Ocular Rhinosporidiosis with Staphyloma Formation: The First Report in Sri Lanka


ABSTRACT

Four rare human cases of primary ocular rhinosporidiosis with staphyloma formation in Sri Lanka are described. Cases 1, 3, and 4 were the first reported cases of ocular rhinosporidiosis, with a river contaminated with the causative organism Rhinosporidium seeberi as the probable source of infection. A contaminated lake was the probably source in case 2. Their unusual features included serial rhinosporidial lesions in multiple sites (palpebral and bulbar conjunctivae), with possible extension to the posterior chamber with uveitis and to the retina with the formation of posterior staphylomas in the same eye. In addition, a possible extension of the infection or immunological reaction against the pathogen to the contralateral, non-rhinosporidial eye occurred in three cases, documented by the development of posterior staphylomas and retinal abnormalities. Only one patient had a significantly elevated IgG titre. (J Infect Dis Antimicrob Agents 2007;24:133-41.)

INTRODUCTION

Rhinosporidium seeberi, the causative pathogen of rhinosporidiosis in humans and animals, was recently and definitively classified as a Protoctistan protozoan, with 10 other parasitic or saprobic microorganisms in the new class Mesomycetozoea.1-3 Some other members of this class cause diseases in amphibia, fish, birds, insects, and crustaceans, sometimes with similar histopathological features. The ocular disease has, however, not been ascribed to them.

Ocular rhinosporidiosis accounts for approximately 15 percent of all cases of rhinosporidiosis. The term ‘ocular rhinosporidiosis’ was suggested,4 but we prefer the term ‘ocular rhinosporidiosis’ because an ocular disease can also be caused by other spore-bearing organisms including microsporidia. Sporadic cases of rhino-
sporidiosis are now being reported from western and other regions, in emigrants and expatriates from endemic areas where they acquired the infection, justifying its recognition as an emerging infectious disease.

This report describes four cases of ocular rhinosporidiosis with staphyloma formation which is very rare, with only nine case reports in the literature. The response to oral dapsone therapy and the pathogenesis of rhinosporidial staphylomas are also discussed.

**MATERIALS AND METHODS**

**Cytodiagnosis**

Smears from the conjunctivae and anterior choanae of the nose were stained with periodic acid-Schiff (PAS) for rhinosporidial sporangia and endospores that appear deep magenta in colour.

**Histopathology**

Excised rhinosporidial tissues were fixed in 10 percent formol-saline and processed for paraffin embedding for staining of 5-μm sections with the hematoxylin and eosin (H and E) stain.

**Anti-rhinosporidial antibody assays**

Anti-rhinosporidial antibodies in patients’ sera were titrated by the dot-enzyme-linked immunosorbent assay (dot-ELISA) method on nitrocellulose discs, with anti-human IgG-, IgM-, and IgA-phosphatase conjugates (Kirkgaard Perry Laboratories, MD, USA) and substrate with chromogen (Wellcozyme, Wellcome, UK).\(^5\) Rhinosporidial antigen was extracted from the endospores by ultrasonic disintegration followed by absorption of bound human immunoglobulin with sepharose G.\(^5\) Sera from asymptomatic persons with no anti-rhinosporidial antibody, and sera from patients with rhinosporidiosis with previously determined titres, were used as controls.

**Ethical clearance**

A written informed consent for the clinical procedures and for publication was obtained from all patients. An ethical clearance was obtained from the Ethics Committee of the General Hospital, Kandy, Sri Lanka.

**RESULTS**

**Case 1**

A 58-year-old, previously healthy housewife presented with a fleshy growth with spontaneous bleeding on the inner aspect of the right lower eye lid for one year. The growth was excised, but histopathological examination was not done. One year later, a similar growth appeared on the sclera of the same eye. It was excised, and a conjunctival graft was placed on the site. Rhinosporidiosis was reported on histopathological results (Figure 1). The patient was myopic on both eyes with a posterior staphyloma on a B-scan on the rhinosporidial eye (Figure 2). There was no family history of myopia. The intra-ocular pressure was 10 mmHg. One year later, a dark blue-black, cystic anterior staphyloma (Figure 3) with scleral thinning on the same eye was noted at the site from which the original rhinosporidial growth had been excised. Anterior and posterior uveitis were observed on slit-lamp examination, while a retinal involvement was suspected on account of the presence of posterior uveitis. No penetration of the lesion into the anterior chamber was detected. Smears of both conjunctivae and anterior nasal choanae stained by PAS showed no evidence of rhinosporidial elements.

The patient was treated with oral dapsone (100 mg/day) for one month, with topical prednisolone acetate every six hour for three months. A repeat
Figure 1. Histopathology of the bulbar conjunctival rhinosporidial growth on the sclera of the right eye showing a degenerate intermediate (immature) sporangium containing degenerate endospores; the pore (arrow), surrounded by the annulus, through which the endospores exit was visible. Initial magnification x 400. H&E stain.

