JOURNAL OF NEUROSURGERY:
Case Lessons

J Neurosurg Case Lessons 5(3): CASE22400, 2023
DOI: 10.3171/CASE22400

Transorbital drillout to the cavernous sinus: an approach for squamous cell carcinoma with perineural spread. Illustrative cases

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BACKGROUND This study describes a transorbital apical approach to the cavernous sinus, where the greater wing of sphenoid (GWS) and superior orbital fissure (SOF) are drilled out to access the interdural incision zone and lateral wall of the cavernous sinus.

OBSERVATIONS This was a retrospective series of 3 patients with periocular squamous cell carcinoma (SCC) and radiological evidence of perineural spread to the cavernous sinus. Following an orbital exenteration, the GWS was drilled to reach the lateral border of the SOF. The meningo-orbital band, a periosteal transition between the frontotemporal basal dura and periorbita, was incised to enter the lateral wall of the cavernous sinus. The relevant cranial nerves were biopsied to provide an accurate zonal classification of disease.

LESSONS The transorbital apical approach via the SOF provides a corridor of access to the cranial nerves within the lateral wall of the cavernous sinus. This technique was successfully performed on 3 patients with periocular SCC. One case had radiological evidence of intracavernous oculomotor nerve involvement, 1 patient demonstrated nasociliary nerve enlargement at the SOF, and another had frontal nerve involvement extending into the cavernous sinus. Cerebrospinal fluid leak occurred in 1 case addressed with fat packing and fascial closure.

https://thejns.org/doi/abs/10.3171/CASE22400

KEYWORDS transorbital apical drillout; perineural invasion; squamous cell carcinoma

Periocular squamous cell carcinoma (SCC) with perineural spread is an important disease that carries significant risk of regional morbidity and mortality. Perineural spread with orbital apical extension usually necessitates an orbital exenteration. Following the exenteration, the intracavernous cranial nerves and their branches can be biopsied to determine the true zonal extent of disease. The transorbital approach to the skull base has engendered significant interest in recent years. An apical drillout to reach the cavernous sinus and its respective cranial nerves obviates invasive approaches such as a craniotomy or lateral orbitotomy.[1,2]

The incidence of perineural invasion in periocular SCC is 4.3–14.4%,[3–7] although studies from tertiary centers have reported much higher rates ranging from 23.8% to 36.7%.[8–10] While the terms “perineural invasion” (PNI) and “perineural spread” (PNS) are at times used interchangeably, they are 2 separate entities. PNI is a histological finding that provides prognostic information, whereas PNS refers to symptomatic or radiological involvement of named nerves that alters the management paradigm.

Conceptually, the management of periocular SCC with PNS can be guided by its zonal classification. Pertaining to the orbit, zone 1 disease extends to the superior orbital fissure (SOF), zone 2 defines PNS up to the trigeminal ganglion, and zone 3 encompasses any disease proximal to the trigeminal ganglion.[11] Overall, PNS portends a poor prognosis. The 5-year local control rate for cutaneous SCC (cSCC) of the head and neck with PNS is 57–64%, while the 5-year overall survival declines from 88% for zone 1 disease to 51% for zone 2 to 3 disease combined.[11–13]

In this series, we present 3 patients with periocular SCC and PNS extending beyond the SOF. All cases underwent an orbital exenteration to the orbital apex with adjuvant radiotherapy. At the time

ABBREVIATIONS cSCC = cutaneous squamous cell carcinoma; CSF = cerebrospinal fluid; CT = computed tomography; MOB = meningo-orbital band; MRI = magnetic resonance imaging; PNI = perineural invasion; PNS = perineural spread; SCC = squamous cell carcinoma; SOF = superior orbital fissure.

INCLUDE WHEN CITING Published January 16, 2023; DOI: 10.3171/CASE22400.
SUBMITTED September 21, 2022. **ACCEPTED** October 24, 2022.

of exenteration, an apical drillout was performed to biopsy the relevant cranial nerves within the cavernous sinus. This technique and its outcomes are herein described.

