Orbital Apex Lesions: A Diagnostic and Therapeutic Challenge

Sung-Woo Cho¹ Won-Wook Lee¹ Dae Joong Ma² Ji-hoon Kim³ Doo Hee Han¹ Hyun Jik Kim¹
 Dong-Young Kim¹ Seong-Joon Kim² Sang In Khwarg² Sung-Min Kim⁴ Sun Ha Paek^{5,6}
 Chae-Seo Rhee⁷ Chul Hee Lee⁷ Peter H. Hwang⁸ Tae-Bin Won^{1,6}

¹Department of Otorhinolaryngology, Head and Neck Surgery, Seoul National University Hospital, Seoul, Korea

²Department of Ophthalmology, Seoul National University Hospital, Seoul, Korea

³Department of Radiology, Seoul National University Hospital, Seoul, Korea

⁴Department of Neurology, Seoul National University Hospital, Seoul, Korea

⁵Department of Neurosurgery, Seoul National University Hospital, Seoul, Korea

⁶Center for Minimally Invasive Skull Base Surgery, Seoul National University Hospital, Seoul, Korea

⁷Department of Otorhinolaryngology, Head and Neck Surgery, Seoul National University Bundang Hospital, Seongnam, Korea

⁸Division of Rhinology and Endoscopic Skull Base Surgery, Department of Otolaryngology-Head and Neck Surgery, Stanford University, Stanford, California, United States

Address for correspondence Tae-Bin Won, MD, PhD, Department of Otorhinolaryngology Head and Neck Surgery, Seoul National University Hospital, 101 Daehak-Ro Jongno-Gu, 110-744, Seoul, Korea (e-mail: binent@snuh.org; bin2000@snu.ac.kr).

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Abstract

Objective To analyze the clinical characteristics of and treatment outcomes for orbital apex lesions according to their pathological diagnosis and identify clinical characteristics that could aid in their differential diagnosis.

Design Retrospective analysis design was used for this study.

Setting The study was conducted in a single tertiary institution.

Participants Patients with pathologically confirmed lesions centered in the orbital apex who were admitted between January 2011 and December 2015.

Main Outcome Measures Clinical characteristics, including demographics, predisposing factors, presenting symptoms, radiological findings, intraoperative findings, biopsy results, and treatment outcomes.

Results Nine patients with invasive fungal sinusitis, six with inflammatory pseudotumor, and six with neoplastic or tumorous lesions were enrolled. The most common presenting symptom was orbital pain or headache, followed by ophthalmoplegia and vision loss, which exhibited overall recovery rates of 62.5% and 33.3%, respectively, after definitive treatment. The prognosis was worse for patients with invasive fungal sinusitis. There was no significant difference in age, underlying medical conditions, absolute neutrophil count, C-reactive protein level, and radiological findings among the three groups. Grossly necrotic tissues around the orbital apex area at biopsy were more frequently found in patients with invasive fungal sinusitis than in the other patients. In most cases, pain ameliorated after surgical intervention. There were no surgery-related morbidities.

Keywords

- ▶ orbital apex
- ▶ invasive fungal sinusitis
- ▶ inflammatory pseudotumor
- ▶ biopsy
- ▶ prognosis

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Conclusions Lesions centered in the orbital apex included invasive fungal sinusitis, inflammatory pseudotumor, and tumorous lesions. However, clinical features that clearly differentiated chronic invasive fungal sinusitis from inflammatory pseudotumor could not be identified. Our findings suggest that prompt biopsy is warranted for timely diagnosis, symptom relief, and early implementation of definitive treatment.

Introduction

The orbital apex is a small, cone-shaped region located between the posterior ethmoidal foramen and the openings of the optic canal and superior orbital fissure. It is contiguous with the superior orbital fissure anteriorly and the cavernous sinus posteriorly. Many neurovascular structures are located in this region, including cranial nerves such as the optic, oculomotor, abducens, and ophthalmic branch of the trigeminal nerve, along with the cavernous sinus, carotid artery, and periarterial sympathetic plexus.

