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CASE REPORT

Orbital Aspergillosis Mimicking Giant Cell Arteritis

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ABSTRAK

Penyakit aspergillosis orbit sangat jarang berlaku tetapi boleh menyebabkan neuropati optik yang sakit. Selain itu, penyakit ini mampu menyerupai giant cell arteritis terutamanya dalam kalangan pesakit tua. Kami ingin melaporkan kes aspergillosis orbit yang berlaku pada seorang lelaki Melayu berumur 65 tahun yang mengadu penglihatan yang kabur secara beransur-ansur dan sakit kepala pada bahagian yang sama. Malangnya, keadaan pesakit tersebut merosot selepas rawatan kortikosteroid dan bertukar menjadi sindrom apeks orbit. Pengimejan dan sampel biopsi menunjukkan aspergillosis orbit. Pesakit menjadi buta akibat diagnosis yang tidak tepat pada peringkat awal. Tujuan laporan ini adalah untuk mengingatkan para doktor agar sentiasa mengambil kira kepentingan epidemiologi penyakit dalam mendapatkan diagnosis yang tepat, terutama apabila pesakit mempunyai tanda-tanda yang luar biasa.

Kata kunci: aspergillosis, giant cell arteritis, kortisosteroid, neuropati optik

ABSTRACT

Orbital aspergillosis is a very rare, debilitating disease which can present solely with painful optic neuropathy and mimic giant cell arteritis in an elderly person. We report a case of orbital aspergillosis in a 65-year-old Malay man who presented with unilateral gradual blurring of vision and ipsilateral headache. Our initial working diagnosis was giant cell arteritis. Unfortunately, patient's condition worsened with intravenous corticosteroid and developed into orbital apex syndrome. Imaging and biopsy results showed evidence of orbital aspergillosis. Patient lost his eyesight due to the wrong initial working diagnosis. This report is to emphasize that although giant cell arteritis is also a sight and life-threatening condition, it is rare among

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Asian populations. We need to take into account the epidemiology of the disease and look into any other differential diagnoses when the presentation is atypical.

Keywords: aspergillosis, giant cell arteritis, corticosteroid, optic neuropathy

INTRODUCTION

Orbital aspergillosis is rare but can be potentially fatal in immunocompromised patient (Ali & Lee 2013). It can present with various vague symptoms but lack of clinical signs which makes the diagnosis difficult, leading to a delayed or inappropriate treatment. In this report, we present a case of orbital aspergillosis which mimics giant cell arteritis (GCA). The initial computed tomography imaging failed to demonstrate an early orbital apex lesion which worsened after administration of high dose corticosteroid with the initial working diagnosis of GCA.

It is well known that 90-95% of the anterior ischaemic optic neuropathy is non-arteritic in origin. It is caused by perfusion insufficiency of short posterior ciliary arteries to the optic nerve leading to visual loss. Besides that, it can also be caused by vasculitis which is known as GCA. However, GCA is very rare especially among the Asian population. It was reported to be 20 times less common in Asian than Caucasian patients (Pereira et al. 2010). In a retrospective study in Korea, it was noted the prevalence of GCA in Korean patients was very low, only contributing about 2.1% in patients who suffered from anterior ischaemic optic neuropathy. (Choi et al. 2019).

The purpose of this case report is to highlight that despite the blinding condition possibly caused by GCA which is relatively rare, clinicians should make a thorough workout and have a higher index of suspicion on other differential diagnoses, such as infection, especially in an immunocompromised patient as it can potentially become a life threatening condition if treatment involves a high dose of corticosteroid.

