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Case Report: Rhinosporidiosis Literature Review

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Abstract. Rhinosporidiosis is caused by *Rhinosporidium seeberi*, a pathogen currently considered a fungus-like parasite of the eukaryotic group Mesomycetozoea. It is usually a benign condition, with slow growth of polypoid lesions, with involvement of the nose, nasopharynx, or eyes. The clinical characteristics of a painless, friable, polypoid mass, usually unilateral, can guide the diagnosis, but the gold standard for diagnosis is histopathological findings. This article reviews the epidemiology, pathobiology, clinical manifestations, diagnostic strategies, and treatment approach for rhinosporidiosis.

CASE DESCRIPTION

A 10-year-old Latin-American boy presented to the outpatient clinic complaining of unilateral epistaxis of 5-month duration through the right nostril without any other symptom. He lived in Murindó, Antioquia, in the rural area. He denied any associated symptoms. He was evaluated by otorhinolaryngologist (ENT) who described a polypoid lesion in the nasal vestibular region with little bleeding. The rest of physical examination was within normal limits, and blood tests were unremarkable. A simple computerized tomography (CT scan) of the head revealed a mass with nodular appearance in the right nostril of soft tissue characteristics (Figure 1A and B). Nasofibrolaringoscopy revealed an area of denuded and friable tissue in the vestibular region (Figure 2A and B). There was no evidence of local extension, the rest of the nasal cavity appeared normal, and the polypoid mass was totally excised. He was sent to our infectious diseases outpatient care clinic in 2018 with the results of histopathology of the nasal cavity with report of numerous and scattered, well-defined, thick-walled, circular structures corresponding to sporangia with internal endospores with mixed inflammatory tissue (Figure 3A and C) in the hematoxylin and eosin staining consistent with rhinosporidiosis.

He was treated by ENT with complete endoscopic excision of the lesion, and in the 6-month follow-up, he has remained asymptomatic and has not had clinical recurrence of the lesion.

DISCUSSION

Rhinosporidiosis is now considered an emerging infectious disease.[1] It is caused by *Rhinosporidium seeberi*, a pathogen that has been known for more than a century; the first report corresponds to the description of an Argentinian physician and has passed through several classifications. It was formerly considered a fungus, then transiently considered an entity caused by a cyanobacterium, and currently, it is classified as a parasitic protist of the eukaryotic group Mesomycetozoea—fungus-like thorough molecular technology; a group of microorganisms grouped along with organisms that cause similar infections in amphibians and fish.[2,3]

It is involved in the development of a chronic granulomatous disease of slow growth and usually exhibits benign behavior of polypoid characteristics mainly with a nasal, nasopharyngeal, and/or ocular involvement.[4]

EPIDEMIOLOGY

It has been reported from about 70 countries with diverse geographical features and involving almost all the continents,[5,6] but its highest incidence and endemicity is in the tropical and subtropical regions, with 90% of the cases reported in India and Sri Lanka, and a pediatric incidence estimated in 1.4%.[7] South America is the next region of endemicity, with the northern area of Brazil (Amazon region) in the state of Marañao being most affected,[8] followed by Paraguay, where it is considered endemic.[9]

It has been frequently reported in Brazil, Colombia, in the departments of Tolima, Purificacion and Magdalena and Venezuela in the region of Barinas and Portuguesa, with more than 100 proven associated with the large number of rivers and lagoons, which explains the watery condition necessary for the growth favoring the development of the microorganism.[10]

It has a male to female ratio of approximately 3:1, and it affects people of all ages, usually between 15 and 40 years; frequently involved in farming or fishing activities; sand workers; and paddy cultivators.[6,11]

PATHOPHYSIOLOGY, LIFE CYCLE, TRANSMISSION, AND IMMUNE RESPONSE

The presumed mode of infection of *R. seeberi* is through the epithelium ("transepithelial infection") most commonly found in nasal sites; it is accepted that the infectious forms probably corresponds to the free endospores released to a previously injured epithelium.[12,13]

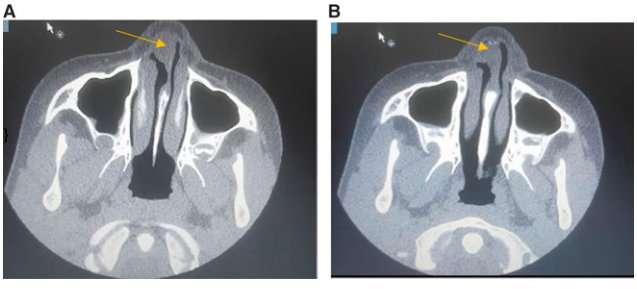

FIGURE 1. Tomography.

