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## **CT of Perineural Tumor Extension: Pterygopalatine Fossa**

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# CT of Perineural Tumor Extension: Pterygopalatine Fossa

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Tumors of the oral cavity and paranasal sinuses can spread along nerves to areas apparently removed from the primary tumor. In tumors of the palate, sinuses, and face, this "perineural" spread usually involves the maxillary division of the trigeminal nerve. The pterygopalatine fossa is a pathway of the maxillary nerve and becomes a key landmark in the detection of neural metastasis by computed tomography (CT). Obliteration of the fat in the fossa suggests pathology. Case material illustrating neural extension is presented and the CT findings are described.

Perineural extension is possibly the most insidious form of tumor spread of head and neck malignancy. After invading a nerve, tumor follows the sheath to reach the deeper connections of the nerve, escaping the area of a planned resection. Thus, detection of this form of extension is important in treatment planning and estimation of prognosis.

The pterygopalatine fossa (PPF) is a key crossroad in extension along cranial nerve V. The second branch of the trigeminal nerve passes from the gasserian ganglion through the foramen rotundum into the PPF. Here the nerve branches send communications to the palate, sinus, nasal cavity, and face. Tumor can follow any of these routes proximally into the PPF and eventually to the gasserian ganglion in the middle cranial fossa.

The PPF contains enough fat to be an ideal subject for computed tomographic (CT) evaluation. Obliteration of this fat is an important indicator of pathology, including perineural tumor spread. Other signs of perineural extension include enlargement of foramina, increased enhancement in the region of Meckel cave (gasserian ganglion), and atrophy of the muscles innervated by the trigeminal nerve.

Adenoid cystic carcinoma is associated with perineural extension most often, but other cell types may exhibit similar behavior.

## Anatomy

The pterygopalatine fossa is a small "cleft" between the posterior wall of the maxillary sinus and the anterior surface of the pterygoid process of the sphenoid bone. The PPF connects directly with the infratemporal fossa lateral to the fossa via the long pterygomaxillary fissure. The smaller sphenopalatine foramen (not seen in fig. 1) connects the PPF with the nasal cavity medial to the fossa. When viewed from a point lateral to the skull, the pterygomaxillary fissure appears to curve anteriorly and continues as the inferior orbital fissure. The inferior orbital fissure represents a direct communication between orbit and infratemporal fossa. The most posterior part of the inferior orbital fissure meets the most superior extension of the PPF, thus forming a direct communication between the PPF and the apex of the orbit. All of the above-mentioned fissures and foramina represent potential pathways of tumor spread.

Of greater importance in perineural tumor spread is the role of the PPF as a

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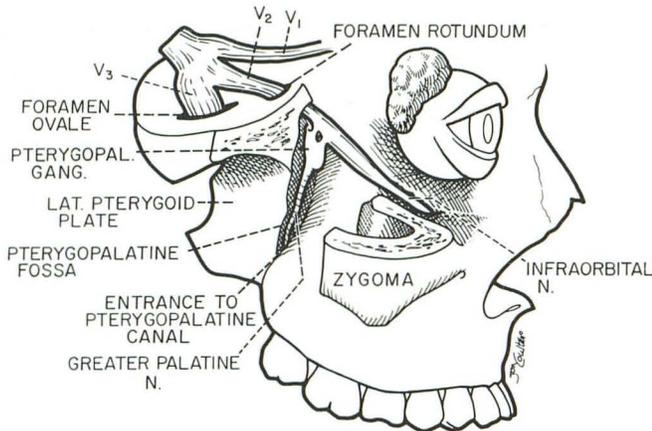


Fig. 1.—Course and major branching pattern of maxillary nerve ( $V_2$ ) as it passes through PPF. Maxillary nerve passes through foramen rotundum and PPF, and continues on as infraorbital nerve, passing into the infraorbital canal in orbital floor. Greater palatine nerve extends inferiorly to entrance of pterygopalatine canal, through which it reaches palate. Superior alveolar nerves (not shown) pass along posterolateral wall of sinus, which they perforate to gain access to maxillary sinus. Specimen is sectioned through inferior orbital fissure with removal of frontozygomatic and zygomatic arches.

branching point of the trigeminal nerve. The maxillary nerve passes directly posteriad from the PPF to the gasserian ganglion in Meckel cave in the middle cranial fossa. The maxillary nerve passes along the lower margin of the inferior orbital fissure until reaching the entrance of the infraorbital canal. Passing through the infraorbital canal, the nerve now called the infraorbital reaches the soft tissues of the anterior cheek. The palatine nerves extend inferiad from the PPF through the pterygopalatine canal and greater and lesser palatine foramina to reach the mucosal surface of the hard palate.