Illustrative Cases

The technique of a transorbital apical approach to the cavernous sinus is herein described. Once the orbital exenteration is completed, the greater wing of sphenoid is drilled with the Midas Rex MR8 instrument (Medtronic). Bone removal is extended toward the lateral border of the SOF. Once this boundary is reached, it can be partially removed by a fine Kerrison rongeur or diamond-tipped drill. The meningo-orbital band (MOB) is thus revealed, a structure that tethers the frontotemporal basal dura to the periorbita along the lateral border of the SOF.[14,15] It is recommended that the incision along the MOB should be made along the periosteal border at the sphenoid ridge, to a maximal length of 4 mm to prevent transection of the lacrimal branch of V1.[16] This incision is continued in a sagittal plane, which leads directly to the interdural space within the bilayered lateral wall of the cavernous sinus. The outer layer is composed of the dura propria, while the inner layer is formed by the confluence of the epineuriums of cranial nerves III, IV, V1, and V2.[14,15] To gain further access to the roof of the cavernous sinus, the optic strut is removed and the optic canal is deroofed until the anterior clinoid process is reached and detached.[17]

Case 1

A 45-year-old man presented with a 5-week history of severe right periorbital pain that was worse in the supine position. He had no ocular history and his past medical history was significant for hypertension and type 2 diabetes. Examination revealed right upper lid partial ptosis with inferior globe dystopia. There was no proptosis. Extraocular motility was globally limited. Visual acuity was 20/20 in both eyes, with no relative afferent pupillary defect. Anterior and dilated posterior segment examinations were unremarkable.

Magnetic resonance imaging (MRI) orbital scans (Fig. 1) revealed a right medial extraconal mass with peripheral enhancement and a central nonenhancing component suggestive of necrosis. The right medial rectus and superior oblique were displaced by the mass, with no intervening fat plane, indicating invasive disease. There was suspicion for PNS to the right cavernous sinus with prominence of the intracavernous oculomotor nerve. The clinicoradiological features were concerning for an aggressive malignant process.

A biopsy of the orbital mass was performed via a retrocaruncular approach, which confirmed invasive SCC. Staging computed tomography (CT) chest, abdomen, and pelvis scans revealed no nodal or metastatic disease. A multidisciplinary decision was made to proceed with an orbital exenteration with reconstruction via a free radial forearm flap.

Following the orbital exenteration, the greater wing of sphenoid was drilled and extended toward the lateral border of the SOF. The optic strut was removed, followed by an anterior clinoidectomy. This enabled access to the superolateral wall of the cavernous sinus to biopsy the oculomotor nerve, which demonstrated a negative posterior margin. A cerebrospinal fluid (CSF) leak was encountered at the optic foramen. This was repaired with fat and rectus fascia harvested from the abdomen. Fat was packed into the region of the leak with an onlay of fascia sutured to the dura with 4–0 Prolene sutures (Ethicon Inc.).

The exenteration specimen revealed a moderate to poorly differentiated SCC with positive margins. There was focal PNI without lymphovascular invasion. Adjuvant radiotherapy of 60 Gy was applied to the right orbit, followed by 2 cycles of cisplatin. One year postoperatively, the patient remains alive with no recurrence. He will continue to undergo 3-monthly MRIs.

Case 2

A 75-year-old immunocompetent woman with a history of multiple keratinocyte cancers was referred to the Oculoplastic service for a right medial canthus SCC that had undergone 2 recent excision

