Intravenous tocilizumab in idiopathic pediatric uveitis with refractory cystoid macular edema – A case report

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A 13-year-old boy with a 4-year history of idiopathic pediatric uveitis and recurrent uveitic macular edema had failed conventional immunomodulatory therapy and presented to us with a vision of 6/24 [right eye (OD)] and 6/9 [left eye (OS)]. Fluorescein angiography showed diffuse vascular leakage along with cystoid macular edema (CME). Intravenous tocilizumab (10 mg/kg body) was given as 14 injections over 12 months. Repeat fluorescein angiography every 3 months showed a dramatic improvement in the vascular leakage and resolution of CME. At 13 months OF follow-up, vision had improved to 6/9p (OD) and 6/6(OS) with no recurrence of inflammation or CME.

Key words: Biologics, cystoid macular edema, idiopathic, pediatric uveitis, tocilizumab

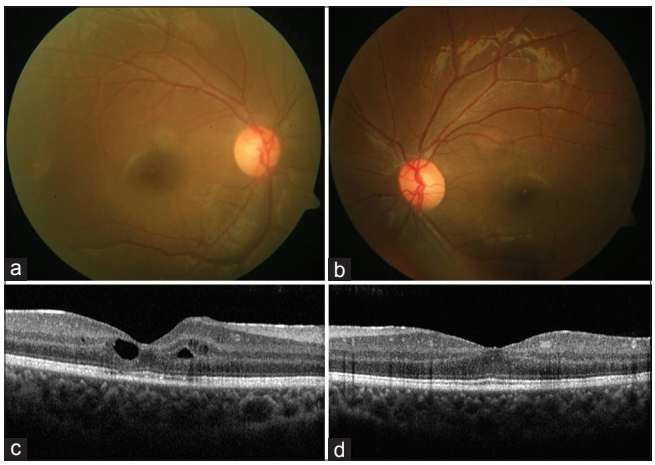

Figure 1: Fundus photographs of right (a) and left eyes (b) showing vitritis in the right eye with otherwise normal looking posterior pole with corresponding OCTs showing cystoid changes in the fovea in the right (c) and hyperreflective dots in the inner retina in the left eye (d)

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Recurrent cystoid macular edema (CME) in pars planitis and in children is difficult to treat and results in poor visual outcome. Initiation of biologics in a developing country like India in idiopathic pediatric uveitis is still nascent. In this case report, we report the improved visual outcome in an idiopathic pediatric uveitis, demonstrated on imaging, with intravenous tocilizumab.

Case Report

A 13-year-old boy was referred to us with a 4-year history of par planitis [both eyes (OU)] and recurrent CME [right eye (OD)]. Over the 4-year period, he did not respond to methotrexate in the past. At the time of examination, he was on a combination of deflazacortisone (24 mg/day), azathioprine (100 mg bd since 21/2 years) and cyclosporine (100 mg bd since 6 months). He also had a history of receiving three intravitreal dexamethasone implants over 1.5 years to the OD (last injection received was 5 months ago). Systemic examination or laboratory investigations did not reveal any significant abnormality. Extensive laboratory investigations including complete hemogram, serum angiotensin converting enzyme, serum lysozyme, mantoux test, ELISA for HIV, antinuclear antibody, HLA B51, ELISA, and western blot (IgG and IgM) for Lyme disease, random blood sugar, urine routine, magnetic resonance imaging orbit and cranium, computed tomography of thorax, and ultrasound abdomen did not reveal any abnormalities.

