Ocular Leishmaniasis

Review Article

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Abstract

***Purpose*:** To introduce the importance and world prevalence of ocular leishmaniasis (OL), its clinical manifestations, and diagnostic and management features with more emphasis on Iranian cases.

***Methods*:** We reviewed all available articles published about OL during recent 50 years.

***Results*:** OL is an ocular protozoal infection which is widespread in the world but is more common in developing countries. All forms of leishmaniasis (cutaneous, mucocutaneous, and visceral) can involve the eye, but ocular lesions are usually seen in cutaneous form. Clinical manifestations of OL include: lid skin ulcer, conjunctivitis, episcleritis, cataract, glaucoma, keratitis, uveitis, and finally eye destruction. Clinical diagnosis of this disease is difficult and any delay in diagnosis and management can cause irreversible damage to the eye and adnexae. From 1950 to 2005 there were limited reports of OL in the literature from: *USA*, *Brazil*, *Germany*, *Spain*, *Turkey*, *India*, *Sudan,* and *Iran*. In *Iran,* four cases were reported, two of whom ended in blindness, because the treatment procedures were not effective. Treatment with combined stibogluconate and allupurinol in early stages of the disease usually leads to complete healing of the lesions and disappearing of parasites from the ocular samples.

***Conclusion*:** Although OL is a relatively rare disease in the world, it is potentially dangerous and affected patients must be followed up closely, especially immunodeficient ones. Early diagnosis of OL and rigorous treatment may prevent blindness. Pentavalent antimonial compounds (combined stibogluconate with allopurinol) can be effective in treatment.

***Keywords*:** Ocular Leishmaniasis, Pentavalent Antimonials, Blindness.

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Introduction

Leishmaniasis is a protozoal disease which is widespread in over 88 countries in the world. It is estimated that 350 million People live in areas where the disease is endemic, 12 million people are presently affected and approximately 1.5 million new cases occur each year.[1] The disease is more common in developing countries. Despite various control measures, the incidence of the disease has increased and new outbreaks have been encountered in areas exposed to immigrants.[1] The microorganism is transmitted by the bite of a sand fly and can cause different clinical entities depending on the species of the Leishmania,[2] and the host immune response.

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These include cutaneous form which is caused by Leishmania Tropica (L Tropica), visceral form caused by *L Donovani* and mucocutaneous form caused by *L Braziliensis*.[2] Some species act as the opportunistic parasites mainly in immunosuppressed patients.[3-5]

In *Iran* visceral leishmaniasis or *Kala-Azar* and cutaneous leishmaniasis are sporadic and endemic respectively.[6,7] *Kala-Azar* has been reported from *Ardebil*, *Fars*, *Khorasan*, Eastern *Azarbaijan*, *Khoozestan*, *Qom*, *Boushehr,* and *Lorestan* provices.[7]

Ocular leishmaniasis (OL) as an old world disease[6] is caused by different Leishmania species.[8,9] The eye may be affected in cutaneous, mucocutaneous and Post *Kala–Azar* Dermal Leishmaniasis (PKDL).[10-18]

Clinical manifestations of OL include lid skin ulcer, blepharitis, conjunctivitis, cataract, interstitial keratitis, anterior uveitis, glaucoma and finally loss of the eye. Clinical diagnosis of ocular lesions is difficult because it has no specific characteristics and can simulate other conditions like chalazion, lid or conjunctival tumors, dacryocystitis or non specific uveitis.[6,7]

The eyelid is involved in 2.5% of cases with cutaneous leishmaniasis. The conjunctiva and episclera are also affected in cutaneous leishmaniasis[6,10,18] by contiguous spread from the lid or by inoculation of the conjunctiva by the patient's own fingers. The conjunctivitis which occurs in visceral form is usually bilateral and the route of infection is hematogenous.

If its eyelid lesions remain untreated, they may spread to the conjunctiva, episclera and even cornea. So OL is a potentially blinding disease and any delay in diagnosis and treatment as well as patient's immune deficiency can cause irreversible damage to the eye or its adnexae.

Therefore, despite the uncommon occurrence of this disease its diagnosis and treatment remain a challenge. This literature search was carried out to provide a general overview of OL in the world, with special glance to *Iran*, including guidelines for its timely diagnosis and management.

Methods

About 30 articles associated with OL could be obtained from Medline and Elsevier websites. The search of the English language literature was conducted using the keywords “ocular leishmaniasis” and “Leishmania” from the years 1956 to 2005. Also 25 papers which were presented in various congresses and meetings in recent 50 years were reviewed. There is a list of their addresses at the end of the article.

Results

Until 1978 there were few reports from Africa and the USA, with ocular manifestation, secondary to systemic leishmaniasis.[19-21]
In 1979 a reported case of interstitial keratitis from the USA indicated that mucocutaneous leishmaniasis can cause blindness.[11]

In 1980 in *Germany* a research on cutaneous leishmaniasis of eyelids was carried out.[12] At the same time 3 cases of uveitis associated with *Kala–Azar* were reported from *India*. 2 of them developed glaucoma.[22]

In 1983 in the *USA* Leishmania Braziliensis Panamensis was isolated from an eyelid ulcer sample. Serologic tests were positive and pentavalent antimony drug was effective in its treatment.[23]

In 1990 an uncommon case of leishmaniasis was reported from *Brazil* with disseminated cutaneous lesions, systemic manifestations and ocular involvement. In spite of satisfactory regression of both systemic and cutaneous signs, ocular lesions did not respond to treatment.[24]

An *Indian* report in 1991 described blepharoconjunctivitis in a patient with nodules of PKDL on the chin. It was suggested that contamination spread from the chin nodules to the eye by fingers.[25]

