Immune-mediated tuberculous uveitis - A rare association with papulonecrotic tuberculid

Prince Yuvraj Singh, Preema Sinha, Sukriti Baveja, Aradhana Sood

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Department of Dermatology, Armed Forces Medical College, Pune, Maharashtra, India

Correspondence to: Dr. Preema Sinha, Department of Dermatology, Armed Forces Medical College, Pune - 40, Maharashtra, India. E-mail: sinhapreema@gmail.com

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The tuberculids are a group of distinct clinicopathological form of skin lesions representing hypersensitivity reaction to hematogenous dissemination of *Mycobacterium tuberculosis* or its antigen from an underlying active or a silent focus of tuberculosis elsewhere in the body in an individual with a strong antituberculous cell-mediated immunity and by definition do not show bacilli on special stains and are culture-negative. Ocular involvement can occur in tuberculosis, both due to direct invasion by the bacilli as well as an immune-mediated reaction; however, immune-mediated tuberculous uveitis occurring as a hypersensitivity response in association with PNT has hardly been reported in the literature. Here we report one such rare case.

Key words: Rare association, tuberculids, tuberculous uveitis

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Various tuberculids include lichen scrofulosorum, erythema induratum of Bazin, and papulonecrotic tuberculid (PNT).[1,2] PNT presents as recurrent crops of papules and nodules which heal with atrophic scars predominantly distributed on extremities but can present on other areas such as buttocks, face, ears, and glans.[3] The diagnosis is based on strong clinical suspicion and is supported by a strongly positive tuberculin skin test, histopathological evaluation, evidence of underlying focus of tuberculosis, and adequate response to antituberculosis treatment.[4,5] Tuberculous uveitis is a readily treatable disease and the consequences of delay in either ocular or systemic diagnosis can be very serious for the patient. Here we report a rare case of PNT associated with uveitis managed adequately with antitubercular treatment and corticosteroids.

Case Report

A 40-year-old male presented with multiple, recurrent swellings over both lower legs of 5 years and recurrent episodes of redness of left eye of 2 years duration. The swellings were painful, occurred in crops over legs, ulcerated in next few days, to heal over next 4–5 weeks leaving behind dark-colored scars. There was history of recurrent episodes of redness of left eye associated with mild discomfort and photophobia for 2 years. He used to get symptomatic relief on taking steroid eye drops but the symptoms used to recur after few weeks on stopping the eye drops. He kept on getting crops of skin lesions despite taking numerous medical consultations in the past.

On examination, he had multiple hyperpigmented to skin-colored papules and nodules of various sizes over both lower legs with few lesions showing ulceration and crusting [Fig. 1a]. Multiple hyperpigmented, atrophic, and varioliform scars of healed lesions were also seen. Examination of left eye revealed a red eye with circumcorneal congestion and exotropia [Fig. 1b]; cells 1 + and flare trace in anterior chamber with posterior synechiae and hypopyon seen on slit lamp examination [Fig. 1c]. Fundoscopic examination was normal. There was no lymphadenopathy and the rest of the systemic examination was normal. Laboratory investigations revealed an ESR of 33 mm fall at the end of first hour and Mantoux test was strongly positive with 22 mm induration. Chest X-ray, computed tomography chest, and ultrasound abdomen were negative.

Biopsy from the lesion showed mixed inflammatory cells infiltrates with focal areas of necrosis, leukocytoclastic vasculitis with fibrinoid necrosis of blood vessels, and few palisading granulomas [Fig. 1d]. Ziehl–Neelsen staining, culturing of mycobacteria by Löwenstein-Jensen (L-J) medium, and polymerase chain reaction for *Mycobacterium tuberculosis* complex done on skin biopsy tissue were negative. Based on clinical findings, strongly positive Mantoux reactivity, and histopathological findings, the patient was diagnosed as a case of PNT and was started on antitubercular therapy in the form of HRZE (isoniazid 300 mg/day, rifampicin 600 mg/day, pyrazinamide 1500 mg/day, and ethambutol 1200 mg/day) for the next 2 months followed by HR for next 4 months. A course of tapering doses of Tab. prednisolone along with topical steroid eye drops was given for uveitis. The patient responded well with marked healing of the lesions after 3 months of treatment without any fresh crops. Eye symptoms resolved within 2–3 weeks and the topical steroids were completely tapered off and stopped after 2 months. There was no relapse of skin lesions or uveitis at 6 months post therapy follow-up.