His best-corrected visual acuity was 6/24 (OD) and 6/9 [left eye (OS)]. Slit-lamp examination showed early cataractous changes (OD) and a quiet anterior segment (OU). Fundus examination showed vitreous cells and CME (OD > OS) confirmed by optical coherence tomography [Fig. 1]. Fluorescein angiography (OU) showed diffuse leakage from the choriocapillaries and the retinal blood vessels along with CME [Fig. 2]. Intravenous tocilizumab (10 mg/kg body) was given as 14 injections over 12 months. The last injection, the dose of intravenous tocilizumab, was reduced to 8 mg/kg. Repeat fluorescein angiography every 3 months showed a dramatic improvement in the vascular leakage with intravenous tocilizumab and resolution of cystoid macular edema [Figs. 3 and 4]. Regular monitoring of blood counts showed decrease in total blood counts though in the normal range. Liver function and renal functions were normal. Cyclosporine was discontinued within 3 months of starting tocilizumab. Deflazacort was reduced in a tapering schedule and azathioprine was continued at 100 mg bd as he continued to receive intravenous tocilizumab injections.

At 13 months of follow-up after initiation of tocilizumab, vision had improved to 6/9p (OD) and 6/6 (OS) with no recurrence of inflammation or CME. He was also on deflazacort (1.5 mg/day) and azathioprine (100 mg bd). Fluorescein angiography did show minimal leakage of peripheral retinal

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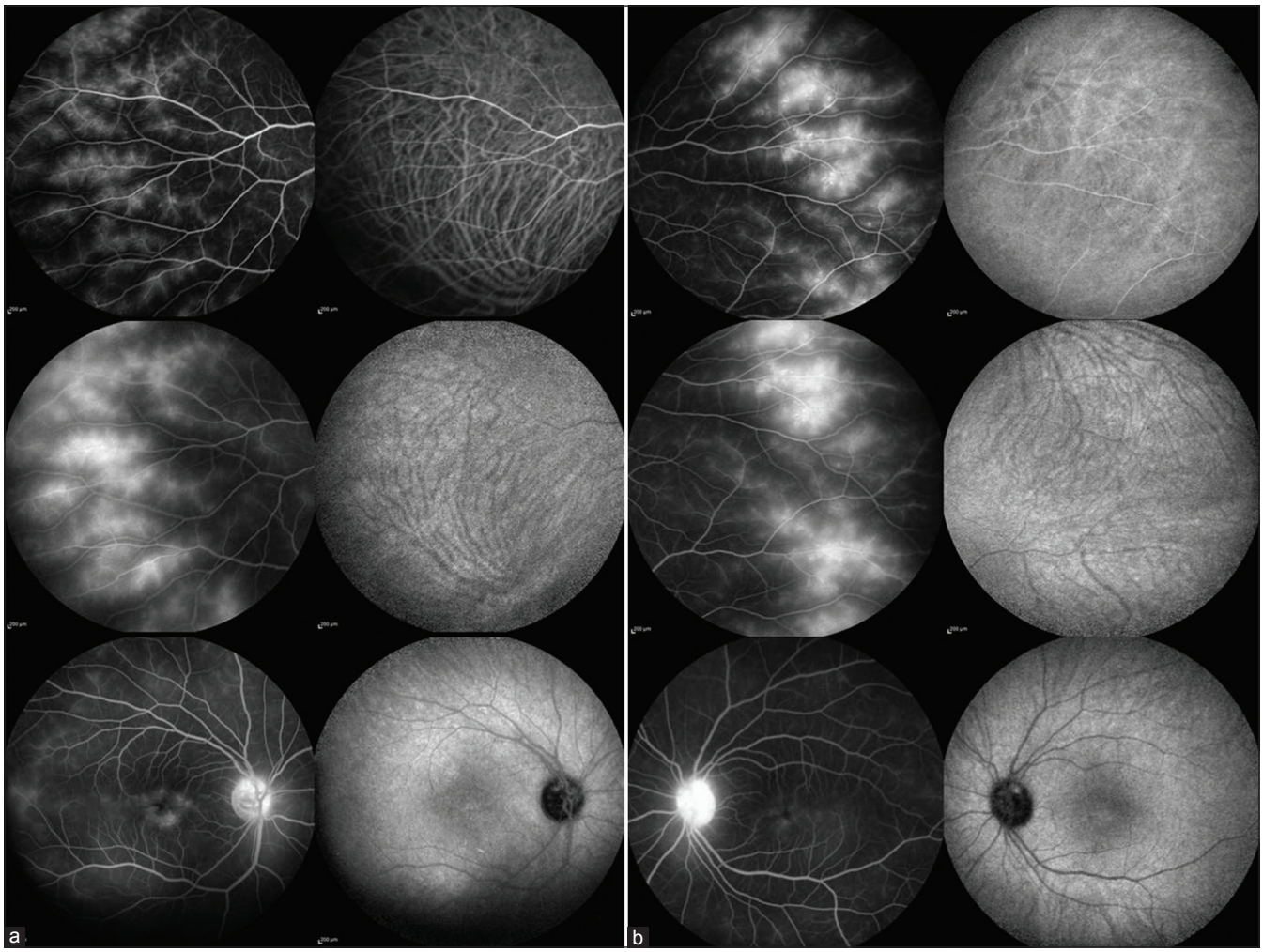

