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Clinicopathological study of parasitic lesions of the eye and ocular adnexa in a tertiary care ophthalmic center in South India

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Purpose: To study clinical and pathological features of parasitic lesions in the ocular adnexa in a tertiary care ophthalmic center in south India. **Methods:** 43 cases of ocular parasitosis were analysed clinically and correlated with the pathological findings (gross morphology and histopathology) over a period of five years (2015–2020). **Results:** Among the 43 cases, the age group ranged from 9 months to 78 years (mean age of 41.6 years). Female patients were more common than male patients, with a percentage of 63% (27) and 37% (16) respectively. Cystic lesion in the lid or orbit was seen in 23 cases (53.4%); solid mass lesions were seen in 17 cases (39.5%); subconjunctival worms in three cases; and subretinal parasite in one. Gross examination and histopathologic study showed Dirofilaria in 23 cases (53.5%), followed by Cysticercus in six cases (14%) and Microfilariae in four cases (9.3%). Exact species identification was not possible in ten cases (23.25%). Correlation between the type of lesion and type of inflammatory cells with the specific parasite was done. **Conclusion:** Our study showed that important clinicopathological correlations can be made from the parasitic lesions in the eye and adnexa, which can aid in definitive diagnosis and prompt identification of the parasite for patient management.

Key words: Cysticercus, dirofilaria, granulomatous reaction, microfilaria, orbital mass, parasite

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Ocular parasitosis is a relatively rare disease even in a developing country like India. These parasites are important as they can cause severe damage to the external and internal structures of the eye. Lesions in the eye can be due to damage directly caused by the parasite, indirect pathology caused by toxic products, immune response incited by infestation, or ectopic parasitism of the pre-adult or adult stages.[1] In certain parasitic infestations, removal of the live worm is important because killing of these parasites by antimicrobial agents can incite severe intraocular inflammation and infection such as endophthalmitis.[2]

While symptomatology and serology are not reliable for diagnosis, surgical removal and histopathological diagnosis are the best ways to identify the parasite. The intact parasite is required for proper identification of the species.[3,4]

We report here clinicopathological correlations of 43 cases of parasitic lesions in the eye and ocular adnexa from a tertiary care ophthalmic center in south India.

Methods

Retrospective analysis of 43 consecutive cases of parasitic lesions in the eye and adnexa from 2015 to 2020 was done. All patients had detailed clinical history and completed ophthalmological examination. Gross morphological examination with measurements and histopathological examination was done by two trained ocular pathologists. Parasite identification was confirmed by a veterinary parasitologist.

Gross examination

The parasite specimens, preserved in normal saline, were subjected to initial washing with water followed by ascending grades of alcohol (30%, 70%, and 100%), and then kept in a clearing agent, lactophenol. In few cases, the worms were thoroughly washed in a physiological solution, and cleaned from mucus and debris before fixation. In case of broken pieces of helminth specimens, they were directly placed in a clearing agent namely lactophenol. Such worms with lactophenol in a slide with cover glass was examined under a stereo zoom microscope directly under low and high power magnification, and measurements were done.

The worms were identified based on gross morphological features like length, cuticular striations, anterior end (head end) and posterior end (tail end) of the worm specimen, and presence of cephalic, caudal and anal alae or protrusions. Male and female worm forms were identified along with the arrangement of papillae, column of granules, somatic cell or nuclei and its pattern of arrangement throughout the body.[5]

The excised mass and tissue specimens were put in formalin and subjected to histopathological processing and examination.