## Representative Case Reports

### Case 1. Adenoid Cystic Carcinoma (fig. 2)

A 33-year-old man with ulceration on the left side of his palate had hypoesthesia in the distribution of the left infraorbital nerve. CT after administration of intravenous contrast material demonstrated the tumor in the inferior part of the medial wall of the maxillary sinus extending through the posterior wall into the lower part of the PPF. There was obliteration of the fat in the PPF. The foramen rotundum was enlarged with some bone destruction of the root of the pterygoid. There was enhancement in the region of the gasserian ganglion, and the foramen ovale was slightly enlarged. Enhancement was seen in the orbital apex. This was not directly contiguous with the abnormality in the PPF. The infraorbital canal was not well visualized on axial CT, and the metallic dental work interfered with coronal sections. Tomography showed an enlarged infraorbital canal.

Biopsy showed adenoid cystic carcinoma, and the patient underwent a left maxillectomy with partial removal of the sphenoid. Pathology demonstrated involvement of the pterygopalatine space with tumor invasion of the neural elements. There was perineural and endoneural extension along the infraorbital nerve. A biopsy of a large nerve in the region of the foramen ovale demonstrated perineural invasion. Postoperatively the patient received radiation therapy.

Tumor is thought to have arisen in the palate or maxillary sinus

and entered the PPF. The tumor followed  $V_2$  proximally to the gasserian ganglion then antegrade along  $V_1$  and  $V_3$ . Tumor also extended distally from the PPF along the infraorbital nerve.

### Case 2. Squamous Cell Carcinoma (fig. 3)

A 50-year-old man had facial pain 2 years after resection of a squamous cell carcinoma of the ipsilateral nasal ala. Plain films showed enlargement of the infraorbital canal. CT showed tumor in the roof of the maxillary sinus in the position of the infraorbital nerve. A small amount of tumor was seen extending along the posterior wall of the maxillary sinus toward the PPF. Though the bony walls of the PPF were not eroded, the fat within the fossa was obliterated. There was a large mass in the middle cranial fossa involving the gasserian ganglion. The foramen rotundum was not defined clearly on any slice, but no destruction of the area was seen.

This case shows proximal spread from the PPF to the middle cranial fossa. The tumor reached the PPF by passing along the infraorbital nerve from a superficial primary. A less likely alternative explanation would require a second primary in the roof of the maxillary sinus eroding into the infraorbital canal and infratemporal fossa.

### Case 3. Adenoid Cystic Carcinoma (fig. 4)

A woman patient had proptosis, sixth nerve palsy, and decreased sensation in the maxillary distribution of the trigeminal  $V_2$ . CT after injection of intravenous contrast material showed a density in the orbital apex and obliteration of the upper PPF. Needle biopsy of the orbital apex was read as adenocarcinoma. The patient received radiation therapy. Follow-up CT again showed an apical density and obliteration of the PPF. Slices were continued through the maxilla, and the mass was seen in the posterior maxillary sinus with irregularity of the posterolateral wall. The ipsilateral pterygoid, masseter, and temporal muscles had atrophied. Biopsy of the mass in the sinus revealed adenoid cystic carcinoma, and the sinus was thought to be the primary site. The extension into the PPF was probably along the superior alveolar nerves, which perforate the bony wall of the maxillary sinus and then proceed along the posterior wall into the PPF.

### Case 4. Mixed Histiocytic Lymphocytic Lymphoma (fig. 5)

A 54-year-old woman had facial pain and fullness in the malar region. Axial CT after intravenous injection of contrast material showed a soft-tissue mass in the malar region. The infraorbital canal was prominent on the axial cut, with apparent enhancement along its length. An enhancing mass replaced the fat of the PPF and protruded laterally into the infratemporal fossa and medially into the nasal cavity. The foramen rotundum was widened, and there was enhancement in the region of the gasserian ganglion. The sphenoid sinus was opacified either by tumor or by obstruction caused by the tumor in the nasal cavity. No connection was found between the sphenoid sinus and the foramen rotundum. Coronal scans showed the enlargement of the infraorbital canal and the foramen rotundum and enhancement in the gasserian ganglion. Pluridirectional tomography confirmed the smooth, concentric enlargement of the foramina. Biopsy of the facial lesion revealed mixed histiocytic lymphocytic lymphoma. The patient did well on radiation and chemotherapy.