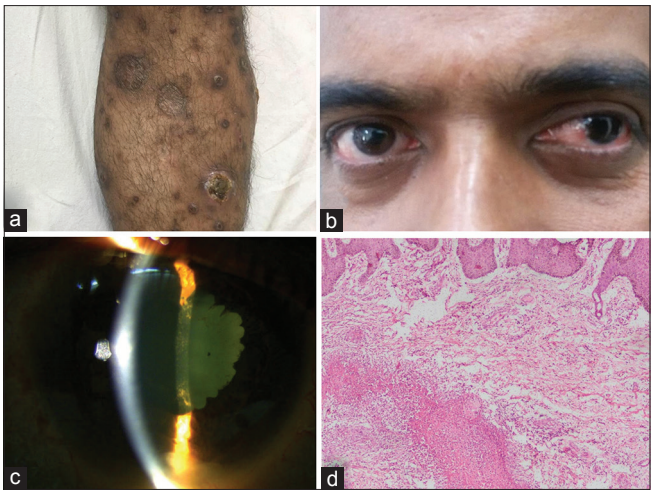

Figure 1: (a) Multiple hyperpigmented to skin-colored papules and nodules present over left the leg with few lesions showing ulceration and crusting. (b) Examination of the left eye revealed a red eye with circumcorneal congestion and exotropia. (c) Cells 1+ and flare trace in anterior chamber with posterior synechiae and hypopyon was seen on slit lamp examination. (d) Biopsy from the lesion showed mixed inflammatory cells infiltrates with focal areas of necrosis, leukocytoclastic vasculitis with fibrinoid necrosis of blood vessels and few palisading granulomas (hematoxylin and eosin ×200)

Discussion

The concept of tuberculids was introduced by Darier in 1896.[1] The tuberculids represent an Arthus-type hypersensitivity reaction to hematogenous dissemination of *Mycobacterium tuberculosis* or its antigen from an underlying active or a silent focus of tuberculosis elsewhere in the body in an individual with a strong antituberculous cell-mediated immunity and by definition do not show bacilli on special stains and are culture-negative. Clinical forms of tuberculids include lichen scrofulosorum, erythema induratum of Bazin, and PNT. PNT is the least common form reported rarely even from countries with high prevalence of tuberculosis.[6] It presents with recurrent crops of symmetrical, hard, dusky red papulonodular, pustular, or necrotic lesions that ulcerate and heal over several weeks to leave behind atrophic varioliform scars. Typical areas of involvement include extensors of extremities, dorsum of hands and feet, face, ears, and glans. Common features on histopathological examination of the lesion include epidermal ulceration, a mixed inflammatory infiltrate in the dermis, coagulative necrosis, palisading granulomas, and leukocytoclastic vasculitis with extravasation of red cells. Polymerase chain reaction (PCR) on the lesional skin for mycobacterial DNA is a sensitive tool to demonstrate the organism and various studies show 0–80% positive rates.[7] A negative result for PCR does not exclude the diagnosis like it was seen in our case.[5] The diagnosis of PNT is made on the basis of a typical clinical picture, a strongly positive tuberculin skin test, consistent

histopathological findings, past history of tuberculosis, or a present focus of *Mycobacterium tuberculosis* infection in the body and adequate response to antitubercular therapy.[4] In our patient, the clinical picture, a strongly positive tuberculin skin test, and the histopathological finding of the skin biopsy were consistent with the diagnosis of PNT. An underlying tuberculous focus can be demonstrated in only 38–75% of cases, most commonly in lymph nodes and it can be negative like in our case.[8] The rapid response to antituberculosis therapy in our patient also supports the diagnosis.[9] The treatment for tuberculids is the same as for any other form of tuberculosis and our patient was given a complete course of antitubercular treatment for 6 months. Intraocular TB is a great mimicker of various uveitis entities and it can be due to direct infection or indirect immune-mediated hypersensitivity response to mycobacterial antigens when there is no defined active systemic lesion elsewhere or the lesion is thought to be inactive. Direct infection may manifest in the form of keratitis, conjunctivitis, acute anterior uveitis, chronic granulomatous anterior uveitis which may be associated with iris or angle granulomas, mutton-fat keratic precipitates and posterior synechiae, intermediate uveitis, macular edema, multifocal choroiditis, choroidal tubercles, vasculitis, vitritis, papillitis, neuroretinitis, endophthalmitis and panophthalmitis.[5,10] Uveitis is underdiagnosed in tuberculosis and the uveitis in our patient also appears to be a hypersensitivity response to mycobacterial antigen as we could not find a defined active systemic lesion elsewhere, and the patient did not have features such as choroidal tubercle, subretinal abscess, endophthalmitis, panophthalmitis which are more consistent with infective etiology, its association with PNT which is itself a cutaneous hypersensitivity reaction to tubercular antigen, and a rapid response to treatment.[10] The association of immune phlyctenular conjunctivitis and leukocytoclastic vasculitis with PNTs has been mentioned commonly but, to the best of our knowledge, there is only one case reported before our patient of hypersensitivity tuberculous uveitis with PNTs by Dar *et al*.[5,11]

Conclusion

To conclude, immune-mediated tuberculous uveitis is a rare form of hypersensitivity response to underlying focus of tuberculosis and its association with PTN is a useful cutaneous marker of underlying focus of tuberculosis.

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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Conflicts of interest

There are no conflicts of interest.

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