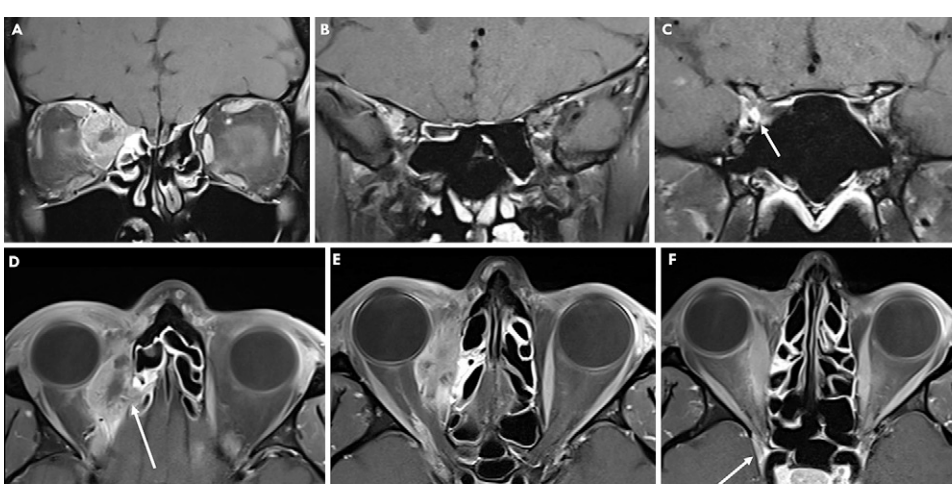

FIG. 1. MRI orbital scans of case 1. T1 fat-suppressed, contrast-enhanced sequences demonstrate a right orbital mass with perineural spread to the anterior cavernous sinus. **A:** There is a right medial extraconal mass with peripheral enhancement and central nonenhancing components, suggestive of necrosis. **B:** The mass extended toward to the superior orbital fissure. **C:** The right intracavernous oculomotor nerve (*arrow*) was prominent. **D:** There was extension of the soft tissue mass with likely perineural spread at the right ethmoidal foramen (*arrow*). **E and F:** The right superior orbital fissure and cavernous sinus (*arrow*) are enlarged with moderate enhancement.

procedures. The lesion was initially excised and repaired with a full-thickness skin graft. Histological analysis revealed a well to moderately differentiated SCC with invasion to a depth of 4.3 mm. There was extensive PNI but no lymphovascular invasion. A positive deep margin necessitated a re-excision, which was reconstructed with a forehead flap.

At the time of the referral to our service, visual acuity was right 20/50 and left 20/20. There was a 4-mm ptosis of the right lid, with ipsilateral sensory loss in the distribution of the frontal nerve. An MRI orbital scan revealed markedly abnormal thickening and enhancement of the right nasociliary nerve, with antegrade extension into the anterior ethmoidal nerve (Fig. 2). Staging CT neck and chest scans revealed no nodal or distant metastasis. Following multidisciplinary discussions, an orbital exenteration with a left vastus lateralis free flap reconstruction was planned.

An orbital exenteration was performed. An intraoperative frozen section of apical tissue showed persistence of moderately differentiated SCC. Further specimens were therefore taken from the anterior cavernous sinus. First, the greater wing of sphenoid was drilled up to the lateral border of the SOF (Fig. 3). The MOB was incised to expose the orbitotemporal and orbitofrontal dura, which enabled access to the anterior lateral wall of the cavernous sinus. A section of V1 was sampled, which showed no malignant changes. Biopsy of the anterior ethmoidal nerve at the level of the foramen was also unremarkable. To prevent a CSF leak, fat and fascia lata were harvested from the thigh and inset into the dura edge with 4–0 Prolene sutures. The socket was reconstructed with a left vastus lateralis free flap and the patient completed adjuvant radiotherapy. However, she subsequently developed leptomeningeal spread and died 6 weeks later.

Case 3

A 78-year-old man with a history of multiple facial skin malignancies presented with a poorly differentiated SCC of the left upper lid and brow, with PNI < 0.1 mm in diameter. MRI demonstrated frontal nerve enhancement and enlargement to the SOF (Fig. 4). Positron emission tomography–CT and MRI neck staging scans were negative. The patient underwent a total orbital exenteration with frozen section control of the skin margins and apex, which demonstrated a positive frontal nerve margin at the apex. An apical drillout was thus performed with excision of the preganglionic V1 from the lateral wall of the cavernous sinus, of which the posterior margin was negative. A radial forearm free flap repair was performed, followed by an uncomplicated recovery. Cumulative radiotherapy of 60 Gy was applied to the orbit, forehead, and cavernous sinus 1 cm beyond the posterior excision margin. There was no clinical or radiological evidence of recurrence at 3-year follow-up.

