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Rhinosporidium seeberi: Is It a Fungi or Parasite?

Rhinosporidium seeberi: Mantar mı, Parazit mi?

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ABSTRACT

Rhinosporidium seeberi (*R. seeberi*) causes rhinosporidiosis, which is manifested as tumor-like polyps developing primarily in the nostrils and conjunctiva in human and animals. This disease is characterized by the presence of large, round-shaped mature stage and small endospores with resistance to culturing. *R. seeberi* was first reported in 1900 as a sporozoan parasite, but later classified as a lower fungi, although its morphological similarity with aquatic parasites were also noticed. According to 18S small-subunit ribosomal DNA sequencing, *R. seeberi* belongs to a group of fish parasite DRIP clade located between the animal and fungal divergence. Histological examination is thus necessary for the definitive diagnosis of rhinosporidiosis, and the first line of treatment is usually total surgical excision and electro-cauterization of the polyp base. Among the drug therapies attempted, remission has been reported in some patients who received only Dapson treatment. This disease is endemic across India, Pakistan and Sri Lanka and occurs sporadically in other parts of The World with a common history of patients bathing in stagnant water. An outbreak in Serbia during 1992-1995 and 5 rhinosporidiosis cases from Turkey have been reported until date. Considering that rhinosporidiosis is associated with exposure to water and the agent belongs to a branch of aquatic parasites, it has been proposed that aquatic animals are the natural hosts and that the mammalian hosts acquire infection by contacting contaminated water. Therefore, there is a need for the investigation of the infection in fish besides mammalian animals as reservoirs as well as to conduct screening of antiparasitic drugs with infected fish or infected cell lines with the nearest phylogenetic relatives of *R. seeberi*.
Keywords: *Rhinosporidium seeberi,* epidemiology, diagnosis, treatment

ÖZ

Rhinosporidium seeberi (*R. seeberi*) insan ve hayvanlarda, öncelikle burun delikleri ve konjunktivada gelişen tümör benzeri poliple karakterize olan Rhinosporidiosis etkenidir. Büyük, yuvarlak şekilli olgun evreler ve daha küçük endosporlar ile karakterize olup; kültürü yapılamamaktadır. Yirminci yüzyılın başında, *R. seeberi* sporozoan parazit olarak düşünülüp daha sonra ilkel fungus olarak sınıflandırılmış, ancak akuatik parazitler ile morfolojik benzerlikleri de fark edilmiştir. *R. seeberi* "18S small-subunit ribosomal DNA" sekans analizi ile hayvan-mantar ayrımı düzeyinde yer alan DRIP grubu balık parazitleri içerisine dahil olmuştur. Kesin tanı ve tedavi için cerrahi eksizyon sonrası polip tabanının elektro-koterizasyonu ve histolojik incelemesi gereklidir. Denenen ilaç tedavileri arasında sadece Dapson ile bazı hastalarda remisyon sağlanmıştır. Hastalık Hindistan, Pakistan ve Sri Lanka'da endemik olarak görülse de diğer ülkelerde de rastlanmaktadır ve hastaların ortak öyküsünün durgun suya girmek olduğu gözlenmiştir. Sırbistan'da 1992 ile 1995 yılları arasında bir salgın meydana gelmiş ve Türkiye'de günümüze dek toplamda beş olgu bildirilmiştir. Rhinosporidiosis bulaş yolunun suyla temas ile ilişkilendirilmesi ve etkenin akuatik parazitlerin bir grubunda olması nedeniyle, akuatik hayvanların doğal konaklar olduğu ve memeli konakların enfeksiyona kontamine su ile kontakt sonucunda yakalandıkları düşünülmektedir. Bu nedenle, *R. seeberi*'ye filogenetik olarak yakın türler ile enfekte hücre serilerinde anti parazitik ilaçların etkilerinin taranması gerektiği gibi, enfeksiyonun balıklarda ve rezervuar olarak doğadaki hayvanlarda araştırılmasına da ihtiyaç vardır.
Anahtar Kelimeler: *Rhinosporidium seeberi,* epidemiyoloji, tanı, tedavi

INTRODUCTION

Microorganism

Rhinosporidium seeberi (*R. seeberi*) is a hydrophilic microorganism causing rhinosporidiosis, a chronic granulomatous disease characterized by slow-growing, tumorlike reddish friable mucosal polyps, that bleed profusely on touch which are developing primarily in nostrils and conjunctiva of human and animal hosts. Rarely, lesions may also develop in nostrils neighboring area, rectum and external genital organs (1-3).

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Türkiye PARAZİTOLOJİ Dergisi

Morphologically, *R. seeberi* is showing similarity to *Coccidioides immitis* with large round shaped mature stages and smaller endospores. Besides this, it can be stained by fungal stains as methenamine silver, periodic acid-Schiff and mucicarmine. *Rhinosporidium seeberi* is resistant to culture and life cycle is unknown (1).

