**Commentary: Ocular toxoplasmosis: From bench-side to clinical practice!**

"Anatomical and functional outcomes of pars plana vitrectomy for inflammatory epiretinal membrane surgery in healed toxoplasmosis infection"[1]

Ocular toxoplasmosis (OT), one of the most intriguing infectious posterior uveitis of public health importance, has varied spectrum and atypical presentations besides the classical lighthead in the fog picture.[2] Acquired OT devoid of chorioretinal scar is more commoner than congenital infection that presents with it. Elkins B S et al. described the clinical pointers for OT over viral retinitis as the lack of retinal hemorrhages, discrete, smooth contoured edges to the lesions. Except for transient inflammatory reaction during infection,[3] OT without retinochoroiditis is a rarity despite few reports[4] in the early stages.

Anticipating the immune status of the host clinically based on the multifocality and scant vitritis[5] in the immunosuppressed is critical to the clinician as the investigational and management strategies are poles apart.[4] When immunosuppressed, it should alert the astute clinician to evaluate for associated central nervous system toxoplasmosis by neuroimaging. The treatment of immunosuppressed is lifelong devoid of steroids.

The intraocular inflammatory response reduces the parasitic burden of the disease.[4] This explains the reason of lower sensitivity of polymerase chain reaction (PCR), which detects the toxoplasma B1 gene in the immunocompetent state than the suppressed. Its results are not influenced by initiation of anti-toxoplasma therapy. On the contrary, the sensitivity of Goldmann-Witmer coefficient (GWC) (which measures the levels of antibodies) is higher in the immunocompetent state than the suppressed. The first test which a clinician needs to order for a suspected toxoplasma is measurement of immunoglobulin G (IgG) using enzyme-linked immunosorbent assay. Absence of it rules the disease effectively out in an immunocompetent, and if the suspicion is strong, it needs to be repeated in 2–3 weeks. A rise in titer of IgG over 2–3 weeks is an indication of recent infection. Measurement of IgM is critical since IgM-positive cases can have a significantly larger reduction in lesion size with oral therapy than with intravitreal clindamycin with dexamethasone (IVCD). Cases which are IgM-negative can have a similar better response with IVCD. The magnitude of the elevated levels of these antibodies or their lower levels at a single point in time does not indicate the chronology of the events. The IgG avidity test detects the highly avid IgG antibodies that develop after 3–4 months. This test could indicate the time of exposure if the IgG and IgM were reactive. This is relevant for evaluating OT during pregnancy. On the flip side, the low IgG avidity test should not be used to confirm the diagnosis of recent infection as the avid antibodies could persist for many months. Both IgG and IgM could also be negative during reactivation. The other investigations of toxoplasma like the various PCR types, GWC, and immunoblotting could be combined[5] to increase the sensitivity up to 97%. What is really intriguing in the modern era is the improved sensitivity (of 85%) of a novel two-step PCR protocol[6] proposed by Sugita et al.

The treatment of OT is a mother of several controversies. Whether or not to treat all toxoplasma cases is the first one, as their efficacy is not proven over the natural course of the disease. With absent consensus on the initial antimicrobial of choice, what is discrete is the synergistic role of the combinations in preventing the development of resistance. Being an infective retinitis, monotherapy with steroids orally and locally is an absolute contraindication.[5] However, oral corticosteroids need to be used in severe vitritis, decreased vision, proximity of lesions to the fovea or optic disk, and the large size of the active lesion. The end point of treatment can be ideally guided by the treatment response meticulously documented using autofluorescence and optical coherence tomogram findings.[5] Literature is replete with contradictory findings on possible toxoplasma reactivation following cataract surgery and pars plan vitrectomy. When treating the toxoplasma sequelae, in potentially sight threatening cases such as recurrent foveal choroidal neovascular membranes and with multiple earlier reactivation of inflammation, a safer strategy of antimicrobial prophylaxis after the inflammation is quiescent is worth a consideration.
Currently, the popular strategy of using IVCD to limit the side effects of oral therapy needs to be appropriately applied for OT in pregnancy. Similar to the analogy in acute retinal necrosis, IVCD may need to be repeated and seldom prevents the other eye/systemic involvement. The exclusion criteria used in the randomized control trial comparing IVCD versus oral therapy\(^{[4]}\) includes the immunosuppressed state and the lesion location within 500 μm of the fovea. The subgroup of patients who could benefit from secondary prophylaxis with half normal dosing of cotrimoxazole for preventing recurrences\(^{[6]}\) needs to be applied in clinical practice. A combination of both local and oral therapies could be an intelligent option as the final visual outcome was not statistically significant in both the groups.\(^{[5]}\) Bosch-Driessen et al. proved that the combination of azithromycin and pyrimethamine has a less frequent and less severe side effect profile than the classical therapy (pyrimethamine, sulfadiazine, oral steroids) with similar outcomes.

As pyrimethamine reduces the scar size over other drugs,\(^{[6]}\) it is logically used for lesions involving papillomacular bundles with monitoring of leucocyte and platelet counts under expert hands with folinic acid. The hepatic and renal functions need to be monitored for most of the antimicrobial drugs. The unique action of azithromycin on both sporozoite and cyst stage in vivo is not evident in vivo. Atovaquone possibly extends the time to recurrences. Spiromycin, the unique placenta-centric drug, does not cross the placenta to reach the minimum effective concentration in the vitreous of the fetus to treat OT. However, it is popularly used to prevent the mother-to-child transmission of toxoplasma if infected within 18 weeks of pregnancy or within 6 months before conception. Before IVCD, the classic triple therapy with folinic acid was indicated in pregnancy at the gestational age of 18 weeks or later due to their teratogenicity during organogenesis. Clindamycin with azithromycin or atovaquone is an alternative too to prevent the Sabin’s tetrad. The potential emerging newer therapies in future for OT include dihydrotriazine, artimiside/artimizone derivatives, fluridone (blocks endogenous abscisic acid), apicoplasts targets using subtractive genomics, and the vaccine research!

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