Leg Ulcers Associated with Positive Lupus Anticoagulant in Two Cases of Klinefelter’s Syndrome

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Klinefelter’s syndrome (KS) is caused by the presence of an extra X-chromosome. Leg ulcers occur in 6–13% of patients with KS (1). The occurrence of leg ulcers is related to a variety of factors, including chronic venous insufficiency (2), platelet hyperaggregability (3, 4) and elevated levels of plasminogen activator inhibitor-1 (PAI-1) (5, 6). We report here 2 KS patients with positive lupus anticoagulant who had leg ulcers, suggesting that immunological abnormalities may be associated with the development of leg ulcers in KS.

CASE REPORTS

Case 1. A 56-year-old Japanese man visited our hospital with painful ulcers on both legs. He had been treated with oral prednisolone at a dose of 5 mg/day for rheumatoid arthritis for the past 24 years. Necrotic ulcers were found in the malleolar and pretibial regions of both legs, along with dense brown pigmentation (Fig. 1a). Laboratory studies revealed a red blood cell count of 3.49 × 10⁶/µl, white blood cell count of 7.07 × 10⁹/µl and platelet count of 2.44 × 10¹²/µl. There were no abnormalities in the prothrombin time, partial thromboplastin time or plasminogen level. Spontaneous aggregation of platelets was not observed, and the PAI-1 activity was normal. There were no abnormalities in coagulation/fibrinolysis pathways, such as high levels of PAI-1 activity (5, 6) and platelet hyperaggregability (3, 4), have been implicated as causes of ulcer formation. In particular, increased PAI-1 activity is a likely pathogenic factor of leg ulcers in KS, because testosterone was reported not only to improve the leg ulcers, but also to normalize PAI-1 activity in KS (7). This effect of testosterone is consistent with the inverse relationship between testosterone and PAI-1 activity (8).

However, our two cases showed normal PAI-1 activity. Instead, positive lupus anticoagulant associated with autoimmune diseases (rheumatoid arthritis and SLE) suggests that immunological abnormalities are probably related to the development of the leg ulcers in these cases. Igawa & Nishioka (9) also reported a case of leg ulcer in KS syndrome that showed immunological abnormalities, such as the presence of antiphospholipid

Fig. 1. (a) A large necrotic ulcer on the left lower leg of case 1. (b) Healed leg ulcer after therapy.
antibodies. Testosterone administration improved the leg ulcer in their case, similar to our case 1. KS is occasionally associated with autoimmune diseases, such as SLE and Sjögren’s syndrome (10), and these autoimmune diseases were also improved by testosterone administration (11). Therefore, the formation of the leg ulcers in KS is attributed not only to the abnormalities of PAI-1 activity and platelet hyperaggregability, but also to immunological defects due to androgen deficiency.

The authors declare no conflicts of interest.

REFERENCES