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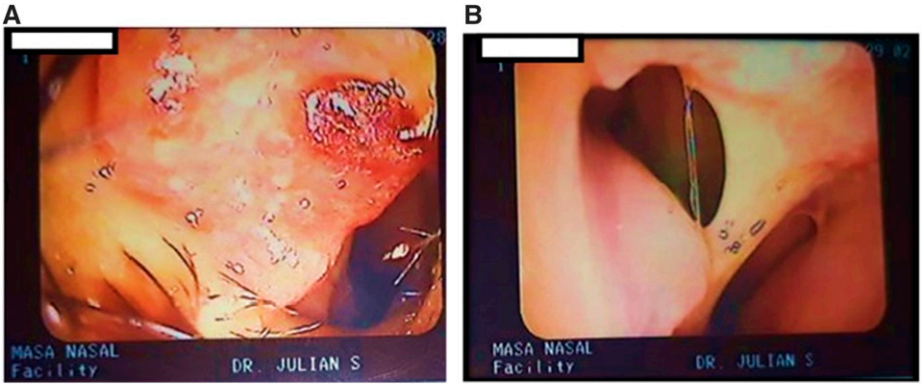

FIGURE 2. Nasofibrolaringoscopy.

The mature form of the microorganism known as sporangia contains multiple sporangiospores or endospores; when rupture of this structure occurs in the epithelial surface, the endospores are released and activated in contact with tissues, and continue with the persistence of local invasion and subsequent maturation into trophocytes (early and late), and the cycle begin again.[13]

As a result of hematologic or lymphatic dissemination, autoinoculation, or direct inoculation, skin lesions distant from the inoculation site (nose) may appear.[14]

There is no definitive known host; in addition to the numerous cases in humans, it is known that it affects birds and other mammals. The mode of transmission is still a matter of debate; cross-infection has never been documented between members of the same family or between animals and humans. Presumably, the contact with the free spore in aquatic or marshy environments in susceptible human and animal hosts could be an explanation[15]; in arid regions, airborne spore transmission has also been suggested.[16]

With respect to the immune response, some data support the endospores, and the sporangia layers are linked with the primary antigenic stimuli in the host and are also dependent on the virulence derived from different strains secondary to its genetic heterogeneity.[17] Both cellular and immune responses are developed in the mammal host.[18]

CLINICAL MANIFESTATIONS AND PHYSICAL EXAMINATION

The disease has four clinical forms—1) nasal, 2) ocular, 3) cutaneous, and 4) disseminated.[7]

The literature reports that approximately 70% of the cases involve the nose and nasopharynx usually in an unilateral form; ocular lesions, particularly of conjunctiva and lachrymal sac, account for 15% cases.[19]

The main characteristic of the disease is the occurrence of a polypoidal, reddish, friable, painless, pedunculated, hyperplastic soft tissue mass in the nasal area, typically with an indolent and chronic progression.[20]

The remaining cases reported correspond to different sites and rare localizations such as lips, palate, uvula, maxillary antrum, epiglottis, larynx, pharynx, and trachea/bronchi ear.

The presence of a disseminated disease with simultaneous involvement of the limbs, trunk, and internal organs, even the brain, is rarely encountered in persons without preexisting immunocompromised conditions.[21]

Recurrence, dissemination to related anatomical site, and bacterial super-infection are frequent complications.[22,23]

LABORATORIES, IMAGING AND DIAGNOSTIC TESTS

No pathognomonic findings are described in the literature for the chemical or hematological analysis.

There is no typical lesion described for rhinosporidiosis, but imaging (contrast-enhanced CT) has an important role in delineating the site and extent of the disease, as well as ruling out the involvement of surrounding bone, nasolacrimal duct, and tracheobronchial tree.[24]

In some low-income areas, the cytology could be helpful, especially in extra-nasal lesions, but the definitive diagnosis is made by histopathology of the resected tissue.[1]

Rhinosporidium seeberi presents as large (50–100-mm) rounded structures that can be seen as yellowish pinhead-sized spots in the polyp. Microscopically, these structures vary in size, corresponding to different stages in the development of the organism, and have a densely eosinophilic wall that encloses smaller rounded structures containing amorphous eosinophilic material. Microscopic features of this organism are enhanced by using Grocott-Gomori's methenamine silver, periodic acid–Schiff, and mucicarmine stains.[25] *Rhinosporidium seeberi* has very similar morphology to *Coccidioides*, but its sporangia and endospores are larger than spherules.[26]

The pathology usually reports lesions localized in the orbital zone, nose, or nasopharynx, with granulomatous inflammation with fibrosis, and granulation tissue and in the disseminated disease, chronic granulomatous inflammation.[26]

Differential diagnosis must include chronic granulomatous diseases, especially those with affection of the rhino-sinusal tract, oropharynx, and ocular system, and even tumoral pathology.[27]

TREATMENT, PROGNOSIS, PREVENTION, AND FOLLOW-UP

The likelihood of spontaneous regression of nasal polypoidal lesions is unlikely in the natural course of rhinosporidiosis.[28]

