Scrofuloderma Associated with Granuloma Annulare-like Lichen Scrofulosorum

Agnes I. Otto[1], Judit Harsing[1], Iren Herjavecz[2], Maria Kiss[3] and Sarolta Karpati[1]
[1]Department of Dermatology, Semmelweis University Budapest, Mária u.41, HU-1085 Budapest, [2]National Institute of Tuberculosis and Pulmonology of Korányi, Budapest, and [3]Department of Dermatology and Allergology, University of Szeged, Szeged, Hungary. E-mail: aot@freemail.hu
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Sir,

Scrofuloderma is a form of cutaneous tuberculosis (TB) resulting from contiguous extension of an underlying tuberculous focus, most commonly over a lymph node. Lichen scrofulosorum is characterized clinically by grouped perifollicular and extrafollicular, pinhead-sized papules over the trunk, which is considered to be a delayed type IV hypersensitivity response to *M. tuberculosis*. Concomitant presentation of these two cutaneous TB entities has not been reported previously in Europe. Granuloma annulare-like lichen scrofulosorum is also a rarity. We report here the case of a patient with scrofuloderma who developed lichen scrofulosorum with an extraordinary morphology.

CASE REPORT

A 66-year-old Caucasian man presented to our clinic in 2008 with multiple yellow-brownish arcuate plaques with beaded morphology on the trunk and back, which had been present for 2 years. (Fig. 1). On dermatological examination, the patient additionally had an oval, 2 cm diameter, non-ulcerative erythematous tumour in the left supraclavicular region with cervical lymphadenomegaly (Fig. 2). During the past 4 years three tumours with identical morphology had appeared over the left supraclavicular region and the jugulum, associated with cervical, left supraclavicular and left axillary lymphadenomegaly. In 2005 lymphadenectomy had been performed in the left supraclavicular region to exclude non-Hodgkin's lymphoma. Histology showed granulomatous lymphadenitis with abscess formation. Malignancy was ruled out. Chest and abdominal computed tomography (CT) scan was negative. In 2007 two skin tumours were excised. Histology showed granulomatous inflammatory infiltration in the subcutaneous tissue. No organisms were observed in tissue sections stained for acid-fast bacilli and fungi. The histologist suggested a granulomatous reaction triggered by a ruptured epidermoidal cyst. Chest radiography was negative. Four months later, axillary block dissection was performed, in which 13, 0.9–5 cm diameter lymph nodes could be identified. Histology in all lymph nodes was evaluated as a chronic granulomatous inflammatory process with caseation. Ziehl-Neelsen, Grocott and periodic acid Schiff (PAS) staining was negative. In February 2008 a 1.6 cm diameter, skin-coloured, ulcerating nodule was excised from the neck. The result of the histopathological examination was identical to the previous findings; granulomatous inflammation. Neck and chest CT scan proved moderately enlarged lymph nodes in the neck and supraclavicular region. The deeply situated lymph nodes composed a conglomerate, formed by multiple, 1 cm diameter and smaller centrally necrotizing lymph nodes. In the left supraclavicular area a trabeculated lesion of 1 cm diameter was described, connected to the skin. The right axillary region, the lungs and the mediastinum were free of abnormalities. Although, the most probable diagnosis was TB, the patient had not received any anti-tuberculous treatment. He had been referred to one specialist after another without establishment of the correct diagnosis. In the following 4 months the patient did not present to the doctor since he was afebrile and his general condition was good. His major concern was the eruption persisting on his trunk and back and the appearance of a new tumour in the left supraclavicular region in the proximity of the neck. He was re-

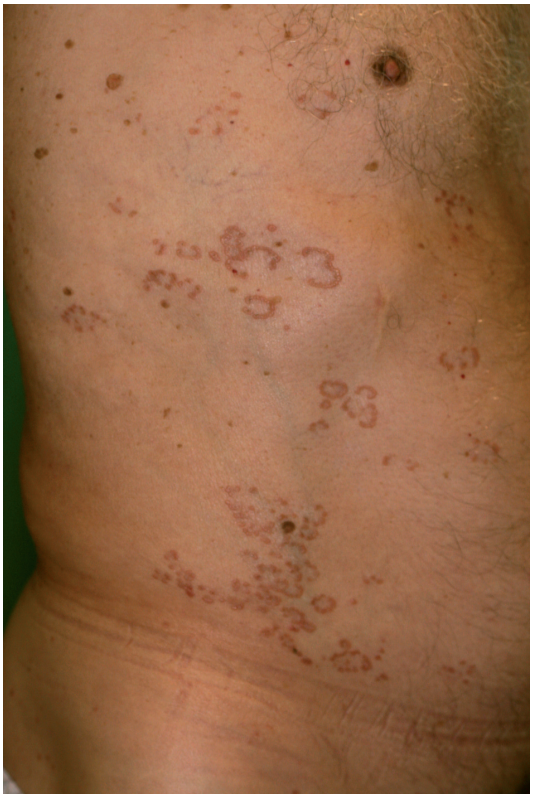

Fig. 1. Arcuate, yellow-brownish plaques with beaded morphology on the trunk; lichen scrofulosorum.

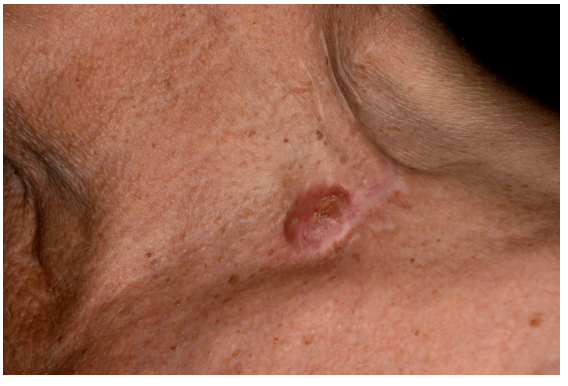

Fig. 2. An oval, non-ulcerative erythematous tumour, 2 cm diameter, in the left supraclavicular region; scrofuloderma.

