 5, 7, 9, 20). The foramen ovale and rotundum, the cavernous sinus, and Meckel's cave should also be carefully examined with high-resolution MR imaging to exclude tumor involvement. In patients presenting with disease in the cavernous sinus, Meckel's cave, or the pterygopalatine fossa, a careful search should be performed clinically and radiologically for a primary lesion of the head and neck that may be causing perineural spread to those locations. Among the sites that need careful examination are the palate and all cutaneous and mucosal surfaces of the head and neck.

Acknowledgments

We gratefully acknowledge the assistance of Donna Stevenson and Melissa Burkett in the preparation of this manuscript, and Ian Suk for art work.

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