Case report

Endogenous Aspergillus endophthalmitis in a healthy individual

Manandhar A, Bajracharya L
Tilganga Institute of Ophthalmology, Gaushala, Bagmati bridge, Kathmandu, Nepal

Abstract

Background: Fungal endogenous endophthalmitis in a healthy individual without any predisposing factors is very uncommon. It can occur in intravenous drug abusers, where Aspergillus is more frequently isolated as the causative organism. Case: We treated an unusual case of culture-proven endogenous Aspergillus endophthalmitis who was immunocompetent and was not an intravenous drug user. The affected eye was successfully treated with repeated intravitreal, intracameral and intrastromal injections of amphotericin B and anterior chamber wash. Conclusion: Endogenous fungal endophthalmitis can occur in healthy individuals.

Key-words: Aspergillus, endogenous endophthalmitis, amphotericin B

Introduction

Fungal endophthalmitis is a serious intraocular infection occurring most commonly in immunocompromised individuals (Gonzales et al, 2000; Schiedler et al, 2004; Binder et al, 2003; Leibovitch et al, 2005; Hashemi et al, 2009)) or in immunocompetent individuals following ocular trauma (Moinfar et al, 2010; Taylor et al, 2002), intraocular surgeries (Muzaliha et al, 2010) or from intravenous drug use (Doft et al, 1980, Roney et al, 1986, McGowan et al, 2010). However occurrence of fungal endophthalmitis in a healthy individual without any of the above three conditions is very uncommon. We are presenting one such unusual case.

Case

A 25 year-old young man, residing in one of the valleys of Nepal with temperate climate, a fruit vendor by occupation presented to us with chief complaints of progressively increasing pain, redness, defective vision and photophobia in his right eye (RE) for one month. He denied suffering from any kind of ocular trauma prior to the start of the symptoms. He was not a contact lens wearer. His treatment had been started a week after the onset of the disease. He was referred to us since his RE problem worsened in spite of medical treatment for almost three weeks. On examination of his RE, visual acuity was 6/24 (unaided) and 6/18 with a pinhole. There was ciliary congestion. Corneal epithelium was intact. Superficial stroma was clear whereas in the infero-temporal quadrant of cornea, deep stroma and endothelium had white infiltration. Corneal sensation was normal. Corresponding to the same quadrant, in the anterior chamber (AC), just underlying the area of infiltrates, there was a collection of thick white fluffy exudate showing finger-like projections at the free edge which were moving freely along with the aqueous current. The infero-temporal sector of the angle from 7 to 9 o’clock meridian was clogged with this collection of exudates. Besides this, 1 mm hypopyon was present [Fig.1]. The aqueous showed about 30-35 cells/HPF and 2+ flare. The depth of the anterior chamber was normal. The pupil was pharmacologically mid-dilated. Lens was clear but vitreous was slightly hazy. The posterior pole and the mid periphery of the fundus were grossly normal. His left eye was within normal limits. IOP in RE was 21 mm of Hg with applanation tonometry. B-scan of RE showed few heterogenous echodensities in an-
terior and mid vitreous. The retinal, choroidal and scleral complex was normal. With the above findings, a provisional diagnosis of fungal endophthalmitis was made.

Figure 1: Deep corneal infiltrate with AC exudate

He denied having any episode of fever prior to the onset of the eye problem. He recalled having a small infected lesion on the dorsum of his right foot 2 months back which healed on self-treatment within a week. On examination, there was a mark on the dorsum. He denied use of intravenous drugs but chewed tobacco regularly. Past ocular history was not significant. Clinical notes in the referral slip showed that on the day of his first visit, he had a small endothelial plaque in the infero-temporal peripheral part of the cornea with mild AC reaction. Even at that time, other than the endothelium, the rest of the cornea was completely normal. The endothelial plaque grew in size progressively, and after a week, infiltration was documented in the deep stroma as well. He was treated as a case of sclerokerato-uveitis with prednisolone acetate 1% and timolol maleate 0.5% eye drops since past 3 weeks. He was started on oral prednisolone with the initial dose of 60 mg daily (in tapering dose) along with anti-tubercular drugs (Isoniazid and Rifampicin) two weeks before he came to us.

Work-up revealed total leukocyte count of 8100/cumm, neutrophil 51%, lymphocyte 49%, erythrocyte sedimentation rate was 5/mm in first hour, negative VDRL, TPHA and HIV (1 and 2). Random blood sugar was 112 mg %. Mantoux test showed 16 mm induration. Examination of urine (routine and microscopy) was within normal limits. Both blood and urine cultures were negative.