Discussion

At its lateral border, the cavernous sinus is composed of 2 membranous layers: an outer dural fold contributed by the temporal fossa dura and an inner wall formed by the epineuriums of cranial nerves III, IV, V1, and V2.[16] The oculomotor nerve is surrounded by a thick layer that can be dissected with relative ease, while the trochlear nerve and ophthalmic division of the trigeminal nerve are encased within a thinner layer that is attached to the outer wall.[18] At the SOF, the 2 layers of the lateral wall of the cavernous sinus diverge.[16] The outer layer inserts onto the lateral border of the SOF, where it is adjacent to the periosteal layer of the periorbita. This transitional periosteal bridge is termed the meningo-orbital band or the orbitotemporal periosteal fold.[15] Therefore, dissection through the MOB will lead to the interdural incision zone, which provides access to the entire lateral surface of the cavernous sinus.[19] Anteriorly, the interdural zone lies 5.3 ± 1.55 mm medial to the SOF.[19] Dissection through the MOB requires care, as it contains a complex vascular plexus comprising the orbitomeningeal artery and small dural veins.[16] A variant of the orbitomeningeal artery will

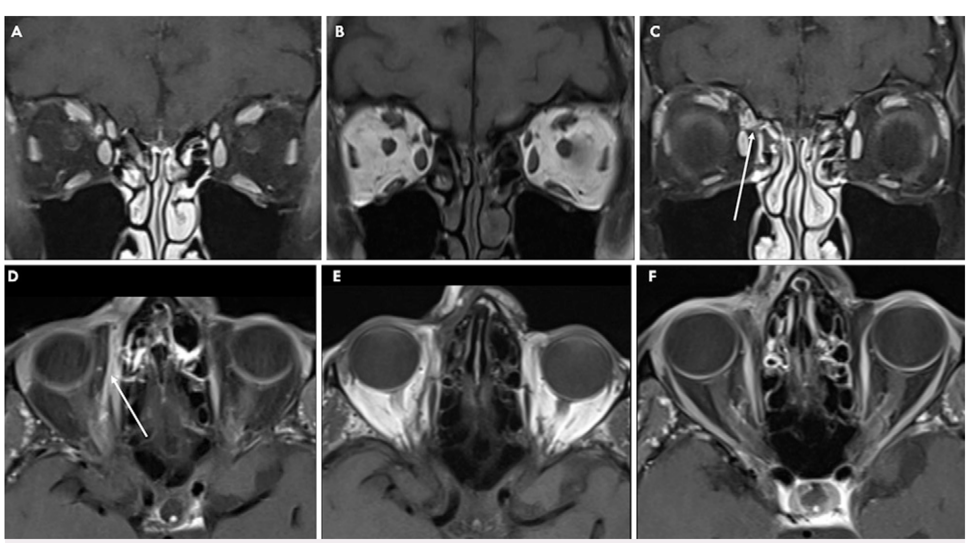

FIG. 2. MRI orbital scans of case 2, following 2 excisions for a right medial canthus SCC. **A:** Coronal T1 fat-suppressed, contrast-enhanced sequence demonstrating enhancement and thickening of the right nasociliary nerve. **B:** T1-weighted sequence demonstrating disturbance of the fat plane in the region of the right nasociliary nerve. **C:** The *arrow* demonstrates antegrade extension of enhancement into the anterior ethmoidal nerve. **D:** Axial T1 fat-suppressed, contrast-enhanced sequence. The *arrow* demonstrates an enhancing and enlarged right nasociliary nerve. There is extension into the right anterior ethmoidal foramen (**E**) and the superior orbital fissure with suspicion for involvement of the anterior cavernous sinus (**F**).

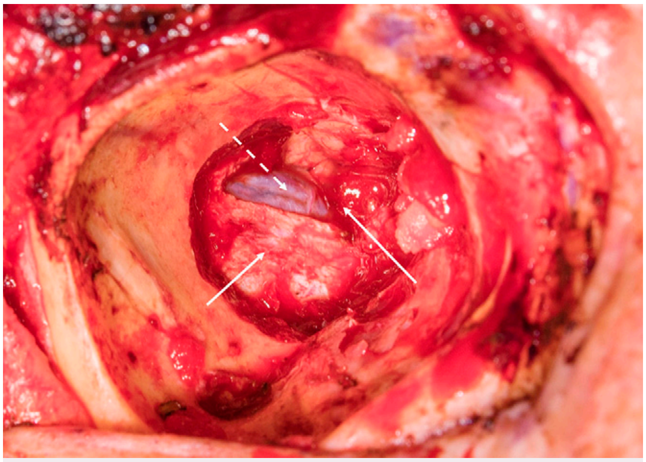

FIG. 3. Intraoperative photograph demonstrating the transorbital apical approach to the cavernous sinus. The greater wing of sphenoid is drilled (*short arrow*) to join the lateral border of the superior orbital fissure, which is then partially removed. Incision through the meningo-orbital band exposes the orbitotemporal dura (*dashed arrow*). To improve exposure of the superolateral wall of the cavernous sinus, the optic strut is removed (*long arrow*) and the anterior clinoid process is removed (not shown).

course through Hyrtl's canal, a small foramen lateral to the superolateral border of the SOF.