CASE REPORT

A 65-year-old Malay man with underlying diabetes, hypertension and ischaemic heart disease presented with a chief complaint of right eye blurring of vision for two weeks. The blurring of vision was generalised, gradual onset and progressively worsened. It was associated with right sided headache for 3 months prior to the presentation. There was no eye pain, redness, haloes or any eye discharge. Patient had nausea but no vomiting. He also had loss of appetite and he lost about 15 kg in 3 months. Patient did not have fever, chills and rigors, night sweat, chronic cough or haemoptysis. There were no constitutional symptoms. Besides that, he did not experience any jaw claudication or scalp pain. On examination, vision of right eye was counting finger with presence of

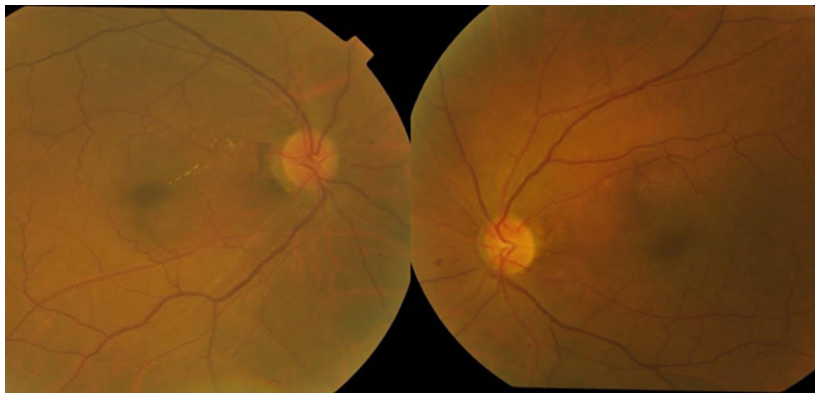

Figure 1: Fundus photo of patient during first presentation showing normal optic disc appearance

relative afferent pupillary defect on the same eye. There was also reduced optic nerve function (reduced red desaturation and light brightness). His left eye vision was good (6/6). Otherwise, patient's anterior segment appeared normal. Intraocular pressure was 10 mmHg in both eyes. The optic discs were not swollen or hyperaemic, there was no sectoral pallor seen and cup to disc ratio was 0.3 (Figure 1). Extraocular movement was full. On systemic examination, patient had prominent temporal artery over right side with mild tenderness. However, there was no loss of pulsation. His vital signs were normal with normal dextrostrix.

Systemic investigation reviewed raised total white cell count (17.2), raised platelet (511) and raised erythrocyte sedimentation rate (91) with his blood sugar level within normal range. C-reactive protein was 4.84. Computed tomography (CT) of the brain was normal.

A working diagnosis of GCA with posterior ischaemic optic neuropathy was made. Temporal artery biopsy was planned after omitting anti-platelet for five days. Meanwhile, intravenous methylprednisolone 250 mg QID was administered in the hope of preventing the fellow eye involvement. Unfortunately, after 2 days of intravenous methylprednisolone, patient's vision deteriorated to no perception of light and he developed right third nerve palsy with evidence by complete ptosis (Figure 2) and total ophthalmoplegia in which there was restricted extraocular movement in all gazes (Figure 3). The right eye pupil was dilated and anisocoria was more