Lesions in the orbital apex may be inflammatory, neoplastic, infectious, iatrogenic, or traumatic.¹ Even a small lesion in this area can cause significant morbidity, with symptoms including orbital pain, headache, and neuro-ophthalmologic symptoms such as ptosis, ophthalmoplegia, and loss of vision.¹

Although the specific neuropathy may vary depending on the underlying etiology and involved cranial nerves, recovery is often unsatisfactory, even after treatment.^{2,3} Therefore, early identification is essential, and appropriate treatment should be initiated as soon as possible.⁴ Establishment of a definitive diagnosis requires surgical biopsy. However, limitations concerning surgical access to the orbital apex have discouraged the use of routine biopsy as the standard of care.

In the present study, we analyzed the clinical characteristics of and treatment outcomes for orbital apex lesions according to their pathological diagnosis and attempted to identify clinical characteristics that could aid in the differential diagnosis of these lesions.

Materials and Methods

This study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. 1701-015-820). The medical records of patients who were admitted to a single tertiary skull base center between January 2011 and December 2015 were retrospectively reviewed. Patients with lesions centered in the orbital apex were included. Patients who did not undergo biopsy via the endonasal approach and patients with Graves' disease, retinoblastoma, or any skull base or sinonasal disease without significant involvement of the orbital apex were excluded. Patient demographics, underlying medical diseases, symptoms, clinical laboratory findings such as C-reactive protein (CRP) levels and absolute neutrophil count (ANC), histopathological diagnosis, and treatment outcomes were reviewed. Computed tomography (CT) and magnetic resonance (MR) images were also reviewed for all patients to assess the presence of bony destruction, coexisting sphenothmoidal disease, infiltration of surrounding tissue,

lesion intensity (MR images), and gadolinium enhancement pattern.

All included patients underwent biopsy via a transnasal endoscopic approach to the orbital apex under imaging guidance. In most cases, biopsy was performed through the nostril ipsilateral to the lesion. When wide debridement with placement of a pedicled septal flap was performed at the time of biopsy, a binostril approach was used in conjunction with posterior septectomy. Following posterior ethmoidectomy and sphenoidectomy, structures such as the lamina papyracea, roof of the skull base, and opticocarotid recess were identified. The lamina papyracea was dissected with a blunt elevator, starting anteriorly from a point midway between the anterior and posterior ethmoidal artery and proceeding posteriorly to the medial orbital apex and, in select cases, the optic canal for optic nerve decompression. An endonasal drill with a 3.2-mm diamond burr was used for egg shelling the thicker bones of the orbital apex and optic canal before removal. When the periorbita was intact, it was incised halfway with a sickle knife; the procedure was completed using fine dissecting scissors exposing the intraorbital contents. For intraconal lesions, blunt dissection between the medial and superior oblique muscles was performed. Necrotic tissue was judiciously debrided, and multiple biopsies were obtained from regions near the periphery of the necrotic tissue. Multiple culture specimens were also acquired using swabs and tissue. In patients who underwent with wide debridement, a nasoseptal flap was utilized to cover the exposed orbital apex. Further definitive treatment was performed individually according to the final pathology.

Neuro-ophthalmologic outcome measures were evaluated at least 3 months after definitive treatment. Visual acuity was measured using a Snellen visual acuity chart and transformed into logarithm of the minimum angle of resolution (LogMAR) values for analysis. The outcome was graded as partial improvement in visual acuity or patient-reported vision) or complete (difference in the LogMAR value after treatment was less than 0.2 when compared with the value for the contralateral unaffected side or values recorded prior to disease onset) recovery. For the evaluation of ophthalmoplegia, patient-reported changes in diplopia and ocular movement restriction were determined on a scale of 0 to -4, with 0 representing no limitation and -4 representing no movement in that field of gaze. The changes were analyzed and graded as partial or complete recovery. Changes in orbital pain relative to the preoperative pain level were evaluated immediately after surgery and 3 months after definitive treatment using a Numeric Rating Scale (NRS).

All data were statistically analyzed using SPSS for Windows, Version 12.0 (SPSS Inc., Chicago, Illinois, United States). The results are presented as medians (ranges). Cross-table analysis with Fisher's exact test was used for categorical variables, while Kruskal–Wallis test and Mann–Whitney U tests were used for continuous nonparametric variables. A *P*-value of <0.05 was considered statistically significant.

