Orbital Apex Syndrome secondary to Chronic Invasive Fungal Rhinosinusitis and its Diagnostic Challenges: A Case Report

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ABSTRACT

Objective: To present a case of chronic invasive infection rhinosinusitis (CIFRS) complicated by orbital apex syndrome, highlighting the significant diagnostic challenges and delays encountered before establishing the diagnosis.

Methods: This is a case report.

Case Presentation: This patient is a 65-year-old diabetic female, status post-kidney transplantation with immunosuppressant use presented with headache and sudden painless vision loss and extraocular limitation of the right eye. Magnetic resonance imaging (MRI) revealed a right-sided ill-defined nasopharyngeal mass, with nasopharyngeal carcinoma as the radiologic consideration. Biopsy revealed bacterial and fungal elements. During admission, antibiotics, antifungals, and tumor debulking was done but symptoms persisted. Histopathology showed reactive inflammatory tissue; hence, a short course of intravenous high-dose steroids was given. Overall health declined and patient eventually expired.

Conclusion: This case highlights the importance of maintaining high clinical suspicion for fungal infection despite non-specific radiologic findings in immunocompromised patients with vague, localized symptoms. Prompt recognition and tissue diagnosis are critical for early intervention.

Key Words: Orbital Apex Syndrome, Chronic Rhinosinusitis, Fungal Infection, Immunocompromised, Nasopharyngeal Carcinoma

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Chronic invasive fungal rhinosinusitis is an indolent infection with slow destructive process, typically from *aspergillus fumigatus.*[1] Aspergillosis is a common fungal infection that can present similarly to malignancy, especially in immunocompromised patients.[2] Risk factors for fungal infection include poorly-controlled diabetes mellitus, human immunodeficiency virus, chemotherapy, and those on chronic oral corticosteroid therapy.[3] Invasive forms can lead to orbital invasion and subsequently orbital apex syndrome that manifests with loss of vision, proptosis and third, fourth, and sixth cranial neuropathy. [4]

CASE PRESENTATION

A diabetic and hypertensive 65-year-old female, status post-kidney transplant, presented with sudden right-sided vision loss. She also has a 6-month history of new-onset headaches and diplopia. Prior to kidney transplant, the patient underwent desensitization for donor-specific antibodies (DSA) using plasmapheresis, intravenous immunoglobulin, and rituximab. She was maintained on cyclosporine, mycophenolate sodium, and low-dose prednisone. A few months prior to consult, she underwent brain Magnetic resonance imaging (MRI) and computed tomography (CT) scan to evaluate new-onset headache which showed unremarkable brain findings and polysinus disease (Figure 1).

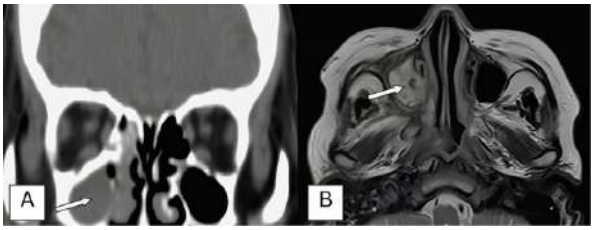

Figure 1. Early Radiologic Findings **A**. Plain Brain Coronal CT scan done 4 months prior to admission showing mucosal thickening in the right ethmoid and bilateral maxillary sinus. **B**. Plain Brain MRI T2 sequence, axial view done 1 month prior to admission, showing fluid signal in the right maxillary sinus.

An ophthalmologist diagnosed her with central retinal artery occlusion, prescribed oral steroids, and requested brain MRI and fluorescein angiography. The patient sought a second opinion and was assessed with proliferative diabetic retinopathy of both eyes, but was advised that blurring of vision is not retinal in origin. The brain MRI showed an ill-defined, infiltrative heterogeneous abnormal signal at the right nasopharyngeal mucosal space, consider nasopharyngeal carcinoma (NPCA). The patient was then referred accordingly for further evaluation.

On physical examination, visual acuity was poor light perception in the right eye and 20/40 (best corrected) in the left eye. The right eye showed 15° exotropia on Hirschberg with mild extraocular muscle (EOM) limitation of gaze, greater on abduction and infraduction. Mild ptosis was present (Marginal Reflex Distance 1 2 mm) bilaterally without proptosis. The patient had right-sided sensory deficit of 90% on the trigeminal nerve distribution (V1-V3), intact bilateral corneal reflex, and decreased right-sided hearing. There was no diplopia, eye pain, or proptosis.

