Journal of Clinical & Experimental Ophthalmology

Paulino et al., J Clin Exp Ophthalmol 2016, 7:4
DOI: 10.4172/2155-9570.1000573

Case Report Open Access

Invasive Aspergillosis in an Immunocompetent Asian Teenager

Jose Antonio T. Paulino, Archimedes LD Agahan*, Felice Katrina Trio-Ranche

Department of Ophthalmology and Visual Sciences, College of Medicine, University of the Philippines Manila, Philippine General Hospital, Ermita, Manila, Philippines

***Corresponding author:** Archimedes Lee D. Agahan, M.D., Sentro Oftalmologico Jose Rizal, Philippine General Hospital, University of the Philippines Manila, Ermita, Manila, 1000, Philippines, Tel: (+63 2) 3022491; E-mail: docagahan@yahoo.com

Received date: April 20, 2016; **Accepted date:** July 12, 2016; **Published date:** July 15, 2016

Abstract

Purpose: To report a case of invasive Sino-orbital aspergillosis in an Immunocompetent Asian teenager

Method: Case Report

Result: An immunocompetent Asian teenager with no comorbidities presented with a unilateral orbital proptosis with orbital cellulitis-like symptoms was unresponsive to medical therapy. Findings on computed tomography demonstrated a fairly homogenous mass occupying the entire left maxillary sinus, with erosion of the orbital floor and medial wall to invade the ethmoids and the orbit. Excision biopsy of the mass showed fungal elements with tissue invasion and granulomatous reactions. Treatment included excision of the mass and systemic antifungals. During the course of treatment, however, the patient lost vision on the affected eye, which did not improve even after excision of mass and treatment of the infection

Conclusion: Clinicians should be aware of the possibility of having a fungal infection mimicking other infections and tumors in immunocompetent host since prompt treatment could possibly save the vision, and, in the long run, the patient's life.

Keywords: Invasive aspergillosis; Maxillary tumor; Retro-orbital mass; Sino-orbital invasive aspergillosis

Introduction

Proptosis due to orbital pathologies have numerous causes, these may include inflammation, infection, tumors or a combination of the above. Classifying the probable cause of proptosis may appear straightforward or may be masked by multiple causes. In an era of numerous medical advancements, treatment should be guided by careful history and physical examinations and further supplemented by diagnostics and imaging, more so, in cases which seem to poorly respond to treatment.

Aspergillosis is the most common fungal infection of the paranasal sinuses; it is also a group of fungal infections with the causative agent coming from the Aspergillus genus. Invasive aspergillosis is a disease wherein fungal spores are inhaled and spread in the nasopharynx and paranasal sinuses. This condition is usually predisposed by an immunocompromised state, diabetes mellitus and human immunodeficiency virus (HIV) infection. Prolonged antibioitic, steroid, anti-neoplastic and immunosuppressive drugs have also been identified as predisposing factors to this infection.

We present a case of an immunocompetent 19-year-old male with no comorbidities, presenting with unilateral orbital proptosis, pain and blurring of vision, previously treated as a case of orbital cellulitis. Computed tomography (CT) scan showed a maxillary mass with orbital extension and excision biopsy yielded granulomatous invasive aspergillosis, which was, treated with complete excision and anti-fungal medications, however, no improvement of vision even after medical and surgical treatment.