Figure 2: Fluorescein angiography showing diffuse vascular leakage, increasing toward the later phases, a hot disc and leakage at the macula suggestive of cystoid macular edema with corresponding indocyanine green angiography of the right (a) and left eyes (b). The ICG pictures are noncontributory

blood vessels, in stark contrast to the pretreatment angiograms but no CME. Complete blood counts monitoring revealed a total white blood counts of 3600 cells/mm^3 at the last follow-up.

Discussion

Tocilizumab is a fully humanized antibody that binds both to soluble and membrane-bound IL-6 receptors and has been approved in moderate to severe forms of rheumatoid arthritis, juvenile idiopathic arthritis (JIA), and Castleman disease.[1-4] IL-6 is elevated in the aqueous and vitreous in autoimmune uveitis. Tocilizumab is also known to decrease the vascular permeability in retinal vessels.[1] Reports of its usefulness in refractory noninfectious uveitis macular edema in JIA, Behcet's disease and bird shot chorioretinopathy have been described in literature.[2-5] In this case report, we describe the improved response of macular edema and vascular permeability in a young boy with idiopathic uveitis and refractory macular edema. Although the follow-up is short (13 months), to our knowledge, we do not have information on the utility of tocilizumab, in idiopathic pediatric uveitis especially pars planitis with refractory macular edema.

In our case, a decision to switch to biologics was made when he failed conventional immunomodulatory therapy. A decision on intravenous tocilizumab was made on the expertise of the treating pediatric rheumatologist and evidence in literature

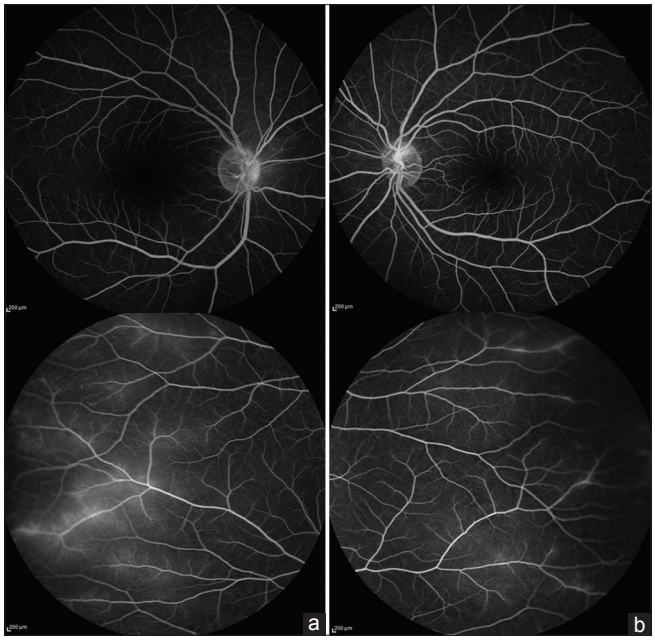

Figure 3: Fluorescein angiography after 3 months of intravenous tocilizumab showing decrease in vascular leakage, resolution of cystoid macular edema and reduced leakage from the optic discs in right (a) and left eyes (b)