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Results

43 cases of parasitic lesions in the eye and ocular adnexa were analyzed. The age group ranged from 9 months to 78 years (mean age of 41.6 years). 27 female (63%) and 16 male (37%) patients had ocular parasitosis. Cystic lesion in the lid or orbit was seen in 23 cases (53.4%); solid mass lesions were seen in 17 cases (39.5%); subconjunctival worms in three cases; and subretinal parasite in one case [Table 1]. 23 cases (53.5%) of Dirofilaria were identified. The species of Dirofilaria that were isolated were *Dirofilaria immitis* and *Dirofilaria repens*. Cysticercus was seen in six cases while Microfilariae were seen in four cases (9.3%). Exact species identification was not possible in ten cases (23.25%). Histopathological study of the specimens showed inflammation with eosinophils (65.2%) and lymphocytes (65.2%), followed by plasma cell infiltration in 39.5% and neutrophilic infiltration in 16.3% of cases. Giant cells were seen in 17 cases (39.5%). The secondary changes that were noticed were granuloma formation in 18 cases (41.8%), necrosis in 11 cases (25.5%), and fibrosis and vascularization in 9 cases each (21%). [Table 2]. Correlation between the type of lesion and type of inflammatory cells with the specific parasite was done [Tables 3 and 4].

Dirofilaria worm was found to be a thin, slender, motile, whitish-yellow-coloured worm. The head was narrower with slight concavity. Rudimentary papillae were seen at this anterior end. The caudal end was rounded. The worm had a thick laminated cuticle on its surface. Longitudinal section showed multi-layered cuticle, lateral chords; the female worm in addition had a uterus [Figs. 1–3].

Microfilaria was a sheathed parasite ranging from 250 to 300 micron in size. They were transparent with a blunt head and pointed tail, and covered by a hyaline sheath [Fig. 4].

Cysticercus cellulosae were found to be ovoid, opalescent, and milky-white, measuring 8–10 mm in breadth and about 5–7 mm in length. The cyst was seen under stereo zoom microscope, and measured. The scolex of the larva, with its suckers, invaginated within the bladder and was seen as a thick white spot. Histopathological study of cysticercosis mostly revealed a cystic cavity containing the larval form, with duct-like invaginations, double-layered lining eosinophilic membrane with a variable granulomatous reaction, inflammatory infiltrate, fibrosis and rare calcification [Fig. 5].

Table 1: Sites of involvement by the parasites

Site of lesion	Number of cases
Lids	16
Orbit	11
Conjunctiva	8
Lacrimal Gland	2
Intraocular	4
Tenon's/Sub-Tenon	2

Table 2: Types of inflammatory cells identified in the tissue

Inflammatory cells	Number of cases
Neutrophils	7 (16.3%)
Lymphocytes	28 (65.2%)
Eosinophils	28 (65.2%)
Giant Cells	17 (39.5%)
Plasma Cells	17 (39.5%)

Table 3: Parasite with the type of lesion

Parasite	Total no. of cases	Cystic lesion	Solid mass lesion
Dirofilaria	23*	10	10
Cysticercus	6	6	0
Microfilaria	4	1	3
Unidentified parasite	10	6	4

*3 cases of Dirofilaria presented as subconjunctival worm

Discussion

Clinical findings, imaging, and serology alone have limitations in identifying a parasite; therefore gross as well as histopathological examinations play an important role in the identification of the parasite or parasite parts in the excised specimen.

Many of the times, the presence of a mass lesion in the orbit with eosinophils and with or without Splendore–Hoeppli phenomenon warrants the pathologist to carefully search for a parasite or degenerated parasite part, and to avoid misdiagnosing it as a mere which will add to specific management of the patient.

It is important to note that apart from eosinophils, other inflammatory cells (both acute and chronic), granulomas and giant cell reactions similar to an inflammation process initiated in a fungal infection or due to a reaction to a foreign body may

