A study of Clinical, OCT and Fluorescein Angiographic Findings in Toxoplasma Retinochoroiditis.

AIM
To determine the clinical, OCT and angiographic findings in Toxoplasma retinochoroiditis and whether these can be used to diagnose Toxoplasma retinochoroiditis.

METHODS
Retrospective chart review of all patients diagnosed and treated as Toxoplasma retinochoroiditis in the period April 2008- March 2012. All patients had typical active retinochoroiditis patches suggestive of Toxoplasmosis. Anti Toxoplasma antibody titers were analyzed in available cases. FFA and OCT features were analyzed in available cases.

RESULTS: Of a total of 86 cases, 53 (61.63%) were primary and 33 (38.37%) secondary. 36 out of 86 (41.86%) were in children under the age of 16 years. Macular involvement occurred in 49 (56.98%). Vasculitis (63.95%) followed by Kylaeriasis arterialis (58.1%) were the most common lesion seen. Single or multiple segmental periphlebitic patches around posterior pole and frosted branch angiitis were significant clinical findings. Multiple spike like protrusions of inner retinal layers on the surface of the lesion were the typical and most characteristic OCT feature observed in 100% of cases tested. Seropositivity was obtained in 91.18 % of cases tested.

CONCLUSION
As clinical features together with angiographic and OCT findings have a better predictive value in the diagnosis of Toxoplasma retinochoroiditis, these rather than serology could be used for the diagnosis and treatment of Toxoplasma retinochoroiditis.

Toxoplasmosis has worldwide distribution, and Toxoplasma retinochoroiditis is the most common form of posterior uveitis in otherwise healthy individuals. The prevalence of seroconversion varies in different regions, depending on socioeconomic, geographic and climatic factors. For example, the prevalence of seropositivity in Brazil ranges from 50% to 83% and that in the US from 30% to 70%.

Toxoplasmosis is caused by T.gondii, an obligate intracellular protozoan. The cat is the definitive host whereas humans along with mice and live stock are intermediate host.

Transmission to humans occur mainly by three mechanisms viz. Ingestion of undercooked meat containing bradyzoites, ingestion of sporozoites from contaminated food or water and transplacental spread of parasite from infected mother.

Classically, Toxoplasma retinochoroiditis appears as a focus of inner retinitis. Healing of the lesion occurs with control of the acute infection and scar formation. The cyst may remain inactive in the scar or adjacent to it for a period of years. Ultimately, the cyst wall may rupture, releasing organisms into the surrounding retina and resulting in recurring retinitis. As a result, the initial lesion can cause damage to the inner retinal layers adjacent to an old chorioretinal scar and can be accompanied by vitritis.

However, considerable variation exists in the clinical features of this disease. Additional clinical insights into the disease may have important implications for the understanding of tissue damage mechanisms, with implications for the management and prognosis, as well as help future research efforts.

This is a study of the clinical, OCT and angiographic findings in Toxoplasma retinochoroiditis and their reliability as compared to serology.

Materials And Methods
Case records of patients who presented to Medical Trust Hospital from April 2008 – June 2011 & Comtrust Eye Hospital from July 2011 – March 2012, diagnosed and treated as Toxoplasma retinochoroiditis were included in the study. All patients had typical active retinochoroiditis patches suggestive of Toxoplasmosis.

The retinochoroiditis was classified as primary or secondary depending on the absence or presence of associated hyper pigmented chorioretinal scar.

All posterior segment findings were noted. Anterior chamber reaction if any was also noted.

Anti Toxoplasma antibody titers were analyzed in available
Fundus photos available were reviewed in all cases. Type and location of lesion, associated Vasculitis and its extend, other features like hemorrhages were careful looked for and noted. Kylaeriasis was noted if intra vascular exudates like material were seen in fundus photo. FFA (n=24) features were analyzed in available cases.

Cirrus 4000 spectral OCT was used. 5 line HD scans and macular cube scans done were reviewed (n=36) in available cases. All available scans in macular cube were analyzed in advanced visualization software of Cirrus OCT.

Results
There were a total of 86 cases in this study. Of these 36 (41.86%) were children under the age of 16 years; 55 (63.95%) were male and 31 (36.05%) were female.

All patients presented with unilateral involvement except one, who had bilateral symmetrical involvement. Out of a total of 86 cases, 53 (61.63%) were primary and 23 (38.37%) were secondary. Macular involvement was seen in 49 (56.98%) whereas 37 (43.02%) were having extra macular involvement.

