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An Invasive Aspergillosis with Large Orbital Abscess with Intracranial Extension in HIV Infection: A Case Report

รายงานผู้ป่วยโพรงหนองขนาดใหญ่บริเวณเบ้าตาร่วมกับการลุกลามในสมองจากการติดเชื้อราแอสเปอร์จิลลัสแบบรุนแรงในผู้ป่วยติดเชื้อเอชไอวี

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Abstract

Objective: To report an unusual finding of orbital invasive aspergillosis with intracranial involvement

Methods: We report a 40-year-old Thai female with human immune deficiency virus (HIV) infection presented with 1 month of left painful proptosis and complete visual loss. Orbital magnetic resonance imaging (MRI) depicted large abscess at posteromedial part of left orbit with intra-cranial involvement, and ipsilateral ethmoid sinusitis. Orbital abscess was urgently drained.

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Results: Tissue biopsy from wall of the abscess revealed fungal hyphae which was confirmed as Aspergillus fumigatus from pus culture. Although prompt systemic antifungal drugs and aggressive sinus debridement were performed, patient underwent orbital exenteration.

Conclusions: This case demonstrates a large orbital abscess with intra-cranial involvement, an uncommon finding of invasive aspergillosis which might misdiagnose as other infection. Early tissue diagnosis should be done for the proper treatment.

Keywords: aspergillosis, fungal infection, orbital abscess, orbital infection, invasive aspergillosis

บทคัดย่อ

วัตถุประสงค์: เพื่อรายงานอาการโพรงหนองในเบ้าตาและการลุกลามในสมอง ซึ่งพบได้น้อยในผู้ป่วยติดเชื้อราแอสเปอร์จิลลัส

วิธีดำเนินการ: รายงานผู้ป่วยหญิงไทยอายุ 40 ปี ติดเชื้อเอสไอวี มาตรวจด้วยอาการปวดบริเวณเบ้าตาซ้าย ตาโปน และตามัวลงประมาณ 1 เดือนก่อนมาโรงพยาบาล จากการตรวจด้วยเครื่องสร้างภาพด้วยสนามแม่เหล็กไฟฟ้าพบโพรงหนองขนาดใหญ่ที่บริเวณเบ้าตาซ้าย ในบริเวณสมอง และในโพรงจมูกเอดมอยด์ ผู้ป่วยได้รับการผ่าตัดระบายหนองทันที

ผลการศึกษา: ผลการตัดชิ้นเนื้อผนังโพรงหนองไปตรวจทางพยาธิพบเชื้อรารูปแท่งซึ่งเพาะเชื้อเข้าได้กับเชื้อราแอสเปอร์จิลลัส ฟูมิกาตัส แม้ผู้ป่วยจะได้รับยาต้านเชื้อราและได้รับการทำผ่าตัดเอาเนื้อเยื่อในโพรงจมูกที่ติดเชื้อออกอย่างเร่งด่วน สุดท้ายแพทย์จำเป็นต้องผ่าตัดเอาลูกตาและเนื้อเยื่อรอบดวงตาออก

สรุป: โพรงหนองบริเวณเบ้าตาและมีการลุกลามในสมองเป็นสิ่งที่พบได้น้อย ซึ่งอาจได้รับการวินิจฉัยคลาดเคลื่อนว่าเกิดจากเชื้ออื่นได้ การเจาะระบายหนองและส่งชิ้นเนื้อตรวจทางพยาธิตั้งแต่ระยะแรก จะช่วยให้เกิดการรักษาที่ถูกต้องได้

Keywords: aspergillosis, fungal infection, orbital abscess, orbital infection, invasive aspergillosis

Introduction

Aspergillosis is a fungal infection caused by Aspergillus species. Non-invasive aspergillosis such as allergic rhinosinusitis and aspergilloma occurs among immunocompetent hosts but invasive and fulminant types are commonly found in immunocompromised patients[1]. The fungus enters the blood stream to the brain or to other organs causing disseminated disease. Orbital involvement worsens the prognosis because of ready availability of pathways for further intracranial spread, such as superior orbital fissure, optic canal that direct to the intracranial space. In general, most of orbital aspergillosis were related to a typical fungal mass or invasive lesion extended from sinus[2] rather than an abscess. Here, we report a rare presentation of orbital abscess with intra-cranial extension from invasive aspergillosis in HIV patient.

