Review Article

Rhinosporidiosis: A Riddled Disease of Man and Animals

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Abstract | Rhinosporidiosis is a non-contagious, sporadic, chronic granulomatous infection of man and large domestic animals, characterised by the production of large polyps with high recurrence rate. Polyps occur mainly in nasal, ocular regions; cutaneous and disseminated forms are relatively rare. Spread of these organisms to other areas in an affected person may involve blood, lymph or auto infection. Rhinosporidiosis has been reported form more than 70 countries and mainly the reports are concentrated from Sri Lanka and Southern India. Surgical removal of the polyp will be the cure and in some cases dapsone has given some cure. From the day of inception of this disease there had been a controversy for causative agent of this condition among eukaryotic protozoan parasite or algae or fungi or prokaryotic blue green algae which finally confirmed as a fungi *Rhinosporidium seeberi*. Recent works by various researchers shows that *R. seeberi* belong to the class Mesomycetozoea. Other mystery remains in its habitat and its inability to be cultured on laboratory media. Similarly, laboratory animal infection does not yield classical form of disease as it does in human and large animals. The pathogen is so mysterious that the mechanism behind evasion of immune mechanism is also not clear. Still various aspects of disease such as mode of transmission, mechanism of infection, biology of rhinosporidiosis, immunological response and laboratory culture techniques are unresolved mysteries due to paucity of documented data which demands more exploration. This review illustrates main features of rhinosporidiosis and systematic approaches for the diagnosis and treatment of this controversial pathogen.

Keywords | Rhinosporidiosis, Nasal polyps, Man, Animals, Diagnosis, Treatment

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INTRODUCTION

Rhinosporidium seeberi is known for causing Rhinosporidiosis yet a disease which is considered as unresolved enigma for over a century and condition was first time reported from Argentina in 1812 by Malbran (Dhayagude, 1941; Branscomb, 2002; Tiwari et al., 2014). Rhinosporidiosis is a non-contagious, sporadic, chronic granulomatous infection of the mucocutaneous tissue caused by *Rhinosporid-*

ium seeberi, yet an unisolated and unclassified fungus (Jain, 1967; Arseculeratne, 2005). It causes a chronic granulomatous disease of man and large domestic animals, characterised by the production of large polyps with high recurrence rate. The nasal cavity is the most commonly affected site (Das et al., 2011). The absence of the Splendore-Hoeppli reaction and specialized mechanisms to escape from immune system makes this pathogen an interesting subject for mycologists. Initially *R. seeberi* was confused with eukaryotic protozoan parasite or algae or prokaryotic blue green algae but later on confirmed as a nearest relative to lower fungi. Based upon polymerase chain reaction, DNA sequencing, cloning, Southern hybridization results, light and electron microscopy evidence of nanocytes (large daughter cells of Microcystis, a cynobacteria) inside the sporangia of rhinosporidiosis lesions were observed concluding as a blue green algae microcystis to be the cause of rhinosporidiosis. Fluorescent in-situ hybridization (FISH) and 18S rDNA sequence based PCR studies emphasizes similarity of *R. seeberi* with member of genus *Dermocystidium,* an aquatic protistan fish parasites of Icthyosporea clade (Ahluwalia, 1992; 1997; Fredricks et al., 2000).