### Case 5. Fibrous Histiocytoma (fig. 6)

A 54-year-old man had nasal obstruction without significant facial pain. CT after intravenous injection of contrast material showed a soft-tissue mass in the right maxillary sinus bowing the floor of the orbit upward. There was erosion of the anterior wall of the maxillary sinus and involvement of the soft tissues of the anterior cheek. Tumor

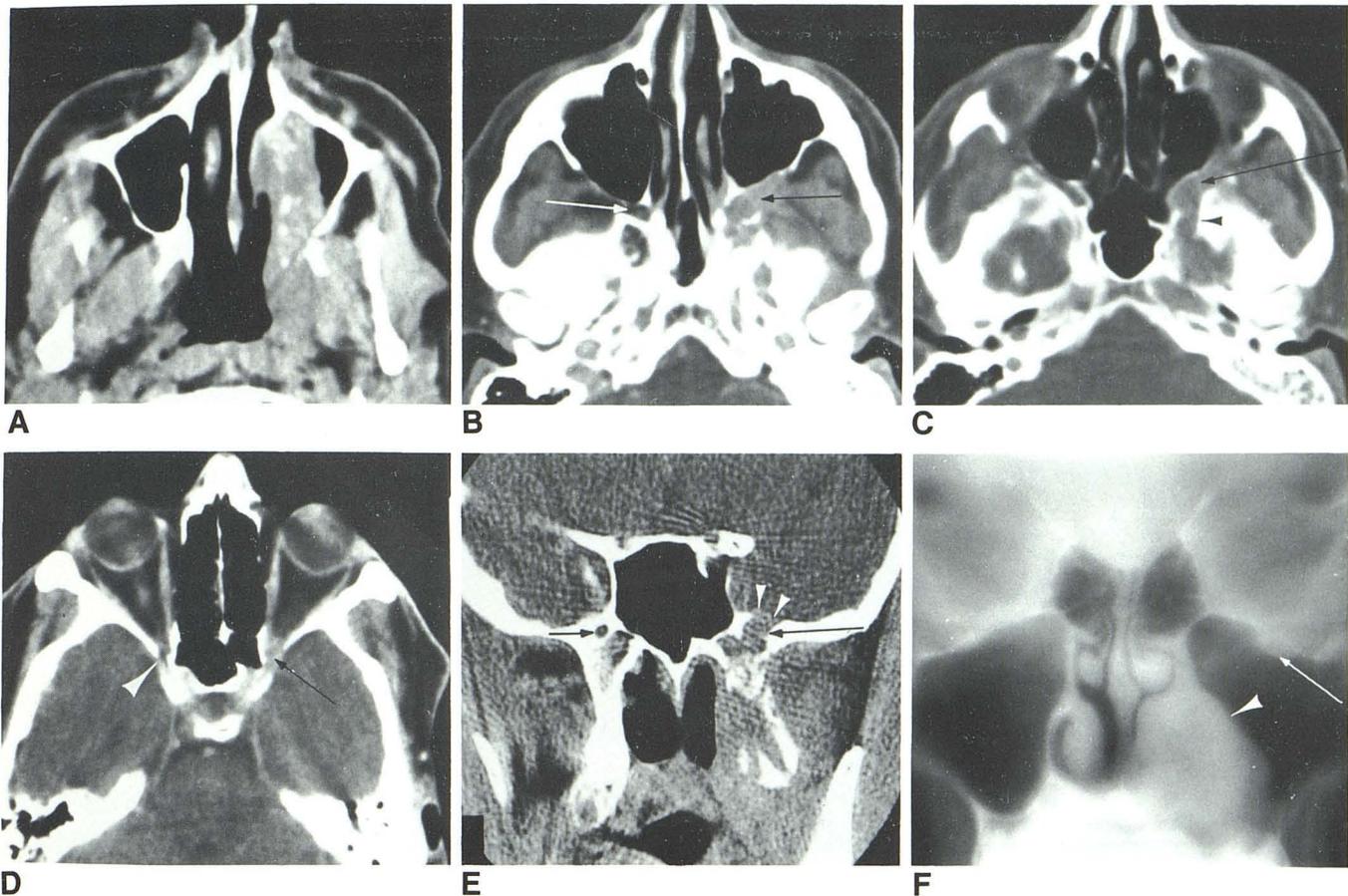


Fig. 2.—Case 1. Adenocystic carcinoma. **A**, After administration of contrast material. Axial slice through tumor in maxillary sinus, eroding posterior wall and pterygoid plate at level of suture just beneath PPF. **B**, Slightly higher slice. Obliteration of fat in PPF (black arrow). Fat is in opposite PPF (white arrow). **C**, Slightly higher cut. Obliteration of fat in PPF (arrow). Enlargement of foramen rotundum (arrowhead). **D**, Axial slice through orbital apex. Enhancement and obliteration of fat in apex (arrow) was not continuous with abnormality in PPF.