On the very day of presentation to our hospital, vitreous and AC tap was taken. Vitreous was clear in colour but watery in consistency. This was followed by a thorough AC wash, intra-vitreal, intra-cameral and intra-stromal injection of Amphotericin-B (5 microgram/0.1ml) under peribulbar block. Smears were prepared from AC and vitreous tap. Each of the specimens was inoculated onto chocolate agar, blood agar, Sabouraud’s dextrose agar and Thioglycolate broth. Smears did not give any clue to the causative organism. The patient was commenced on eye drops of natamycin 5% every hour, amphotericin B 0.15% every hour, moxifloxacin 0.05% every three hours, atropine 1% three times a day and oral fluconazole 150mg once a day.

On day 2, pain in the right eye decreased, and so did the hypopyon. AC exudates decreased to a little extent but IOP measured 26 mm of Hg. So brimonidine tartarate 0.15% eye drop was added. Over the next few days, the IOP kept creeping up requiring oral acetazolamide 250 mg thrice a day and topical dorzolamide 2% eye drops for its control. After three days, fungal growth was seen in few of the culture plates of vitreous specimen.

Since vitreous and fundus examination was difficult due to stromal edema from injections, B-scan was repeatedly evaluated. On day 5, B-scan showed slightly increased vitreous echodensities. Aspergillus flavus was identified from the vitreous growth after a week of incubation. The deep infiltrate of the cornea started to extend anteriorly to involve middle and superficial stroma. A week later after the first dose, he received second dose of intra-vitreal, intra-cameral and intra-stromal injections of Amphotericin-B. AC wash was repeated.

On subsequent follow ups, the corneal infiltrate became full thickness to involve the epithelium with a defect; however the bulk of AC exudate started to decrease. The central small area of cornea underlying the AC exudate started to become thin, and
on the day 12, it gave way. Pseudocornea formed over that slip like opening and iris became adherent to it. The AC became shallow temporally, but was still formed elsewhere. Eye ball was soft with a pressure of 9 mm Hg, but there was no leak. This was self sealed corneal perforation.

Third dose of intra-cameral and intra-stromal (peri-lesional) injection of Amphotericin-B was given on day 14. The pseudo-cornea started to epithelialize and IOP tended to rise up to 20 mm Hg. Exudates in AC started to decrease gradually. He was continued on his topical medications and oral antifungal.

**Figure 2: Resolution of corneal infiltrate and AC exudate**

Over the next one and a half months, the visual acuity in right eye improved to 6/9 with correction, neo-vascularization developed in the cornea around the sealed perforation with iris adherent to the endothelium, the AC exudate got organized [Fig. 2], AC cells came down to 15 to 17 cells/HPF, there was a posterior synechia at 7 to 8 o’clock meridian, lens was clear and vitreous cleared up. The fundus showed healthy optic nerve head with a small cup and healthy macula with a good foveal reflex. However on gonioscopy, angles were found to be closed to 360 degrees. Tab fluconazole was discontinued after a total of 7 weeks of treatment, natamycin, amphotericin B and moxifloxacin eye drops were gradually tapered off, and latanoprost 0.005 % had to be added to rest of the anti-glaucoma medication. Glaucoma filtering surgery was planned.