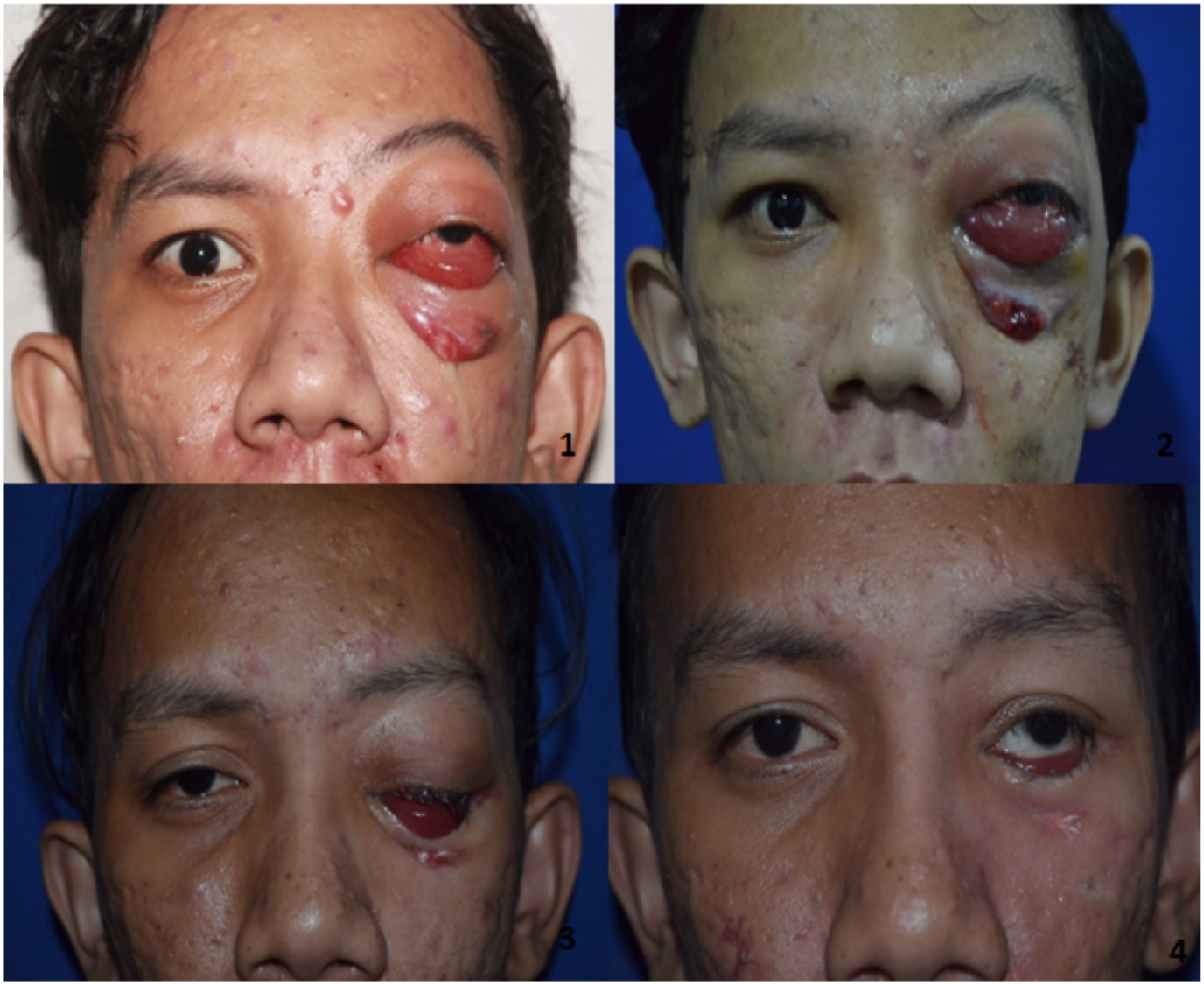
Case Report

A 19-year-old male, with a 6-month history of gradually enlarging fluctuant mass approximately 8 × 8 mm in size was noted inferior to the lower eyelid on the left maxillary area with associated pain (4/10, non-radiating), erythema, rupturing spontaneously with bloody and purulent discharge. He consulted a local doctor after the spontaneous rupture of mass, which, as reported, did not cause the mass to shrink and was treated as a case of preseptal cellulitis and was given co-amoxiclav 625 mg/tab TID for 7 days with no improvement. Another consultation was done 2 months later due to gradual increase in size and non-resolution of above mentioned symptoms, with development of facial numbness with intermittent episodes of pain, gradual proptosis and blurring of vision of the left eye. Extraocular movement was reportedly still full with no note of diplopia. He was diagnosed to have an abscess and was again treated with co-amoxiclav 625 mg/tab TID for 7 days, still with no improvement of symptoms. On follow-up, 5 months after the onset of symptoms, no improvement was noted and the blurring of vision of the left eye with proptosis worsened. MRI of the orbit and sinuses was performed for further management [1-5].