ETIOLOGICAL AGENT

Rhinosporidiosis is a chronic granulomatous clinical condition characterized by fungal infection of mucous membrane in animals and man, caused by *Rhinosporidium seeberi* (Mello, 1949; Mendoza et al., 2001; Branscomb, 2002). *Rhinosporidium seeberi*, was discovered by Guillermo Seeber in 1900 in Argentina, as a protozoan parasite which produces nasal polyp. Later on in 1923, J. Ashworth described that rhinosporidiosis is caused by a fungus and he named it *Rhinosporidium seeberi* in the honor of G Seeber. The travel of *R. seeberi* is huge that during various timeline it has been placed in several families and class. Ashworth suggested that *R. seeberi* was closely related to fungi of lower level like Phycomycetes (Ashworth, 1923). Sooner it was placed in Ascomycetes fungi by Dodge (Dodge, 1935). Later, different workers found that this organism have resemblance with fish pathogens namely *Ichthyophonus* and *Dermocystidium* (Dunkerly, 1914; Carini, 1940). Confusion prevailed and some workers thought the organisms to be fungi, some as protozoa, some as carbohydrate waste and some as Cynobacterium (Ahluwalia, 1992; 1997). Work done by Herr et al. (1999a) finally placed this organism in a clade called DRIP (*Dermocystidium*, the rossette agent, *Ichthyophonus* and *Psorospermium*) which is a recently added fish pathogen group. These workers carried out phylogenentic analysis using 18s ribosomal DNA sequences. It is grouped in the order Chitridiales due to weakly developed or absent mycelia, class Mesomycetozoa family Rhinosporideacae or Olipidicea as each spherical cell is transformed into a single sporangium (Kennedy et al., 1995; Herr et al., 1999b; Ahluwalia, 2001). Class Mesomycetozoa includes numerous parasitic as well as saprophytic microorganisms, which mostly infect fishes and amphibians; although *R. seeberi* is only capable of infecting mammals among other members, though multiple host-specific strains may subsist (Silva et al., 2005).

In *R. seeberi,* 'Sporangia' have been redesignated nodular bodies (NB) and 'spores' as spheres of cellular waste (scw). Two carbohydrates, namely defective proteoglycans synthesized intracellularly and an exogenous polysaccharide ingested through diet of tapioca constitute indigestible material in NB and scw. Polysaccharide in NB which has beta, 1-4 glycosidic bonds between mannose residues is not degraded by gastrointestinal enzymes nor in intracellular lysosomes which break only alpha-glycosidic bonds. A link between NB and dry tapioca has been deduced. Rhinosporidiosis is a complex phenotype with perhaps no parallel in medical science. This report erases 99 years (1892-1991) of controversies regarding 'causal organism' of rhinosporidiosis (Ahluwalia, 1992).

Rhinosporidium equi and *R. ayyari* names were given to the strains isolated from rhinosporidiosis of horses and buffaloes, respectively. Minchin and Fantham called them *R. kinealyi* when obtained from rhinosporidial affected tissue while Vanbreuseghem named as *R. amazonicum* (Minchin and Fantham, 1905). Though today all these four names have been replaced by one common name *R. seeberi.*

GEOGRAPHICAL DISTRIBUTION, EPIDEMIOLOGY AND HOST RANGE

Literature suggests that disease has been reported from approximately 70 nations with diverse geographical distribution and clinical features. Although disease is evident sporadically in parts of Europe, Africa, southern United States, South Africa and South American