Vasculitis (63.95%) followed by Kylaeriasis arterialis (58.54%), anterior chamber reaction (40.70%) and vitritis (39%) were the commonest clinical findings.

Neuroretinitis (8.34%) as well as frosted branch angitiis (5.83%) were seen. These findings as well as pars planitis (32.14%) were seen always in patients with active retinochoroiditis patch. Intraretinal hemorrhages (5.83%) were seen in few eyes in the absence of CNVM but sub retinal bleed when present was always associated with CNVM.

FFA was available in 24 cases. Mainly two types of angiographic patterns were seen. One was the early hypo fluorescent lesions followed by late hype fluorescence. The other pattern was very early hyper fluorescence followed by late further increase in hyper fluorescence. 14 of 24 (58.33%) showed early hypo fluorescent lesions followed by late hype fluorescence whereas 9 (37.5%) showed very early hyper fluorescence followed by late further increase in hyper fluorescence. 1 (4.17%) patient had cystoid macular edema. CNVM was present at presentation along with active disease in 3 cases. All were classic CNVM. One patient developed CNVM on follow up.

Other findings as well as pars planitis (32.14%) were seen always in patients with active retinochoroiditis patch. Intraretinal hemorrhages (5.83%) were seen in few eyes in the absence of CNVM but sub retinal bleed when present was always associated with CNVM.

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OCT was available in 36 patients. Characteristic finding of toxoplasmosis on OCT was Multiple spike like protrusions of the inner retina overlying the lesion. This was found in 36 (100%) out of 36 patients where OCT was analyzed. The other OCT findings were vitreous cells in 33 (91.66%) and sub retinal fluid in 5 (13.88%) cases. The commonest site of lesion was Inner & Outer retina in 17 (47.22%) (some view of outer retinal layers present); followed by Inner retina, outer retina and choroid in 12 (33.33%) and predominantly Inner retina in 7 (19.44%) cases (hyper reflectivity of inner retinal layers complete shadowing of outer retinal layers and choroid).

Of 68 patients in whom serology was done Ig G titer for Toxoplasma antibody was positive in 62 (91.18%), whereas Ig M Toxoplasma antibody titer was positive in only 7 (10.29%). Rest 6 (8.82%) didn’t show seropositivity.

Figure - 2 OCT of Ocular Toxoplasmosis

Discussion
Toxoplasmosis is the most common form of posterior uveitis encountered in clinical practice. Most common presentation is active retinochoroiditis patch near the old hyper pigmented chorioretinal scar or denovo.

Toxoplasmosis can present with variety of other clinical features as well. In our study Vasculitis (63.95%) was the most common clinical finding followed by Kylaeriasis arterialis (58.54%), anterior chamber cells (40.70%) and vitritis (39%). Whereas Anterior chamber reaction was most common finding as per study by Monet et al and Juliana et al.

Vasculitis when present was phlebitis predominantly with single or multiple segmental lesions clustered around the primary retinitis patch mostly on normal retina. We feel this is more inflammatory response rather than due to organism directly. Also we had cells on OCT in some eyes were Anterior chamber and vitreous reaction was absent. This also indicates the tendency for immune response indicators to be confined close to the lesion in toxoplasmosis.

Even though there are reports in literature of isolated pars planitis, neuroretinitis and frosted branch angiitis due to toxoplasmosis, we did not have any case were these findings were seen in the absence of retinitis patches. Even though we don’t have enough numbers to definitely conclude, there is a tendency for peripheral toxoplasma lesions to be more associated with pars planitis and posterior lesions to be more associated with neuroretinitis and frosted branch angiitis. Again all these findings are more likely to be immune response reactions to the primary lesion especially since toxoplasma is an intracellular organism.

We have few eyes which had secondary CNVM along with active retinitis lesion, which is also not well reported in literature. Suspicion of CNVM should be raised whenever there is an associated intra retinal hemorrhages and in such cases. FFA should always be advised.

