Tubercular subretinal abscess in a pediatric intermediate uveitis patient on methotrexate

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Pediatric intermediate uveitis (IU), usually idiopathic, can also be associated with tuberculosis (TB) and sarcoidosis. A 14-year-old girl was diagnosed with idiopathic IU after ruling out TB and sarcoid. She was treated with oral steroids and methotrexate (MTX) with good inflammation control. One year later, she presented with subretinal (SR) abscess. Lab tests were still negative but aqueous polymerase chain reaction confirmed TB. With antituberculosis treatment, complete resolution of the lesion was noted. The likelihood of a change in phenotype of ocular TB, from an IU to TB SR abscess or a possible reactivation of latent TB due to MTX are discussed.

Key words: Idiopathic intermediate uveitis (IU), Methotrexate, Subretinal abscess, Tuberculosis (TB), Juvenile Idiopathic arthritis

Juvenile idiopathic arthritis (JIA) and pediatric intermediate uveitis (IU) are two common noninfectious uveitides in children.[1,2] IU in children is usually idiopathic but common associations are sarcoidosis and tuberculosis.[3] Although systemic steroids help treat the acute inflammation, immunomodulatory treatment remains the mainstay for long-term disease remission and to minimize complications.

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We report an uncommon presentation of a young girl with idiopathic IU on methotrexate (MTX), who developed tuberculous subretinal (SR) abscess during the course of treatment which was proven by aqueous polymerase chain reaction (PCR).

Case Report

A 14-year-old girl was referred to us as IU, with a history of blurring of vision, redness, and pain in the left eye since 1 month. She was on topical steroids at presentation. Although there was a transient history of pain in the small joints, there was no skin or malar rash or contact history with tuberculosis (TB). On examination, her best-corrected visual acuity (BCVA) was 20/20, N6 in both the eyes. Slit-lamp examination of right eye (OD) was normal and left eye (OS) revealed anterior chamber (AC) reaction-1+ and vitreous cells-2+. Intraocular pressure by applanation tonometry was 17 mmHg in both eyes (OU). Right eye fundus was normal and left eye revealed grade-1 vitreous haze, disc hyperemia, and snowball exudates in the inferior vitreous and pars plana.

Laboratory investigations revealed a normal hemoglobin, normal total and differential counts with an erythrocyte sedimentation rate of 55 mm/hour, negative rheumatoid factor, normal serum angiotensin-converting enzyme levels, a weakly positive antinuclear antibody (ANA) (in 1:80 dilution), and a positive anti-ds DNA. Her Mantoux test showed no induration at 48 hour and chest X-ray was also normal. With a clinical diagnosis of idiopathic IU, she was started on a tapering course of oral prednisolone (1 mg/kg body weight). Two weeks after starting oral steroids, she was initiated on tablet MTX 15 mg/week which was stepped up to 20 mg/week by 1 month, under the care of a pediatric rheumatologist. At 2 months follow-up, her ocular inflammation had resolved completely. The oral steroids were tapered and stopped. She was continued on tablet MTX 20 mg/week, with regular monitoring. Ocular inflammation was well under control for 1 year.

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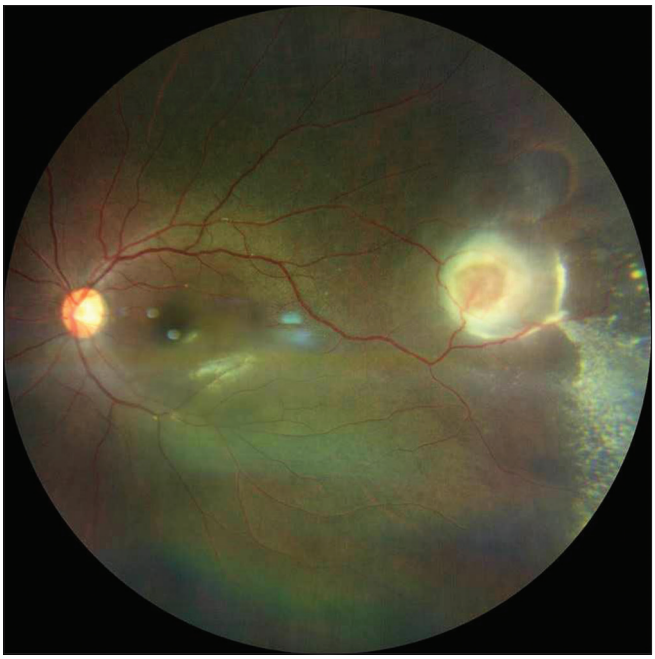

Figure 1: Widefield fundus photograph (Zeiss CLARUS™ 500) of the left eye showing subretinal abscess with subretinal exudates

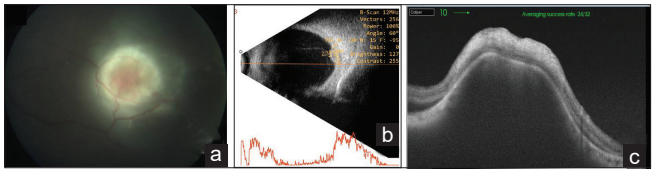

Figure 2: (a) SR abscess in temporal quadrant (b) Ultrasound B-scan showing a few low reflective dot and clump echoes in the vitreous with a localized mass lesion noted in the temporal quadrant with medium surface and internal reflectivity with no shadowing. Retina is attached throughout. (c) Swept source-optical coherence tomography (SS-OCT), a vertical scan taken through the lesion in the superotemporal quadrant showing an elevated retinochoroidal contour with subretinal fluid surrounding the lesion