History

In 1900, Seeber described rhinosporidiosis firstly and when he discovered sporangium structure of *R. seeberi* he considered this organism as a sporozoan parasite belonging to the coccidia group taxonomically. After that, *R. seeberi* was classified in the lower fungi (Phycomycetes) such as Chytridineae and belonging to suborder near to the Olpidiaceae. Then Dodge classified *R. seeberi* as an ascomycetous fungus because of the similarity of sporangia to multispored asci (2). Besides this, similarities between *R. seeberi* and aquatic parasites like *Ichthyophonus* and *Dermocystidium* have noticed also by some researchers. Because of taxonomic controversies, *R. seeberi* has been considered in a wide range as protozoan, fungus and cyanobacterium. Sequence analysis of 18S small-subunit (SSU) ribosomal DNA (rDNA) (GenBank accession no. AF118851) placed it within a recently described fish parasite group DRIP (Dermocystidium-Rosette agent-Ichthyophonus-Psorospermium) clade that proposed to rename as Mesomycetozoa (2). In Herr's study (2), 18S SSU *rDNA* gene could not amplified by PCR with NS1 (nu-SSU-0038-5'; 0020-0038):5'-GTAGTCATATGCTTGTCTC-3' and NS8 (nu-SSU-1769-3'; 1788-1769): 5'-TCCGCAGGTTCACCTACGGA-3' primer set (4) and amplification was succeeded after degeneration of NS8 primer as S14R: 5'-TCCGCAGGTTCACC(TA)ACGGA-3' (5). Amplification of 1790 bp, nearly full length of 18S SSU rDNA sequence of *R. seeberi* was succeeded using NS1 and the modified reverse primer set. Phylogenetically, the nearest relatives of *R. seeberi* were found to be two *Dermocystidium* species while it was also clustered closer to the other members of the DRIP clade like the rosette agent, *Ichthyophonus*, and *Psorospermium*. DRIP clade covering unknown organisms situated between the animal-fungal divergence, and *R. seeberi* is near to the choanoflagellates placed in lowest branch of the Animalia kingdom. Common features of DRIP group (i) spherical parasitic stages (some have endospore-like structures) showing similarity with fungus characteristics; (ii) they are resistant to culture except *Ichthyophonus hoferi* and (iii) all are parasites showing aquatic habitats (2). However, later Ahluwalia (6) commented on the article published by Herr et al. (2) that the sporangia DNA was extracted without enzymatic digestion, which is insufficient for removing human cells, therefore these contaminating human cells could be the source of amplified 18rDNA in their study. Contrary to Ahluwalia's letter, Herr's team (7) responded Ahluwalia's letter as the sequence in their study (GenBank accession no. AF118851) was unrelated with 18S SSU rDNA nucleotide sequences of human. Additionally, the sequences of *R. seeberi* from human (GenBank accession no. AF118851) and a dog (GenBank accession no. AF158369) with rhinosporidiosis, were identical to each other (1).

Diagnosis

Detection of *R. seeberi*'s endosporulating sporangia ranging from 60 and 450 μm or more in diameter in histological sections of polyps is pathognomonic for diagnosis. In the mature sporongia, approximately up to 12.000 endospores between 7 and 15 μm diameter that discharge from a pore and repeat *in vivo* life cycle in surrounding tissue is contained. After excision of the polyp, in histopathological examination of the smear stained by hematoxylin and eosin method, numerous thick-walled sporangia with different stages of maturation showing inflammation in surrounding tissue were observed (2,3).

Treatment

First line treatment is total surgical excision and electro-cauterization of polyp base. However, recurrens of the lesions are reported (3,8). Sonkhya et al. (8) stated that, previously antifungal agents were found to be ineffective in treatment while complete remission was achieved in a study with Dapsone therapy for a year in rhinosporidiosis patients.

Epidemiology

The disease is showing endemicity primarily in India, Pakistan and Sri Lanka. However, it also occurs in other parts of The World, including Africa, South America, Middle East and Europe. Common history of the patients was bathing in the local pond or stagnant water (3,9).

Males are more frequently infected than females. It is stated that the content of chloride, a potent inhibitor of microorganism growth, in endemic country India is very less when compared to western countries where rhinosporidiosis is only seen as sporadic cases mostly have diagnosed in expatriate Indians (10).

Rhinosporidiosis occurs rarely in European countries. However, an outbreak affected 21 individuals between 1992 and 1995 and common behavior of the patient group is bathing in the same stagnant water in Serbia (Former Yugoslavia) (9).

Rhinosporidiosis in Turkey: There were totally five rhinosporidiosis cases reported from Turkey so far. The first case was published in 1955, a 12 years old girl of a farmer family who gained the lesion in her nose by accidentally felling into a stagnant water after occurrence of a trauma in her nose (11,12). Than two male cases were reported in 1979 from Turkey. The lesions were arisen from maxillary sinus and spread to nasopharynx in 78 years old patient and to ethmoidal area in other 53 years old patient. They were treated by surgical excision (13). Another case reported from Turkey is 47 years old male patient. His history was to contact with soil for three days during an earthquake after losing his right molar teeth. He admitted to hospital with erosion of the anterior wall of the right maxillary antrum. Rhinosporidiosis was diagnosed by cytological and histopathological examinations and the lesion was removed by surgical excision without any recurrence in two years follow up period (12). The last case from Turkey published in 2008, was a 75 years old female with grape-like mass in her right nostril. After totally excision of the lesion that histopathologically diagnosed as squamous papilloma, recurrence was occurred in six weeks. It was suspected from rhinosporidiosis and diagnosis was confirmed by histopathological examination after total excision of the lesion and electro-cauterization of the base of it. The patient diagnosed as Alzheimer disease five years ago, did not have any history of previous surgery and contact with pond water or pets (14).

CONCLUSION

Analysis of 18S *rRNA* gene suggests that this organism is not a fungus but rather is the first known human pathogen from a

novel aquatic parasite branch located near the animal-fungal divergence in the phylogenetic tree. Fredricks et al. (1) proposed that, the natural hosts of *R. seeberi* are aquatic animals and mammalian hosts acquire infection via contacting contaminated water. This hypothesis is depending on the observations that rhinosporidiosis is associated with exposure to water and the agent belongs to a branch of aquatic parasites. Therefore, there is a need for investigation of the infection in fish in ponds and rivers besides mammalian animals as reservoirs in disease endemic areas as well as screening antiparasitic drugs using infected fish or infected cell lines with nearest phylogenetic relatives of *R. seeberi* in DRIPs clade.

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*** Ethics**

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