

Paradoxical worsening of a case of TB subretinal abscess with serpiginous-like choroiditis following the initiation of antitubercular therapy

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A 37-year-old immunocompetent male patient presented with the blurring of vision, both eyes for the past 1 year. Fundus examination revealed bilateral multiple subretinal abscesses with areas of healed serpiginous-like choroiditis. Laboratory investigations showed positive tuberculin skin test, positive QuantiFERON TB-Gold Test, and high resolution computed tomography chest showed enlarged mediastinal lymph nodes. The aqueous sample revealed polymerase chain reaction (PCR) positive for *Mycobacterium tuberculosis* (MTB) (MPB64 genome). He was treated antitubercular therapy (ATT) along with oral steroids. Although he responded well initially, he had recurrent inflammation and paradoxical worsening. This was managed with a high dose of intravenous corticosteroids, immune suppressive and ATT. He also had a diagnostic vitreous biopsy which was also PCR positive for MTB (IS6110 gene). He subsequently continued ATT along with corticosteroids and immune suppressive and responded well. We present this case report for its unusual presentation.

Key words: IS6110 gene, MPB64 genome, paradoxical worsening, subretinal abscess

Paradoxical reaction to anti-tubercular therapy has been observed in various forms of ocular tuberculosis (TB), including serpiginous-like choroiditis, intermediate uveitis, granulomatous anterior uveitis, retinal vasculitis, and panuveitis and has been documented frequently in extrapulmonary TB.^[1-3] It is believed to be mediated by the host's immune system due to an enhanced delayed hypersensitivity of the host, decreased suppressor mechanisms, and as a response to mycobacterial antigens. We report, a case of bilateral paradoxical reaction in serpiginous-like choroiditis with multiple subretinal abscesses.

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Case Report

A 37-year-old male patient presented with the complaints of defective vision in both eyes associated with pain for the past 1 year. He was previously diagnosed and treated by his local ophthalmologist, as serpiginous choroiditis, with multiple courses of oral steroids. His previous investigations revealed a positive QuantiFERON TB-Gold Test, positive tuberculin skin test (10 mm × 10 mm induration with five tuberculin units), and high resolution computed tomography chest revealed subcarinal granulomatous lymph node enlargement with calcification. However, other investigations for syphilis, toxoplasmosis, HIV was negative.

On examination, we recorded a best-corrected visual acuity (BCVA) of 20/200 in the right eye and 20/40 in the left eye. Slit lamp examination of both eyes revealed a quiet anterior chamber. However, both eyes had plenty of vitreous cells in anterior vitreous. Fundus examination with indirect ophthalmoscopy, showed multiple subretinal abscesses with few areas of healed serpiginous-like choroiditis patches in both eyes [Fig. 1a]. On B-scan ultrasonography, we noted a retinochoroidal elevation nasally with moderate surface and internal reflectivity in the right eye and inferiorly and temporally in left eye, respectively [Fig. 1b]. Magnetic resonance imaging brain was found to be normal. The patient was referred to a chest physician, who initiated first-line antitubercular therapy (ATT) (isoniazid 300 mg rifampicin 450 mg, pyrazinamide 750 mg). Ethambutol was not added by the chest physician, probably due to its potential optic nerve toxicity. We started the patient on systemic steroids 1 mg/kg body weight/day which was tapered gradually. The patient was closely followed up every week. On the second visit at 3 weeks, his BCVA was 20/125 and 20/63 in the right and left eye, respectively. Fundus examination of both eyes showed resolution of the subretinal abscess noted earlier. However, we noted reactivation of serpiginous-like choroiditis lesions in the left eye [Fig. 2a and b]. Aqueous sample revealed polymerase chain reaction (PCR) positive for *Mycobacterium tuberculosis* (MTB) (MPB64 genome). Paradoxical reaction was suspected, ATT was continued, and the dose of oral steroid was stepped up. On the third visit at 4 weeks, his BCVA was 20/63 and 20/80 in the right and left eye, respectively. Fundus examination of both eyes revealed the progression of active lesions and appearance of new lesions in the left eye [Fig. 2c and d]. The patient was given 3 doses of 1 g intravenous methylprednisolone at this visit followed by of oral steroids 1 mg/kg body weight, and ATT was continued.

On the fourth visit at 6 weeks, his BCVA was 20/63 and 20/200 in the right and left eye, respectively. Fundus

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examination showed regressing lesions in the right eye and relentless progression of lesions in the left eye [Fig. 2e and f]. We added immunosuppressive azathioprine 50 mg thrice a day along with oral steroids and continued ATT. On the fifth visit at 10 weeks, his BCVA decreased to 20/200 and 20/400 in the right and left eye, respectively. Fundus examination showed few new active lesions in right eye threatening fovea, and left eye also showed active lesions [Fig. 2g and h]. Diagnostic vitrectomy was done and vitreous biopsy was also PCR positive for MTB (IS6110 gene); however, the culture did not show any growth. On the sixth visit at 12 weeks, his BCVA remained at 20/400 and 20/125 in the right and left eye, respectively [Table 1]. Fundus examination revealed regression of all abscesses and regression of serpiginous-like choroiditis in both eyes [Fig. 3a and b]. The patient presented at 4 months with his BCVA being 20/630 and 20/32 in the right and left eye, respectively, with fundus showing healed lesions in both eyes.