temperate regions, western and middle eastern countries however it has endemic status in many Asian countries especially tropical regions, India, Brazil, Argentina, Uganda, Texas and Sri Lanka (Karunaratne, 1939; Ramchandra et al., 1975; Londero et al., 1977; Vukovic et al., 1995). In United Kingdom disease has been reported from ponies and horses (Leeming et al., 2007). International travel increases the risk of disease transmission from endemic areas to virgin soil. Disease can be distributed at large scale due to trading, international import, inter-continental movement of affected animals or human beings. Principally rhinosporidiosis affect mammals predominantly human beings but have been reported from other domestic and wild animals and birds species *viz.,* cattle, equine, caprine, canines, felines & avian species such as water fowl, swans, geese and wild ducks as well. In fishes also disease has been seen (Rao, 1938; Karunaratne, 1964; Myers et al., 1964; Pal, 1995; Das et al., 2011). Disease rarely affects young ones; mostly it is seen in humans of 20-40 years of age group, with uncertain reasons. Europe, Africa, United States. Diseases has endemic nature in Sri Lanka and Southern part of India (Shetty and Mohan, 2013). The disease is also reported from Sri Lanka in humans, the maximum human cases on population basis. Reports of animal rhinosporidiosis from Sri Lanka is missing but a recent sero-epidemiological study result using dot-Elisa showed that antibodies against the pathogen are present in cattle and buffalo (Sudasinghe et al., 2011). Inter-continental immigration and frequent travel is one important cause of global spread of this disease. In India first case was reported from Bihar and since then many states as Madhya Pradesh, Maharashtra, Orissa, Pondicherry, Rajasthan, Uttar Pradesh, Haryana, Kerala, Tamil Nadu and Chhattisgarh have witnessed the disease except Delhi, Punjab and H.P till date (Andleigh, 1951; Ramchandra et al., 1975; Ratnakar et al., 1992). In humans and swans one outbreak of rhinosporidiosis was reported in 1990. Similarly clinical manifestation of nasal and ocular rhinosporidiosis occurred as an outbreak in human beings in Serbia, likewise one outbreak of ocular and cutaneous rhinosporidiosis was also evidenced from Florida, USA in swans. Some workers demonstrated that incidences in humans are related with ABO Blood group also and O^+ blood group individuals are more (70%) prone to disease followed by AB^+ for the disease as compared to other blood groups in India (Jain, 1967). An epidemiological study at Malappuram district of Kerala, India revealed that among the 504 nasal masses operated in hospital in a period of 3.5 yrs, 54 cases (10.71%) were confirmed as rhinosporidiosis. The survey showed an age preponderance to the age group 21-35 years and majority (88%) were males. Among the 6 taluks of this district the majority of cases were reported from taluks of Perinthalmanna (31%), Ernad (22%) and Tirur (20%). The study revealed the endemic nature of this disease in Malappuram district and the careful history revealed frequent pond baths by all the patients (Ahmad et al., 2013).

One study reported that the number of patients in an epidemic exceeded the total number of autochthonous cases of rhinosporidiosis ever recorded in Europe. The male-to-female ratio was 10:7 and, except for a middle-aged man, all patients were in the age range 6-16 years. Preponderance of ocular (12) over nasal (5) localization of the disease in this epidemic indicates that the real number of cases may be much higher. The only experience all patients had in common was that they spent their holiday preceding the onset of symptoms bathing in the same accumulation of stagnant water of the Silver Lake (Vukovic et al., 1995). Human reports are documented worldwide periodically. Though ocular form of human infection was first time reported from India, now reports from various parts of the globe especially from African countries have emerged (Gichuhi et al., 2014). Studies regarding their habitat are less and it is thought to be prevalent in water and soil. A study conducted recently had showed that *R. seeberi* is prevalent in ground water (Kaluarachchi et al., 2008).

TRANSMISSION

R. seeberi is natural inhabitant of contaminated water and dust particles harbouring spores. Soil and water harbor the spores of these pathogens and hence water and soil act as reservoir for this pathogen (Rath et al., 2015). While drinking water, abraded nasal mucosa may get the infection (70% cases) and through dust fomites conjunctiva may gave rise to ocular form (15%) of disease. It is neither contagious nor transmitted through sexual contact. In arid countries such as arid India and Iran the most common form is ocular form through dust fomites. Incubation period is very long. Cases are more frequently observed in communities residing near swamp areas as contaminated water serves as source of infection, hence earlier it was

considered as aquatic fungus. It indicates possibility of probable synergism among aquatic micro-organisms and *Rhinosporidium seeberi* for the spread of infection through stagnant water. No direct transmission between humans and animals is reported yet, however transmission may occur by direct contact with fungal spores through aerosols, inhalation of dust particles, infected clothing and through swimming in torpid contaminated water (Reddy and Lakshminarayana, 1962; Venbreuseghem, 1976). Autoinoculation into breached skin or traumatized epithelium through transepithelial infection, lymphatic and haematogenous routes may also significantly contribute as predisposing factor in the entry and dissemination of fungal spores in the body. Auto-inoculation into adjacent epithelium may takes place if endospores may come out from polyps after any trauma or surgical intervention. For anatomically distant sites in the body of host haematogenous dissemination from a subclinical form of upper respiratory focus of infection (nasal or nasopharynx) can be one probable route of spread. Though few workers have suggested probability of lymphatic spread into regional parts of body but this route is yet not confirmed (Ashworth, 1923; Arseculeratne, 2002).

