

Takayasu's arteritis overlapping with systemic sclerosis

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ABSTRACT

We describe an unusual case of overlap between Takayasu's arteritis (TA) and systemic sclerosis (SSc). TA has been found in association with several diseases, but not with SSc. To our knowledge this is the first case report of TA associated with SSc in the literature. It is possible that the expression of the two diseases in our patient was influenced by the presence of genetic factors predisposing to both TA and SSc.

Introduction

Takayasu's arteritis (TA) is a necrotizing and obliterative segmental panarteritis of unknown etiology involving the aortic arch and its major branches, the thoracic aorta and, less frequently, the pulmonary arteries. Ueno *et al.* (1) classified the disease into four basic types. Type I includes the aortic arch and its branches, type II the thoracic and abdominal aorta without involvement of the aortic arch, type III cases present type I and type II lesions, and type IV shows involvement of the pulmonary arteries (2).

Systemic sclerosis (SSc) is a connective tissue disorder of unknown cause and uncertain pathogenesis characterized by vasculopathy, abnormally increased deposition of collagen and extracellular matrix proteins in the skin and internal organs, and immunologic abnormalities. TA is a rare pathology occasionally associated with other autoimmune diseases

such as systemic lupus erythematosus (3), rheumatoid arthritis (4), seronegative spondylarthritis (5), Crohn's disease (6) and Behçet's syndrome (7). To the best of our knowledge there are no reports so far describing the simultaneous presence of SSc and TA.

We report here the case of a patient who developed SSc 8 years after the diagnosis of TA.

Case report

A 29-year-old woman was referred to our department in May 1997, complaining of Raynaud's phenomenon, arthralgias and small ulcerative lesions on both hands which had started 18 months previously. She had been hospitalized at the General Hospital of Cagliari in 1989 and was discharged with a diagnosis of TA (type II according to Ueno *et al.*). Despite continuous treatment with corticosteroids, after 6 years the patient showed stenosis of the left subclavian artery and marked narrowing of the abdominal aorta in the subrenal tract (Fig. 1). Consequently in 1996 she underwent an aorto-bifemoral bypass graft and a left humeral-subclavian bypass graft, which was subsequently extended to the homolateral radial artery. She was discharged from the hospital on low dose corticosteroid treatment.

At the time of her referral to our department, clinical examination revealed dyschromia and thickening of the skin involving the face, upper anterior chest and, in particular, the upper limbs. The

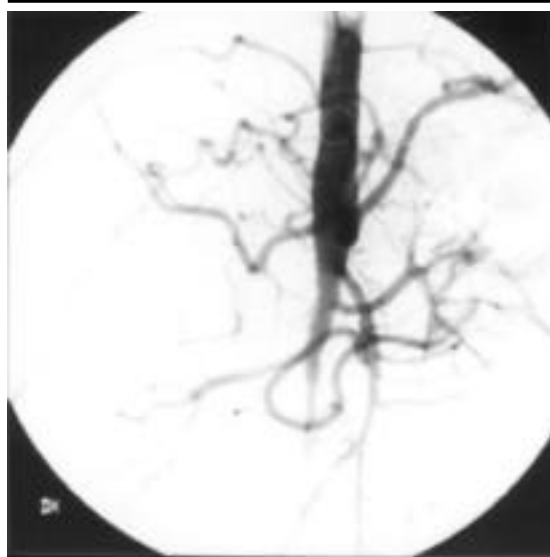


Fig. 1. Arteriography showing narrowing of the abdominal aorta in the subrenal tract.



Fig. 2. Sclerodactyly and dyschromia of the skin.

patient also presented sclerodactyly with small ulcerative lesions on the I, IV and V fingers of the left hand and on the V toe of the right foot (Fig. 2).

Hematochemical tests were positive for antinuclear (titer 1:320; nucleolar pattern) and anti Scl-70 antibodies; low titers of p-ANCA antibodies were also present; the erythrocyte sedimentation rate and C-reactive protein were slightly increased. The HLA serological typing was: HLA-A2,24; Cw4,-; B35-39; DR11-16; DR51-52.

Esophagogastroduodenoscopy showed

hiatal hernia associated with gastroesophageal prolapse and antral gastritis. Nailfold capillary microscopy was compatible with a scleroderma pattern (marked disorganization of the normal capillary architecture, increased inter-capillary loop distances with frequent avascular areas, neoangiogenesis and enlarged loops) (Fig. 3).