Case Report

A 40-year-old Thai female presented with a 1-month history of retro-orbital pain and proptosis on her left eye. Her medical history included 1-year diagnosis of HIV infection without antiretroviral therapy due to ongoing treatment of active pulmonary tuberculosis infection. She was in conscious, looked cachexia. Eye examination revealed 20/40 vision in the right eye and counting fingers at 1 foot with positive relative afferent pupillary defect in the left eye. Proptosis with exophthalmometer measurement 14 mm. right eye and 17 mm. left eye (base 98 mm.), complete ptosis, total ophthalmoplegia and eyelid swelling were found on the left side, but normal lower eyelid and cheek sensation. Anterior segments were unremarkable, but decrease corneal sensation in left eye. The posterior segment of right eye showed exudate and hemorrhage at the posterior polar area suggesting a cytomegalovirus infection. On the other hand, the fundus and optic disc of left eye looked pale without swelling. Tortuous retinal vessels were presented. Blood examination showed anemia (Hemoglobin 8.2 g/dl), platelet count 387,000/ml, negative results for serum cryptococcal antigen, aerobic hemoculture, sputum AFB and modified AFB. Her HIV viral Load was 2412 copies/ml. Absolute CD4 count was 35 cells/mm^3. MRI brain and orbit revealed a 3.0x2.2x1.8 cm. irregular rim enhancing intraconal lesion at posterior aspect of left globe encasing the optic nerve, inhomogeneous intermediate intensity on contrast-enhanced T1-weighted images (Figure 1a, 1b), a 3.0x2.8x2.0 cm. lesion with hyperintensity on T2-weighted images visualized at left frontal lobe. A minimal hemorrhage in an affected brain parenchyma was suspected (Figure 2a, 2b). Intravenous ganciclovir for right CMVR was given. The patient underwent left anterior orbitotomy with abscess drainage promptly.

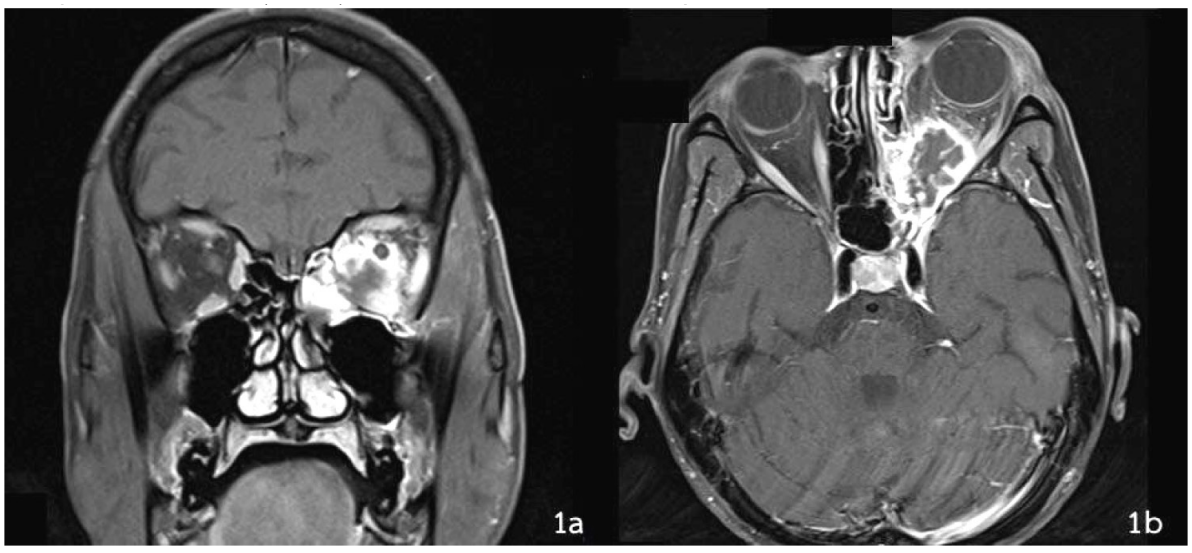

Figure 1 **a:** and **b**: Coronal and axial contrast-enhanced T1-weighted MR image shows an irregular peripheral contrast enhancing lesion in left orbit, involving both intra- and extraconal spaces, encasing left optic nerve, associated with thickened enhanced mucosa of nearby ethmoid sinus