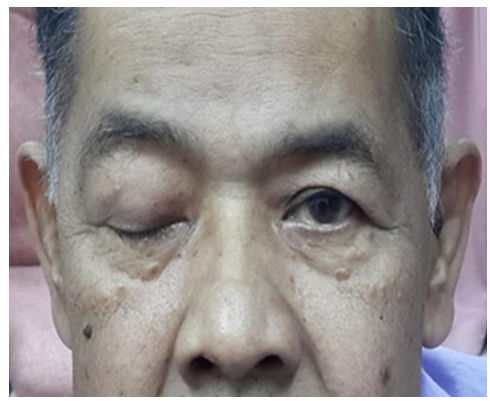

Figure 2: Photo showing right complete ptosis

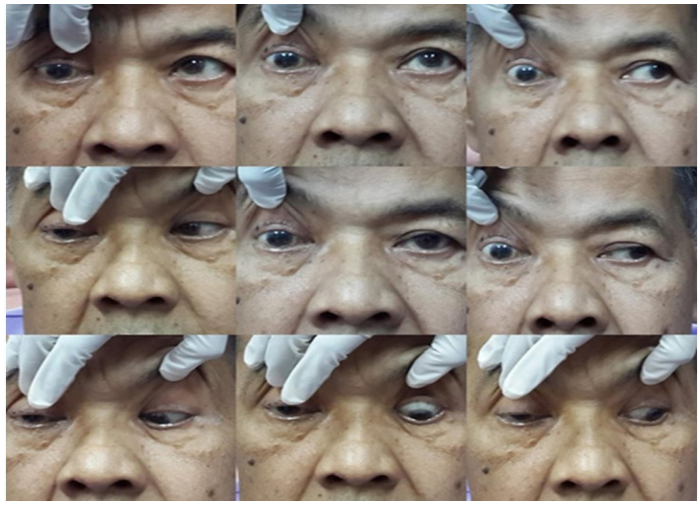

Figure 3: 9-gaze photos showing right total ophthalmoplegia

prominent in a bright room. Right tochlear, abducens and ophthalmic division of trigeminal nerve were affected as well. Other cranial nerves were normal. In view of sudden onset of right sided multiple cranial nerve palsy, patient was arranged for magnetic resonance imaging (MRI) of the brain and orbit. MRI of brain and orbit showed right orbital apex enhancing lesions causing crowding of orbital apex with extension into inferior aspect of right cavernous sinus and into the right inferior orbital fissure and pterygopalatine fossa (Figure 4). There was mucosa thickening of right posterior ethmoidal, sphenoid, maxillary sinus, as shown in the MRI as well as CT scan of paransasal sinuses (Figure 5). IV methylprednisolone was discontinued and patient was referred to the otorhinolaryngologist. Right endoscopy was performed under general anaesthesia and showed fungal

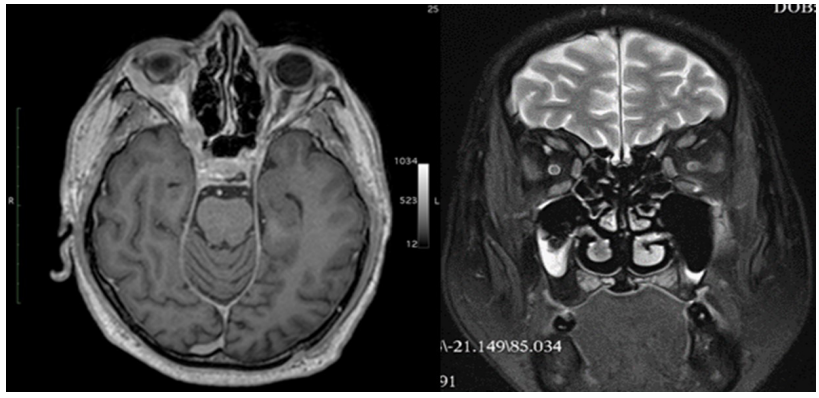

Figure 4: MRI brain/orbit of patient after commencement of high dose corticosteroid. Left: Enhancing lesion crowding right orbital apex. Right: Mucosal thickening of maxillary sinuses

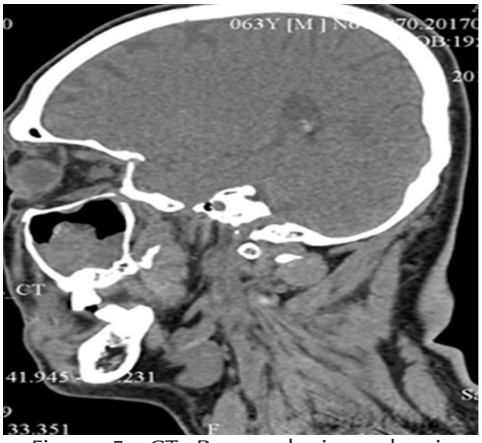

Figure 5: CT Paranasal sinus showing marked mucosa thickening of right maxillary sinus with almost circumferential enhancing mucosal layers and specks of calcification highly suggestive of fungal sinusitis.

ball over the right maxillary sinus which had breached the lamina papyracea. Biopsy of the mass was taken and histopathological examination reviewed hyphae, with the culture yielding *Aspergillus fumigaitus*.

With the diagnosis of orbital apex syndrome secondary to aspergillosis, patient was started with intravenous variconazole. Patient was then maintained with oral itraconazole. He responded well, however, vision remained as no light perception and he developed hospital acquired pneumonia. Fortunately, he recovered and was discharged home.