Results

A total of 21 patients with orbital apex lesions were included in this study. The median age was 71 years (range: 14–89), and the male to female ratio was 10:11. Invasive fungal sinusitis (IFS) and inflammatory pseudotumor (IPT) were the most common disease entities involving the orbital apex. The remaining lesions were heterogeneous lesions, including true neoplastic and tumorous lesions with expansile properties involving the orbital apex. The most common initial presenting symptom was orbital pain and/or headache (19/21 patients). During the course of the disease, neuro-ophthalmologic symptoms (ophthalmoplegia and/or vision loss) developed in 20 of the 21 patients. Ophthalmoplegia was observed in 16 patients and vision loss in 15. The median interval between the onset of initial symptoms and the onset of neuro-ophthalmologic symptoms was 33.5 (2–1350) days, and the median interval between the onset of neuro-ophthalmologic symptoms and diagnosis was 22 (6–274) days. The patients' characteristics are summarized in ►Table 1.

Invasive Fungal Sinusitis (*n* = 9)

All patients presented with headache or orbital pain as an initial symptom and developed at least one neuro-ophthalmologic symptom during the disease course. Eight of the nine patients exhibited ophthalmoplegia and seven exhibited vision loss.

With regard to the disease course, five patients exhibited a chronic disease course of more than 12 weeks, three exhibited a subacute disease course of 4 to 12 weeks, and one exhibited an acute disease course of less than 4 weeks.⁵ None of the patients demonstrated features of IFS, including gray to black discoloration of the nasal mucosa, ulceration, and necrotic tissue, on routine endoscopic exams. Eight patients showed evidence of ipsilateral sphenoid or posterior ethmoid disease on initial imaging, and eight patients showed infiltrative lesions (►Fig. 1A) on MR imaging (MRI) and CT. The remaining one patient exhibited a mass-like, space-occupying lesion. Four patients exhibited signs of bone destruction on CT (►Table 2). Predisposing medical conditions^{6,7} were identified in seven patients; these included diabetes mellitus (DM) in four, chronic steroid use for rheumatologic disease in two, and myelodysplastic syndrome in one. None of the patients with DM exhibited ketoacidosis or a hyperosmolar hyperglycemic state. The median glycated hemoglobin (HbA1c) level was 6.3% (range: 6.0–6.7%) in the four patients with DM, indicating relatively well-controlled blood sugar levels. Only one patient exhibited neutropenia at the time of initial presentation; this patient had underlying myelodysplastic syndrome with an ANC of 264/μL. Disease progression

Table 1 Clinical features of orbital apex lesions according to their pathological diagnosis

Parameters	Total (<i>n</i> = 21)	Invasive fungal sinusitis (<i>n</i> = 9)	Inflammatory pseudotumor (<i>n</i> = 6)	Tumorous lesion (<i>n</i> = 6)
Age (Years)	71 (range: 14–89)	81 (range: 15–94)	75 (range: 57–84)	36 (range: 14–72) ^b
Male: Female	10:11	5: 4	4: 2	1: 5
Prevalence of underlying disease	12 (57.1%)	7 (77.8%)	4 (66.7%)	1 (16.7%)
Orbital pain/Headache ^a	19 (90.4%)	9 (100%)	6 (100%)	4 (66.7%)
Ophthalmoplegia ^a	16 (76.2%)	8 (88.9%)	4 (66.7%)	4 (66.7%)
Visual loss ^a	15 (71.4%)	7 (77.8%)	4 (66.7%)	4 (66.7%)
Ophthalmoplegia + Visual loss	11 (52.4%)	6 (66.7%)	3 (50.0%)	2 (33.3%)
Median interval between initial symptom development and neuro-ophthalmologic symptom development (days)	33.5 (range: 2–1350)	26 (range: 15–94)	60 (range: 2–290)	38.5 (range: 10–1350)
Median interval between neuro-ophthalmologic symptom development and diagnosis (days)	22 (range: 6–274)	137 (range: 24–274) ^b	9 (range: 6–60)	55 (range: 28–1363)
ANC(counts/μL)	4572 (range: 265–9841)	5173 (range: 265–7872)	4990 (range: 1981–7620)	3009 (range: 1720–9841)
CRP(mg/dL)	0.76 (range: 0.03–19.10)	1.04 (range: 0.03–19.10)	0.94 (range: 0.11–1.32)	0.36 (range: 0.07–0.43)

Abbreviations: ANC, absolute neutrophil count; CRP, C-reactive protein.

^aNumbers are mutually not exclusive.