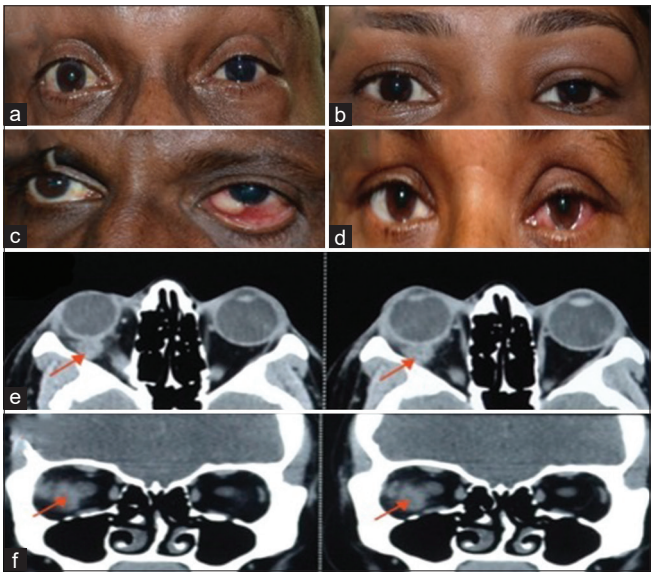

Figure 1: Presentations of Dirofilaria (a) Pre-treatment lid swelling of a case of parasitic lesion in the left lower eyelid. (b) Pre-treatment lid swelling of a case of parasitic lesion in the left upper eyelid. (c) External photography showing a Tenon's cyst in the left eye. (d) Dirofilarial conjunctival cyst in the left eye with chemosis. € CT scan image showing the parasite in the orbit (red arro–) - Axial section. (f) CT scan image showing the parasite in the orbit (red arrow) - Coronal plan

Table 4: Parasite and corresponding type of inflammation on microscopy

	Neutrophils	Eosinophils	Other inflammatory cells	Giant cells and granuloma	Necrosis
Dirofilaria	+/-	+	+/-	+	+
Cysticercus	+/-	Usually absent	Lympocytes +	-	-
Microfilaria	-	+	+/-	+	+

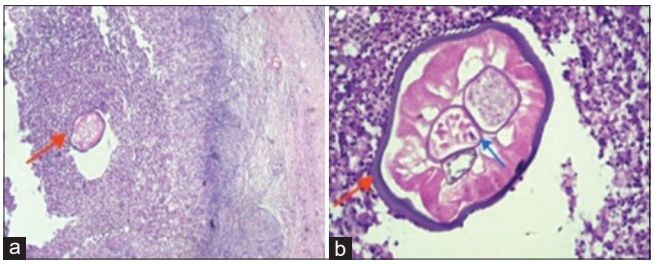

Figure 2: Histopathological findings in Dirofilaria (a) Microphotograph showing adult female filarial nematode cyst (red arrow) in the conjunctival tissue with severe inflammation around the parasite (Hematoxylin and Eosin stain, X100) (b) Microphotograph showing an oval cystic structure (red arrow) with cuticle, longitudinal ridges organelles (uterus and intestine) shown by blue arrow (Hematoxylin and Eosin stain, X400)

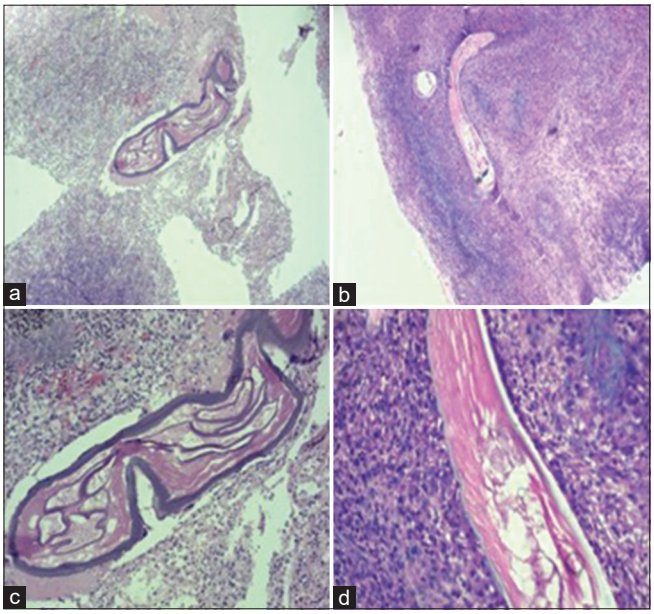

Figure 3: Histopathology of Microfilaria (a) and (b) Microphotograph showing an irregular parasite surrounded by acute inflammatory cells (Hematoxylin and Eosin, X200). (c) and (d) Microphotograph showing a chitinous structure and inner organelle (Hematoxylin and Eosin, X400)

be seen. So absence of eosinophils does not exclude absence of parasite, and the pathologist should look for a degenerated parasite.