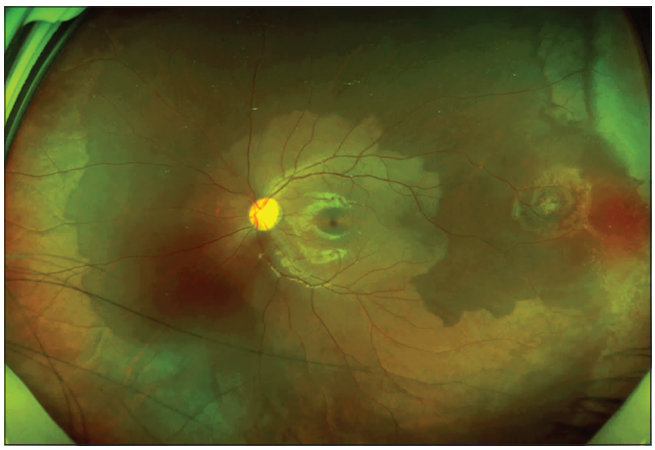

Figure 3: Widefield fundus photograph of the left eye showing complete resolution of the sub retinal abscess with a chorioretinal scar after completion of 9 months of antitubercular treatment

After 1 year from the primary presentation, while on MTX 20 mg weekly, she came with symptoms of increased floaters and redness in the left eye since 1 week. Her BCVA was 20/20, N6 in OU. Right eye was normal and left eye showed an AC reaction of 1+. On fundus examination, a three disc diameter (DD) heterogenous subretinal (SR) yellow lesion in the temporal mid-periphery was noted which was suggestive of SR abscess [Fig. 1 and 2a]. Ultrasound B-scan and enhanced depth imaging-optical coherence tomography confirmed clinical findings [Fig. 2b and 2c]. She was re-evaluated for TB. Her Quanti-FERON TB gold (QFT-G) test was negative and high resolution computerized tomography (HRCT) chest was within normal limits. Aqueous tap PCR for *Mycobacterium tuberculosis* was positive for MPB64 genome. MTX was withdrawn and she was started on appropriate antitubercular therapy (ATT) along with tapering oral steroids. At 1 month, the lesion was showing early signs of resolution. The SR abscess had regressed completely by 6 months with the formation of chorioretinal atrophy. At her recent follow-up, she had completed 9 months course of ATT without recurrences [Fig. 3].

Discussion

It is important to rule out TB before initiation of immunomodulators in any child, especially in an endemic country like India. We had a child treated as idiopathic IU, based on negative lab tests for TB, presenting with SR abscess after an inflammation free period of 1 year while on MTX.

Two possibilities were considered in this patient; either a case of an ocular TB which presented initially as IU and changed phenotype to a SR abscess later during the course of disease or of MTX-induced immunosuppression leading to TB uveitis.

While her mantoux test was negative and chest Xray was normal at the first visit, even in the subsequent visit, when she presented with SR abscess, her HRCT and QFT-G were negative. False-negative QFT-G or tuberculin skin test (TST) has been noted in patients in association with severe systemic illnesses, immune-deficiency states and in those with extrapulmonary TB (EPTB) among others.[4,5] Studies have noted QFT-G false negativity in almost up to about 28.8% EPTB patients, which varied according to the anatomic site of involvement.[5]

Our patient was an otherwise healthy 14-year-old girl with no other systemic evidence of immune-deficiency state. Our case shows the limitations of current diagnostic tests as supportive evidence for ocular TB. SR abscess, being a more classical presentation, with a higher degree of suspicion of TB, AC tap was done which confirmed ocular TB.

MTX-induced iatrogenic immunosuppression was considered as the other possibility. MTX has been found to be safe and efficacious in pediatric uveitis,[6] but interestingly few authors have noted that as compared with non-JIA children, JIA children on MTX without TNF inhibitors had a significantly increased tuberculosis infection rate.[7,8] Our patient had no other signs of systemic immunosuppression or of systemic TB. In our case, the SR abscess responded well to ATT and completely resolved with no recurrences till the follow-up period. Hence, this possibility seems less likely in our case.

She also had a weakly positive ANA but without any active systemic lupus disease and is under the care of a pediatric rheumatologist. ANA positivity has been noted in as many as 33% healthy children in various studies.[9]

Thorough fundus evaluation should be done periodically in children on immunosuppressives. Peripheral fundus lesions

as seen in this case, can otherwise be missed. Widefield fundus photographs can help detect and monitor course of these lesions in children.[10]

Conclusion

Idiopathic IU is a diagnosis of exclusion. This is an uncommon presentation of a probable ocular TB, managed initially as idiopathic IU due to false-negative test results. While on MTX, this changed to a SR abscess, a classical phenotype of ocular TB, confirmed by PCR from intraocular fluid. A child with adequate uveitis control on MTX for a year, ANA positivity and non-contributory systemic or laboratory evidence compounded the dilemma. Our case also stresses the need for regular follow-up of children on immunosuppressives. With an increasing trend towards the use of immunomodulators and biologicals, newer lesions developing either as part of the disease course or a reactivation of latent TB must be considered.

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.

Conflicts of interest

There are no conflicts of interest.

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