**Discussion**

Fungal endophthalmitis is an uncommon, but a sight threatening disease. Endogenous fungal endophthalmitis is usually seen in immune-compromised individuals suffering from HIV, uncontrolled diabetes mellitus, cancer chronic obstructive pulmonary disease, end stage renal disease, individuals with prosthetic cardiac valves, permanent pacemakers or with indwelling catheter, patients on immune-suppressive therapy for autoimmune disorder like rheumatoid arthritis, lupus (Gonzales et al, 2000; Schiedler et al, 2004; Binder et al, 2003; Leibovitch et al, 2005), or after organ transplant (Hashemi et al, 2009), via endogenous spread of the organism (most frequently Candida and Aspergillus sp.) to the eye from distant site of infection through blood stream, and also in immune-competent individual from intravenous drug use where the organism (usually Aspergillus sp.) reaches the eye from the injection site through blood stream (Doft et al, 1980; Roney et al, 1986; McGowan et al, 2010). Of course, traumatic and post-operative fungal endophthalmitis can occur in immune-competent individuals from penetrating ocular trauma (Moinfar et al, 2010; Taylor et al, 2002) or intraocular surgeries (Muzaliha et al, 2010) respectively due to direct inoculation of the organism into the eye from the external environment. On extensive literature search we found three articles (from indexed journals) on culture proven endogenous fungal endophthalmitis occurring in healthy individuals. One article wrote about the endogenous candida endophthalmitis occurring in a healthy woman (Kostick et al, 1992). The only ailment she was found to be suffering from was the vaginitis and onychomycosis. Transient or intermittent candidaemia from vaginitis was thought to be the cause of endophthalmitis in that lady. The second article wrote on endogenous zygomycosis endophthalmitis that occured in a healthy young male in whom the source of organism could not be identified (Gupta et al, 2009). The only history he gave was about receiving intravenous dextrose infusions while undergoing a surgical procedure for post-traumatic hydrocele elsewhere a week prior to that
episode. The third case report was on endogenous scedosporium endophthalmitis in an elderly diabetic patient who was labeled as immune-competent since her diabetes was under control at that time (Shankar et al, 2007). Other reports on endogenous candida endophthalmitis occurring in healthy individuals are in women after induced abortion (Chen et al, 1998; Sikiæ et al, 2001). The causative organism was Candida sp in those cases, where the organisms from the genital tract were said to have inoculated into the venous system. In cases of endogenous fungal endophthalmitis, blood culture is positive in only 33 % (Binder et al, 2003).

Our patient was not immune-compromised by any kind of systemic disease or by any immune-suppressive treatment. To support that his blood works were all normal. He was not a diabetic and was HIV negative. He was not suffering from any systemic infection at that time. Although he gave history of having an infected lesion a month prior to the onset of his eye problem, the blood culture showed no growth of any organism. He was not an intravenous drug user. Just to make sure that that was not a case of traumatic fungal endophthalmitis it would be important to highlight the fact that our patient did not have trauma to his affected eye. On examination also, we found not even a scar in the epithelium or in the anterior stroma of the cornea. The involvement of the endothelium and the posterior stroma of the cornea clinically looked like secondary to intraocular infection.

In terms of the prominent anterior segment involvement our case is quite similar to the case of scedosporium endophthalmitis (Shankar et al, 2007). That case also had a fluffy white exudative mass in the AC just like in our case. Even in that case, the macula was spared, unlike in many endogenous fungal endophthalmitis cases.

Our case is one of those unusual ones, where the site of inoculation of the organism into the body is unknown. Another uniqueness of this case is the management part. Our case recovered very nicely only with repeated intra-vitreal and intra-cameral injections of Amphotericin-B, AC wash and other medical treatment, without vitrectomy. In almost all the cases report on fungal endophthalmitis, vitrectomy was part of the management (Doft et al 1980; Roney et al, 1986; Weishaar et al, 1998) and it is suggested as the part of management of fungal endophthalmitis (Riddell 4th et al, 2011). The treatment outcome of endogenous aspergillus endophthalmitis (EAE) is generally poor (Weishaar et al, 1998). But in our case, the infection healed completely. Use of steroid definitely makes the favorable environment for any fungus to grow (McGowan et al, 2010; McLean, 1963) which is very clearly evidenced in the sequential OCT of a patient with candida endophthalmitis, before and after the use of systemic steroid (McGowan et al, 2010). Even in our case the anterior chamber lesion grew rapidly to form a filamentous mass after the use of oral steroid. However, un-involvement of macula in our case resulted in a good treatment outcome. Otherwise EAE cases usually have a characteristic chorio-retinal lesion located in the macula (Weishaar et al, 1998). After resolution of the infection, the only sequele were peripheral adherent leucoma and ocular hypertension from angle closure. Although Voriconazole is the best antifungal for EAE (Riddell 4th et al, 2011), intra-vitreal amphotericin-B also has high local antifungal action (Weishaar et al, 1998; Riddell 4th et al, 2011). This seems to have been proved also in our case, since the infection healed completely.

Conclusion
Endogenous fungal endophthalmitis should be suspected even in healthy individuals. This high level of suspicion prevents the use of oral steroid in such cases. White plaque in the corneal endothelium should arouse a suspicion of fungal infection, particularly when it grows in size despite using adequate dose of topical steroid.

References

Binder MI, Chua J, Kaiser PK, Procop GW, Isada CM (2003). Endogenous endophthalmitis: an 18-year review of culture-positive cases at a ter-