^b*p* < 0.05 with the Kruskal–Wallis test and *p* < 0.05 after post hoc analysis with the Mann–Whitney U test.

Fig. 1 Representative case of a 73-year-old man diagnosed with invasive fungal sinusitis. (A) T1-weighted magnetic resonance image with gadolinium enhancement shows a diffuse infiltrating lesion in the right retro-orbital apex region (white arrow). (B) Intraoperative findings reveal mixed pale and grayish necrotic tissue over the left orbital apex (black arrow) and right optic nerve (black arrowhead).

was acute in this patient, with a poor response to appropriate antifungal therapy. He died 4 months later because of disease aggravation and multiorgan failure. The ANCs for the remaining eight patients were within normal limits (median: 5367/ μ L, range: 3086–7872/ μ L). Initially, they were clinically diagnosed with inflammatory lesions of the orbit and treated with systemic corticosteroids. Four of the eight patients who were symptomatically treated showed an initial improvement with the treatment. However, subsequent treatment failure and aggravation of symptoms led to referral for surgical biopsy. Mucosal thickening in the lateral wall of the sphenoid sinus abutting the orbit was a frequent intraoperative finding. Gross necrotic tissue was identified in the orbital apex in every patient ($\rightarrow$ Fig. 1B). Endoscopic debridement of the necrotic tissue was performed, followed by antifungal treatment after confirmation of the pathological diagnosis. No fungal organism was identified at the time of initial biopsy in two patients, who were subsequently diagnosed with IPT. These patients showed both symptomatic and radiological disease aggravation despite immunosuppressive therapy, which necessitated repeated biopsies. The causative pathogens were *Aspergillus* species in all nine patients. The pathological diagnosis was confirmed by the presence of dichotomous branching of hyphae invading the mucosal layer on Grocott's methenamine silver staining. Tissue culture was positive only for three among seven patients.

Of the eight patients with ophthalmoplegia, one exhibited partial recovery and one exhibited complete recovery. Two of the seven patients with vision loss showed partial recovery; complete vision recovery was not achieved in any patient.

Inflammatory Pseudotumor ($n = 6$)

The initial presenting symptom was headache or orbital pain in every patient. Five of the six patients developed at least one neuro-ophthalmologic symptom. Four patients exhibited ophthalmoplegia and four exhibited vision loss.

On MR and CT images, three patients showed an infiltrative pattern and three showed a mass-like pattern ($\rightarrow$ Fig. 2A). One patient showed definite bony destruction.

Intraoperative findings at the time of surgical biopsy included fibrotic inflammatory tissue in three patients ($\rightarrow$ Fig. 2B) and gross necrotic lesions around the orbital

apex in three patients. Chronic inflammation was the major pathological feature in all patients, with one showing vasculitis. Patients were treated with systemic corticosteroids (3/6) alone or in combination with other immunosuppressive agents (3/6) such as cyclophosphamide, mycophenolate mofetil, and rituximab. Among the four patients with vision loss, only one showed complete recovery, while the remaining showed no changes. Neuro-ophthalmologic symptoms did not worsen after definitive treatment.

Neoplastic and Tumorous Lesions ($n = 6$)

These lesions include one osteosarcoma, one rhabdomyosarcoma, one ossifying fibroma, two mucocoeles, and one vascular malformation. Four of the six patients in this group initially presented with pain, while one presented with proptosis and the other with hyposmia. All patients exhibited at least one neuro-ophthalmologic symptom. Four patients presented with vision loss and four with ophthalmoplegia. All patients exhibited an expansile, mass-like lesion in the orbital apex ($\rightarrow$ Fig. 3). Treatment of these lesions included endoscopic resection or endoscopic marsupialization, with orbital/optic nerve decompression. Complete resolution of ophthalmoplegia was observed in all patients. Among the four patients with vision loss, one each showed partial and complete recovery, respectively.