LIFE CYCLE OF PATHOGEN

Life cycle of *R. seeberi* is still mysterious as no well-established natural reservoir is documented and it cannot be cultured *in vitro*. Histological sections reveal all developmental stages of this pathogen. *R. seeberi* is an endospore forming pathogen which range from 60-450 micron or more. There may be around 12,000 spores inside mature sporangia. These spores may range from 7- 15 micrometre in diameter which can be passed out through pores (Herr et al., 1999b). Life cycle involves two stages first is of "Trophocyte" measuring about 7 microns in size and second is mature thick walled cyst called "sporangium" of 300 µm in size filled with numerous spores (Mishra et al., 1968). Spores are sometimes referred as electron-dense inclusion, electron dense body, electron-dense circular structure, germinative body, spherical body, protrusion of cell wall or sporozoites. Fully developed sporangia acting as source of spores are found on the external surface while the developing sporangia are present deep inside (Grover, 1970; Kutty and Gomez, 1971; Vanbreuseghem, 1973). Once the spores are released from the sporangia they can harbour the nearby tissue and can repeat their life cycle (Herr et al., 1999b).

MODE OF DISSEMINATION

Various ways by which *R. seeberi* spreads throughout the body of the affected person or animals have been documented by several workers. Karunaratne (1964) reported auto infection of *R. seeberi* according to which a trauma at the polyp causes spread of organism to various regions of the body. The trauma may occur as accident or during surgery for the removal of the polyp. This type of infection is mainly seen in the respiratory tract infection. Reports of spread of *R. seeberi* to remote organs have also been documented. Spread of organism from respiratory tract to the limbs of the affected individual through blood has been reported (Rajam et al., 1955). Ashworth (1923) suggested possibility of involvement of lymphatics in the dissemination of the pathogen but no study reported similar results to support the hypothesis. Later in 2002, a study showed that there is involvement of regional lymph nodes at the site of lesion (Arseculeratne, 2002). The lymph node had fibrous capsule along with presence of sporangia.

PATHOGENESIS, CLINICAL SYMPTOMS AND LESIONS

After entry of pathogen or it's spores main target sites are mucous membrane of nasal cavity and nasopharynx (in 70% incidences), less frequently conjunctiva or ocular mucous membrane but other sites such as oral mucosa of palate, lips, epiglottis, bronchi, larynx, trachea, external genitalia, bone, rectum and urethra may also get the infection, though ears, buccal cavity, pharynx, anus, vulva, penis and cutaneous tissue rarely gets the infection (Srinivasa, 1962; Rao et al., 1965). In a rare reported study parotid salivary duct system has also shown unusually extra nasal presentation due to rhinosporidiosis (Mahadevan, 1952; Kini et al., 2001). Clinical symptom may begin with epistaxis, discomfort, nasal obstruction and mucopurulent rhinorrhea. Pain occurs due to large sized papillomatous lesion obstructing nasal passage or affected site and applying pressure on nearby nerves and vascular vessels. Depending upon stage of life cycle, host status and site affected the symptoms may vary. Disease begins with the formation of small mass which degenerate into friable polyps of different colours as per the colour of sporangia varies from white, yellow, grey,

and pink to purple. Clinically disease can be presented in four forms: nasal, ocular, cutaneous and disseminated form.

Nasal Form

This is most commonly occurring form of rhinosporidiosis, characterized by epitaxis and development of sessile, pink to purple, peduncular polyps like nasal obstruction which can be unilateral or bilateral mostly in the upper respiratory tract remarkably on the anterior nares, nasal septum, inferior turbinate and at floor of the nasal cavity filled with opaque grey or white granular material. Polyps may also be situated on soft palate, larynx and nasopharynx. Due to obstruction of nasal passage discomfort and pain is also experienced by affected being. Natural regression of nasal polyp may also take place sometimes.

