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CORRESPONDENCE

A case of widespread unilateral subcutaneous sarcoidosis with ocular and pulmonary involvements with seropositivity for anti-double strand-DNA antibody and rheumatoid factor: A revisit of gap between humoral autoimmune abnormalities and clinical findings

Subcutaneous sarcoidosis is a rare clinical variant of the disease (1%–6% of all sarcoidosis),[1] characterized by predominant involvement in the fat and/or underlying fascia of the skin. The pathogenesis is considered not only to harbor a cellular immune response to certain antigen(s),[2,3] but also postulate an increased incidence of various autoimmune diseases.[4] This report presents a female case of subcutaneous sarcoidosis on the unilateral limb with pulmonary and eye involvements, who was seropositive for anti-double strand(ds) DNA antibody and rheumatoid factor (RF), updating the pathogenic significance of humoral autoimmune background in the disease.

A 64-year-old Japanese woman presented a 6-month history of asymptomatic, board-like subcutaneous induration and nodules distributed broadly on the extensor aspect of the right extremities (Figure 1A,B) and right buttock. She had otherwise no systemic symptoms. Laboratory test showed elevated levels of angiotensin I-converting enzyme (51.1 IU/L, normal 7.7–29.4 ng/ml) and sIL-2 receptor (728 U/ml, normal 122–496 U/ml). Serum antinuclear antibody was less than 1:40 titer, and autoantibodies to topoisomerase I, centromere, RNA polymerase III, ribonuclear protein, ss-DNA, Smith, SS-A/SS-B, and CCP were all negative,

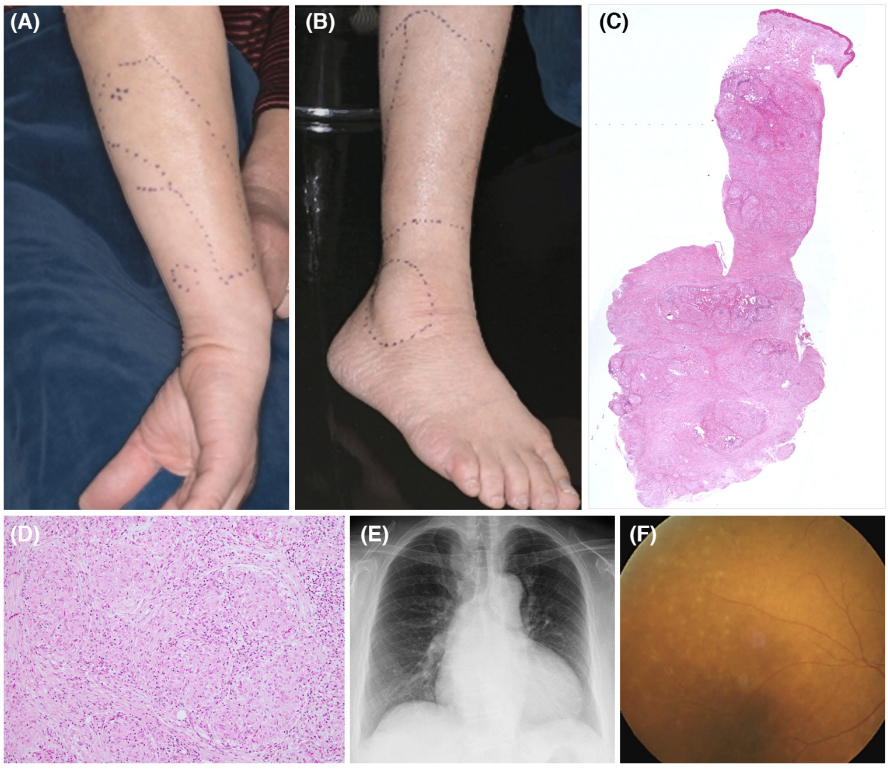

FIGURE 1 Clinical and histological presentation. (A) Clinical appearance of broad board-like induration and subcutaneous nodules on the right forearm and (B) lower leg. *Dotted lines* indicate the location of the skin lesions. (C) Histopathology showing granulomatous infiltration distributing broadly from the lower dermis to the subcutaneous tissue (HE, ×2) and (D) non-caseating granulomatous lesion (HE, ×200). (E) Radiographic finding revealing typical BHL. (F) Ophthalmologic finding revealing posterior uveitis with multiple chorioretinal lesions

except for elevated anti-dsDNA antibody (23.7 U/ml, normal 0–12.0 U/ml) and RF (73.9 IU/ml, normal <15 IU/ml), albeit without clinical features suggestive of SLE or RA. Skin pathology showed multiple, round epithelioid granulomas with faint lymphocytic infiltration, localized exclusively to the subcutis (Figure 1C,D). She had a negative tuberculin skin test but exhibited bilateral hilar lymphadenopathy (BHL) on gallium scintigraphy (Figure 1E). Ocular examination revealed posterior uveitis with multiple iris and trabecular nodules, and chorioretinal lesions (Figure 1F). We finally diagnosed as subcutaneous sarcoidosis with ocular and pulmonary involvements. Because of normal visual performance and lack of pulmonary symptoms, corticosteroid eye-drops were only administrated. During 3 years of follow-up, the oculocutaneous lesions had gradually improved with persisted seropositivity of anti-dsDNA antibody and RF.

It remains unclear whether the presence of serum autoantibodies is pathogenic significance in the specific variant of cutaneous sarcoidosis or an epiphenomenon co-occurring within aberrant immunological basis. Retrospective studies have revealed increased incidence of hypergammaglobulinemia (<41.3%),[5] and seropositivity of anti-nuclear antibody (1.3%–32.0%),[6,7] anti-dsDNA antibody (~6%),[6,8] and RF (7.4%–16.7%)[8,9] in the overall sarcoidosis. However, these serological parameters are unrelated to the skin phenotype and the development of corresponding collagen diseases, as well as serum ACE and soluble IL-2 receptor levels,[5] but tend to be detectable at higher age.[6,9] Besides, higher immunoglobulin levels were significantly found in patients with corticosteroid-resistant sarcoidosis and/or disease relapse, implicating a possible biomarker for the disease activity.[5]

A growing evidence has emerged the aberrant B-cell function in sarcoidosis (e.g., predominance of naïve/activated B-cell subsets and decrease in memory B cells).[4] This was strengthened by the favorable clinical efficacy of anti-CD20 therapy (rituximab) in the disease affecting various organs. Combing a database review that part of patients with subcutaneous sarcoidosis (6/21 cases, 28.6%) have later or preceded history of various autoimmune diseases,[10] the subcutaneous disease may represent the clinical variant associated with autoimmune predisposition. Immunological screening in subcutaneous sarcoidosis is required for unraveling of complicated humoral autoimmunity in the disease-modulating pathology.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DECLARATION SECTION

Approval of the research protocol: N/A.

Informed Consent: The patient diagnosed at Fukui University Hospital with written informed consent.

Registry and the Registration No.: N/A.

Animal Studies: N/A.

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