An Unusual Form of Lupus Erythematosus Profundus Associated with Antiphospholipid Syndrome: Report of Two Cases

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Lupus erythematosus profundus (LEP) is a rare clinical feature of cutaneous lupus erythematosus (CLE), characterized by multiple hard subcutaneous induration with panniculitis as the main clinical manifestations of the disease. We describe here two cases of LEP with solitary hard induration extending over a wide area of the back. Both cases showed fibrin thrombosis of the subcutaneous vessels and positive test results for anti-phospholipid antibody. Based on these findings, we thought that the thrombosis associated with antiphospholipid syndrome (APS) was responsible for the peculiar clinical findings in our cases.

CASE REPORTS

Case 1
A 22-year-old Japanese woman was referred to our hospital with a 5-month history of a subcutaneous induration in the left lumbar region, associated with mild pain. At the time of the first consultation, dark-red erythema with a subcutaneous hard induration measuring approximately 16 × 8 cm in size was observed in the left lumbar region (Fig. 1A). She also had polyarthritis. Biopsy specimens obtained from the induration in the lumbar region revealed lobular panniculitis with infiltration by lymphoid cells and plasma cells, thickening of the septa, and multiple prominent lymphoid follicular indurations extending from the deeper layers of the dermis to the subcutaneous tissue (Fig. 1B). Fibrin thrombi were evident in the intra-lobular vessels. A diagnosis of LEP was made based on these findings.

There were skin indurations measuring approximately 4 mm in size on the right middle finger only one week after the first consultation. Biopsy of the finger indurations revealed thrombosis of the dermal vessels. Since thrombi were found in both skin lesions, we conducted specific tests for antiphospholipid antibody (e.g. lupus anticoagulant, anti-cardiolipin beta-2 glycoprotein I antibodies), and the results revealed seropositivity for lupus anticoagulant (1.39 ratio (normal: within 1.3)) while the cardiolipin test for syphilis was negative and the activated partial thromboplastin time (APTT) was not prolonged. There was no evidence of thrombosis of the internal organs. Laboratory investigation revealed leucopenia (3,400/μl), positive test results for ANA (1:320 homogenous, speckled pattern), anti-U1 RNP antibody, anti-Sm antibody, anti-SS-A antibody, and double-stranded DNA IgG antibody (35 IU/ml; normal <12). Serum complement levels were slightly low in C3 (CH50 28.0 U/ml (normal 25.0–45.0), C4 74 mg/dl (normal 76–160), C1 14 mg/dl (normal 14–44)). Based on the findings, the diagnosis of LEP associated with systemic lupus erythematosus (SLE) and APS was made. The patient was started on combined therapy with oral prednisolone 30 mg/day and aspirin 100 mg/day. The indurations at both sites began to disappear gradually following the initiation of this treatment.

Case 2
A 59-year-old Japanese woman was referred to our hospital with a 4-month history of a large subcutaneous induration in the left lumbar region. She showed positive test results for antinuclear antibody and anti-double-stranded DNA antibody. She did not fulfill the diagnostic criteria of the American College of Rheumatism (ACR) for SLE. The patient had a large hard induration, measuring approximately 40 × 16 cm in size, with dark-red erythema extending from the lumbar to the hip region, associated with mild pressure pain (Fig. 2A). Biopsy of the induration in the lumbar region revealed lobular panniculitis with hyaline necrosis, thickening of the wall of the septa, and marked lymphocytic cell plus plasma cell infiltration (Fig. 2B). Thrombosis of the veins in the subcutaneous fat tissue was seen, as in Case 1. From these findings, the skin induration was diagnosed as LEP.

Laboratory findings demonstrated positive test results for ANA (1:80 homogenous, speckled pattern) and anti-double-stranded DNA IgG (59; normal <12), but negative results for...
anti-sm antibody and anti-U1 RNP antibody. Serum levels of complements were within normal limits (CH50 38.5 U/ml (29.0–48.0), C3 118 mg/dl (65–135), C4 20 mg/dl (13–35)). Since the patient had no systemic symptoms, she did not fulfill the ACR diagnostic criteria for SLE. Based on the findings on histopathological examination and the prolonged aPtt (46 s (25.0–36.0)), we conducted tests for antiphospholipid antibody, and positive results were obtained for lupus anti-coagulant (1.42 ratio (normal; within 1.3)), and anti-cardiolipin beta-2 glycoprotein I antibody (5.5 U/ml (normal < 3.5 U/ml)).

The patient was diagnosed as having LEP associated with APS. The standard first-line therapy for CLE is hydroxychloroquine (HCQ); however, because HCQ is still not approved in Japan, she was initiated on oral treatment with prednisolone 30 mg/day and aspirin, 100 mg/day. The subcutaneous induration gradually decreased in size, but did not disappear entirely; she was continued on treatment with prednisolone, 20 mg/day.

DISCUSSION

LEP is a rare condition of CLE and the main target of this disease is the subcutaneous tissue. The lesion in Case 1 was associated with SLE, while Case 2 did not fulfill the ACR diagnostic criteria for SLE. According to a population-based cohort of CLE (1), 18.1% of CLE patients were diagnosed with SLE during a 3-year observation period. Therefore, we need to observe Case 2 carefully for the onset of SLE.

Both of the cases reported here presented with a large hard subcutaneous induration in the lumbar region. Histologically, fibrin thrombosis was seen in the lobular lesion of subcutaneous fat, and both cases showed evidence of APS. There have been no reports to date about the relationship between LEP and APS.

The most common sites of occurrence of LEP are the face and upper arms (2, 3), and onset in the lumbar region is relatively rare. Each eruption of LEP usually measures 1 to several cm. Development of a subcutaneous induration over an extensive body region, such as in the cases reported here, is rather rare.

Blood tests for lupus anticoagulant were positive in both of our cases. We recognized no other risk factors (e.g. hormonal therapy) for thrombosis. We could not find livedo reticularis or skin ulcers (4), such as the common skin manifestations of APS. Furthermore, no evidence of thrombosis in any other organs was found in either of the 2 cases. Although fibrin thrombosis has been reported to occur in approximately 10% of lesion in LEP (5), we detected thrombosis not only in the lesions in the lumbar region, but also in the induration in the right middle finger in Case 1. These findings suggest that the thromboses in our cases were correlated not only with LEP, but also with APS, which was confirmed by its correlation with the disease activity of APS in Case 1. Since Case 2 also showed thrombosis and peculiar clinical feature similar to Case 1, we thought that APS may have played an important role in the pathogenesis of LEP in our 2 cases.

The authors declare no conflicts of interest.

REFERENCES