DISCUSSION

GCA is a systemic vasculitis which involves medium to large sized vessels, most commonly the extracranial branches of carotid arteries usually in patients above 50 years old (Calvo-Romero 2003). The incidence of GCA ranges from 0.5-27 cases in 100,000 people aged above 50 years old, with higher incidence among the Scandinavian countries and North American population (Borchers & Gershwin 2012). It is twice more common in women than men with HLA-DR4 haplotype as the genetic predisposition (Chew et al. 2009). The lower incidence observed in Asian population implies that environment and genetic factors play an important role in pathogenesis of GCA (Pereira et al. 2010). Epidemiology is a crucial tool to assess the environmental and genetic risk factors when it comes to a list of differential diagnoses (Choi et al. 2019).

GCA is a cell-mediated immune response in which it causes the destruction of blood vessel wall, ultimately leading to vascular stenosis or occlusion. Common clinical manifestations of GCA are low grade fever, constitutional symptoms, headache, abnormal temporal arteries, jaw claudication, amaurosis fugax, irreversible blindness and polymyalgia rheumatica. There are five criteria listed by the American College of Rheumatology for the diagnosis of GCA, which are age at onset more than 50 years old, new and persistent headache, temporal arteries abnormalities, erythrocyte sedimentation rate more than 50 mm per hour and a positive temporal artery biopsy (Hunder et al. 1990). In our patient, 4 criteria were fulfilled despite being unable to perform a temporal artery biopsy; thus, an initial diagnosis of GCA was made.

However, this patient did not have

typical symptoms of GCA such as scalp tenderness and jaw claudication with no symptoms of polymyalgia rheumatic. Although his temporal artery was prominent, it was not pulsatile. During the presentation, patient came with poor vision and positive relative afferent pupillary defect, but did not have the typical chalky white disc or optic disc swelling. His optic discs appeared to be normal. Hayreh (1990) reported that in patients with GCA, 80% of them loss their vision due to anterior ischaemic optic neuropathy. There are 10% of patients that develop central retinal artery occlusion whereas only less than 5% of cases presented with posterior ischaemic optic neuropathy, in which optic disc appearance is normal. Hence, the diagnosis of GCA should be re-evaluated before the administration of intravenous corticosteroid.

Our patient did not have temporal artery biopsy done due to his bleeding tendency secondary to anti-platelet consumption. However, it is not necessary for patient to have a negative biopsy to rule out GCA as previously there were cases with negative temporal artery biopsy reported (Saedon et al. 2012). As a result, patient was treated with intravenous methylprednisolone before the temporal artery biopsy with the intention to protect the fellow eye from having the similar attack. Unfortunately, he developed multiple cranial nerve palsy which involved oculomotor, trochlear, abducens and ophthalmic branch of trigeminal nerve after the commencement of steroid. GCA can manifest as an ocular motility problem infrequently, but multiple cranial nerve involvement should warrant a repeated imaging. Brain MRI of the patient in this case showed right orbital apex enhancing lesions which corresponded to the clinical findings if the biopsy of the fungal ball in orbital apex, which was as confirmed *A. fumigatus*.

Previously, there were similar cases reported in the western countries in which orbital aspergillosis has been misdiagnosed as GCA. Most of the cases presented symptoms of headache and vision loss and their initial CT-scans were also normal (Zhou et al. 2016). Clinicians should consider the possible diagnosis of orbital aspergillosis if patient is in an immunocompromised state such as diabetes mellitus, leukaemia, acquired immunodeficiency syndrome (AIDS), prolonged systemic immunosuppressant, excessive environmental exposure and advanced age (Levin et al. 1996). In our patient, he has diabetes and advanced age as risk factors. Besides that, persistent symptoms or deteriorating vision despite optimal immunosuppressive treatment should alert the clinician that it could be an orbital aspergillosis rather than a GCA (Ali et al. 2013). Negative temporal artery biopsy was unable to rule out GCA but should make the clinician reconsidering other possible diagnosis.

