Papulonecrotic Tuberculide in a Three-year-old Child

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Date:	9 June, 1999
Venue:	Yaumatei Skin Centre
Organizer:	Social Hygiene Service, DH; Clinico-pathological Seminar

CASE SUMMARY

History

A three-year-old girl presented with a two-year history of recurrent, bilaterally distributed, asymptomatic papules mainly affecting the extensor surfaces of the upper and lower limbs. The lesions progressed to form pustules, crusts and were increasing in number. Some of these lesions healed with scarring and pigmentation. The girl was otherwise healthy with no systemic complaint or respiratory symptom. There was no significant past medical history or family history. Allergy history was negative. She was born in China. Her mother had recently moved from China with her to Hong Kong. BCG and other childhood vaccinations had been given in China.

Examination

On physical examination, the child had multiple, symmetrically distributed, erythematous papules and plaques on the upper and lower limbs (Figure 1). These lesions were non-tender on palpation and did not show any ulceration. Scars and pigmentary changes were evident (Figure 2). The clinical differential diagnosis included papulonecrotic tuberculide, PLEVA, lymphomatoid papulosis and papular urticaria.

Investigations

A full thickness, deep incisional skin biopsy was performed. There was a well circumscribed zone with dermal and fat necrosis in concert with a mixed cell infiltrate consisting of lymphocytes and neutrophils in the middle and lower dermis, and superficial subcutis. There were also epithelioid histiocytes in palisades, and multinucleated giant cells with granuloma formation. Vasculitis was not seen. The overlying epidermis was intact. Special stains for acid-fast bacilli, fungi and bacteria were negative. There was no refractile foreign body. The histological diagnosis was granulomatous dermatitis with dermal and fat necrosis consistent with **papulonecrotic tuberculide**.

Swab and tissue cultures were all negative. Polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* was performed which was also negative. Chest radiograph, early morning urine for acid-fast bacilli, baseline haematology and biochemistry were

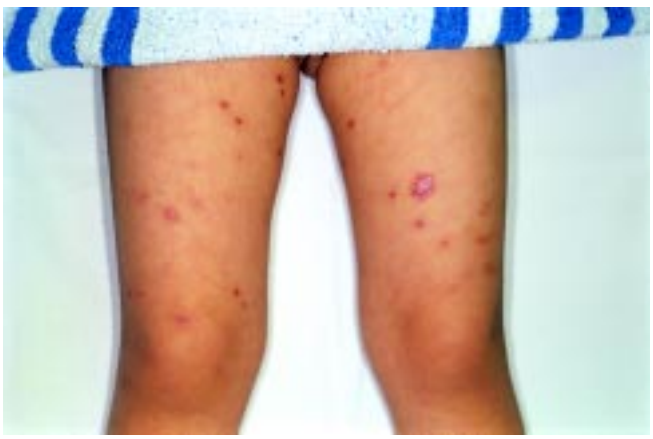

Figure 1: Multiple, symmetrically distributed, erythematous papules and plaques over both thighs

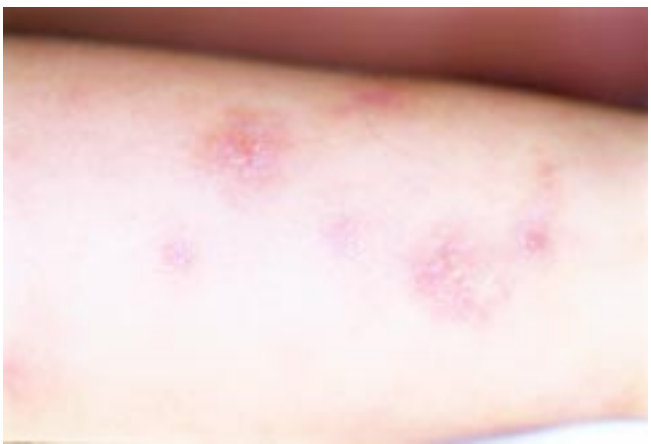

Figure 2: Lesions healed with scarring and pigmentary changes

all negative. Tuberculin test (Mantoux test) performed by the chest physician was strongly positive. It showed an induration of >15mm after 48 hours. The diagnosis was papulonecrotic tuberculide.

Management

Once the diagnosis was confirmed, anti-tuberculous multi-drug therapy (MDT) was started. This included pyrazinamide (25mg/kg/day), rifampicin (10mg/kg/day), and isoniazid (5mg/kg/day). The minimum duration of therapy was for six months. Her parents had given full consent on the above MDT regime. She showed good compliance with the regime. On subsequent follow-up examination, some of the lesions subsided with residual scarring and pigmentary changes but some persisted. Overall, general health remained good and there was no new lesion.

A REVIEW OF PAPULONECROTIC TUBERCULIDE (PNT)

The concept of tuberculide was first introduced by Darier in 1896. Later, Pautrier established that papulonecrotic tuberculide was a tuberculosis associated condition.