Comparison of IFS, IPT, and Tumorous Lesions

The age of patients in the IFS and IPT groups was significantly higher than that of patients in the tumorous lesion group, with the median age in each group being 81 (15–94), 75 (57–84), and 36 (14–72) years, respectively ($p = 0.017$ with the Kruskal-Wallis test; $p = 0.008$ for IFS vs tumorous lesions and $p = 0.026$ for IPT vs tumorous lesions after post hoc analysis with Mann-Whitney U tests). There were no significant age differences between the IFS and IPT groups. The disease duration before diagnosis, underlying disease status, and ANCs did not differ among groups. Despite the absence of statistical significance, neuro-ophthalmologic symptoms tended to present earlier in the IFS group (26 days, range: 15–94 days), followed by the IPT (60 days, range: 2–290 days) and tumorous lesion (38.5 days, range: 10–1350) groups. However, the interval between the

Table 2 Imaging features of IFS and IPT

	Spheno-ethmoidal lesion ^a	PPF lesion ^a	Bone destruction ^a	Overall character		MRI signal						Gd enhancement	
				Infiltrative	Mass-like	T1 hi	T1 low	T1 iso	T2 hi	T2 low	T2 iso	Homogeneous	Heterogeneous
IFS	8 (89%)	2 (22%)	4 (44%)	8 (89%)	1 (11%)	2 (22%)	2 (22%)	5 (56%)	2 (22%)	7 (78%)	0	5 (56%)	4 (44%)
IPT	5 (83%)	2 (33%)	1 (17%)	3 (50%)	3 (50%)	1 (16%)	2 (33%)	3 (50%)	4 (67%)	2 (33%)	0	5 (83%)	1 (17%)

Abbreviations: Gd, gadolinium; IFS, Invasive fungal sinusitis; IPT, Inflammatory pseudotumor; PPF, pterygopalatine fossa.
^aNumbers are mutually not exclusive.

onset of neuro-ophthalmologic symptoms and definitive diagnosis was significantly longer for the IFS group (137 days, range: 24–274 days) than for the IPT (9 days, range: 6–60 days) and tumorous lesions (55 days, range: 28–1363) groups ($p < 0.001$ with the Kruskal–Wallis test; $p = 0.004$ for IFS vs IPT and $p < 0.001$ for IFS vs tumorous lesions after post hoc analysis with Mann–Whitney U tests). The imaging characteristics of IFS and IPT are summarized in ►Table 2. IFS cases were more likely to demonstrate bony destruction on CT and more likely to present as an infiltrative lesion. However, these characteristics were not statistically significant. The presence of sphenoethmoidal lesions, pterygopalatine fossa lesions, and signal intensity and enhancement patterns on MRI showed no significant differences among groups. The intraoperative finding of gross tissue necrosis was more frequently associated with IFS ($p = 0.044$, ►Table 3). The recovery rate for ophthalmoplegia was significantly lower in the IFS group than in the other two groups [odds ratio (OR): 0.250, 95% confidence interval (CI): 0.075–0.830, $p = 0.007$]. The recovery rate for vision was also lower in the IFS group, although the difference was not significant (OR: 0.762, 95% CI: 0.175–3.327, $p > 0.99$; ►Table 4).

Overall Pain Outcome

Nineteen of the 21 patients had initially presented with headache or orbital pain. Twelve of these exhibited pain relief immediately after the surgical intervention, with a median change of –1 (–4 to 2) in the NRS score. An overall improvement in pain after definitive treatment was achieved in 16 (IFS: 8, IPT: 4, tumorous lesions: 4) of the 19 patients.

Discussion

In the present study, we analyzed the clinical characteristics of and treatment outcomes for orbital apex lesions according to their pathological diagnosis and identified clinical characteristics that could aid in the differential diagnosis of lesions. Because of the rarity of these lesions, relevant literature is scarce.

We identified three distinct lesions in our series, namely IFS, IPT, and neoplastic and tumorous lesions centered in the orbital apex. Although the diagnosis differed, the clinical presentation of all lesions was similar. The presenting symptom was usually orbital pain or headache, followed by neuro-ophthalmologic symptoms such as ophthalmoplegia and vision loss. These symptoms reflect the proximity of neural structures in this area and are consistent with the findings of previous case series.^{3,8,9} An accurate diagnosis is the first and most important step in the treatment of these lesions. The primary objective of the present study was to identify clinical characteristics that could aid in the differential diagnosis of lesions centered in the orbital apex. To the best of our knowledge, this is the first study that aimed to differentiate the clinical features of chronic IFS and IPT, the two most common disease entities in the orbital apex in our series.