Traditionally, access to the cavernous sinus was dependent on a formal craniotomy approach. Variations of the craniotomy include the frontotemporal (pterional), subtemporal, and orbitozygomatic routes.[1] The frontotemporal or pterional craniotomy is centered on the sylvian fissure as the primary pathway to the sphenoid ridge.[1] The frontal and temporal lobes are retracted, followed by an anterior clinoidectomy, which exposes the roof of the cavernous sinus.[17] Indeed, the pterional approach is a versatile technique that provides excellent exposure to the cavernous sinus. However, notwithstanding the risks of meningitis and CSF leak inherent to a craniotomy with extensive bone removal, possible adverse outcomes include temporalis atrophy and neurovascular injury, including palsy of the oculomotor nerve as it crosses the inferior border of the anterior clinoid process.[17]

A variation of the frontotemporal craniotomy is a subtemporal craniotomy. This technique involves removal of the greater wing of

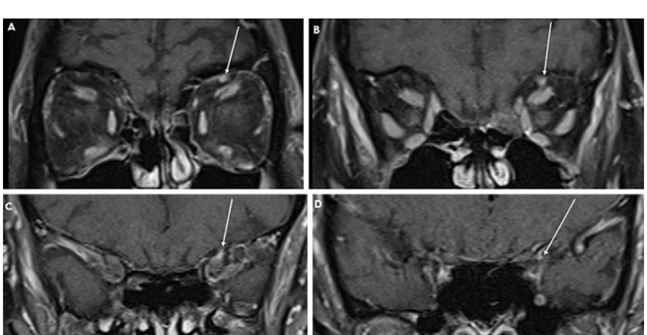

FIG. 4. MRI orbital scans of case 3. **A–D:** T1 fat-suppressed, contrast-enhanced sequences demonstrating enhancement and enlargement of the left frontal nerve (*arrows*) extending to the superior orbital fissure.

sphenoid to reach the base of the middle cranial fossa, thereby minimizing temporal lobe retraction to gain access to the lateral wall of the cavernous sinus.[17] A unilateral or bilateral supraorbital craniotomy utilizes an intradural subfrontal pathway to the cavernous sinus from a superomedial approach.[17] However, this method requires retraction of the frontal lobe and optic nerve. An orbitozygomatic osteotomy has also been described to maximize exposure of the periorbita but is another invasive procedure that is obsolete in the context of exenteration.[14]

An endonasal transsphenoidal approach to the cavernous sinus has been described, but the access pathway is narrow and direct visualization is limited by the angulation of the endoscope lens. Removing the lateral wall of the sphenoid sinus exposes the dura overlying the medial wall of the cavernous sinus.[18] Recently, the middle meatal approach has been described in cadaver studies, whereby the inferomedial wall of the bulla ethmoidalis is removed and an ethmoidectomy is extended to a sphenoidotomy. The pathway is further extended laterally to the pterygopalatine fossa to access the lateral wall of the cavernous sinus.[20] This maneuver requires medial retraction of the carotid artery to expose cranial nerves III and IV. Potential sequelae include carotid arterial injury and sympathetic nerve palsy.

Observations

The zonal classification of head and neck cSCC with PNS provides a management framework. For disease that extends beyond the SOF, access to the cavernous sinus provides an opportunity for intraoperative sampling of the relevant cranial nerves, to determine the posterior extent of disease. The technique presented in this series is centered on the SOF and the MOB as the primary access points to the interdural space and cranial nerves within the lateral wall of the cavernous sinus (Fig. 5).