Results

Initially, the patient had a visual acuity (VA) of 20/20 for the right eye, and 20/40 improved to 20/30-2 for the left eye via Snellen chart. The left eye was immobile, proptosed by 3 mm compared to the right, and also displaced superiorly and temporally. There was chemosis and lagophthalmos (Figures 1-4). The left pupil was sluggish with a grade 3 RAPD. Intraocular pressure (IOP) on the left was slightly increased (with a reading of 23/24/25 mmHg by rebound tonometry). Slitlamp

and fundus findings were normal for both eyes. Systemic findings were unremarkable.



Figures 1-4 : 1) Day 1. Patient admitted in Institution with IV Therapy of Piperacillin-Tazobactam. 2) Day 18. Development 3 days post Excision biopsy via inferior Orbitotomy, subciliary approach. 3) Day 130. Patient on follow-up and 58 days post Maxillary sinus debulking via Caldwell Luc approach. 4) Day 228. Patient on follow-up with no proptosis noted.

Diagnostic tests were ordered such as complete blood count, urinalysis, chest x-ray, Mantoux skin test, electrolytes, fasting blood glucose, Venereal Disease Research Laboratory (VDRL), HIV status were ordered showing normal results.

On the 7th day of admission the patients vision on the left eye has diminished to a VA of 20/100 with intraocular pressure still at 23 mmHg. The patient was able to undergo imaging, and the CT scan showed a fairly homogenous mass occupying the entire left maxillary sinus, with erosion of the orbital floor and medial wall to invade the ethmoids and the orbit. The globe was deformed and was displaced anteriorly, superiorly and temporally (Figures 5-7).

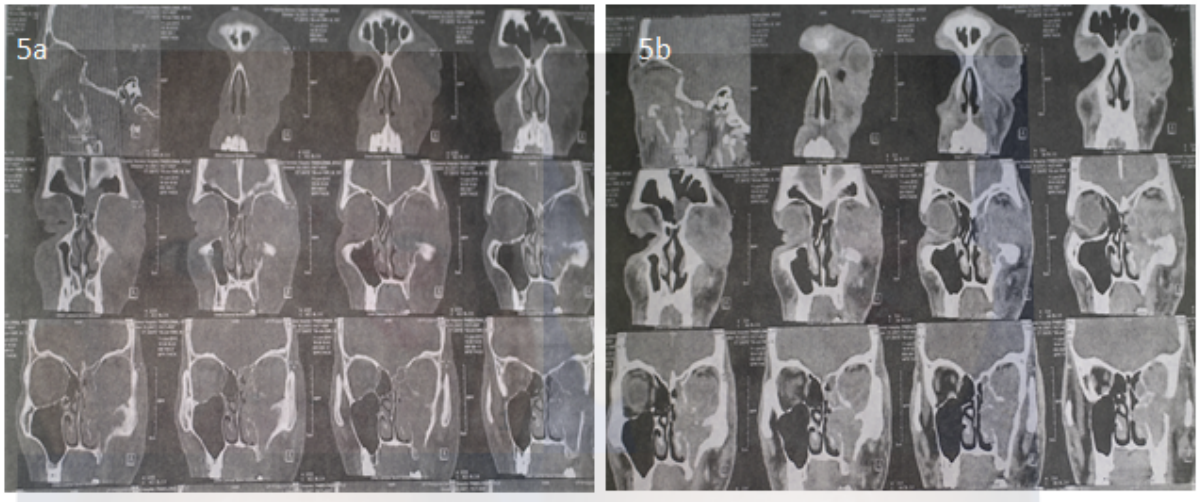


Figure 5: (a) Facial CT scan with Orbital cuts, Coronal View, Bone window showing lysis of bone and tissue invading the maxillary and nasal sinus with extension to the left orbit **(b)** Facial CT scan with Orbital cuts, Coronal View, showing lysis of bone and tissue invading the maxillary and nasal sinus with extension to the left orbit.