Various parasites can infest the eye and adnexa. Protozoa like Acanthamoeba spp., Leishmania species, helminths that include round worms like the Angiostrongylus species, *Loa loa*, Dirofilaria species, and flat worms like *Taenia solium* and Schistosoma spp. have been reported to cause ocular lesions.[1] *Loa loa*, Onchocerca, and Dirofilaria are some of the parasites that are found subconjunctival and even intraocular.[1,2] Ocular dirofilariasis has been reported in India from Kerala, Karnataka. and Gujarat.[2]

Dirofilaria is a dog filarial worm that is transmitted to humans via mosquitoes. The immature female worm is found to have a thick laminated cuticle, broad lateral chords, and female genital system.[6] Male and female heartworms are distinguished based on morphometric and morphological characteristics; for example, in adult *Dirofilaria immitis*, the male is shorter with a spirally coiled posterior end, whereas the female is larger and straight on both ends. Spicules and pre-anal papillae are found in male worms.

Ophthalmic manifestations that have been described are periorbital, subconjunctival, sub-Tenon's and intraocular lesions.[7] The worm is identified after excision of the lesion and tissue analysis. It can also mimic a lacrimal sac mucocele, and biopsy is diagnostic in such cases.[8] We have earlier described multifocal choroiditis due to dead Dirofilaria which was later removed and the diagnosis was confirmed by histopathology and polymerase chain reaction.[9] It has also been reported to be found in the vitreous cavity.[10] We found Dirofilaria lesions involving the lids, lacrimal gland, orbit, as a conjunctival cyst and a Tenon's cyst. Clinically, they were found to be both cystic and solid mass like lesions. The common symptoms were recurrent eyelid swelling, redness, and itching.

Cysticercosis is an infection caused by the larval form of *Taenia solium* (*Cysticercus cellulosae*). Common presentations include loss of vision, periorbital pain, scotoma and photopsia.[7] The patient can present with neurocysticercosis or subcutaneous/muscular cysticercosis.[11] The cyst is usually localized to the subconjunctival space and orbit, but may sometimes invade the globe and present in the anterior or posterior segment. In this study, out of the six cases, four were intraocular, one epibulbar, and another presented as a conjunctival cyst. If the retina is involved, hemorrhages and edema are seen. Histologically, the necrotic cysticercus is surrounded by a zonal granulomatous inflammatory reaction with an abscess that contains eosinophils.[12] The vesicle wall shows hyaline degenerations, inflammatory cell infiltration, neuroglial fiber, and glial cell proliferation layers from the inside to outside.[13] Death of the larva causes severe immunological reaction and sometimes endophthalmitis. Cases of submacular parasite masquerading as posterior pole granuloma have been reported.[14] Rarely, a degenerated cysticercus cyst with chronic inflammation may simulate endogenous endophthalmitis.[15] It can also present as fibrinous anterior uveitis with secondary glaucoma. The uveitis resolves with removal of the cyst.[16] Our study had a subretinal presentation of cysticercosis.

Microfilaria was seen in four cases in our study. These included *Loa loa*, *Brugia malayi* and *Wucheria bancrofti*. *L. loa* is a filarial parasite that is endemic in Africa and causes Loiasis. It occurs due to the bite of *Chrysops silacea*.[17] The worm is filiform, cylindrical, and has a semi-transparent body with numerous