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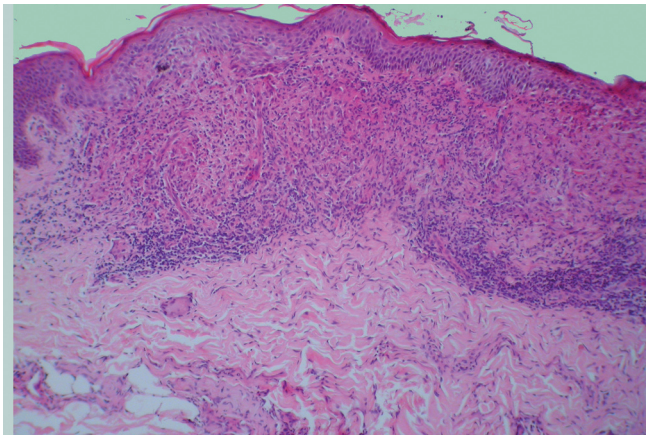

Fig. 3. Histopathology of lichen scrofulosorum with tuberculoid structures in the upper dermis (haematoxylin-eosin (H&E) ×80).

ferred to our clinic in June 2008. Significant laboratory findings included a raised erythrocyte sedimentation rate (ESR) (98 mm in the first hour) and an elevated immunoglobulin A serum level of 580 mg/dl (normal 70–370 mg/dl) and a moderate anaemia combined with iron deficiency. Serology for syphilis (RPR, TPHA, TP-ELISA) and human immunodeficiency virus was negative. The tuberculin test was positive after 48 h (18 mm: the patient had a history of BCG vaccination). Surgical excision of the tumorous nodule was performed in our clinic. Histology showed large, caseating, necrotizing granulomatous inflammation. Ziehl-Nielsen staining was negative. Histology of the skin specimen taken from the granuloma annulare-like plaques proved perifollicular tuberculoid structures with Langhans type giant cells and a non-specific inflammatory cell infiltration (Fig. 3). Nested polymerase chain reaction (PCR) assay targeting IS6110 insertion DNA sequence of *M. tuberculosis* DNA was positive in the scrofuloderma sample, but proved negative in lichen scrofulosorum. On the basis of the clinical picture, laboratory findings, histology and positive PCR result performed from the tissue of the skin tumorous lesion, the diagnosis of scrofuloderma associated with lichen scrofulosorum was made. The patient was treated with pyrazinamide 2500 mg daily, isoniazid 300 mg daily, rifampicin 600 mg daily, and ethambutol 1500 mg daily for 2 months. Isoniazid and rifampicin were continued for another 4 months. The patient showed an excellent response to anti-tuberculous therapy, even after 2 months: the arcuate plaques faded and later dissolved, and the control chest CT scan showed no pathological lymph nodes in the left axillary region, only residual scarring.

DISCUSSION

Extrapulmonary TB constitutes 10% of cases of TB (1). Cutaneous TB is still a rarity in Europe and North America. The host's immune status defines the clinical presentation of the tuberculous infection of the skin similarly to the route of infection. In the classification system proposed by Tappeiner & Wolff (2, 3) exogenously and endogenously acquired true cutaneous TB exists. Scrofuloderma belongs to the second group, since it has been reported that it occurs most commonly after cervical lymph node infection via contiguous extension. (4). The relationship between TB and tuberculids is still enigmatic. Tuberculids are generalized exanthems in the skin, resulting from hypersensitivity reactions to *M. tuberculosis* or mycobacterial antigen in an individual with strong anti-tuberculosis cell-mediated immunity (5). This group includes lichen scrofulosorum, papulonecrotic tuberculid, erythema induratum (Bazin's disease – subcutaneous form) and superficial thrombophlebitic tuberculid (first described by Hara in 1997 (6)). Winkelmann described a case of TB associated with granuloma annulare in 2002 (7). Tsai described a cutaneous tuberculid clinically resembling granuloma annulare in 2007 (8). We present here a patient who had a subcutaneous form of skin TB and consecutively and concomitantly a rare type of tuberculid, which reflects the hyperergic state of the immune system. Our case serves as an example to demonstrate the complexity of the immune defence mechanisms in TB. Coexisting scrofuloderma and lichen scrofulosorum has been reported previously only in India (9). We are the first to present such a case in Europe. Granuloma annulare-like lichen scrofulosorum was reported once before in an immunocompromised patient in 2007 (8). Taken together with our case, a new form of lichen scrofulosorum is described: the granuloma annulare-like variant. The rarity of TB, especially extrapulmonary TB in Hungary, serves as an explanation for the delayed diagnosis and treatment. Finally, not only the HIV-positive population is prone to TB in developed countries. With the use of tumour necrosis factor (TNF) antagonists (biologic agents, e.g. infliximab, etanercept, adalimumab) attention was focused on the role of TNF-α in activating macrophages and preventing the dissemination of infection by stimulating granuloma formation (10). Thus, atypical presentation of TB, such as extrapulmonary disease including skin TB, might be expected in the future with a higher incidence. Cervical lymphadenitis is the most common form of extrapulmonary TB (11) and can play a significant role as a primary focus associated with cutaneous manifestations.

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