Ocular Form

This form begins as a sessile growth, which worsen to friable peduncular polyps in the eye. As per the size of outgrowth symptoms of tearing, discharge, redness of eye, photophobia, lid eversion, and conjunctival infection may appear. Polyps formed in the eyes are mostly flat, comparatively soft, bluish or pinkish to reddish in colour, lobular and express pin head sized spots due to presence of underlying mature sporangia. Usually 15% of rhinosporidial infections subsist on bulbar and palpebral conjunctiva, lacrimal sac and naso-lacrimal duct comprising ocular form of Rhinosporidiosis. There is evidenced that the primary predilection site of rhinosporidiosis is lacrimal sac from which infection spreads downward through the naso-lacrimal duct to the nasal passage for polyp formation.

Cutaneous Form

These lesions usually occur as tiny papule which becomes wart-like with a friable crenulated surface, which easily develop into ulcer and get infected but rarely become peduncular.

Disseminated Form

This form is **r**arely reported and whenever present is characterized by presence of spherules of *R. seeberi* in the bone, liver, lung, viscera, spleen, trunk, limbs and brain upon autopsy. If brain is involved, disease can be fatal, while if limbs are affected gradual demolition of underlying bone is an important feature. In males introvert polyps can also be present on the external urethral meatus (Agarwal et al., 1959; Nayak et al., 2007). Grossly cutaneous manifestation may occur in form of painless large, single or multiple, sessile or pedunculated, pseudotumoral polypoid lesions on the mucosa, papillomatous vascular lesions of nasal or urethral polyps, papilloma or slowly growing warts like noninfiltrating growth mostly in nasal cavity (Vallarelli et al., 2011). Sometimes, friable soft tissue masses resembling to strawberry or reddish colour due to enhanced vascularity either unilaterally or bilaterally or micro-abscesses can also be present in nasal cavity. Besides nasal obstruction, systemic and cutaneous form of disease is also documented (Rajam et al., 1955). Histologic microscopic examination reveal multifocal hyperplasia and ulceration on the mucosa, hyperplastic epithelium mainly within the mucosae of lamina propria, highly vascularized with fibromyxomatous connective tissue, large number of *R. seeberi* with variable morphology within juvenile and mature sporangia may be seen by PAS and Mayer's Mucicarmin stain. Sometimes, mild hyperemia, mild multifocal hemorrhage suggestive of vascular invasion, necrotic focal areas on the submucosa or occasionally mild multifocal hemosiderosis may also be present. Inflammed nasal mucosa can be infiltrated with neutrophils (polymorphonuclear cells), eosinophiles, lymphocytes, plasma cells (plasmocytes), mastocytes, giant cells and histiocytes along with edema and numerous fungal sporangiospores inside the sporangium. Sporangium size may range from 10 to 180 µm in diameter, enclosing sporangiospores of approximately 2 to 5 µm size or may vary oftenly. The mature sporangia came out through the epithelial surface and release many endospores into the nasal exudates. Numerous neutrophils are present surrounding the free endospores while chronic inflammatory cells including macrophages, giant cells and lymphocytes form major part of fibro-myxomatous or fibrous stroma. In the stroma giant cells may occur within sporangia also with prominent fibrosis mainly in non-respiratory locations of body.

In one clinicopathological study of 34 cases of rhinosporidiosis, generally a lymphoplasmacytic response was observed in all cases. Polymorphonuclear leukocytic response mostly observed at the site of rupture of sporangia. Epithelioid cell granulomatous and giant cell response observed in 47% of cases. Transepithelial migration of sporangia observed in 76% of cases (Makannavar and Chavan 2001).