A transorbital approach to the cavernous sinus has been previously described. Instead of a formal craniotomy, Goldberg et al.[21]

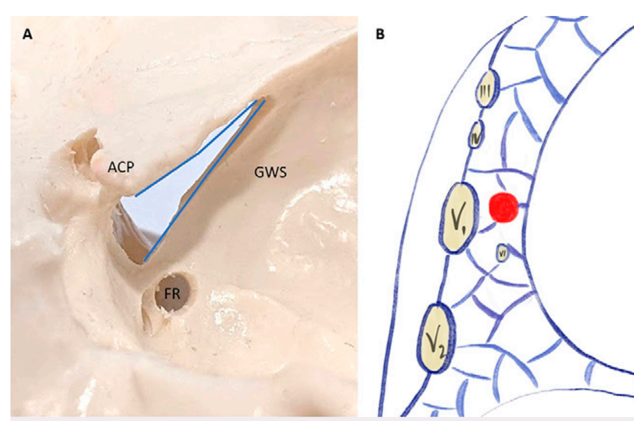

FIG. 5. A: Cranial view demonstrating the meningo-orbital band, which is composed of the confluence of the periorbita and frontotemporal basal dura periosteum, located along the edges of the superior orbital fissure (indicated by *lines*). **B**: Schematic diagram of the right cavernous sinus. The lateral wall is composed of 2 dural layers. The inner layer is composed of the epineurium of cranial nerves III, IV, V1, and V2. The interdural zone enables access to the intracavernous cranial nerves without disturbing the venous component of the cavernous sinus. ACP = anterior clinoid process; FR = foramen rotundum; GWS = greater wing of sphenoid.

proposed a lateral orbitotomy with drillout of the greater wing of sphenoid. Altay et al.[22] described a similar approach; in addition, upon reaching the SOF, the inferior border was removed and recognition of the MOB led to the exposure of the interdural space. A transorbital approach to the cavernous sinus via a lateral retrocanthal corridor has also been described: the greater wing of sphenoid is drilled out to improve exposure of the SOF, and further removal of the optic strut and superomedial portion of the optic canal leads to the superior border of the cavernous sinus.[23]

There are several advantages to the transorbital approach: importantly, it provides access to the inner layer of the lateral cavernous sinus wall without the need to enter the venous compartment. Second, it enables extensive bone removal to allow excision of dura along the floor of the anterior cranial fossa and anterior wall of the middle cranial fossa, as well as posterior visualization of the optic nerve up to the chiasm. No retraction of the brain is required. Furthermore, it avoids the need for a craniotomy, which, in combined cases, has a greater incidence of infection and CSF leak.

The risk of operative complications such as CSF leak is mitigated by the use of a spinal CSF drain and a fat graft to fill in the dead space within the intradural compartment followed by an overlay of fascia lata secured to the remaining dura/periosteum. Further packing of fat at the orbital apex will also ensure contact with the free flap, minimizing the amount of dead space. The temporalis muscle is left intact, which eliminates any risk of atrophy. Finally, if the defect in the greater wing of sphenoid requires reconstruction, it can be done with relative ease by neurosurgical colleagues using the insertion of a fat graft or thin resorbable material such as polydioxanone foil.[23]

Lessons

This series demonstrates the feasibility of a transorbital apical drillout approach to the cavernous sinus in patients with periocular SCC complicated by extensive perineural spread. An orbital exenteration facilitates the field of view in this approach, which is relatively less invasive and provides an opportunity for intraoperative biopsy to determine if there is true marginal clearance. The SOF and MOB provide a window of direct access to the cranial nerves enveloped within the lateral wall of the cavernous sinus. Removal of the anterior clinoid process together with the optic strut further exposes the entire roof of the sinus. The venous compartment of the cavernous sinus is preserved, the risk of neurovascular injury is minimized, and the need for a formal craniotomy is obviated.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Selva. Acquisition of data: Tong, Slattery, Vrodos. Analysis and interpretation of data: Tong. Drafting of the article: Tong, Slattery. Critically revising the article: Slattery, Vrodos, Selva. Reviewed submitted version of the manuscript: Tong, Vrodos, Selva. Approved the final version of the manuscript on behalf of all authors: Tong. Administrative/technical/material support: Slattery. Study supervision: Slattery, Vrodos, Selva.

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