Photoplethysmography of the hands and feet revealed alterations indicative of severe obliterative vasculopathy. Colour doppler ultrasonography showed a normal blood flow velocity in the epiaortic

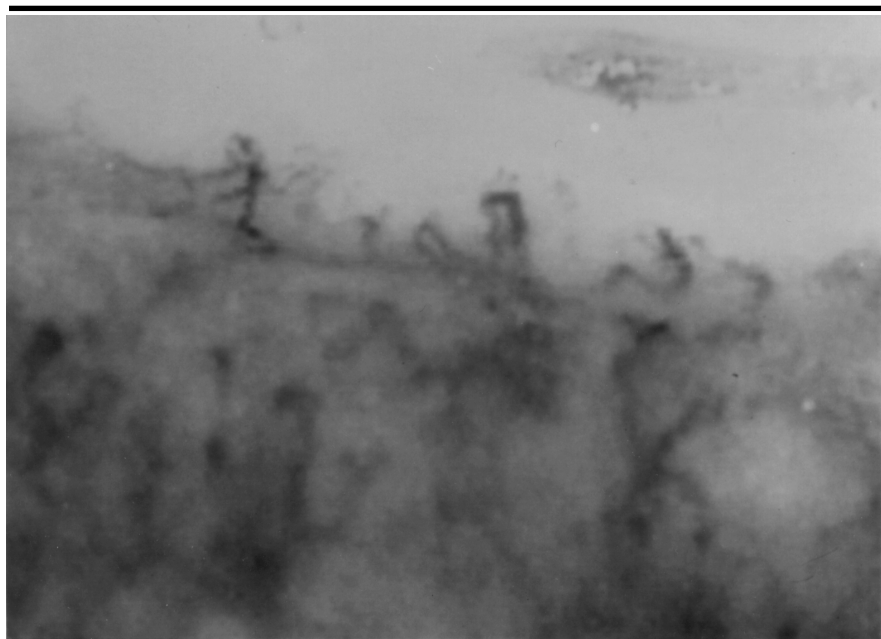


Fig. 3. Nailfold capillary microscopy; note the marked disorganisation of the normal capillary architecture, increased inter-capillary loop distances with frequent avascular areas, neoangiogenesis, and enlarged loops.

and in the upper and lower limb arteries, including the left humeral subclavian bypass. Only a slight stenosis of the post-anastomotic tract of the humeral artery with a considerable reduction of the downstream flow velocity was detected; the aorto-bifemoral bypass was open with a post-stenotic flow in the lower limb vessels.

Chest x-rays, echocardiography, pulmonary function tests including CO transfer, and sequential renal scintiscans were all normal.

Hence, the patient met the American College of Rheumatology (ACR) criteria for the classification of both SSc, with diffuse cutaneous scleroderma, and TA (8, 9) and was discharged from the hospital on a treatment schedule with cyclosporine A (3 mg/Kg/day) and prednisolone (10 mg/day).

Discussion

TA was first described by Takayasu in 1905 during the annual Conference of the Japanese Society of Ophthalmology and was for many years considered to be a disease confined to Eastern countries. It has since been demonstrated that this vasculitis is also present in Europe and America, although with a lower incidence (1 to 2 cases per 1,000,000 inhabitants/years). The etiopathogenesis of the disease remains unclear. Some authors have suggested an infective etiology based on the detection of an increased immune response to *Mycobacterium tuberculosis* and the correlated heat shock protein 65 Kd (10). However, the pathology of TA seems to be immune-mediated. A possible role of cell-mediated immunity is supported by the presence of natural killer and cytotoxic cells and the increased expression of intercellular adhesion molecule-1 in the aortic walls of TA patients.

The importance of changes in humoral immunity is still uncertain despite the detection of anticardiolipin, antiendothelium and antiaortic wall antibodies. The prevalence of ANCA in TA is low and in some series was not even detected (11); therefore the pathogenetic role of these antibodies remains unclear (12). TA has been found to be associated with class I and class II HLA antigens in Japanese (HLA-B3902, B5201, DRB1*

1502, DPB1*0901) (13) and in Indians (B5) (14).

Another characteristic of TA is its extravascular manifestations. Several reports describe skin lesions such as erythema nodosum, malar rash or erythema induratum; however, there are no reports describing scleroderma-like lesions (15). The involvement of the large arteries in systemic sclerosis is very rare. In the literature there is only one case of SSc presenting panaortitis and aortic valvulitis (16), but this case did not fulfill the criteria for the diagnosis of TA.

In our patient the diagnosis of TA, formulated in 1989, was based on arteriography and clinical parameters and approximately 8 years later she also met the ACR criteria for the diagnosis of SSc (8). Our patient had the DR5 (DR11) and DR52 and B39 HLA antigens, which have been shown to be associated with SSc (17, 18) and TA (19), respectively. The HLA B39 antigen is rare in the Sardinian population, suggesting the association of B39 with TA also in Caucasoid populations.

TA has been found in association with several connective tissue disorders and other autoimmune disease, but not with SSc. To our knowledge this is the first report of TA overlapping with SSc. It is possible that the development of the two diseases in our patient was influenced by

the presence of a genetic background predisposing to both TA and SSc.

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