HOST IMMUNE RESPONSE

Though in patient anti-rhinosporidial antibodies are present in high titers but unlike fungal or mycotic infections, Splendore-Hoeppli phenomenon is absent, which is indicated by absence of any antibody-mediated eosinophilic deposition around rhinosporidial bodies in the host system. Studies project that cell mediated immune response is activated but simultaneously with the immuno-suppression or with evidence of immune deviation means switch from CMI to HI also takes place; from activation of CD4+ Th-0 cells, production of CD4+ Th-2 cells begin probably mediated by cytokines towards the production of anti-rhinosporidial antibodies (Chitravel et al., 1981; Chitravel and Sundararaj, 1982; De Silva et al., 2001; Jayasekera et al., 2001). *R. seeberi* evokes immune mechanism in human, still it evades from host immunity through various suggested mechanisms. *R. seeberi* sporangia have a very thick outer wall which encompasses the antigenic structures inside so there is less chance for antibodies to act over it (Arseculeratne, 2002). When there is destruction of the wall there is exposure of these antigens. This phenomenon is called as antigen sequestration. Herr et al. (1999b) reported that *R. seeberi* possess the ability to vary their antigenic structures, and suggested that there is emergence of new antigenic structures when new sporangia emerge. *R. seeberi* also causes immune suppression (Sharmini et al., 2001). Other mechanisms like immune distraction, immune deviation, etc., are also suggested for this pathogen (De Silva et al., 2001).

DIAGNOSIS

Presumptive diagnosis is based on initial history, specific clinical symptoms, histo-pathology and confirmatory diagnosis is on the basis of specimen processing and microscopy. Definitive diagnosis requires help of histopathology for identification of *R. seeberi* in various diverse life stages, however if rhinosporidial bodies are not present in the selected portions of polyps histology may led to false-negative diagnosis. *Rhinosporidium seebri* is an obligate parasitic fungus, which unlike other fungi does not grow over artificial media rather needs tissue culture and epithelial cells for growth and cultivation (Datta, 1965; Levy et al., 1986; Ahluwalia, 1999). Few reports regarding the isolation of these organisms over the laboratory media are documented, however, no confirmation was made over these claims hence it remains uncultivable in media like other organisms (Levy et al., 1986; Arseculeratne and Ajello, 1998). Appropriate specimens involve biopsy tissue from affected areas for punch biopsy, fine-needle aspiration biopsy (FNAB), histochemical studies, cytological and histological examination (Narayanarao, 1966; Bader and Grueber, 1970). Histopathology shows multiple budding sporangia entrenched in fibrovascular stroma infiltrated with chronic inflammatory cells. The histopathological findings of animal rhinosporidiosis resembles with the human disease.

Endoscopic examination involving rhinoscopy and CT scan is helpful in identifying appropriate lesions of tissue overgrowth. CT scan confirms the soft friable mass without bone involvement either in nasal cavity or at the affected site (Ayub-ur-Rehman et al., 2012). Direct microscopy of stained smears with a drop of 5-10 per cent KOH reveals presence of typical double wall cystic spherules of approximately 300 µm size filled with innumerable endospores. Affected tissue or nasal exudates when examined directly with 10% KOH demonstrate empty sporangia and free endospores. There Cytological diagnosis is based upon presence of 5 to 10 µm sized endospores within sporangium of 50 to 100 µm. Lactophenol cotton blue, Alcian blue, PAS and Mucin staining technique make the features of cystic wall and spores more distinct. Other colorants which can facilitate the diagnosis of rhinosporidiosis include PAS, HE, Grocott, Mayers Mucicarmin and GMS. Periodic acid-Schiff stain provides magenta color to endospores while epithelial cells remain PAS-negative.

No growth is observed over Sabouraud's dextrose agar (SDA) medium (Moses et al., 1988). No specific serological tests or culture techniques are available for confirmatory diagnosis. A molecular technique as PCR amplification is helpful by using *R. seeberi*–specific primers for confirmatory diagnosis (Arseculeratne, 2002). Indirect immunofluorescence tests by using sonicated endospores and sporangia as antigens, double diffusion and counter immunoelectrophoresis (CIE) tests are also useful for detection of anti-rhinosporidial antibodies.