Most of the time, *Aspegillus sp.* is considered a harmless organism that can be found anywhere in the environment. It does not usually cause an infection in immunocompetent human (Kamble et al. 2015). Orbital aspergillosis can either non-invasive

or invasive. Examples of be of a non-invasive type, such as sinonasal aspergilloma and allergic aspergillus sinusitis. It may destruct the mucosa and cause bony expansion but there will be no invasioninto the bone or adjacent tissue. On the other hand, invasive type can be localised or of the fulminant form. Localised invasive infection can cause bony erosion and can spread through blood vessels, causing stroke and death. Bony erosion can be due to pressure necrosis or destruction by the mediators released in the process of inflammation (Sivak-Callcott et al. 2004). If there are multiple organ involvement, it is considered as a fulminant form with the pulmonary infections being most common. Other organs which can be involved are the brain, orbit and paranasal sinuses (Levin et al. 1996). In our case, the patient had a localised, invasive orbital aspergillosis.

Neuroimaging is mandatory in cases of orbital apex syndrome secondary to infection. It is helpful in differentiating orbital aspergillosis from other diagnosis with similar presentation. CT scan is best used to evaluate bony structures and paranasal sinuses. Typical finding on the CT scan is heterogeneous soft tissue lesion with calcification and bony erosions (Johnson et al. 1999). MRI is preferable to visualise the soft tissue involvement with focal enhancement of the lesion (Ali et al. 2013). More recently, orbital MRI has been used as an adjunct in the diagnosis of GCA. The most characteristic pattern of enhancement is the perineural enhancement in GCA which is less common in other types of optic neuropathy (Serrano Alcalá et al. 2020). Besides imaging, biopsy is important for a definitive diagnosis. It can be sent for fungal culture to isolate *Aspergillus,* which is the gold standard (Sivak-Callcott et al. 2004). A potassium hydroxide test can be performed to look for hyphae while awaiting biopsy result (Johnson et al. 1999). However, clinicians should bear in mind that the diagnosis could be difficult and sometimes repeated biopsies are required if clinical suspicious is high. (Sivak-Callcott et al. 2004)

Primary treatment for orbital aspergillosis should be surgical debridement and systemic anti-fungal medications (Johnson et al. 1999). If the disease is extensive, surgical debridement might not be feasible. Clinicians should keep in mind that debridement may not totally eradicate the lesion, especially when the extend of the lesion is not well defined. Studies have shown that medical therapy alone is as effective as combined therapy (Marr et al. 2004). Currently intravenous amphotericin B remains the primary choice of antifungal agent in treating this infection. However, it should be discontinued if presence of toxic side effects on the kidneys. Liposomal amphotericin B and variconazole are the newer medication with less side effects (Hay 1994). Both of them were shown to be effective against aspergillosis. Another alternative therapy is oral itraconazole which is a synthetic triazole. It can be used in patients who are unable to tolerate amphotericin B with the results being comparable (Denning et al. 1994). Furthermore, intralesional injection

of amphotericin B can be a palliative option in patients who are not fit for surgery (Cahill et al. 1994). There is no optimal duration of antifungal therapy in orbital aspergillosis but it should be continued until the fungus is totally eradicated (Sivak-Callcott et al. 2004). Aspergillosis has a very poor prognosis in which many patients pass away due to the disease despite surgical debridement and systemic antifungal treatment. Most of them died as a result of intracranial extension (Teh et al. 1995).

CONCLUSION

Giant cell arteritis is a very rare condition especially among the Asian population with the aims of systemic corticosteroid are to prevent progression of ipsilateral vision, protect the fellow eye and prevent large artery involvement. However, if the clinical scenario is atypical or suspicious, clinicians should keep an open mind and consider other disease that can mimic GCA before prompt therapy can be initiated. It is crucial to rule out infective causes before starting patient on systemic corticosteroid. Orbital aspergillosis can be lethal. Initial presentation of orbital aspergillosis is usually non-specific and can be similar to other systemic disorders such as GCA. Neuroimaging can be helpful in confirming diagnosis with the gold standard being the biopsy of the lesion to send for fungal culture. Once the diagnosis is confirmed, surgical debridement and systemic antifungal should be commenced to prevent lethal complications.

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