The current belief is that the tuberculide is a cutaneous autoimmune type IV hypersensitivity reaction to the bloodstream dissemination of mycobacterial fragments. The criteria for defining a true tuberculide are as follows:

1. Evidence of tuberculosis elsewhere showing granulomatous inflammation in the skin biopsy.
2. A strongly reactive tuberculin test.
3. Resolution of the lesions with systemic anti-tuberculous therapy.[1]

Although many conditions have been suggested to be tuberculides, only the conditions erythema induratum of Bazin (EIB), papulonecrotic tuberculide (PNT) and lichen scrofulosorum (LS) are considered to be genuine tuberculides (Table 1).

Epidemiology

Papulonecrotic tuberculide is a rare condition. It is more often seen in areas where *Mycobacterium tuberculosis* infections are prevalent, e.g. South Africa, India, South East Asia including Hong Kong. PNT is more often reported in adults than in children. Apart from a few isolated case reports, only one study in South Africa reported a series of 8 children presented with PNT.[2] In this series, there was a male to female ratio of 2:1. The mean age of the patients was 47.5 months and the median time from onset of lesions to diagnosis was four weeks. In a 10-year retrospective survey on the incidence of cutaneous tuberculosis in Hong Kong from 1983 to 1992, PNT accounted for only 4.0% of all cases of cutaneous tuberculosis diagnosed within this period.[3] The total number of patients diagnosed to have PNT in this survey was seven and they were all adults. Their age ranged from 18 to 43 years with a mean of 29 years. In this study, 85.2% of all cutaneous tuberculosis were tuberculides, in which EIB was the commonest, PNT ranked second and LS third. True cutaneous tuberculosis other than tuberculides like LV, TVC and SFD were all declining in incidence in Hong Kong.

Table 1. Classification of cutaneous tuberculosis[2]

Inoculation tuberculosis (exogenous source)	• Tuberculous chancre • Tuberculosis verrucosa cutis • Lupus vulgaris (some)
Secondary tuberculosis (endogenous source)	• Scrofuloderma • Orificial tuberculosis
Haematogenous tuberculosis	• Acute miliary tuberculosis • Lupus vulgaris (some) • Tuberculous gumma
Tuberculides	• Papulonecrotic tuberculide • Erythema induratum of Bazin • Lichen scrofulosorum
Other	• BCG-related complications

Clinical features

The characteristic morphology of individual PNT lesion consists of papule or papulopustule with size ranging from 1 to 5mm in diameter. Some of these lesions may undergo necrosis to form crusted ulcers, and some may heal with scarring. The lesions of classical PNT are symmetrically distributed on the extensor aspects of the skin of all four limbs. Lesions can appear at unusual sites like the ear lobes and the penis. However, the trunk, oral mucosa, and the face are seldom involved. The lesions follow a characteristic distribution in the various types of tuberculide. EIB is predominantly distributed over the lower extremities especially over the calves. LS is mostly distributed over the trunk and lower extremities. In PNT, the lesions are distributed over the upper and lower extremities and seldom involve the trunk, head or neck. The patient is usually well. A detailed search for underlying tuberculosis is usually not rewarding. Some of these tuberculous foci may be hidden. Recent advances in PCR can help to elucidate the underlying aetiology of these lesions. In adult PNT, concomitant skin eruption with EIB and LV has been documented in the same patient. Conditions that may be confused with PNT include PLEVA, papulopustular syphilid, miliary TB, EIB, papular urticaria, reactive perforating collagenosis and post-BCG vaccination.

Histopathology

The commonest histological feature of PNT is a granulomatous inflammation with palisading granuloma formation There is usually deep dermal fat necrosis but vasculitis and panniculitis are not seen. The cellular infiltrates are usually mixed and consist of histiocytes, lymphocytes, neutrophils and sometimes eosinophils. Fibrosis is absent. Acid-fast bacillus is not detected in routine Ziehl-Neelsen stain or Lowenstein culture. Recent advances in immunohistochemistry suggested that UCHL-1, KP1 and CD3 antibody specifically bind to these tissues. This suggests that specific cell types like T lymphocytes, macrophages and monocytes to which these monoclonal antibodies bind are involved in the pathogenesis of PNT. B lymphocytes and plasma cells are not present in the infiltrates.

Polymerase chain reaction in the diagnosis of cutaneous tuberculosis

PCR is an invaluable tool in the diagnosis of cutaneous tuberculosis including the tuberculides. PCR has been shown to provide reliable, rapid and accurate results in the diagnosis of different types of cutaneous tuberculosis, especially the paucibacillary form. However, it is of paramount importance to carry out internal controls for both positive and negative cases of PCR to avoid biologically false positive and false negative results. It has been shown that in cases where the histological features shows granulomatous dermatitis and in which the routine cultures and special stains were uncertain of the underlying diagnosis, PCR can accurately diagnose lupus vulgaris, erythema induratum of Bazin and papulonecrotic tuberculide.[4] It is suggested that PCR for *Mycobacterium tuberculosis* should be performed on cases of granulomatous inflammation suspicious of tuberculosis origin and the technique should be available in pathological laboratory.

Learning points:
The presence of symmetrically distributed, asymptomatic, necrotic papules over the limbs in patients from tuberculosis-prevalent area may be suggestive of tuberculide. A deep skin biopsy and tuberculin test should be performed.

References

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