Patients with IFS tended to develop neuro-ophthalmologic symptoms at an earlier disease stage compared with patients with IPT or tumorous lesions. However, the mean duration from the onset of neuro-ophthalmologic symptoms to

Fig. 2 Representative case of a 73-year-old woman diagnosed with inflammatory pseudotumor. (A) T1-weighted magnetic resonance image with gadolinium enhancement shows a mass-like infiltrating lesion in the left orbital apex (white arrow). Note the presence of sphenoiditis (white arrow head). (B) Intraoperative findings reveal fibrotic and inflammatory tissue in the left orbital apex (black arrow) and left optic nerve (black arrowhead).

definitive diagnosis was significantly higher for the IFS group than for the IPT and tumorous lesion groups. This may explain why the mean duration from the onset of initial symptoms to definitive diagnosis did not differ among groups. Possible causes for the delay include the use of empirical treatment based on clinical findings and difficulties in establishing a pathological diagnosis, with repeat biopsies required for some cases.

When the recovery rates were analyzed for each of the three groups, the IFS group showed worst outcomes. The pathological process involved in a neuropathy may differ according to the disease entity and involved cranial nerve. Passive compression of nerves, with subsequent early decompression, would be associated with the highest chances of recovery.¹⁰ Lesions such as IFS, which directly involve the nerve, exhibit a poor prognosis.^{2,5,11} This was also shown in our study, where recovery from neuro-ophthalmologic symptoms was better

in the expansile tumorous lesion and IPT groups than in the IFS group. We speculate that IPT is associated with a combined mechanism according to the disease stage, beginning with compression neuropathy and followed by direct nerve invasion as the disease progresses. Delays in diagnosis and definitive medical treatment may have worsened the neuro-ophthalmologic treatment outcomes for the IFS group.

The differentiation of patients with IFS or IPT from those with expansile neoplastic or tumorous lesions was possible with imaging studies. Expansile tumorous lesions showed distinct, well-defined, mass-like features on CT, and/or MRI. However, IFS and IPT shared similar clinical characteristics that did not allow distinction on the sole basis of one trait. Specifically, IFS with an indolent course was difficult to differentiate from IPT. Again, we emphasize that many IFS cases in our series were initially diagnosed with and treated for IPT using systemic corticosteroids. With regard to age and underlying medical conditions, there was no difference between the two groups. Moreover, ANC, a marker of immunocompetence, did not show a marked difference. This is a surprising finding, given the conventional association between IFS and an immunocompromised host. Initial nasal endoscopic exams also revealed no significant differences between the two groups, and imaging studies exhibited limitations in differentiating the two lesions. When the imaging characteristics were investigated, three patients with IPT presented diffuse infiltration and three presented mass-like lesions. This finding is in accordance with the study of Li et al,⁹ who described the characteristic findings of eight IPT patients with retro-orbital involvement.

Table 3 Intraoperative findings for invasive fungal sinusitis and inflammatory pseudotumor

	Necrotic tissue	Inflammatory tissue
Invasive fungal sinusitis (<i>n</i> = 9)	9 (100%) ^a	7 (78%)
Inflammatory pseudotumor (<i>n</i> = 6)	3 (50%)	3 (50%)

^a*p* < 0.05 with Fischer's exact test. Numbers are mutually not exclusive.

Fig. 3 Representative case of a 17-year-old girl with venous malformation, classified as a tumorous lesion in our series. Fat-suppressed T2-weighted magnetic resonance image shows a lesion with a high signal intensity (arrow) in the left orbital apex, with optic nerve compression. The patient developed sudden orbital pain and rapidly progressing vision loss and ophthalmoplegia. Following endoscopic orbital and optic nerve decompression, her neuro-ophthalmologic symptoms resolved completely.

Table 4 Treatment outcomes of neuro-ophthalmologic symptoms

	Invasive fungal sinusitis	Inflammatory pseudotumor	Tumorous lesion
Improvement rate of ophthalmoplegia (partial or complete)	2/8 (25%) ^a	4/4 (100%)	4/4 (100%)
Improvement rate of vision (partial or complete)	2/7 (29%)	1/4 (25%)	2/4 (50%)

^a $p < 0.05$ by Fischer's exact test. Numbers are mutually not exclusive.