On admission, brain CT scan showed the same right-sided ill-defined enhancing mass in the right mucosal pharyngeal space, including the right orbital apex with compression of the right optic nerve and hyperdensities surrounding the right medial and inferior rectus. (Figure 2). Malignancy was the assessment on admission. The patient underwent endoscopic sinus surgery with biopsy of nasopharyngeal mass with intraoperative findings of submucosal mass with friable tissue and purulent discharge (Figure 3). Gram stain and culture showed hyphal elements and *Klebsiella pneumoniae*, respectively. Intravenous cefepime was started and stepped down to oral ciprofloxacin after negative blood cultures. Histopathology revealed septate hyphae and atypical round cell proliferation (Figure 4). Therefore, amphotericin B was started but shifted to isavuconazole due to intolerable headache despite appropriate pain medication. Immunohistochemical stains were positive for CD68, and negative for S100, CK, and p63. This pattern is consistent with a reactive inflammatory process, therefore, malignancy was ruled out.

During admission, the patient had complete right vision loss, and worsening headache, ptosis, and EOM limitation. Repeat brain MRI showed the mass had enlarged to involve the sphenoid sinus, with risk of erosion to the left side. Amphotericin B was subsequently restarted and headache was managed through analgesics. Due to suspicion of orbital apex abscess, endoscopic sinus surgery and orbitotomy with biopsy was performed to debulk the tumor. This revealed congestion in the sinuses

and orbital apex without abscess or purulent discharge. The sinus sample revealed *Aspergillus fumigatus*, and orbit biopsy revealed inflammation. Post-operatively, the patient still had persistent headache which was attributed to the inflammatory process. This prompted initiation of high-dose intravenous methylprednisolone (1 gram daily for 3 days) on day 5 of amphotericin after clearance from all services. The headache improved, but vision, EOM, and ptosis remain unchanged. The patient started to have progressive systemic complications of body weakness and decreasing sensorium. Due to decreasing sensorium, the patient was intubated but the patient's health continuously declined and she eventually expired due to septic shock.

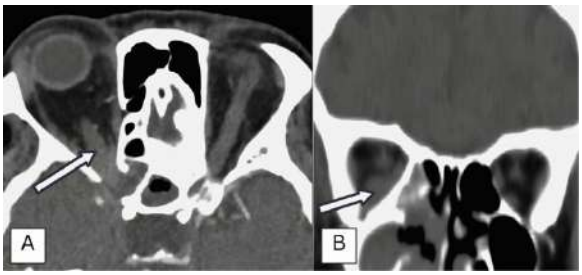

Figure 2. Brain CT Scan with gadolinium contrast done Day 5 of admission showing ill-defined enhancing mass centered in the right mucosal pharyngeal space, with mass effect, 6.7 x 3.9 x 5.2 cm (AP x T x CC), including the right orbital apex with resultant compression of the right optic nerve at axial view **(A)**, and hyperdensities around the right medial rectus and inferior rectus at coronal view **(B).**

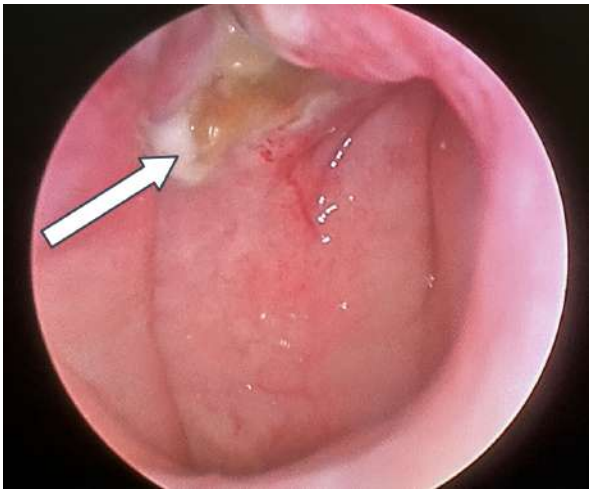

Figure 3. Intraoperative finding during nasopharyngeal biopsy done Day 7 of admission which showed submucosal mass with friable tissue and purulent discharge (white arrow).

