Cutaneous Manifestations of Takayasu Arteritis

Sir,
Takayasu arteritis (TA) is an uncommon chronic 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, atrophias or hyperpigmentation (4). The following skin diseases were considered to be specifically associated with the vascular inflammatory process in TA: erythema nodosum, erythema induratum, tuberculoïd-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 hypertonous 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 Wassermann-manoeuvre of the left arm was positive (pathological result).

Selected normal laboratory findings showed an elevated white blood count (11,700/ul) 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 cytoplasmic antibodies and rheumatoids. Negative serology was found with Borrelia burgdorferi, Chlamydia, Yersinia or Campylobacteri antibodies.

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 leuкоkocytes. 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. Pernicaro 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 nodule 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...
Bullous Pemphigoid and Diabetes Mellitus

Sir,

Bullous pemphigoid (BP) is an immunobullous disorder mainly affecting subjects over 60, and its association with other diseases is controversial for the already critical high incidence of pathologies such as diabetes, neoplasms, cardiopathies, etc., in this age range.

We have studied the possible association between BP and diabetes mellitus in a retrospective case-controlled study.

Sixty-six patients over 60 years of age (mean age 79, range 60–95, 27 men and 39 women) with BP who attended our Institute between 1985 and 1993 were investigated. The diagnosis in all patients had been confirmed by histological examination and direct and/or indirect immunofluorescence test. Each patient was age- and sex-matched with 2 controls recruited from subjects hospitalized in the same period with a diagnosis of contact dermatitis or urticaria. Controls were the first ones whose names appeared in the hospital record books within 3 months before or after the name of each of the BP patients. Controls receiving steroid therapy were excluded from the study.

Diabetes mellitus was assessed through positive past medical history and/or fasting plasma glucose value > 140 mg/dl conducted before steroid treatment.

As reported in Table I, 21 patients (32%) with BP had an associated diabetes mellitus compared to 12 of the control subjects (9%). This difference was statistically significant (p < 0.001 with Yates’ correction).

The prevalence of diabetes in our patients was also relevant when compared to a large population-based survey of known diabetes mellitus in our town of Verona (1), which found 9% diabetes in 48,580 subjects over 60 (9% in men, 8.5% in women).

There are few reports of BP and diabetes mellitus association with different results.

Table I. Subjects with diabetes mellitus (DM) compared as to age and sex

<table>
<thead>
<tr>
<th>Age</th>
<th>Male DM</th>
<th>Female DM</th>
<th>Male Controls</th>
<th>Female Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>60–69</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>70–79</td>
<td>4</td>
<td>9</td>
<td>2</td>
<td>4</td>
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<tr>
<td>&gt;80</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>7</td>
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<tr>
<td>Total</td>
<td>11</td>
<td>27</td>
<td>5</td>
<td>7</td>
</tr>
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</table>

Downham & Chapel found an adult-onset diabetes mellitus in 14 of 34 (41%) patients (2).

Chuang et al., in a case-controlled study, found an increased frequency of diabetes in their series of 30 patients with 20% diabetes in BP compared to 2% of controls (3).

On the contrary, Taylor et al. did not find a difference for the frequency of diabetes in a series of 108 patients with BP when compared with controls (4).

Further statistical and clinical studies are then required to evaluate whether this association could share a pathogenetic mechanism.

REFERENCES


2. Savory WS. Case of a young woman in whom the main arteries of both upper extremities and of the left side of the neck were throughout completely obliterated. Med Clin Trans London 1856; 39: 205–219.