Although chronic IFS is known to present as a mass like lesion,¹² most IFS lesions in the orbital apex in our study presented with diffuse infiltrative features on MRI, with the exception of one patient. The frequency of bone destruction and sphenoethmoidal lesions ipsilateral to the orbital apex lesion was higher in the IFS group than in the other two groups, although the difference was not statistically significant. Bone erosion and mucosal thickening may occasionally be very subtle, and IFS can present with normal CT images and intact bony walls.¹² Furthermore, in some patients, bone erosions may occur with disease progression.¹³ IPT lesions appear isointense on T1-weighted images and hypointense on T2-weighted images,¹³ whereas IFS lesions appear hypo- or isointense on T1-weighted images and hypointense on T2-weighted images.¹² Our study showed similarities as well as differences when compared with previous reports. Therefore, it was difficult to differentiate the two lesions using their signal intensities on MRI.

Nevertheless, findings favoring IFS over IPT included a relatively short duration until the development of neuro-ophthalmologic symptoms, elevated CRP levels, radiological findings of infiltrative lesions with bone destruction and heterogeneous enhancement, and intraoperative findings of gross tissue necrosis in the orbital apex. Although only the last finding showed statistical significance, one can argue the value of statistical comparisons for a relatively small number of patients.

The prognosis of our patients with IFS involving the orbital apex was better than that previously published.^{3,14} This may be the result of multiple factors. First, only one patient in our series exhibited an acute presentation, while the others presented with an indolent course, which is characteristic of chronic IFS.^{12,13} Second, the causative organisms in all affected patients were *Aspergillus* species. Lesions caused by *Mucor* and *Scedosporium* species exhibit aggressive features and are associated with a poor prognosis.¹⁵ Third, although the orbital apex was involved, suggesting an advanced stage, the lesions were relatively localized, allowing for surgical debridement in most patients. Finally, and maybe most importantly, the immune status was relatively well maintained in all but one patient, with a mean ANC that was within normal limits and well-controlled sugar levels (mean HbA1c, 6.3%).

Orbital pain may reflect direct involvement of the ophthalmic (V1) branch of the trigeminal nerve.¹ However, pain can also result from stretching of the sensory nerves in the periorbital. Immediate amelioration of pain after surgical decompression of the medial orbital apex in 13 of the 19 patients in our series suggests that both mechanisms may be involved.

There were no acute complications associated with surgery in our patients. With recent advances in endoscopic endonasal

approaches to the skull base, surgical biopsy from the medial orbital apex can be effectively performed using the endonasal corridor, with minimal patient morbidity. The primary reasons for performing surgery in patients presenting with orbital apex lesions include tissue acquisition for pathological diagnosis, identification of responsible microorganism, and implementation of definitive treatment as soon as possible, while secondary reasons include debridement of nonviable tissue, if present, and decompression of the orbital and/or optic nerve to relieve pain and improve visual loss. Finally, intraoperative findings are expected to aid in diagnosis. In the present study, gross necrotic tissue was more frequently associated with IFS. However, commencement of empirical antifungal therapy on the basis of intraoperative findings is not adequately justified because IPT can also show necrotic features; furthermore, antifungal treatment is associated with noticeable side effects. In the present study, one patient exhibited acute renal insufficiency after the administration of intravenous amphotericin B. In view of the relative safety and positive role of surgery, we advocate early surgical intervention for patients with orbital apex lesions. In addition, orbital apex lesions with negative biopsy findings for fungi should still be considered for a diagnosis of IFS, and repeated biopsies should be performed for lesions not responding to immunosuppressive therapy.

At the time of interpreting the incidence of lesions in the orbital apex, we should consider the possibility of a referral bias. Patients with IPT involving the orbital apex who responded well to corticosteroid therapy or patients requiring approaches other than the endonasal approach may not have been referred and consequently not included in our study. The relatively small sample size is another weakness of our study, although this was a result of the rarity of these lesions. Future studies can overcome this limitation by gathering cases from multiple institutions.

Conclusions

In summary, lesions centered in the orbital apex included IFS, IPT, and tumorous lesions, and we could not identify clinical features that could clearly differentiate chronic IFS from IPT. However, a diagnosis of IFS was favored by the presence of necrosis at the time of biopsy, elevated CRP levels, and radiological findings of infiltrative lesions with bone destruction and heterogeneous enhancement. Our findings suggest that prompt biopsy is warranted for timely diagnosis, symptomatic relief, and early implementation of definitive treatment for patients presenting with orbital apex lesions.

Conflicts of Interest

None.

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