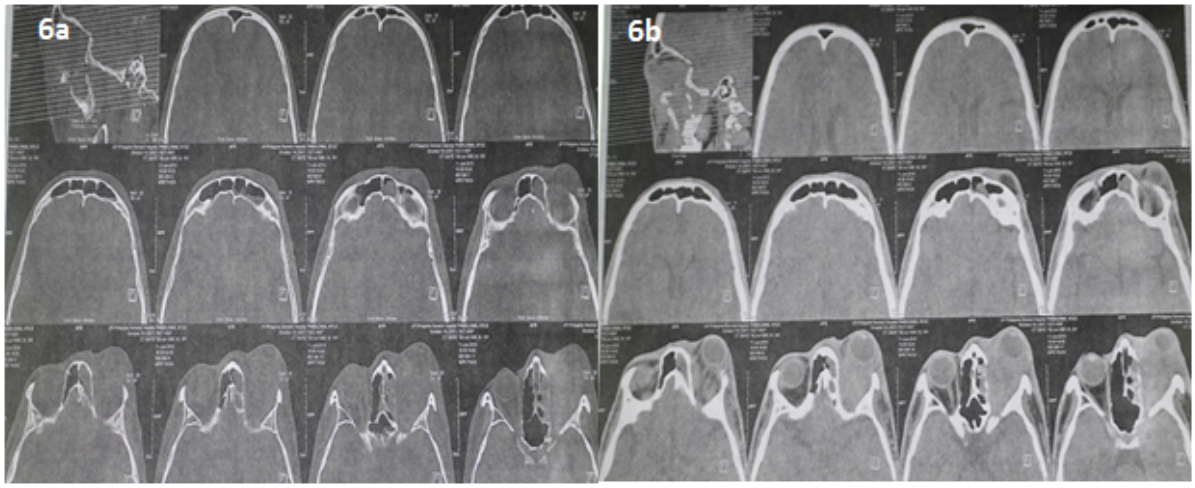


Figure 6: (a) Facial CT scan with Orbital cuts, Axial View, bone window showing proptosis of globe **(b)** Facial CT scan with Orbital cuts, Axial View, showing proptosis of globe with soft tissue occupying the retroorbital area.

A maxillary sinus malignancy was the primary working impression at this point, however, no mass was seen via endoscopy. The patient underwent section biopsy with debulking via inferior orbitotomy; subciliary incision was done (day 15) (Figure 8). At this time, the visual acuity was already No light perception owing to the prolonged compression of the orbital. Histologic examination was done, showing numerous hyphal elements interspersed with normal, granulation and necrotic tissue (Figures 9-11). This was signed out as invasive aspergillosis. A diagnosis of Sino-Orbital invasive aspergillosis was given based on the clinical and histopathologic findings. Patient underwent maxillary sinus debridement via Caldewell Luc approach (day 72) was treated with IV amphotericin B 0.8 mg/kg/day for 42 days and 2 months treatment of oral Voriconazole 200 mg BID was given. The patient on follow-up (day 228) (Figure 4) had no signs of proptosis, VA is no light perception, no pain and with normal IOP of both eyes.