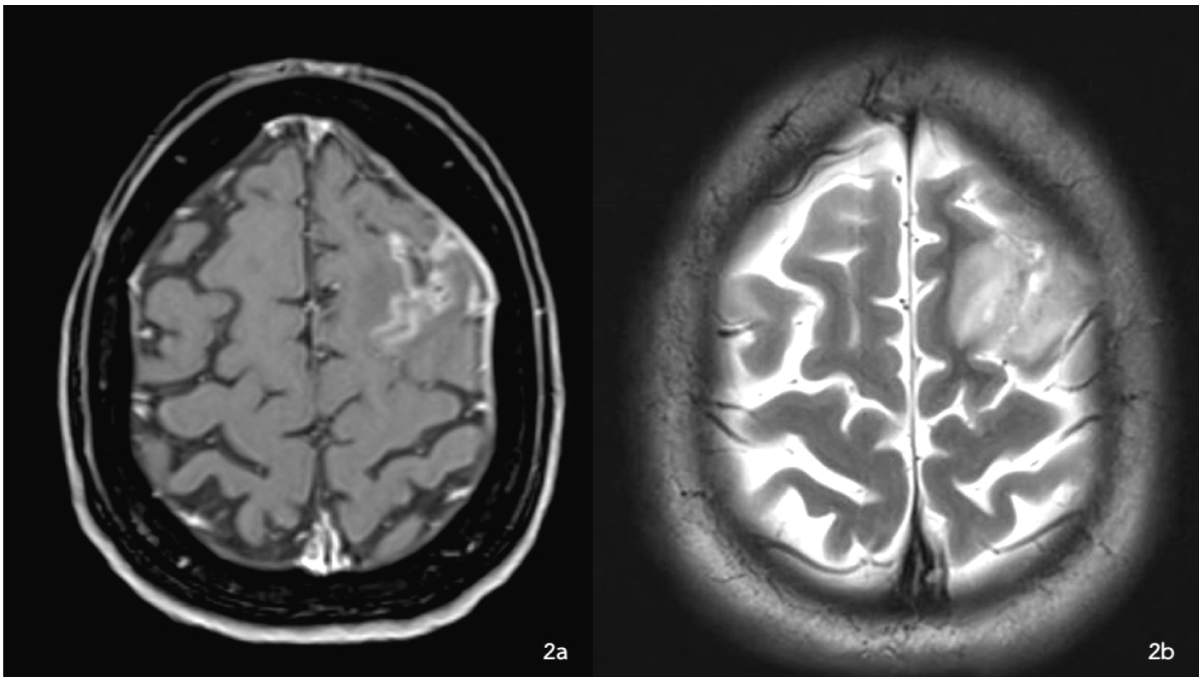

Figure 2 **a:** and **b:** Axial contrast-enhanced T1-weighted MR image and T2-weighted MR image shows an irregular contrast enhancing lesion involving left high frontal lobe and adjacent cortical sulci, associated with vasogenic edema of adjacent brain

Intraoperative findings showed whitish, debris tissue with minimal pus underneath the globe. Intravenous amoxycillin/ clavulanic acid were prescribed after drainage. However, 30 mg/day intravenous amphotericin B was started on the third day of admission after KOH stain and initial report from hematoxylin and eosin histopathologic findings were reported. Histopathological study showed massive septate fungal hyphae branching at 45 degrees angle with positive Gomori's Methenamine Silver (GMS) stain. (Figure 3a, 3b). Pus culture yielded Aspergillus fumigatus and with positive serum galactomannan antigen test. Although the degree of proptosis seemed to be stabilized, left vision was diminished to no light perception. On admission day 8, the patient underwent endoscopic sinus surgery for tissue debridement and retro-bulbar amphotericin B injection. Tissue histopathology was the same. Despite aggressive anti-fungal drugs and debridement, the lesion has become greater in size with extended fluid collection in the left frontal sinus, bilateral ethmoid, sphenoid and maxillary sinuses in a follow-up imaging. Exenteration of left eye with further paranasal sinus debridement were performed on admission day 15. Whitish frail and solid tissue with ill-defined border was found adhering to the optic nerve intraoperatively. The same histopathological pattern was found. One week after exenteration, fever has subsided and the surgical wound was gradually healed with granulation tissue formation. Intravenous amphotericin B was switched to 5 mg/kg of oral voriconazole every 12 hour on admission day 27. Unfortunately, 1 month after discharge from the hospital, patient died from multi-organ failure.