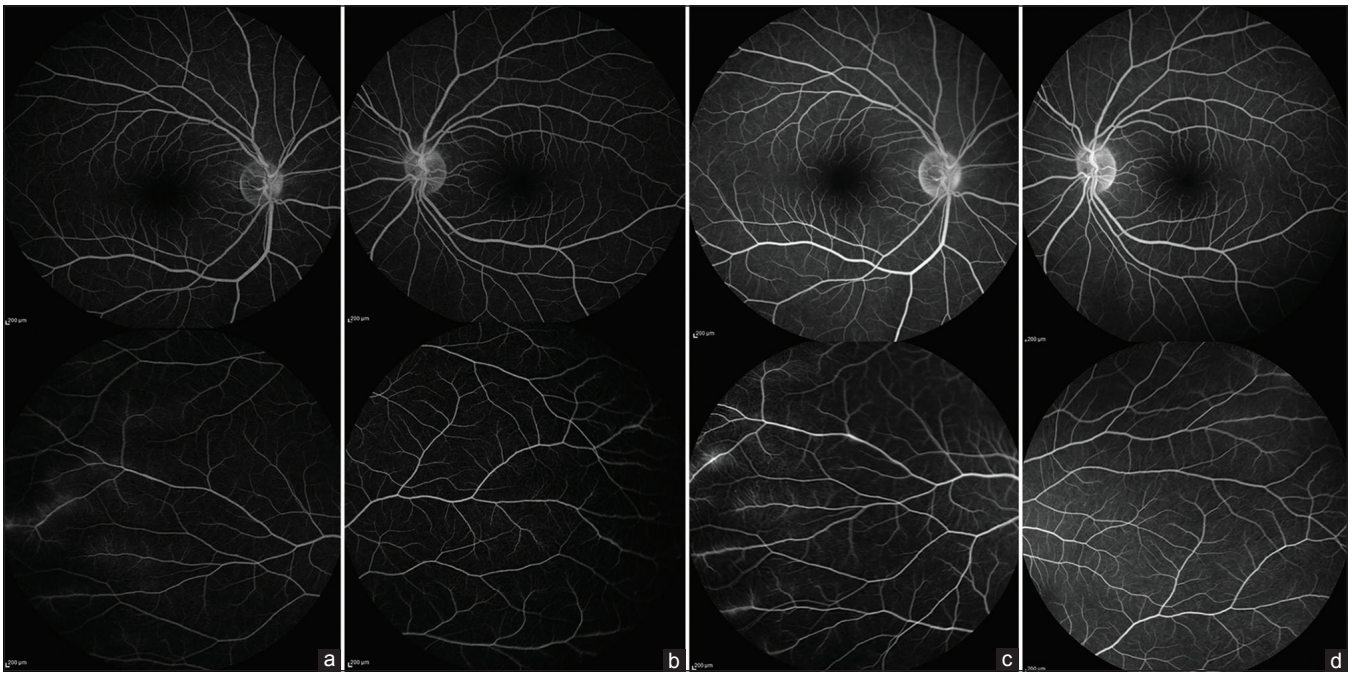

Figure 4: Fluorescein angiography at 6 months (a and b) and 13 months (c and d) after initiation of intravenous tocilizumab, showing further decrease in vascular leakage, no cystoid macular edema or leakage from the optic discs in right and left eyes

on its usefulness in refractory uveitic macular edema and on vascular permeability.[1,3] There was resolution of CME and gross reduction in the diffuse leakage on fluorescein angiography. At the end of 13 months, there was no recurrence of inflammation or CME. Tocilizumab was well tolerated with no severe side effects. The total white blood counts dropped over 13 months while on tocilizumab and this will govern the timing and doses of subsequent injections. Increasing cost due to the drug and hospitalization will definitely be a limiting factor in our patient population.

Conclusion

Intravenous tocilizumab is useful in refractory uveitic macular edema in idiopathic pediatric uveitis. The response to therapy with tocilizumab in this case of idiopathic pediatric uveitis with refractory macular edema will definitely influence management decisions, as initiation of biologics in uveitis is still nascent in India.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflict of interest

There are no conflict of interest.

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