Characteristically, the surgical removal of the lesion with cautherization of the attachment base is almost curative in at least 90% of the cases,[29] but in endemic areas, recurrence is variable, ranging between 5% and 67%; especially in mucosal

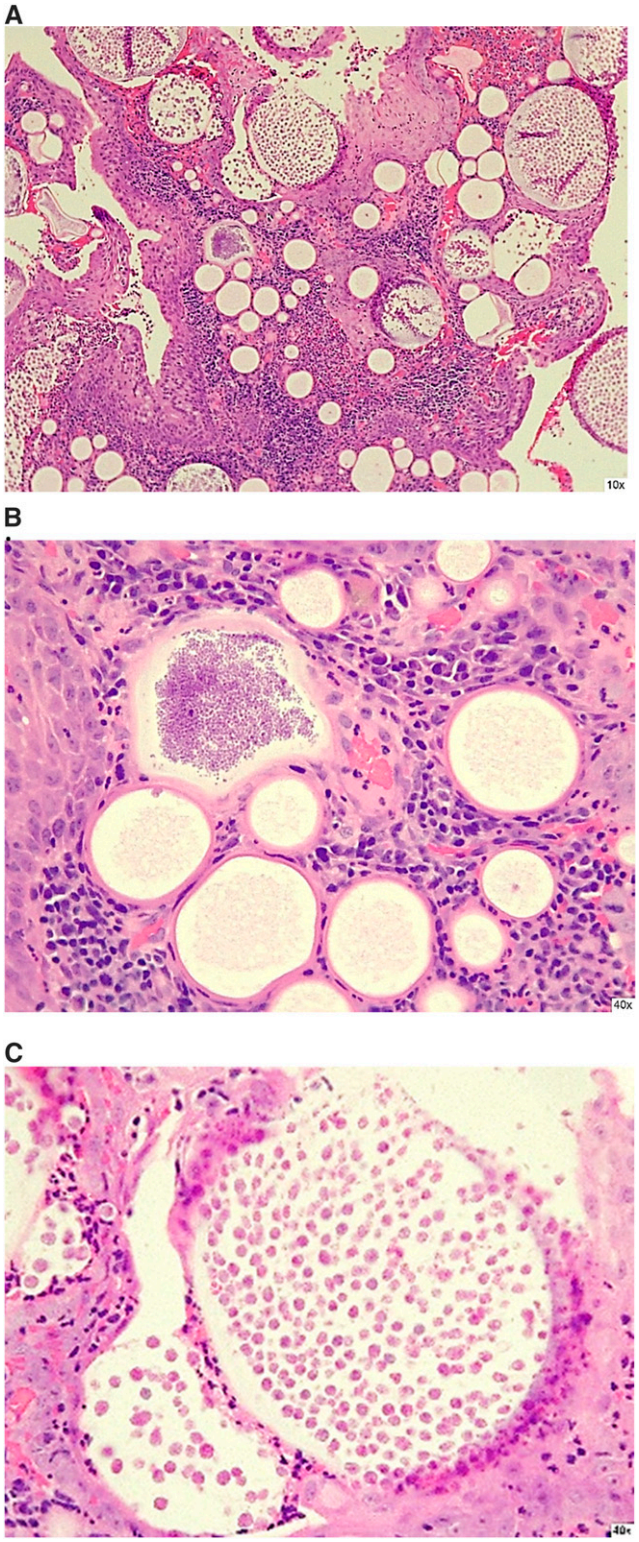

FIGURE 3. Biopsies. This figure appears in color at www.ajtmh.org.

sites (oropharynx and paranasal sinuses), apparently related to the difficulty to achieve complete excision[28,30]; and with disseminated involvement, it reaches 100%.[31]

For that reason, some authors raise the question of a systemic compromise in this pathology, suggesting a more detailed laboratory evaluation and aggressive surgical approach at the first assessment and recommending the complementation of the surgical management with pharmacological treatment of probably remaining reservoirs in the body (blood or the lymphatics) that could explain the relapses.[32]

Studies have shown that at least with dapsone, there is in vitro evidence of degenerative changes and total inactivation of free endospores with in vivo variable responses probably due to pharmacokinetics and pharmacodynamics, still without sufficient evidence to support its use[33]; the time of the treatment is always prolonged (at least 6 months to 1 year).[34]

More recently, because of the occurrence of refractory cases, multidrug approaches in the management of disseminated disease are being considered using cycloserine, dapsone, and ketoconazole among others combinations with good clinical results.[35] In vitro studies report that ketoconazole, trimethoprim–sulfamethoxazole, and amphotericin B deoxycholate do not have endosporostatic or endosporicidal lytic activity.[36]

In general, the prognosis of this disease is good, but given potential for recurrences, clinical data suggest the need for a prompt diagnosis with aggressive treatment and long-term follow-up of the patients to detect relapses and avoid complications.[22]

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