Figure 2. Posterior staphyloma (white arrow) in rhinosporidial eye.

examination after two months of therapy showed no further thinning of the sclera and no evidence of uveitis. No recurrence of the rhinosporidial growth was observed, 11 years after discontinuation of dapsone therapy when the anterior staphyloma was noted on the right eye. Fluorescence angiography of the retina showed no evidence of the leakage of the dye, the myopic degeneration was still present. One year later, no new or recurrent rhinosporidial growths were detected. The right rhinosporidial eye remained stable.
A gradual deterioration of the vision and a large posterior staphyloma of the left eye were noted, indicating a possible spread of the disease to the contralateral eye. Her eye condition remained stable at present.

Serum anti-rhinosporidial IgG and IgM antibodies were 1/400 and 1/100, respectively, but serum IgA antibody was negative (<1/100).

**Case 2**

A 18-year-old man presented with a symptomless, red-coloured, granular conjunctival mass in the left sclera for 3 months. Adjacent to and below the mass was a large, cystic, bluish-black non-vascular staphyloma of one cm diameter (Figure 4). A visual acuity and the fundus of both eyes were normal. Histopathology of the excised mass revealed rhinosporidiosis. Nasal passages and smears showed no evidence of rhinosporidiosis.

Oral dapsone (100 mg/day) was given for three days, but was discontinued due to a development of hemolytic anaemia. The patient remained asymptomatic, three years after excision of a rhinosporidial mass.

**Case 3**

A 34-year-old man presented with a scleral growth on the right bulbar conjunctiva, diagnosed as rhinosporidiosis. It has increased in size for 16 years when the vision of the right eye was impaired. A large anterior staphyloma adjacent and superior to the cornea of the right eye was also present, in association with a choroidal effusion. A scleral graft was placed over the staphyloma. The visual acuity of the right eye slightly improved. Eight years later, there was an impairment of the visual acuity of the left eye, in association with a choroidal effusion and an inferior retinal detachment shown on a B-scan (Figure 6). Fundoscopy showed a macular hole and a retinal fold between the disc and the macula (Figure 7). A possible spread of the rhinosporidial infection from the right to the left eye was suspected, and thus dapsone (100 mg/day) was given for two months. One year later, the visual acuity of the left eye slightly improved. His eye condition remained stable during a two-year follow-up.

Serum anti-rhinosporidial IgG and IgM antibodies
were 1/200 and 1/75, respectively, but serum IgA antibody was negative (<1/50).

**Case 4**

A 34-year-old man presented with a growth of the upper conjunctiva of the right eye for one year. Histopathology of the resected tissue showed rhinosporidiosis. An anterior staphyloma with a dark blue-black-coloured, cystic, swelling was seen beneath the rhinosporidial mass. One year later the visual acuity of the left (non-rhinosporidial) eye was impaired, and fundoscopy and B-scans showed no abnormality.
Figure 6. B-scan of contralateral (non-rhinosporidial, left) eye showing a retinal detachment (R) adjacent to a choroidal effusion (black arrow).

Figure 7. Fundus of contralateral (non-rhinosporidial, left) eye showing a Grade II macular hole (M), retinal ridge (R) and traction bands.

Smears from both eyes and from the anterior nares showed no rhinosporidial elements. Oral dapsone (100 mg/day) was given for two months when there was an improvement of the visual acuity of the left eye. His eye condition remained stable during a three-year follow-up.

The overall clinical features of all four cases are summarized in Table 1.

**DISCUSSION**

The four cases in this report are among 22 cases of ocular rhinosporidiosis in our series of 120
Table 1. A summary of the salient features of the four patients of ocular rhinosporidiosis with staphyloma formation.

<table>
<thead>
<tr>
<th>Case</th>
<th>Residence</th>
<th>Probable source of pathogen</th>
<th>Recurrence of rhinosporidiosis</th>
<th>Retinal involvement</th>
<th>Staphyloma of affected eye</th>
<th>Contralateral eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Non-endemic</td>
<td>River</td>
<td>Yes</td>
<td>Possible</td>
<td>Anterior and posterior</td>
<td>Posterior staphyloma</td>
</tr>
<tr>
<td>2</td>
<td>Endemic</td>
<td>Lake</td>
<td>No</td>
<td>No</td>
<td>Anterior</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Non-endemic</td>
<td>River</td>
<td>No</td>
<td>Yes</td>
<td>Anterior</td>
<td>Macular hole, traction bands, and retinal fold</td>
</tr>
<tr>
<td>4</td>
<td>Non-endemic</td>
<td>River</td>
<td>No</td>
<td>No</td>
<td>Anterior</td>
<td>Posterior uveitis</td>
</tr>
</tbody>
</table>