Fat in superior orbital fissure (arrowhead). **E**, Coronal slice using bone algorithm through pterygoids and sphenoid. Irregularity of root of pterygoid and enlargement of foramen rotundum (long arrow). Slight enhancement at middle cranial fossa opening of foramen (arrowheads). Normal foramen rotundum on opposite side (short arrow). **F**, Anteroposterior tomogram shows mass in inferior nasal wall (arrowhead) and enlargement of infraorbital nerve (arrow). (Tomogram is in usual tomogram orientation.)

eroded the posterior wall of the maxillary sinus but did not extend through the pterygoid. There was enlargement of the pterygopalatine canal and obliteration of the pterygopalatine fat. Tumor passed through the posterolateral wall of the maxillary sinus gaining access to the infratemporal fossa. Biopsy showed a malignant fibrous histiocytoma with neural invasion, and the patient underwent a maxillectomy. The patient returned to the hospital 6 months later with a large recurrence. The case is shown to demonstrate an enlarged pterygopalatine canal that was involved either by neural extension or direct extension.

## Discussion

Malignancy arising in the region of the face, sinus, and oral cavity can spread by perineural extension, direct encroachment, or hematogenous or lymphatic pathways [1–5]. After invading a nerve, tumor can spread along the route of the nerve, gaining access to deeper areas not directly contiguous with the original neoplasm. Recognition of spread along neural pathways is critical to appropriate treatment planning.

Though referred to as perineural extension, the malignancy

can follow either the perineural or endoneural spaces [1]. There is some controversy as to the mechanism of perineural spread [5]. Some authors believe the tumor spreads along a lymphatic system associated with the nerve. Others think the nerve simply represents the line of least resistance.

Adenoid cystic carcinoma has a known propensity for following neural pathways [5–8]. Though these tumors may occur in the parotid or submandibular glands, 60%–70% arise in the minor salivary glands [5, 8], which may be localized in the palate, paranasal sinuses, and nose.

In the region of the face, sinuses, or palate, perineural tumor spread usually follows the maxillary division of the trigeminal nerve (fig. 1). Neoplasm can follow the branches of the trigeminal back to the PPF, a key landmark in detection of perineural extension. Tumor arising in the face can follow the infraorbital nerve (cases 2 and 4). Tumors of the palate follow the palatine nerves through the greater and lesser palatine foramen and the pterygopalatine canal, passing superiorly from the palate to the PPF. Tumors of the maxillary sinus follow the superior alveolar nerves, perforating the

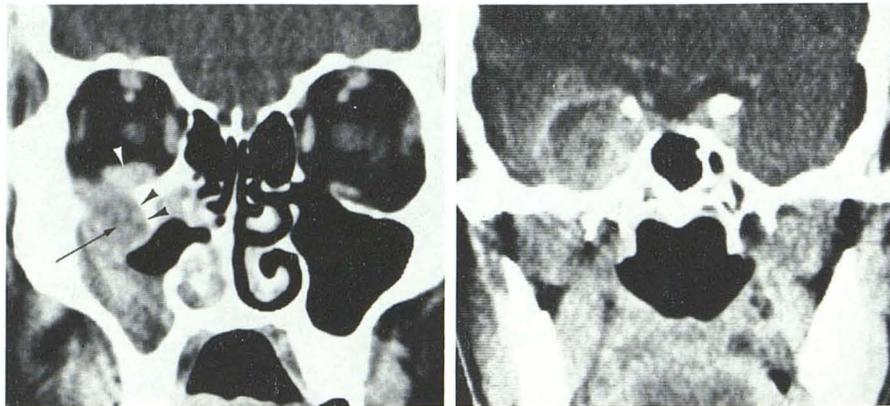


Fig. 3.—Case 2. Squamous cell carcinoma. **A**, Coronal section after intravenous administration of contrast material. Tumor in region of infraorbital canal and maxillary sinus (*arrow*). Tumor erodes floor of orbit, pushing inferior rectus (*white arrowhead*) slightly superiorly. Bony spicule (*black arrowheads*) may represent medial bony wall of expanded infraorbital nerve. **B**, Axial slice. Tumor at posterior end of infraorbital canal (*long arrow*). Tumor (*arrowheads*) follows posterior wall of maxillary sinus toward PPF (*short arrow*). Tumor displaces infratemporal fossa fat. Normal fat plane posterior to wall of opposite maxillary sinus (*white arrow*). **C**, Higher cut (just below inferior orbital fissure). Opacification of upper PPF (*arrow*). No bone destruction in skull base. **D**, Coronal slice through middle cranial fossa. Large mass extending from region of gasserian ganglion is accompanied by some edema of surrounding brain tissue.