Differential diagnosis should be made from other fungal infections of granulomatous rhinitis or polypoid lesions caused by *Coccidioides immitis* or adiaspiromy-

cosis caused by *Chrysosporium parvum,* Cryptococcus polypoid tumor, condylomata, malignancy, myospherulosis (subcutaneous spherulo-cystic disease), hemorrhoids and neoplasia. The anatomopathological study with histopathological examination revealing nasal polypoid lesion should be differentially diagnosed (Crosara et al., 2009). Size of spherules of R. seeberi should be differentially diagnosed from spherules of *Coccidiodes immitis* (30 to 60 mm, comparatively larger in diameter).

TREATMENT

Chemotherapy is not much successful due to inappropriate penetration of the sporangial wall of spherules, thus no effective antifungal or antimicrobials are available. However dapsone has some anti-rhinosporidial effect as it can seize maturation of sporangia along with encouraging fibrosis in the stroma and so the recurrences can be prevented by prolonged use of dapsone (4, 4-diaminodiphenyl sulphone). In one clinical trial with dapsone on 32 patients, 20 patients (71.4%) did not have recurrence in a three year period and none of them needed surgery in that period. Thirty-two patients were used as controls, and 93% of them needed surgery for recurrent rhinosporidiosis in the same three year period. Dapsone (diaminodiphenylsulfone) is a relatively safe drug to use, and no major side effects were noticed in this trial (Nair, 1979). In one study, dosage of 100 mg/day of dapsone for several months is recommended in human patient to prevent the recurrence of disease after surgical removal (Job et al., 1993; Crosara et al., 2009; Madke et al., 2011). Immunological response is not of much value. Recurrences are common, probably due to incomplete excision or intraoperative contamination of adjacent tissues or cells with residing endospores making condition further grave, hence electro cauterization at the site of excision is recommended as a future preventive measure. Surgery by hot or cold snare technique is the treatment of choice and endoscopic removal of naso-oropharyngeal polyps is also practiced (Arun et al., 2009). Treatment is done by cryosurgical excision of lesion to check the recurrence and spread of infection. As *R. seeberi* is notoriously sporadic relapses are common in absence of timely & proper treatment. Recurrence of the disease after surgical treatment is only 10% and if properly taken care of prognosis is good. Morbidity is low and generally due to secondary bacterial infection of the lesion. Death is rare only in disseminated form of disease when multiple organs are involved & severely affect the functioning of vital organs.

Rhinosporidiosis is a condition which both clinicians and pathologists should keep in mind when managing patients from endemic countries with nasal masses. Moreover, it is very interesting in such cases to follow the clinical course: an eventual recurrence of the lesion in our patient would mean a true relapse, excluding the possibility of a reinfection, more probable in the endemic areas (Morelli et al., 2006). As the habitat of *R. seeberi* is identified as ground water, people who use these sources either for swimming or drinking purposes should be free from injuries as the pathogen gains entry through wounds (Kaluarachchi et al., 2008).

CONCLUSION

The etiological agent of rhinosporidiosis, *R. seeberi*, has been a riddle from past 9-10 decades. Though causative agent is now being confirmed as a fungus but yet this pathogen cannot be successfully grown over artificial media under laboratory conditions. Here we have discussed in brief regarding possible mode of transmission, epidemiology, geographical distribution, life-cycle of the pathogen, clinical features and diagnostic and remedial approaches against this disease. Prevention will be the best option to be safe from this organism as the disease takes a chronic course which makes diagnosis difficult. Hence swimmers and persons who are frequent visitors to water bodies should have safety precautions as this organism get transferred through cut wounds. Questions remain open for the scientific community to answer and solve the mystery behind this pathogen. Questions like: is there any host preference, age preference, sex preference, site of predilection as it targets face mainly, information regarding the spread through lymphatics, role in immune suppression need attention. Chronic nature of the pathogen is another ramp which delays its diagnosis as its clinical feature is the clear indicate of the disease. Newer diagnostic assays for various other pathogens including fungal pathogens are now used commonly hence newer assays should be developed to detect this pathogen early both in human and animal so as to control the disease effectively. Hopefully knowledge will probably lead to the development of suitable culture methodology, less time demanding

precise diagnostic laboratory techniques and more efficient therapeutic modalities and sound protocols for the prevention of this disease.

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