Confusion arises when it comes to aid the clinical diagnosis and to start the specific treatment. Serology, including Ig G and Ig M Anti Toxoplasma antibody, is till now the most widely used test to aid the diagnosis. In our study we found Ig G Anti Toxoplasma antibody titer was positive in 91.18% of cases tested whereas Ig M Anti Toxoplasma antibody titer was positive in 10.29% cases only. The study by Juliana et al also showed a nearly similar result of Ig G titer positivity in 100% and Ig M in 13.33% of tested cases. From our study as well as reported literature we see that Ig M has very low sensitivity in ocular toxoplasmosis. This is possibly because eye is a very small organ affected and antibodies produced are probably less to be detected on routine serology. IgG even though has high sensitivity has low specificity as it can be high in normal population without ocular disease also, especially in endemic population like ours.

Although PCR of vitreous and aqueous tap can be used having both high sensitivity and specificity in these cases but being invasive and costly, is not popular as other methods.

Mainly two types of angiographic patterns were seen in our series. One was the early hypo fluorescent lesions followed by late hypo fluorescence. The other pattern was very early hyper fluorescence followed by late further increase in hyper fluorescence. Early hyper fluorescence in toxoplasma retinochoroiditis is unusual when compared to other inflammatory lesions where we expect early hypo fluorescence. This is probably due to more severe involvement of inner retinal layers. In these eyes OCT also showed more profound inner retinal involvement with backscattering of all outer layers.

Further we have analyzed the entire surface of the lesion with advanced visualization of macular cube in cirrus OCT. Spike like protrusion of inner retina somewhere over the lesion were seen in 100% of cases. This retinal spikes are actual protrusions of very superficial retina, into the vitreous and are not due to vitreous traction or vitreous adhesions. Vitreous adhesions and overlying vitreous debris/ cells
were seen as separate findings. Though such findings not reported before in literature we have observed it in each case analyzed. Study by Juliana et al have mentioned “Hairy appearance” over lesion in 20% of cases but no other detail regarding it had mentioned. OCT finding of retinal spikes has not been reported for any other macular inflammatory or non inflammatory lesions. We feel this finding alone can be diagnostic in macular toxoplasmosis.

Vitreous cells/strands in OCT overlying the lesion was second most characteristic finding seen in 91.66% of patients. These thought to be appeared earlier than clinically visible cells on fundus examination.

Our study showed most common location of lesion was inner & outer retina followed by involvement of choroid. Exact location and involvement of layers is difficult by OCT since once inner retina is involved, it tends to cause sever shadowing preventing further visualization of outer retinal layers. But an approximate assessment can be made if entire lesion is scanned or as lesion is healing when inner layer reflectivity decreases. We have made such an attempt but it may be far from accurate.

### Conclusion

Being non invasive and having more sensitivity and specificity, OCT together with clinical features and angiographic findings, can be considered superior in the diagnosis of Toxoplasma retinochoroiditis. These rather than serology could be used to aid the diagnosis and guide treatment of Toxoplasma retinochoroiditis.

### References:


2. Garcia CA, Ore´fice F, Lyra CO, et al. Socioeconomic conditions as determining factors in the prevalence of systemic and ocular toxoplasmosis in northeastern Brazil.


### Dr. Jayesh, fromSurendranagar, Gujarat was one of the most dedicated, intelligent and hardworking postgraduate students, we have seen in recent times, but fate took him away from us in a very unfortunate road traffic accident on 14-10-2012.


### Table: Comparative analysis of OCT based studies on Ocular Toxoplasmosis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Present study</th>
<th>Monnet et. al</th>
<th>Julianna et. Al</th>
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<tbody>
<tr>
<td>Type of study</td>
<td>Retrospective</td>
<td>Prospective</td>
<td>Prospective</td>
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<tr>
<td>Number of cases (n)</td>
<td>86</td>
<td>25 (16 Active and 9 Scared)</td>
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<tr>
<td>Mean age of study group</td>
<td>25.08 (±15.37)</td>
<td>25.5 (±9.9)</td>
<td>25.7 (±11.3)</td>
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<tr>
<td>Male</td>
<td>63.0%</td>
<td>56%</td>
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<td>Female</td>
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<tr>
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<tr>
<td></td>
<td>Extra macular</td>
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<td>NR</td>
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<tr>
<td>Clinical findings</td>
<td>Vascuities</td>
<td>18.75% (A)</td>
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<tr>
<td></td>
<td>Kylaeriasis</td>
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<td>A/C reaction</td>
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<td>Hairy appearance</td>
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<td>Ig M positivity</td>
<td>10.29%</td>
<td>13.33%</td>
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NR = Not Revealed, (A) = Active lesions, SRF = Sub retina fluid.