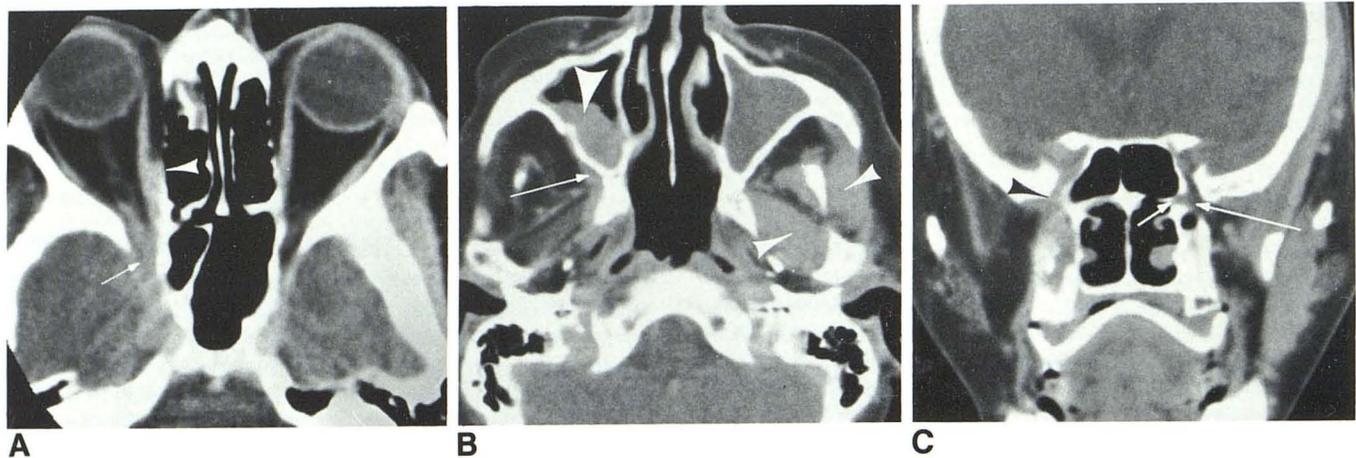
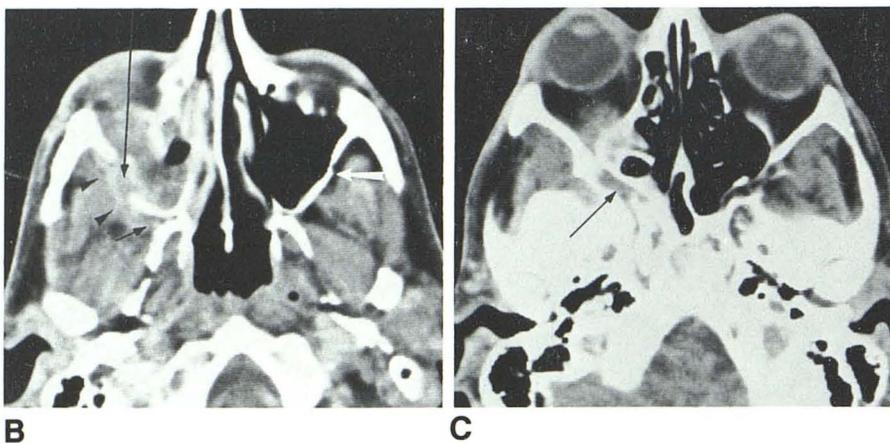


Fig. 4.—Case 3. Adenoid cystic carcinoma. **A**, Axial slice through orbital apex after injection of intravenous contrast agent. Enhancement in orbital apex extending through superior orbital fissure and also medial to medial rectus (*arrowhead*). Superior orbital fissure (*arrow*). Density was noted obliterating fat in upper PPF (not shown). **B**, Lower cut. Mass in maxillary sinus (*large arrowhead*). Density behind posterolateral wall of maxillary sinus (*arrow*). Opposite maxillary sinus was opacified but had lower CT density and was

thought to represent retention phenomenon. (Slightly higher cut showed obliteration of fat in PPF.) Atrophy of masticator muscles. Normal masticator muscles on opposite side (*small arrowheads*). **C**, Coronal slice. Irregularity of posterolateral wall of maxillary sinus and obscuration of fat in PPF. Direct extension from PPF into orbital apex (*arrowhead*). On normal side, note sphenopalatine foramen (*short arrow*) and fat in PPF (*long arrow*).

lateral maxillary sinus wall (case 3) before passing along the posterior wall of the maxillary sinus and entering the PPF. Alternately, a tumor of the maxillary sinus may erode directly into the infraorbital canal or PPF, gaining access to the neural

elements [8]. From the PPF, tumor can follow the trigeminal nerve through the foramen rotundum to gain access to the middle cranial fossa at the gasserian ganglion in Meckel cave (cases 1, 2, and 4).