patients (18%) with rhinosporidiosis seen at our hospital over an eleven-year period from 1995 to 2006. This is the first report of ocular rhinosporidiosis with a staphyloma formation in Sri Lanka. There were four significant features. First, three of four patients were from a non-endemic region, in contrast to those with rhinosporidiosis of the respiratory tract and other sites. Second, the ocular rhinosporidiosis was a primary infection, and was not secondary to the disease of the respiratory tract. Third, there was a retinal involvement in two cases (case 1 and case 3). Fourth, an involvement the contralateral, non-rhinosporidial eye was noted in cases 1, 3, and 4. However, in all these cases, a definitive diagnosis of the extension of rhinosporidiosis to the contralateral eye could not be established due to the impossibility of obtaining intraocular samples.

Eight case reports\textsuperscript{4,6-12} of ocular rhinosporidiosis with a staphyloma formation were from India, and only one\textsuperscript{13} was from the Netherlands. In all these patients, the staphyloma was located adjacent to the scleral rhinosporidial growth. In three Indian reports\textsuperscript{6,7,10} and one Dutch report\textsuperscript{13}, the retina and choroid were unaffected, in contrast to our case series. A Dutch patient had also rhinosporidiosis in the contralateral nasal cavity that might have been the primary site of infection, although the spread of infection was probably through an external route and not through the ipsilateral naso-lacrimal duct. An Indian patient\textsuperscript{10} had a previous history of nasal rhinosporidiosis from which the ocular infection could have been developed by the ascending spread of infection through the naso-lacrimal duct or by an inhalation of the endospores through the anterior nares. Two Indian patients\textsuperscript{11} had probably acquired the infection, as in our patients, from contaminated ground water in the ponds.

The extension of the disease to the retina in our case 1 was similar to the previous reports. This could have been due to an immunological reaction as suggested by its subsidence with steroids and the removal of the rhinosporidial lesion. In addition, we observed a disappearance of a bullous lesion on the eye lid after an excision of the palpebral rhinosporidial growth of the same eye (Arseculeratne 2000,
unpublished). Such an immunological reaction might also explain the retinal detachment, probably due to an exudative Type I hypersensitivity reaction caused by the rhinosporidial antigens in our case 3. The spread of either the microorganism or the antigens to cause the immunological reactions of the contralateral non-rhinosporidial eye in cases 1, 3, and 4 could conceivably have occurred through the venous cavernous sinus.

The posterior staphylomas in our case series, were morphologically different from the rhinosporidial granulomas on palpebral or scleral sites. This difference suggests that the posterior staphylomas are probably not due to the direct spread of the infection. De Doncker and colleagues\(^1\) speculated that a staphyloma formation was due to an immunological or enzymatic dissolution of the scleral tissues caused by the overlying \textit{R. seeberi}. An enzymatic histolytic action was also invoked\(^1\) to explain the phenomenon of ‘trans-epidermal (epithelial) elimination’ of the mature sporangia in palpebral rhinosporidiosis. The staphylomas of congenital or non-infective origin have also been described.

Ground water as in rivers and lakes is the probable natural habitat of \textit{R. seeberi}. The postulated aquatic natural habitat of \textit{R. seeberi} was recently confirmed by in situ hybridization with \textit{R. seeberi}-specific hybridization probes applied on deposits of lake water.\(^1\) River water was probably the source of infection in our cases 1, 3, and 4 that are the first case reports of ocular rhinosporidiosis causally related to river water. A trauma has been reported as a predisposing factor in ocular rhinosporidiosis\(^6\), while minor abrasions of the nasal mucosa of river-sand dredgers\(^7\) conceivably by microscopic, sharp-edged sand particles that we have observed in lake-water deposits could be another example of the role of trauma in localization of nasal rhinosporidiosis in these sand workers.

Dapsone acts by inhibiting the metabolic para- amino benzoic acid cycle, and is considered to be bacteriostatic although a weak bactericidal action has been mentioned. We reported evidence that dapsone was endosporicidal on \textit{R. seeberi} from in vitro tests using the (3-[4, 5-dimethyl-2-thiazolyl] 2, 5-diphenyl-2H tetrazolium bromide) MTT-reduction test of viability, in which dapsone had the lowest IC50 of 7 \(\mu\)g/mL on rhinosporidial endospores.\(^20,21\) Dapsone therapy as an adjunct to surgery has been used successfully on patients with rhinosporidiosis in non-ocular sites.\(^22-24\)

To our knowledge, only two previous reports existed on therapy of ocular rhinosporidiosis with dapsone. Job and colleagues\(^24\) reported two patients with ocular rhinosporidiosis with successfully treatment with dapsone (100 mg/day) for six weeks. The second report was described by John and Mohandas\(^12\) on two patients with rhinosporidial staphyloma the successfully with and cryoapplication and dapsone (100 mg/day) for six months.

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