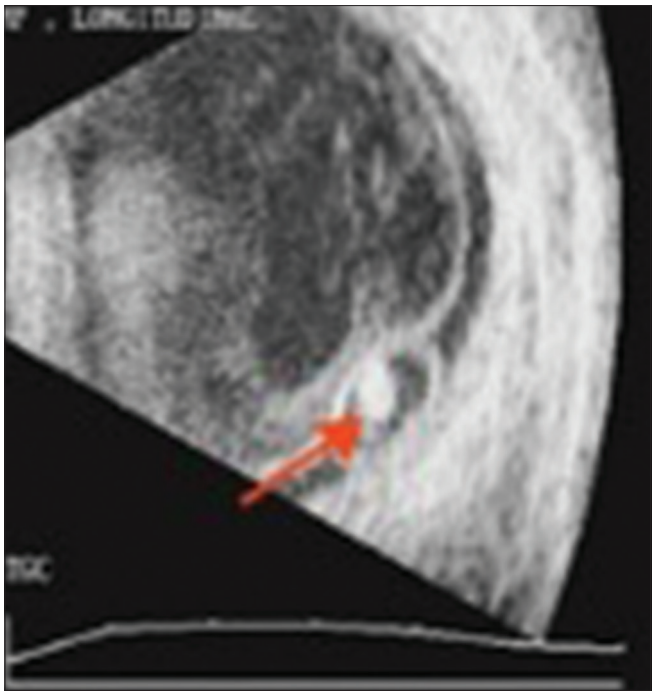

Figure 4: B scan imaging. B scan ultrasonogram of a case of subretinal cysticercus showing a subretinal cystic structure with central hyper reflective area (shown by red arrow)

round and smooth protuberances, and a blunt tail. The cuticle is covered with small bosses, which distinguishes *L. loa* from other filarial parasites. Marked eosinophilia is seen in association with liberation of microfilaria from the female worm.[7]

There are two manifestations of the disease: Calabar swelling, that is localized angioedema caused by hyperemic reaction to adult worms, and subconjunctival migration of the worm. A worm in the subconjunctival space leads to itching, foreign body sensation, and hyperemia.[18] The dead worm induces an acute angioedema, pictured peri-orbitally, and can induce conjunctival nodule formation; after the worm dies, the eye may show signs of extensive iridocyclitis associated with cloudy aqueous, vitreous opacities, and raised intraocular pressure.[7] There can be posterior segment involvement such as extensive hemorrhagic lesions associated with retinal detachment, retinal neovascularization, vitreous hemorrhage, and subretinal exudates. Various systemic manifestations such as lymphangitis, nephropathy, cardiomyopathy, encephalopathy, and arthritis have been reported.[19]

Brugia malayi is a nematode that is transmitted by mosquitoes of the genera Mansonia, Anopheles, and Aedes. Man is the definitive host, and the mosquito is the intermediate host. The common presentations are chemosis, lid edema, orbital cellulitis, anterior uveitis, or a worm in the anterior chamber.[20] It can sometimes be found in the vitreous cavity too and can cause severe immediately.[3,4] The presentations we saw of the filarial worms in our study were both cysts and mass lesions on the lid and sub-Tenon's region.

Six cases of cysticercus were seen in our study. In a study of 102 patients with ocular cysticercosis, extraocular lesions were most commonly found in the orbit, with restriction of ocular movements (46%) and diplopia (28%) being the most