At the same time in India another study presented two cases of ocular cutaneous leishmaniasis and post *Kala–Azar* anterior uveitis. Leishmanial parasite was isolated from the lesion.[26,27]

In 1992 in *Germany*, there was a report of an eastern immigrant, 4-year-old boy with a 5 months history of blepharitis. He had left Lebanon 9 months before. The Lesion did not respond to aminoglycoside antibiotics. Pathological investigations of lesion revealed amastigotes in macrophages. Therapy with gamma - Interferon, which was used for the first time in the treatment of this disease, was effective without any side effects.[28]

In 1993, 3 cases of OL were reported from *Iran*. The first one was a 5-year-old girl from *Shiraz* who was suffering from a small non-healing ulcer on the right lower bulbar conjunctiva for one month. Pathologic investigation showed leishmaniasis infection but the patient did not receive any treatment. Two months later she lost her vision and eventually the right eye was enucleated. Further pathologic examination showed, total destruction of the eye by leishmaniasis.[6]

The second case was a 13-year-old boy with complaint of a non–healing ulcer on the right lower conjunctiva for one and a half months. Meanwhile he was suffering from Cooley's anemia. In pathologic exam, Leishmania SPP was detected in samples from the lesion. He did not receive any treatment and returned after 4 weeks with visual loss. After 2 days he died due to severe anemia. Post mortem enucleation of the right eye revealed complete globe destruction. In histopathologic examination of the eye, a huge population of Leishmania bodies was detected.[6]

The third one was a 10-year-old girl with fever, and hepatomegaly that examination of bone marrow, revealed visceral leishmaniasis. The patient was treated with glucantime and discharged in good health condition after a month. The disease relapsed after 3 years. So glucantime and gentamicin were prescribed for 4 weeks and the patient responded well to the treatment. During relapse of *Kala-Azar*, patient had decreased vision of the right eye due to keratitis that was treated with gentamicin and prednisolone. In spite of improvement in her general condition, she lost her vision completely and after 1 year the eye was enucleated. Final pathologic examination revealed total destruction of the eye by leishmaniasis.[6]

In 1998 in the *USA*, a case was reported with disfiguration of the face, cheeks, nose and eyelids due to cutaneous leishmaniasis. The lesions responded to itraconazole with satisfactory results.[29,30]

In 1998 in Sudan 6 cases with post *Kala-Azar* OL were identified. 4 Patients had Leishmanial blepharoconjunctivitis. Utilizing PCR, causative agents were diagnosed as Leishmania Donovani. The other 2 patients had post Kala-Azar anterior uveitis. Clinical manifestations like blepharoconjunctivitis and uveitis, history of previous treatment with anti–Leishmanial drugs, association with PKDL and positive Leishmania tests, all of them, confirmed other cases of OL. The Patients were treated with systemic stibogluconate. Cases with anterior Uveitis were also treated with corticosteroid and atropine eyedrops. The response to treatment was satisfactory.[10]

In 2001 in *Brazil*, 4 patients were referred with dacryocystitis. Nasal mucocutaneous leishmaniasis was identified as the main cause. All of them were treated successfully with conventional treatment.[31]

In 2002, a patient with non–tender reddish mass in his right lower lid associated with conjunctivitis and nodular episcleritis was referred to an eye hospital in *Tehran*. Leishmania Protozoa was isolated from the lid lesion. Treatment with stibogluconate did not cause obvious improvement. Therapy with combined stibogluconate and allopurinol was started with good results.[18]

In the same year in the *USA*, a kidney transplant patient was reported who received immunosuppressive drugs and suffered from fever and pain in the legs and thorax. Meanwhile he complained of ocular pain and low vision due to keratitis which was caused by Leishmania Viania Braziliensis. After diagnosing OL, biopsy of the iliac crest was performed that showed amastigotes in the sample. Treatment did not provide satisfactory result and the patient died soon from the infection.[4]

In 2003 in *Spain* a patient with sudden visual loss caused by retinal hemorrhage was presented. On systemic evaluation, he was found to have visceral leishmaniasis and treated with pentavalent antimonials. 2 months later, best corrected visual acuity was $^{20}/_{25}$, with no residual scotoma.[32]

In 2004 there was a study in *Turkey* to determine the rate of ocular involvement in cutaneous leishmaniasis. Its results showed 1.93% of all cutaneous lesions and 3.57% of facial lesions were located on the eyelids, and periorbital region.[33]

At the same time there was a report on the fulminant OL in a HIV–1- positive patient in *Turkey*.[34]

Discussion

Patients with leishmaniasis should be followed every few months either by serologic tests or bone marrow examination[6] especially in the immunodeficient cases because of the possibility for reactivation of disease and producing atypical clinical manifestations. In immunosuppressed patients, parasites may spread to other organs easily.[4] Some reports have ignored the need to specify the type of organism with adequate sampling and have treated suspected cases of OL as soon as possible.[35]

So OL may be missed, because it has been almost very difficult to be differentiated among the various types of eye diseases caused by other pathogens. Meanwhile Leishmania may be the cause of intraretinal hemorrhage and should be considered in areas where leishmaniasis is endemic.[32]

Conclusion

The clues for diagnosis are the clinical aspect of the lesions, the epidemiologic data, and a positive Leishmania skin test. Demonstration of the parasite is not always possible.[36,37] Early diagnosis and vigorous treatment may prevent blindness.[18]

Various ocular involvements in cutaneous and mucocutaneous leishmaniasis must be studied further.[38]

Pentavalent antimonial compounds are the drugs of choice[40] and multiple drug therapy especially combined stibogluconate and allopurinol is recommended.[18,39]

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