Cutaneous Manifestations of Takayasu Arteritis

Sir,

Takayasu arteritis (TA) is an uncommon chronical inflammatory arteriopathy with giant cells of unknown etiology. It affects mainly the aorta and its main branches, causing marked fibrosis and thickening of the vessel walls. Some reports suggest that the vascular inflammatory process is not always confined to the arteries but may also involve other vessels, especially small cutaneous vessels (1). The first case was reported by Savor in 1856 (2). Takayasu noted ocular involvement in 1908 (3).

The frequency of skin lesions in TA is estimated at 2.8% to 28% of cases (1, 5). Some skin diseases described in TA have probably occurred independently, such as hand dermatitis, urticaria and angioedema, psoriasis, viral warts, folliculitis, tinea pedis, atrophia or hyperpigmentation (4). The following skin diseases were considered to be specifically associated with the vascular inflammatory process in TA: erythema nodosum, erythema induratum, tuberculoid-like eruptions, pyoderma gangrenosum, and cutaneous signs of necrotizing or granulomatous vasculitis.

In this report we present the case history of a female patient who had suffered from erythema nodosum for years before more specific symptoms of TA developed.

CASE REPORT

A 48-year-old female patient of Turkish origin suffered from arthralgia of the large joints and recurrent red or purple nodules at the lower legs, which had been diagnosed as erythema nodosum for 10 years. Moreover, for some months she had noticed a loss of strength in her left arm and of dizziness when raising the left hand over her head. A hypertonus had been treated with β blockers for 3 years. On the neck, the upper arms and upper legs disseminated maculopapulous or nodulous red or purple lesions were found (Fig. 1). On the lower legs there were multiple dark-red nodules resembling erythema nodosum. Pulses of the radial and ulnar arteries of the left arm were not palpable, while normal findings were noted on the right arm. Blood pressure of the left and right arm was 120/80 and 180/105 mmHg, respectively. The Ratschow-manoeuvre of the left arm was positive (pathological result).

Selected normal laboratory findings showed an elevated white blood count (11.700/µl) and a slightly elevated sedimentation rate of 38 mm after the first hour. Hemoglobin was low (10,4 g/100 ml) and antinuclear factors were positive (1:160, speckled pattern), with associated anti-Scl-70 antibodies. Normal results were obtained on testing of anti-DNA-, anti-ENA- (except anti-Scl-70), anti-cardiolipin and anti-neutrophilic cytoplasmatic antibodies and rheumafactors. Negative serology was found with *Borrelia burgdorferi*-, *Chlamydia*-, *Yersinia*- or *Campylobacter* antibodies.

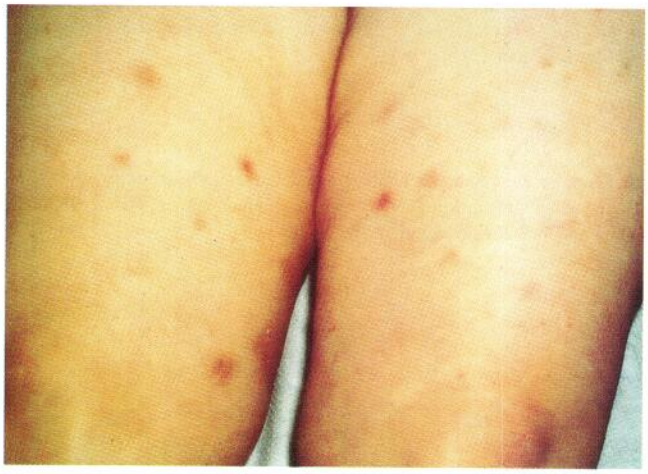

Fig. 1. Nodulous lesions of the upper legs in the late phase of TA.

Arterial digital normal subtraction angiography showed a subtotal stenosis of the left vertebral artery and of the left subclavian artery.

A deep excision biopsy from a nodulus of the lower leg showed dense lympho-histiocytic infiltrates surrounding the vessels of the deep dermal plexus and infiltrating the vessel walls. Some giant cells with multiple nuclei were visible but only few granulocytes and no leukocytoclasia. Some vessels were completely occluded by fibrinoid precipitates. A less extensive vasculitic involvement of the superficial vascular plexus was noticed in this biopsy and in a biopsy taken from a nodus at the upper trunk. No deposition of immunoglobulins or complement (C3c) was detectable in the skin by immunofluorescence. A biopsy which had been taken 3 years before from a nodule of the lower leg could be reviewed and showed the typical features of erythema nodosum without vasculitis.

A marked improvement of the skin symptoms and arthralgia was induced by treatment with 60 mg prednisolone per day. Since the patient suffered from marked soar esophagitis and gastritis soon after the beginning of this therapy, the dose was reduced to 30 mg per day but this led to a relapse of the skin symptoms and arthralgia. A complete remission of skin lesions and arthralgia was achieved by treatment with 40 mg prednisolone per day and 10 mg methotrexate per week.

DISCUSSION

TA is a rare, chronic inflammatory disease. The cause of this systemic disease, which involves mainly the large blood vessels, is unknown. Many patients suffer from symptoms which cannot directly be attributed to vasculitic changes such as arthralgia or weight loss. Lack of specific laboratory parameters makes the diagnosis of TA mainly based on clinical findings. Inflammatory skin nodules as manifestation of the disease appear to be a common feature. Approximately 50% of patients with TA respond to glucocorticoid therapy. Patients with glucocorticoid-resistant disease may achieve remission by additional weekly given low-dose methotrexate.

The occasional involvement of small cutaneous vessels in TA has been described during the last 10 years. Perniciaro et al. found skin lesions caused by vasculitic changes in 7 out of 8 patients with TA (1): 5 patients suffered from erythema nodosum-like lesions, one patient had a pyoderma gangrenosum-like ulcer and one patient developed Churg-Strauss granuloma. The histological investigation of the erythema nodosum-like lesions did not support the clinical diagnosis: in 2 cases necrotizing vasculitis was described, in 2 cases acute panniculitis and in one case a granulomatous vasculitis. Frances et al. reported 4 patients with TA and noduli on the legs which had been biopsied (5): in 2 patients granulomatous inflammatory processes were described, in 2 further cases acute panniculitis. In many published cases of erythema nodosum-like lesions in TA histopathological changes remain unclear since biopsies had not been taken.

A biopsy which had been taken in the early phase of the disease from the patient described here had shown typical

histopathological changes of erythema nodosum. The histopathological findings changed in the late phase of TA: a granulomatous vasculitis with occlusion of small vessels and giant cells was now detectable at the site of erythema nodosum-like lesions and in the maculopapulous and nodulous lesions at the upper extremities and trunk.

Our report shows that nodules which appear early in the history of the disease can be clinically and histologically indistinguishable from erythema nodosum. But later on they may be a sign of true granulomatous giant cell vasculitis. Therefore, histopathological investigation of such nodules is mandatory.

Since granulomatous vasculitic changes reflect persistant activity, histopathological investigations can give additional information about the disease activity of TA. Such changes may be the reason for more intense systemic therapy, especially if combined with necrotizing lesions. All skin lesions in TA should therefore be carefully investigated. On the other hand all erythema nodosum-like lesions and necrotizing skin lesions of unknown origin should lead to the inclusion of TA into the list of differential diagnoses, especially if associated with the histological finding of granulomatous vasculitic changes.

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