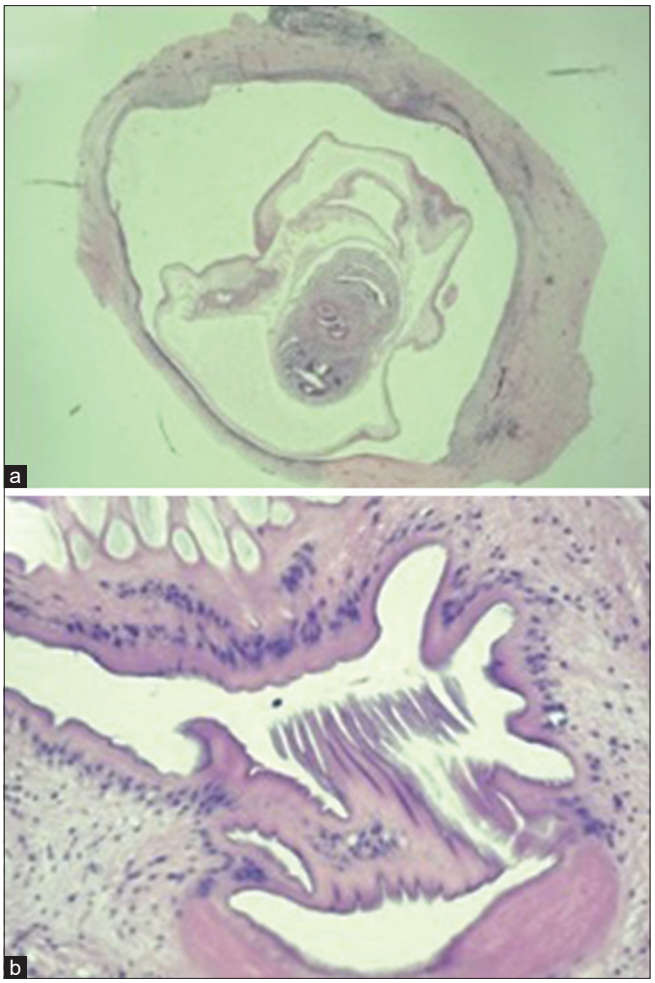

Figure 5: Histopathology of Cysticercosis (a) Microphotograph showing cystic cavity containing larval form of *Cysticercus cellulosae* (x20) (b) Higher magnification showing invaginated scolex suckers and hooklets (x200)

common clinical presentations.[21] Redness, pain, and loss of vision were less common. Proptosis, periocular swelling, ptosis, lid edema, squinting, and conjunctival swelling were all noted signs in reducing frequency. Amongst intraocular lesions, the vitreous and subretinal space were the most favored sites, with diminution of vision (100%) being the most common symptom. 40% showed signs of panuveitis, 20% had retinal detachment, and a few had anterior uveitis with one eye presenting with leukocoria. In a study of 171 patients with orbital cysticercosis, the three main symptoms at presentation were periocular swelling (38%), proptosis, and ptosis.[22] The three main signs at presentation included ocular motility restriction (64.3%), proptosis, and diplopia. The cyst locations in the decreasing order of frequency were anterior orbit (69%), subconjunctival space, posterior orbit, and the eyelid. In all, 80.7% of patients had cysts in relation to an extraocular muscle. In another study of 21 patients with intraocular cysticercosis from south India, 20 patients presented with blurred vision, with headache, redness, pain, and floaters being less common.[23] Vitritis was seen in almost all patients, followed by a retinal detachment and a ruptured cyst. The cyst was located in the vitreous cavity in 36.4% of cases and

in the subretinal space in 63.6%. In our study, cysticercus was seen intravitreal and subretinal location.

In our study, species identification was not possible in ten cases (23.25%) on histopathology since we did not find an intact parasite, which is required for proper identification of the species. Associated degeneration and necrosis also made it difficult to identify the parasite.

Our study showed that parasitic lesions can produce severe acute inflammation of the surrounding tissue which can masquerade an inflammatory mass[8,14,15] since most of the ocular signs are not specific and a high index of suspicion is required for clinical diagnosis. Careful search for the parasite should be done in all nodular and cystic lesions of the eye. It is seen that parasitic lesions of the eye and adnexa have varied presentations and multiple sites of involvement.

Removal of a live parasite is not always feasible, especially when it is intraocular or when a parasite has resulted in host inflammation and mass lesion. In such cases, the mass/cyst along with the dead parasite can be subjected to histopathology and parasite identification can be done by microscopic examination.

Only in exceptional cases do we find a degenerated parasite wherein on microscopy, we fail to accurately clinch the specific parasite. Based on presence of the inflammatory cells especially eosinophils, Splendore–Hoeppli phenomenon, or granulomas along with degenerated parasitic structures, we still can conclude it as a parasitic mass or cyst which would aid in patient management.

Identification of the parasite is of paramount importance in treatment since the choice of anti-parasitic drug is based on the type of parasite. The first line of treatment of dirofilariasis is Ivermectin while in patients with microfilaremic dirofilariasis and in those who cannot tolerate oral ivermectin, Doxycycline is the drug of choice. Diethylcarbamazine (DEC) is the treatment of choice for microfilariasis while for cases of cystecercosis, oral Albendazole usually with steroids is the treatment of choice.[20,21,24]

Conclusion

To conclude, clinicopathological correlations made from the parasitic lesions in the eye and adnexa aid in definitive diagnosis and prompt identification of the parasite for patient management and better outcome.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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