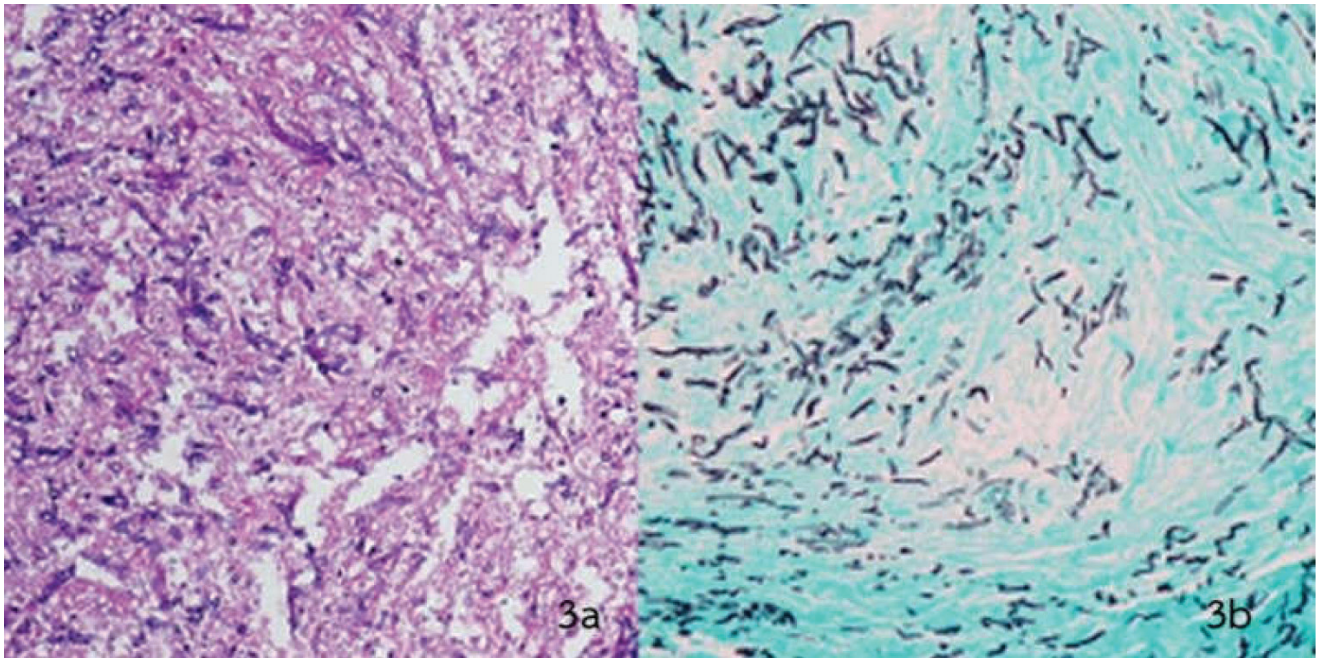

Figure 3 **a:** and **b:** Photomicrograph of the surgical specimen stained with hematoxylin and eosin reveals findings of septate, acute-angle branching aspergillus hyphae invading tissue with confirmed by GMS stain in 3b

Discussion

Invasive aspergillosis is a fungal infection which occurs in many organ system. Rhino-orbital area is one most common site of infection which can extend to the orbit and the brain. Visual deterioration, proptosis and orbital pain as the presented case are common presentations of orbital aspergillosis[2]. Imaging is important to diagnose this disease and determine the extension of lesion. Siddiqui et al described MRI characteristic of Aspergillus mass of nasal and/or sino-nasal origin. In their series, the lesion had iso- to hypo-intense signals on T1-weighted images, intensively hypo-intense on T2-weighted images (relatively hypo-intense to muscles and neutral tissue) and bright homogenous Gadolinium enhancement[3]. Choi HS et al. also reported the similar findings[2]. Bone erosion was frequently seen[4,5]. The decreased signal intensity on a T2-weighted image was due to the presence of ferromagnetic elements such as iron, zinc, magnesium and manganese in fungal amino-acid metabolism or the dehydration effect that occurs in chronic inflammatory disease. Rarely has orbital invasive aspergillosis been described as abscess seen as a rim enhancing lesion in CT or MRI[6,7].

Tissue histopathology is crucial to confirm the diagnosis. Fungal hyphae invaded orbital tissue and vessels which was found in hematoxylin and eosin and Gomori's methenamine silver (GMS) stains. Serum galactomannan can be detected during fungal growth. These help diagnose invasive aspergillosis[2]. As the current case, patient underwent tissue biopsy and blood test which

were confirmed the diagnosis.

A few case reports described orbital invasive aspergillosis in HIV infection. Orbital lesions might be orbital mass[5], intra-orbital abscess as the current case[6,8], and orbital apex syndrome[9]. All of these cases had adjacent sinusitis which might be the origin of infection, but intracranial extension was rarely found. Our case represents an uncommon characteristic of orbital abscess caused by invasive aspergillosis with intracranial invasion. Most of them were acquired immune deficiency patients. As we know, poor immune status is an important risk factor of disease deterioration. The prognosis of this patient attributes to the status of her immune system. Timing of the diagnosis and efficient treatment are also important. Multiple therapeutic strategies were used. Recommendations have ranged from medical antifungal therapy alone to radical surgery in conjunction with systemic and local antifungal chemotherapy[10–12]. Voriconazole has become the drug of choice for the treatment of invasive aspergillosis due to lower toxicity and more tolerability compared with amphotericin B. Surgical debridement was one modality to eradicate the infection. Area of tissue debridement depended on many factors, such as extension of disease, response to medical therapy, and eye function. Orbital exenteration with paranasal debridement and irrigation might be suitable to exterminate all the fungal infected tissue in patients with poor visual prognosis after informed discussion[13]. However, aspergillosis with cerebral involvement has high mortality rates especially in immunocompromised patient[14]. Closed monitoring during medical therapy and after radical debridement are important.

In conclusion, large orbital abscess with intracranial extension in HIV infection is an uncommon finding of invasive aspergillosis. Early tissue diagnosis and prompt treatment is necessary to achieve the clinical improvement.

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