INTRODUCTION

Papulonecrotic tuberculid is a rare condition regarded as a hypersensitivity reaction to *Mycobacterium tuberculosis* following haematogenous spread from a focus of infection in individuals with significant immunity manifested by a strongly positive tuberculin test. It typically affects young adults, involving symmetrically the extremities, ears and the extensor aspects of joints. The individual lesion is an inflammatory papule, which becomes necrotic, ulcerates and involutes over weeks, leaving scars in many cases. A tuberculous focus may not be detected in all the cases and the relevant tests may be negative. Hence, a high index of suspicion of tuberculous etiology should be maintained. Associated clinical features described are lymphadenopathy, phtyctenular conjunctivitis and leukocytoclastic vasculitis.

Immune mediated uveitis is also a hypersensitivity phenomenon but has not been described in tuberculosis in association with papulonecrotic tuberculids. We report a case of papulonecrotic tuberculids associated with immune mediated unilateral uveitis in which all investigations were negative for tuberculosis except a strongly positive tuberculin test. The association between papulonecrotic tuberculids and uveitis, both responding to anti-tuberculosis therapy has not been recognized previously to the best of our knowledge.

CASE REPORT

A 29 years old male presented for a rash, which had persisted and spread for more than one year despite taking different treatments. The rash started from the face and then progressively spread to involve the buttocks, groins and external genitalia. The lesions were painful but not itchy. Ten days before admission, he developed blurring of vision along with redness in left eye.

On examination, multiple erythematous flesh coloured papular lesions of various sizes were present mostly over the buttocks, groins and external genitalia. Scattered lesions were also observed over trunk, limbs and face. Some of the lesions showed central necrosis and crusting. A few atrophic scars of healed lesions were also seen (Figure 1a). Eye examination revealed a red eye with circumcorneal congestion (Figure 2a). Large mutton fat keratic precipitates were seen on the left cornea more dense on inferior and middle zones. Anterior chamber showed cells++ and flare+. Fundoscopic examination did not reveal any abnormality. Lymph nodes were enlarged in the cervical region and were discrete and firm. Rest of the systemic examination was within normal limits.

Laboratory investigations revealed an ESR of 16 mm fall at the end of first hour by Westergren method and Mantoux test was strongly positive with 5 IU (Figure 1a-arrow). Serology for tuberculosis (by Elisa, Omega diagnostics, Pathozyme TB complex plus) and blood PCR (DNA extraction by Lite diagnostics, Bacterial X press nucleic acid extraction kit/DNA amplification by Biotub kit for *Mycobacterium tuberculosis* DNA detection-amplification mixture included primers) for *Mycobacterium tuberculosis* were negative. Biopsy from the lesion showed a mixed inflammatory cell infiltrate and PCR for *Mycobacterium tuberculosis* was negative in the biopsy specimen (DNA extraction by Lite diagnostics, Bacterial X...
Bacterial X press nucleic acid extraction kit/ DNA amplification by Biotub kit for *Mycobacterium tuberculosis* DNA detection-amplification mixture included primers). X-rays chest, ultrasound abdomen and pelvis and blood chemistries were within normal limits.

Despite the negative laboratory parameters, the patient was started with anti-tuberculosis treatment with 4 drugs on the basis of morphology suggestive of papulonecrotic tuberculids and a strongly positive Mantoux test. The regime included Rifampicin 600 mg once daily and Isoniazid 300 mg once daily for 06 months and Pyrazinamide 1500 mg daily and Ethumbutol 1200 mg daily for initial 02 months along with Rifampicin and Isoniazid. Topical steroid eye drops were started for uveitis. The patient showed remarkable improvement with marked healing of the lesions after 3 months of treatment. He gained 13 kilograms of weight during the treatment. His uveitis also responded quickly and the topical steroids were completely tapered off after 1 month and the patient had no relapse of uveitis despite being off steroids. There was no relapse of skin lesions or uveitis at 6 months posttherapy follow-up (Figure 1b, 2b).

**DISCUSSION**

According to Yates and Rook, the concept of tuberculids was introduced by Darier in 1896. In contrast to skin tuberculosis, tuberculids are explained on the basis of hypersensitivity reaction to *Mycobacterium tuberculosis* or its products in a patient with significant immunity. The main features of tuberculids are a compatible clinical picture, positive tuberculin test, evidence of manifestation or past tuberculosis and a positive response to anti-tuberculosis treatment. Tuberculous focus may not be evident in all cases. Tuberculids are uncommon manifestations of tuberculosis in Pakistan and may present clinically in different ways. Papulonecrotic tuberculids consist of recurring crops of symmetrical, hard, disky red papules. These crust or ulcerate heal in weeks leaving behind hyperpigmented or atrophic varioliform scars. Crops may recur over months or years. Epidermal ulceration, dermal coagulative necrosis, granulomatous infiltrate (often resembling granuloma annulare), granulomatous vasculitis and extravasation of red cells are common histological findings. *Mycobacterial* DNA can be demonstrated in lesional skin using a PCR technique. A negative result does not exclude the diagnosis but the whole pathogen has never been isolated. The overall positivity of nested PCR was 35.2% in one study done on extra-pulmonary tuberculosis. In this patient, investigations including skin biopsy, PCR studies and serology were not supportive. Mantoux test was strongly positive. However, no tuberculous focus could be demonstrated. An associated tuberculous focus cannot be demonstrated in all cases of papulonecrotic tuberculids and different studies quote a range of association from 38-75%. The rapid response to anti-tuberculosis therapy leaves no doubt of the diagnosis in this patient despite lack of support by investigations. The treatment has to be completed as for any other form of tuberculosis.

Ocular manifestations of tuberculosis are protean. Ocular involvement is mainly due to direct involvement of eye structures by the organism leading to keratitis, conjunctivitis, anterior uveitis, choroiditis, choroidal tubercles, vasculitis, vitritis, papillitis and panophthalmitis. Tuberculosis is usually under-diagnosed as a cause of uveitis. In this patient, the uveitis appeared to be a hypersensitivity response similar to that seen in papulonecrotic tuberculids as there was a rapid response to treatment, which paralleled improvement in skin lesions. Uveitis appeared approximately one year after appearance of papulonecrotic tuberculids and it did not recur after tapering off the steroids, whereas the uveitis due to actual invasion of the organism is always recurrent. Immune phlyctenular conjunctivitis and leukocytoclastic vasculitis has been seen in association with papulonecrotic tuberculids but hypersensitivity uveitis has not been reported before.

A high index of clinical suspicion is required for diagnosis of papulonecrotic tuberculids; a cutaneous marker of an underlying focus of tuberculosis, as laboratory support may fail to contribute to diagnosis as was illustrated in the present case. Also immune mediated uveitis may be added to the clinical spectrum of papulonecrotic tuberculids.
REFERENCES


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