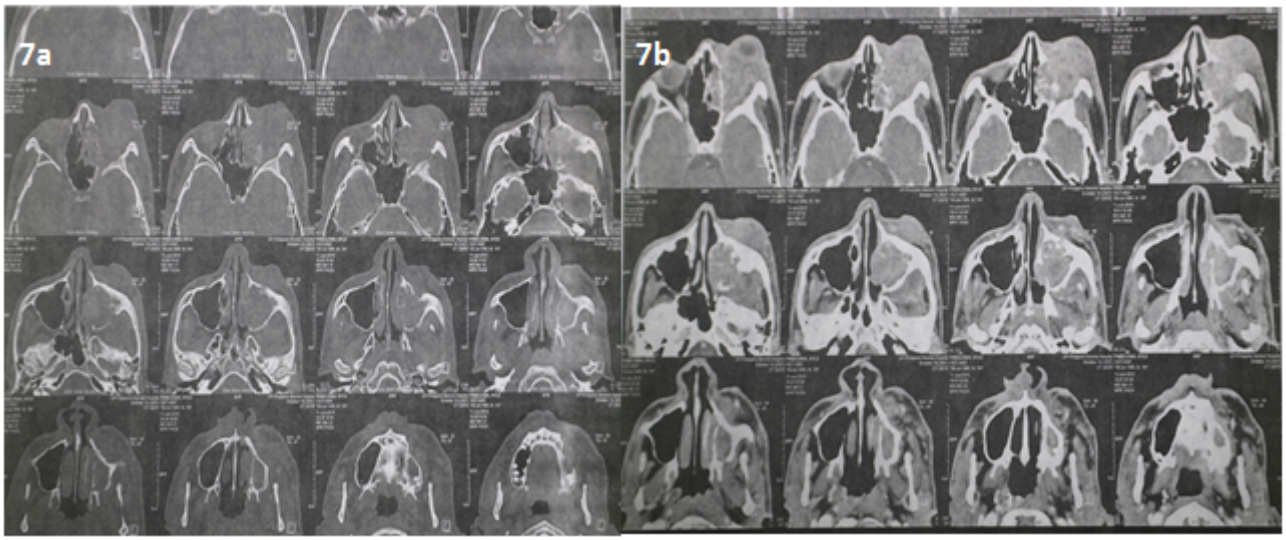


Figure 7: (a) Facial CT scan with Orbital cuts, Axial View, bone window showing proptosis of globe and maxillary sinus and ethmoid bone lysis **(b)** Facial CT scan with Orbital cuts, Axial View, showing proptosis of globe and maxillary sinus and ethmoid bone lysis and homogenous mass occupying the retroorbital area and maxillary sinus.

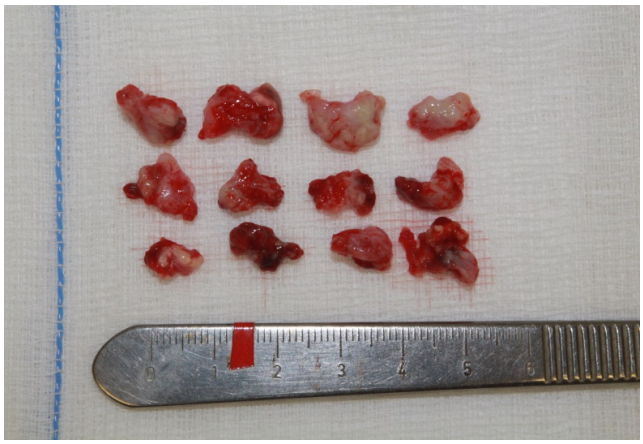


Figure 8: Tissue removed via Inferior Orbitotomy. Multiple, firm, cream white tissue with aggregate diameter of 28 mm.

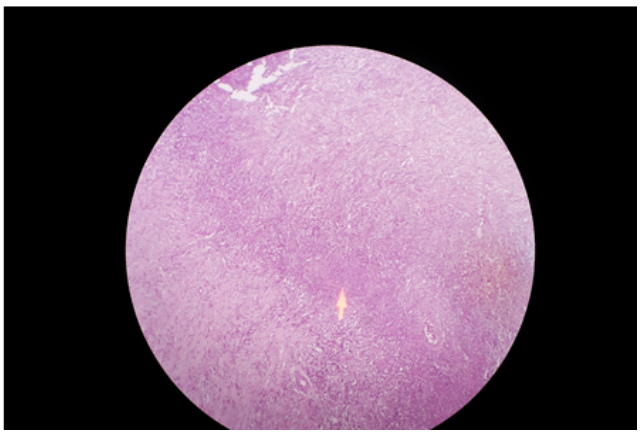


Figure 9: H&E stain of orbital mass at 10x magnification. Demonstrates widespread hyphal elements across normal and necrotic tissue, indicative of invasion.

Discussion

The incidence of Invasive sino-orbital aspergillosis in immunocompetent patients is rare, with only 21 cases found in the English literature since 1966 [6]. Aspergillosis often presents with vague complaints and the absence of clinical findings, making diagnosis difficult. Subsequently, treatment may be delayed, or steroids may be inappropriately given thereby accelerating the disease [2,5,6].

Presenting symptoms for these cases may include; unilateral facial or retrobulbar pain that eventually becomes sharp, constant, and severe enough to require narcotic analgesics. The pain antecedes ophthalmic signs and is consistent with a lesion arising in the sphenoid sinus, which commonly is the site of origin. This presentation suggests a long differential diagnosis, including other infectious, inflammatory, neoplastic, vascular, and neuro-ophthalmic disorders [5-9].