Discussion

To summarize, we report a case of bilateral TB serpiginous-like choroiditis with multiple subretinal abscesses (PCR proven MTB) with paradoxical reaction on initiation of ATT that was managed with high doses of oral corticosteroids, intravenous methylprednisolone, and immunosuppressive agents. Hawkey *et al.* found that a higher bacillary load or a persistent antigenic stimulus that is poorly cleared from the diseased site may be responsible for the development of paradoxical worsening.^[4] Our case presented as serpiginous-like choroiditis with multiple subretinal abscesses with a higher bacillary load that could have attributed to the paradoxical reaction. The other

factor that could have contributed to the paradoxical reaction, was that our patient was on rifampicin, which is reported to reduce the bioavailability of corticosteroids.^[5] Reports by Basu *et al.* and Gupta *et al.*, on analysis of paradoxical reactions to ATT, describe paradoxical reactions in various forms, however, they have not reported any paradoxical reaction in cases of serpiginous-like choroiditis with associated subretinal abscess.^[2,6]

Table 1: Best-corrected visual acuity both eyes corresponding to the fundus pictures in all six visits

Visit	BCVA OD	BCVA OS	Comment
First visit baseline Figure 1a	20/200	20/40	At presentation
Second visit at 3 weeks Figure 2a and b	20/125	20/63	Vision drop due to vitreous haze Aqueous biopsy done
Third visit at 4 weeks Figure 2c and d	20/63	20/80	IV methylprednisolone was given
Fourth visit at 6 weeks Figure 2e and f	20/63	20/200	Azathioprine was added
Fifth visit at 10 weeks Figure 2g and h	20/200	20/400	Diagnostic vitrectomy done Vitreous biopsy done
Sixth visit at 12 weeks Figure 3a and b	20/630	20/32	Vision drop in right eye due to foveal scar