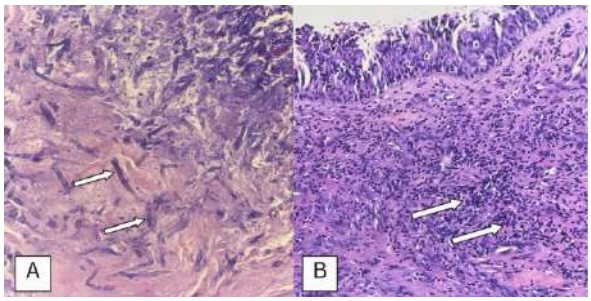

Figure 4. Nasopharyngeal mass histopathology (hematoxylin and eosin stain) from nasopharyngeal biopsy done on Day 7 of admission. (A) Microscopic examination showing branching, septated hyphae under 40x view, which is consistent with a fungal infection. (B) Prominent histiocytic reaction attributed to a reactive inflammatory process.

DISCUSSION

The chronic and indolent course of CIFRS may obscure early recognition, such as in this case as it masqueraded as NPCA radiologically and clinically.[2] On admission, she was initially managed as a case of malignancy. Antimicrobial therapy was initiated only after histopathologic results, highlighting the importance of prompt tissue biopsy and microbiologic evaluation.

Repeat brain MRI showed a pattern of infiltration of the mass from nasopharynx extending to the trigeminal nerve, cavernous sinus, and foramen ovale (Figure 5) which is consistent with NPCA.[5] Biopsy remains the gold standard since fungal infections can mimic characteristics of a malignancy. Both histopathology and microbiologic tests such as potassium hydroxide microscopy, fungal culture, and polymerase chain reaction should still be done, as histopathology alone has limited sensitivity. [6]

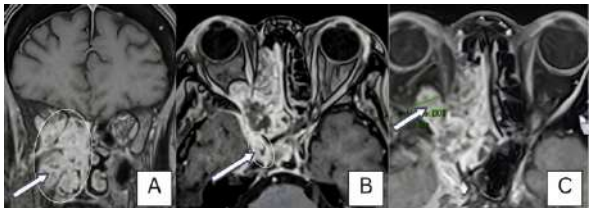

Figure 5. Brain MRI T1 sequence with gadolinium contrast. Day 22 of Admission. **A.** Extensive transpatial soft tissue abnormality involving the right nasopharyngeal wall. **B.** The right cavernous sinus shows prominent enhancement, possibly due to perineural spread via the trigeminal nerve at the right foramen ovale. **C**. A peripherally enhancing focus measuring 2 x 1.5 cm at the right orbital apex region.

Review of CT scan imaging 4 months prior to admission showed polysinus disease and right-sided hyperattenuating paranasal sinus opacification which is concurrent with clinical complaints of new-onset headache. The headache could be due to sinus pressure from blocked drainage, and inflammatory mediators that stimulate local nerves.[7] In elderly patients, new-onset headaches are often attributed to more common causes such as neurological or vascular disorders. Therefore, this patient previously underwent CT and MRI to exclude intracranial structural lesions leading to underdiagnosis of early sinonasal or orbital abnormalities.

Continued progression of the fungal sinusitis led to extension to the orbital apex that caused vision loss from compressive optic neuropathy, and affectation of the origin of the extraocular muscles that led to EOM limitation. Further progression of ptosis and near-complete restriction of EOM movement was attributed to extension of the mass beyond the orbital apex and congestion of the rectus muscles (Figure 6). The rapid progression of the lesion along with culture and histopathology results, favored an infectious etiology, with malignancy considered as unlikely.