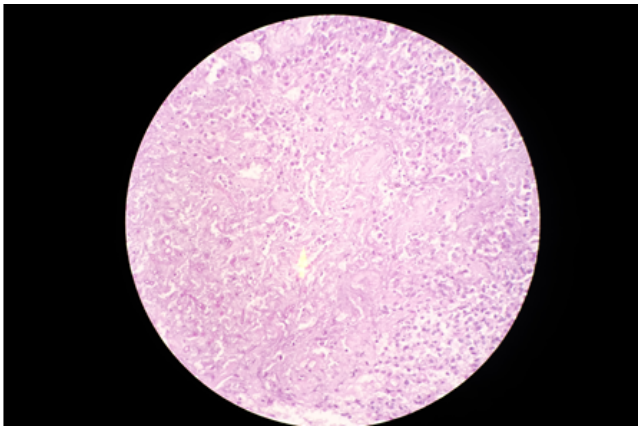


Figure 10: PAS stain of orbital mass at 40x magnification. Noted Hyphal elements surrounding granulation tissue and normal tissue.

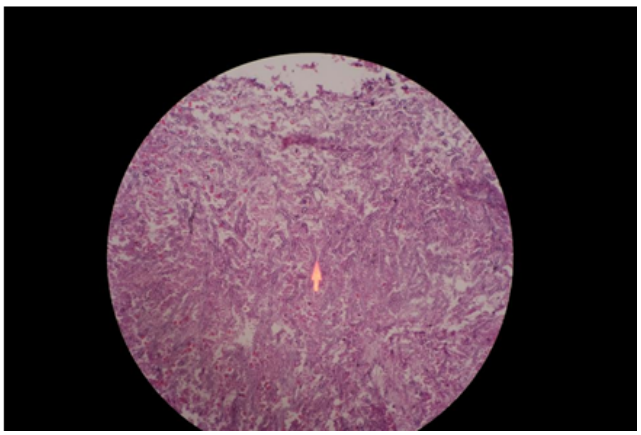


Figure 11: H&E stain of orbital mass at 40x magnification. Note that there are hyphal elements scattered around blood and soft tissue. Aspergillus hyphae have a uniform thickness and typically branch at a 45 degree angle. Also noted are spores found at the superior portion of the slide.

Some of these lead to corticosteroid administration, which worsens aspergillosis infection. In the study conducted by Choi and Choi, 3 patients in the case series were initially treated with high dose steroids for several months since biopsy results showed inflammatory reaction without fungal growth. This caused progression of the disease since further immunosuppression occurred and the infection was not addressed properly, ultimately, giving the patients poor prognoses [5].

Once the infection spreads to the orbit, patients manifest adnexal/orbital signs, often losing all vision over 5-10 days. Ultimately, cavernous sinus and other contiguous structures may be invaded [5].

Aspergillosis is the most common fungal infection of the paranasal sinuses; it is also a group of fungal infections with the causative agent coming from the aspergillus genus. Primary risk factor for Invasive Aspergillosis is Neutrophil Defects and Corticosteroid use; other predisposing conditions include HIV infection, diabetes mellitus, use of prosthetic devices, excessive environmental exposure and possibly advanced age [6].

Invasive rhinosinusitis caused by aspergillus could be further classified into 3 types: acute invasive fungal rhinosinusitis (fulminant), chronic invasive fungal rhinosinusitis, and granulomatous invasive fungal rhinosinusitis (Table 1).

Acute Invasive Fungal Rhinosinusitis	**Granulomatous Invasive Fungal Rhinosinusitis**	**Chronic Invasive Fungal Rhinosinusitis**
Less than 4 weeks to develop	Develops after 12 weeks	Develops after 12 weeks
Commonly affects Immunocompromised	Immunocompetent	Immunocompromised
Histopathology findings:		
Invasion of blood vessels such as the cavernous sinus and carotid arteries, vasculitis, thrombosis, hemorrhage and tissue infarction	Non-caseating granuloma with Langhans-type giant cells, vascular proliferation, vasculitis and perivascular fibrosis	Dense accumulation of hyphal elements, occasional invasion of blood vessels and surrounding tissue

Table 1: Types of Invasive Fungal Rhinosinusitis.

Acute invasive aspergillosis usually takes less than 4 weeks to develop, which commonly affects the immunocompromised, however, there are documented cases wherein immunocompetent individuals have been affected. Invasion of blood vessels such as the cavernous sinus and carotid arteries, vasculitis, thrombosis, hemorrhage and tissue infarction are the histopathologic evidences for this disease entity.