BCVA: Best-corrected visual acuity, OD: Oculus dexter, OS: Oculus sinister

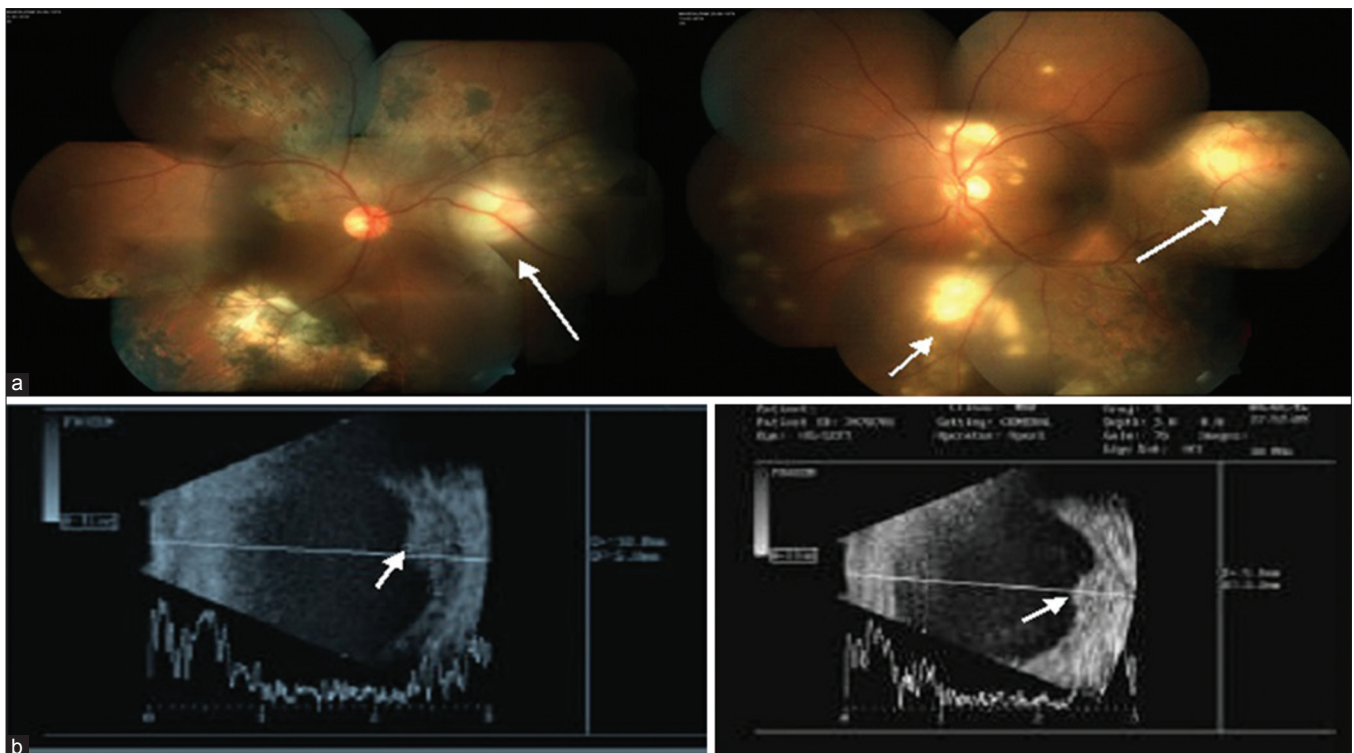


Figure 1: (a) At presentation, fundus photograph both eyes showing multiple subretinal abscesses with serpiginous-like choroiditis patches. (b) corresponding B scan ultrasonography showing retino choroidal elevations suggestive of multiple sub retinal abscesses in both eyes. Right eye measuring 10.1 mm × 9.1 mm × 5.1 mm, left eye measuring 10.6 mm × 5.8 mm × 4.1 mm, moderate internal reflectivity

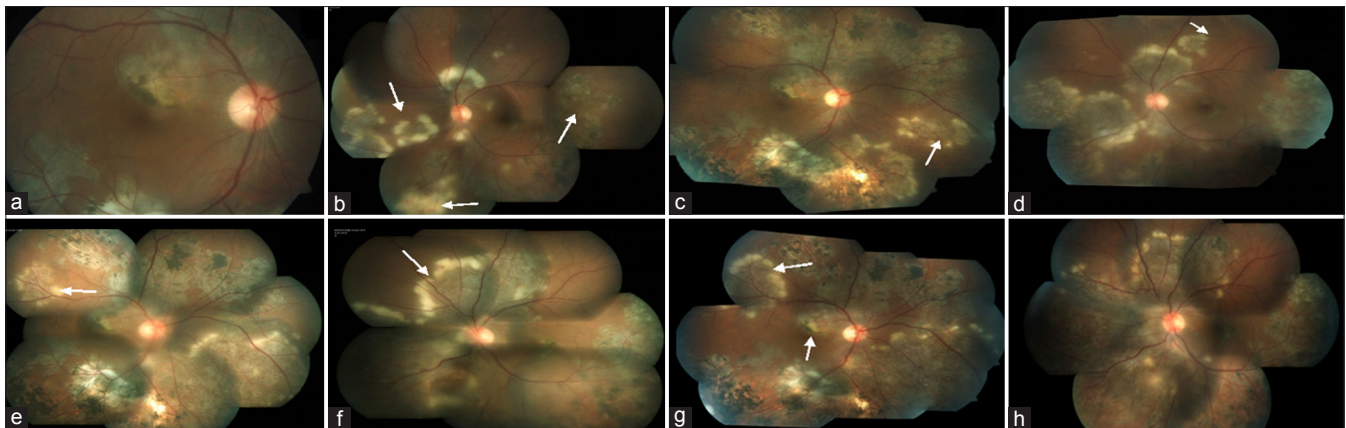


Figure 2: (a and b) Fundus photograph at 3 weeks, revealed resolving sub retinal abscess in both eyes, left eye had reactivation of serpiginous-like choroiditis, a paradoxical reaction, (c and d) fundus photograph at 4 weeks, showing formation of new lesions and progression of old lesions, (e and f) fundus photograph at 6 weeks, showing relentless progression of active lesions and appearance of new lesions, (g and h) fundus photograph at 10 weeks showing formation of the new active lesions in right eye involving fovea



Figure 3: (a and b) Fundus photograph both eyes at 12 weeks showing resolution of the lesions with scarring over fovea in right eye

Our case of bilateral TB serpiginous-like choroiditis with multiple subretinal abscesses was PCR positive for MTB in the aqueous sample as well as the vitreous biopsy. However, we found two different genome sequences by PCR in aqueous (MPB64) and vitreous samples (IS6110), respectively, which is unique to this case. The probable reason for the positivity of IS6110 in vitreous and presence of MPB64 in aqueous aspirate could be due to variation in the initial load of MTB-DNA in vitreous and aqueous samples.^[7]

When our patient had relentless, recurrent paradoxical reactivation of inflammation, we did not consider intravitreal methotrexate as suggested by Julian *et al.*^[8] as our patient probably had a higher bacillary load in the eye, indicated by the presence of subretinal abscesses. We started oral steroids concomitantly with anti-tubercular therapy and not later as suggested by Siantar *et al.*^[5] Intravenous methylprednisolone was given on the third visit and immunosuppressives were used in the fourth visit, when the paradoxical reaction appeared to be relentless and recurrent. Gupta *et al.* in her case series had used Azathioprine as a second-line immunosuppressive in cases not controlled with corticosteroids.^[6] Esen *et al.*^[9] had reported paradoxical

reaction in serpiginous-like choroiditis, who later developed macular edema and serous macular detachment. However, our patient developed a macular scar in the right eye that was responsible for poor visual recovery.

Our case is unique, as we report, the bilateral paradoxical reaction in PCR proven serpiginous-like choroiditis with multiple subretinal abscesses, that was successfully managed with ATT, oral and intravenous steroids and immunosuppressives.

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Conflicts of interest

There are no conflicts of interest.

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