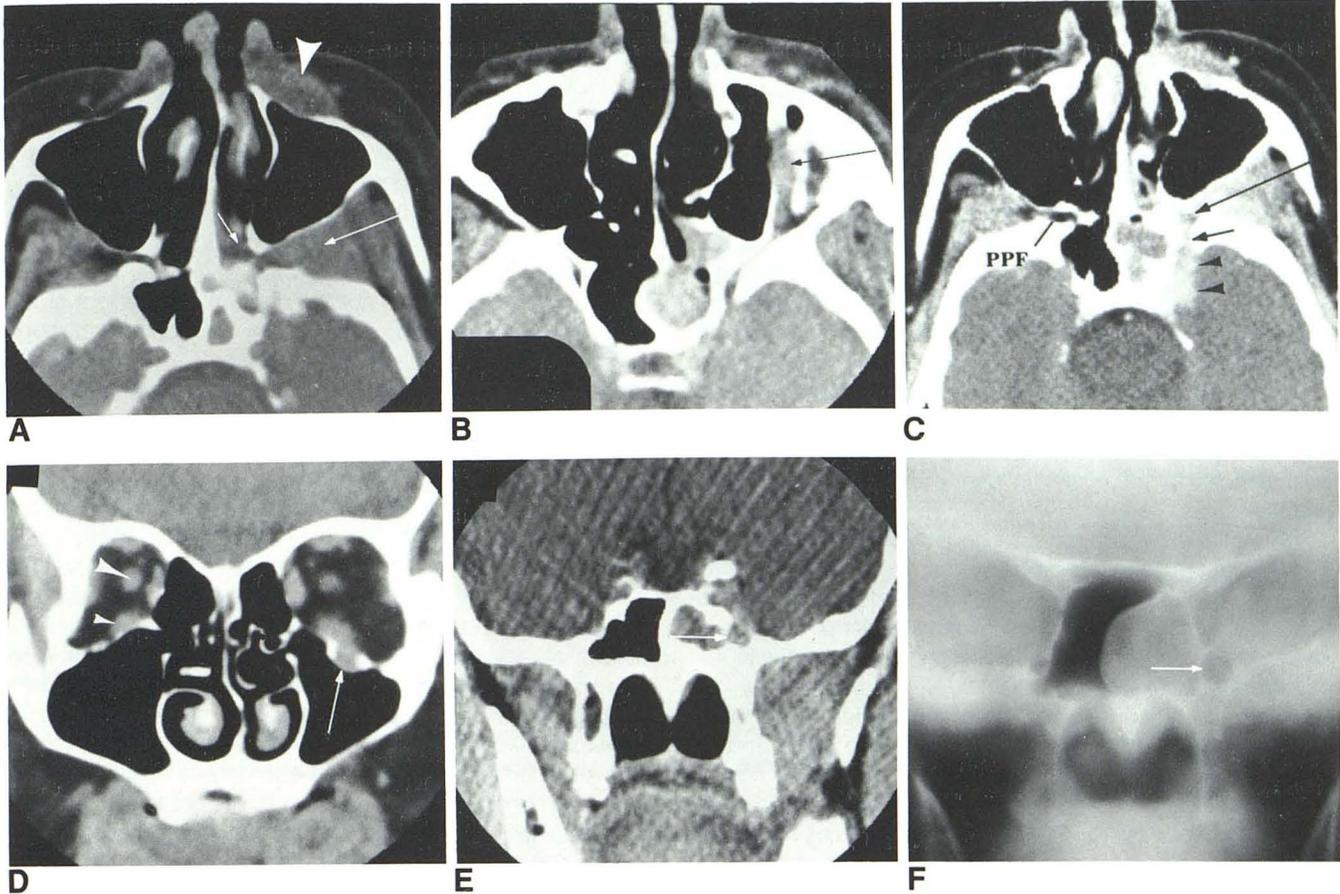
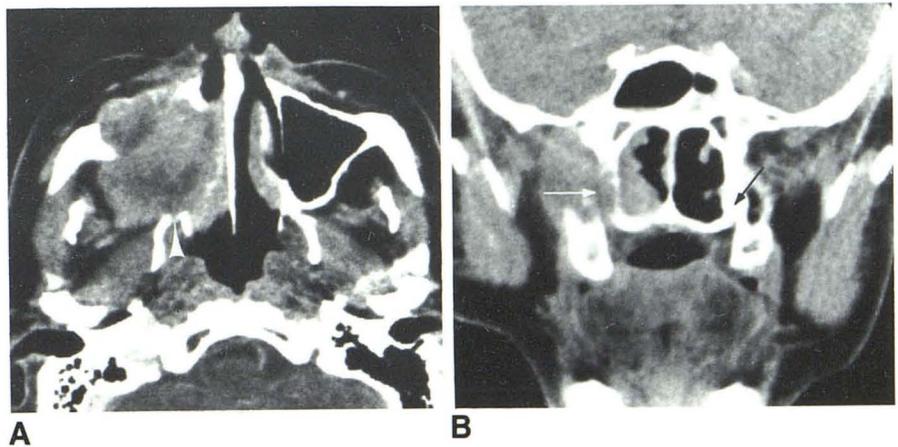