Granulomatous invasive fungal sinusitis and chronic invasive fungal rhinosinusitis both take a longer course which develops after 12 weeks with only the histopathological findings separating these disease entities. In Chronic invasive fungal rhinosinusitis, dense accumulation of hyphal elements, invasion of blood vessels and surrounding tissue are seen, while, in granulomatous invasive fungal rhinosinusitis, non-caseating granuloma with Langhans-type giant cells, vascular proliferation, vasculitis and perivascular fibrosis. Granulomatous invasive type usually occurs in the immunocompetent while chronic invasive fungal rhinosinusitis occur in the immunocompromised [6, 9].

According to Sivac-Calcott et al. CT is superior to magnetic resonance imaging (MRI) for evaluating the sinonasal anatomy and identifying the surgical landmark. The imaging findings of chronic and granulomatous types are similar. These findings are analogous to those of malignant lesions and include bony destruction and extension beyond the sinus, which was also demonstrated in this case. By contrast, the acute type is occasionally associated with very subtle and no significant bone destruction and mucosal thickening compared to the other types of invasive fungal rhinosinusitis.

As proven by the imaging and histopathology, the diagnosis of the patient is Granulomatous Invasive fungal Rhinosinusitis with orbital extension. Compared to the acute and chronic type of invasive fungal rhinosinusitis, the granulomatous type will have good results with surgery alone, however, recent journals note that a combination of: (a) Surgical debridement of affected area, (b) aeration, and (c) antifungal agents is best. Prognosis is generally poor for invasive fungal

rhinosinusitis due to high relapse rate, however, the granulomatous type responds better compared to the acute and chronic type [5,10].

Acute and Chronic Invasive fungal rhinosinusitis is treated by surgical removal of the affected area with administration of anti-fungal agents such as; IV amphotericin B (0.8 mg/kg/day) or voriconazole (200 mg BID), with treating the underlying condition which causes the immunosuppression [6,10].

Conclusion

Invasive fungal disease can mimic other conditions, and is not generally suspected in healthy individuals. Once present, the immune status of the patient must be established, and the disease treated with a combination of surgical and medical measures.

References

1. Nucci M, Marr KA (2005) Emerging Fungal Infections. Clin Infect Dis 41: 521-526.
2. Badiee P, Hashemizadeh Z (2014) Opportunistic invasive fungal infections: diagnosis & clinical management. Indian J Med Res 139: 195-204.
3. Nahar S, Pillai AK, Kumar JA, Goyal N, Singh SK, et al. (2013) Orbital Invasive Aspergillosis – A Rare Fungal Infection of Eye. International Journal of Scientific Study 1.
4. Kim TH, Jang HU, Jung YY, Kim JS (2012) Granulomatous Invasive Fungal Rhinosinusitis extending into the pterygopalatine fossa and orbital floor: A case report. International Society for Human and Animal Mycology.
5. Choi HE, Choi JY, Yoon JS, Kim SJ, Lee SY (2008) Clinical Characteristics and Prognosis of Orbital Invasive Aspergillosis. Ophthalmic Plastic and Reconstructive Surgery. 24: 454-459.
6. Sivak-Callcott JA, Livesley N, Nugent RA, Rasmussen SL, Saeed P, et al. (2004) Localised Invasive Sino-Orbital Aspergillosis: Characteristics Features. Br J Ophthalmol 88: 681-687.
7. Middlebrooks EH, Frost CJ, De Jesus RO, Massini TC, Schmalfuss IM, et al. (2015) Acute Invasive Fungal Rhinosinusitis: A Comprehensive Update of CT Findings and Design of an Effective Diagnostic Imaging Model. AJNR Am J Neuroradiol 36:1529-1535.
8. Valera FC, do Lago T, Tamashiro E, Yassuda CC, Silveira F, et al. (2011) Prognosis of acute invasive fungal rhinosinusitis related to underlying disease. Int J Infect Dis 15: e841-e844.
9. Gupta AK, Lynrah ZA, Kalsotrika G (2009) Invasive Sino-Aspergillosis in Immunocompetent Individuals: Atypical Presentation. Clin Rhinology 2: 27-31.
10. Kim TH, Jang HK, Jung YY, Kim JS (2012) Granulomatous invasive fungal rhinosinusitis extending into the pterygopalatine fossa and orbital floor: A case report. Medical Mycology Case Reports 1: 107-111.