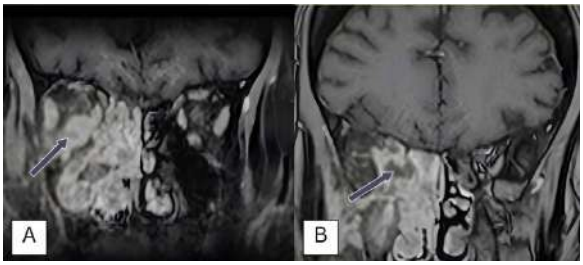

Figure 6. Brain MRI T1 sequence with gadolinium contrast, coronal view, done on Day 22 of admission due to progression of extraocular muscle limitation and ptosis which shows congestion of the extraocular muscles from mass compression (as pointed by the arrow) (**A**) and extension of mass to right orbital apex. The arrow points to the structure that initially was radiologically thought as abscess **(B).**

Due to rapid progression of the mass despite initiation of appropriate antimicrobials, tumor debulking was done. This was performed to decompress the lesion and alleviate the patient's intolerable headache, while also reducing fungal burden to optimize antifungal penetration. Intraoperative retrobulbar triamcinolone was placed since the mass appears inflammatory on nasal endoscopy and imaging (Figure 7). Since the headache persisted post-operatively, high-dose steroid therapy was started for symptomatic control, as both intraoperative findings and histopathology showed inflammatory tissue.

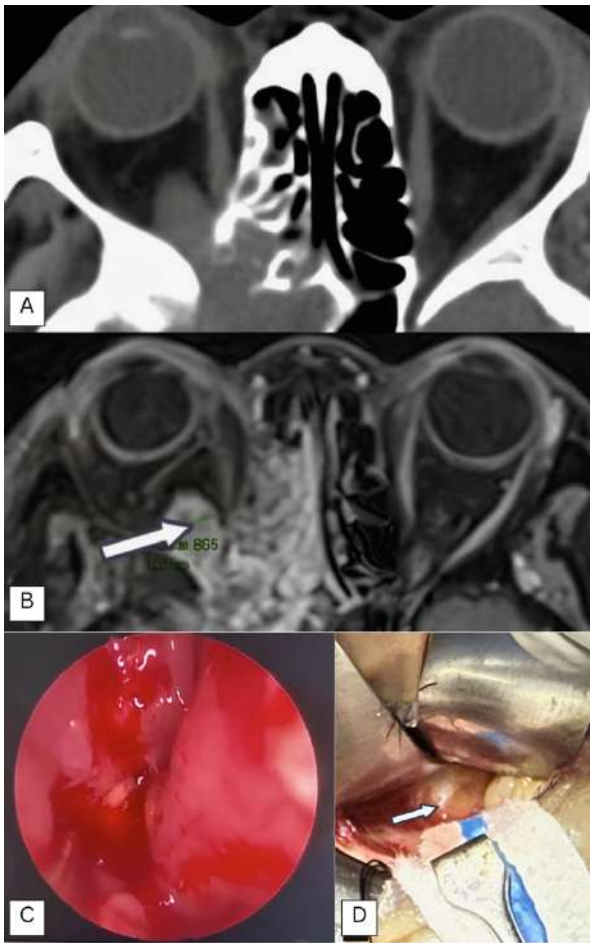

Figure 7. Day 29 of admission. Orbitotomy with incisional biopsy was performed at the site of the hyperdense signal on brain CT (**A**) and hyperintense signal on brain MRI (**B**), which radiologically mirrored the maxillary sinus lesion. Intraoperative endoscopy (**C**) primarily revealed inflammatory tissue without purulent discharge. A yellow fleshy mass was noted during orbitotomy, corresponding to the inflammatory tissue identified on CT and MRI scan **(A, B)**.

CONCLUSION

Given the insidious progression of chronic invasive fungal infection and its occurrence in patients with complex comorbid profiles, early recognition remains challenging. Having a high index of suspicion in immunocompromised individuals presenting with new-onset headache, facial pain, or chronic nasal congestion is important for timely diagnosis and improved clinical outcomes.

ETHICS COMPLIANCE STATEMENT

The authors affirm that this case report was prepared in accordance with the ethical standards of the Philippine Journal of Ophthalmology, the principles outlined in the Declaration of Helsinki, and applicable institutional and national guidelines on research involving human participants.

The patient described in this report is deceased. Written informed consent for publication was not obtained prior to the patient's death. The authors confirm that all identifying information has been removed or anonymized to protect patient privacy. The authors declare that the case report did not require formal institutional review board (IRB) approval, as per the policies of the authors' institution, because it describes a single clinical case without experimental intervention.

The authors further certify that there are no conflicts of interest related to the preparation of this manuscript, and that the work has not been previously published nor is it under consideration by another journal.

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