Fig. 5.—Case 4. Mixed histiocytic lymphocytic lymphoma. A, Axial slices after administration of intravenous contrast material. Tumor on anterior cheek (*arrowhead*). Tumor in infratemporal fossa (*long arrow*). Tumor extending through sphenopalatine foramen into nasal cavity (*short arrow*). B, Infraorbital canal in longitudinal section is quite large with apparent enhancement (*arrow*). C, Fat in PPF is obliterated (*long arrow*). Enhancement extends through

enlarged foramen rotundum (*short arrow*) and is in region of gasserian ganglion (*arrowheads*). Normal PPF on opposite side. D, Coronal CT slice through orbital floor. Infraorbital canal (*arrow*) enlarged compared with opposite side. Inferior rectus (*small arrowhead*). Optic nerve (*large arrowhead*). E, Posterior slice. Enlarged foramen rotundum (*arrow*). F, Enlarged foramen rotundum (*arrow*).

Fig. 6.—Case 5. Fibrous histiocytoma. A, Tumor in maxillary sinus eroding posterolateral wall. Pterygoids only minimally eroded (*arrowhead*). B, Pterygopalatine canal enlarged (*white arrow*) in longitudinal section. Compare with opposite side (*black arrow*).



Most of the neural pathways can be evaluated by CT. In a normal patient, the PPF can be seen on axial slices as a space between the pterygoid plates and the posterior wall of the maxillary sinus. The fossa contains mostly fat, which can

be identified by CT [9, 10]. On successive superior slices, the fat density can be followed into the apex of the orbit. Axial slices show the greater and lesser palatine foramina and the pterygopalatine canal in cross section. The foramen rotundum

is seen in longitudinal section, especially if thin slices are used. On axial sections the infraorbital canal can sometimes be seen in longitudinal section as it passes along the floor of the orbit. Coronal images give an excellent cross-sectional image of the infraorbital canal and foramen rotundum.

Perineural extension is usually detected by enlargement of a neural foramen or by detection of a "resurfacing" phenomenon in the PPF or middle cranial fossa.

Perineural involvement often enlarges the nerve. As the nerve enlarges, the respective foramina may be remodeled showing concentric, smooth enlargement or eventually destruction [1]. Enlargement of the canal or foramen is easiest to visualize in cross section (figs. 2E, 3A, 5D, and 5E), but the enlargement is often detectable in longitudinal section as well (figs. 2C, 5B, 5C, and 6B). This is important, as many important neural pathways, including infraorbital canal and foramen rotundum, are seen in longitudinal section in routine axial views.

The spatial resolution of CT using bone algorithm software is now comparable to pluridirectional tomography. This helps detect foraminal enlargement. Direct coronal CT views of the infraorbital canal in patients with metallic dental work can have considerable artifact, and at times pluridirectional tomography is necessary (case 1).

Tumors can "resurface" on the opposite side of the foramen. In the case of the foramen rotundum, the target area is the gasserian ganglion in Meckel cave in the middle cranial fossa (case 3). The other potential location for this "resurfacing" phenomenon is the PPF, as this area is not as tightly confined as is a nerve within a canal. Obliteration of the fat in the fossa must be regarded with suspicion, even when no bone destruction is seen in the immediate area.

Obliteration of the fat within the PPF is considered to be abnormal [11-13]. The PPF normally contains the branches of the maxillary nerve and pterygopalatine (sphenopalatine) ganglion and the terminal branches of the external carotid (internal maxillary) artery. These are seen as small densities in the PPF fat. Rarely, if the PPF is very narrow, these normal structures may fill the fossa and appear to obliterate the fat. This should be symmetric bilaterally and should not be present on all slices.

Once a tumor has "resurfaced" more centrally, for instance in the PPF, further extension can occur along more central pathways or by erosion directly into bone.

The infraorbital nerve passes along the posterior wall of the maxillary sinus paralleling the inferior orbital fissure as the nerve traverses the short distance from the posterior opening of the infraorbital canal to the PPF. Similarly, the superior alveolar nerves, after perforating the lateral wall, pass along the outside of the posterior wall of the maxillary sinus. Both nerves are bordered by the infratemporal fossa fat. Enlargement of a nerve may thus be detected as a density contiguous with the wall of the sinus (cases 2 and 3). This may be difficult to differentiate from direct extension of a tumor of the maxillary sinus.

Although most attention is paid to retrograde (proximal) extension, antegrade (distal) spread of tumor has also been described [1]. Tumor reaching the gasserian ganglion via the foramen rotundum can then follow the mandibular division

(V<sub>3</sub>) back out of the skull via the foramen ovale as in case 1. Also in case 1 the primary tumor was separate from the infraorbital canal, which was nonetheless enlarged. Tumor was thought to have reached the maxillary nerve in the PPF and then to have extended along the nerve in a peripheral direction. The orbital apex lesion may well represent antegrade neural extension from the gasserian ganglion along the ophthalmic division of the trigeminal (V<sub>1</sub>). This would explain why the orbital lesion was not continuous with the PPF involvement.

Perineural extension is not the only way into or out of the PPF [14, 15]. Malignancy reaching the PPF can pass through the fissures superiorly into the orbital apex [14], laterally into the infratemporal fossa, or medially through the sphenopalatine foramen into the nasal cavity. Case 3 presented as a tumor of the orbital apex. Because the upper PPF was involved, slices were continued through the maxillary sinus. A tumor was found in the maxillary sinus, which is considered the primary because the cell type was adenoid cystic carcinoma. The slight irregularity of the posterolateral wall and the soft-tissue density paralleling the posterior surface of the wall was believed to represent extension along the superior alveolar nerves. Adenoid cystic carcinoma may pass through marrow spaces and along the periosteum; however, this is less likely because of the apparent directed spread to PPF. Involvement of the orbital apex may have been by direct extension superiorly from the PPF. Alternately, a more circuitous route following the maxillary nerve to the gasserian ganglion and then the ophthalmic (V<sub>1</sub>) through the superior orbital fissure can be postulated. The fat collection just anterior to the cavernous sinus was obliterated by tumor (fig. 3A), but the direction of tumor extension at this location is not clear.

Adenocystic carcinoma is noted for its propensity for perineural extension; however, other tumors can exhibit similar behavior. Neural extension of squamous cell carcinoma is well documented. Case 4 illustrated a lymphoma that spread along neural pathways to reach the PPF and then the gasserian ganglion. Case 5, a malignant fibrous histiocytoma, is less clear. Tumor definitely involved the nerve in the surgical specimen. The case is included as an example of enlargement of the pterygopalatine canal, though this may have been from direct extension rather than from enlargement of the nerve itself. No evidence of central spread along the nerve was found in this case.

Involvement of the maxillary nerve can cause pain or numbness in its sensory distribution. Involvement of the gasserian ganglion or V<sub>3</sub> can cause atrophy of the masticator muscles (pterygoid, masseter, and temporal). The decrease in muscle size can be detected by CT, as in case 3.

In conclusion, perineural spread can be very insidious. Tumor can leave the region of the primary tumor and resurface at some distance. CT is the best tool for detecting this important phenomenon, but the findings may be subtle. The obliteration of the fat in the PPF, even without destruction of the bony walls, is an ominous sign. Other signs include enlargement of neural foramina, enhancement in the region of Meckel cave, and atrophy of the muscles of mastication. Obliteration of fat at the orbital apex is probably also a sign, but biopsies large enough to show actual involvement of

nerves are unusual in this region. More experience is needed before a statement can be made about the possibility of tumor passing through the PPF without obliterating the fat within.

The routine orientation for CT is axial. Therefore, familiarity with the appearance of the infraorbital nerve and foramen rotundum in longitudinal section is important, as they are important potential pathways for perineural extension.

In cases of tumors in the region of the face, sinuses, and palate, the radiologist must direct his attention to evaluation of the PPF and the neural foramina if perineural spread is to be detected.

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