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Rheumatoid arthritis and prednisone-induced scurvy

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A MASSIVE gastrointestinal haemorrhage occurred as a complication of scurvy which developed 8 days after prednisone therapy for rheumatoid arthritis. A dramatic response to vitamin C was seen.

Case report

A 43-year-old female was admitted to hospital on 15 July 1969 with an exacerbation of joint pains of rheumatoid arthritis from which she had been suffering for 8 years. For 3 months prior to admission she was bedridden and anorectic and had been treated at home with betamethazone 0.5 mg b.d. and indomethacin 25 mg t.i.d.

On admission her Hb was 10.0 g/100 ml, WBC 9000/mm³, neutrophils 60%, lymphocytes 39%, monocytes 1%. A latex fixation test was strongly positive. LE cell tests were negative on three occasions. Serum iron was 71 µg/100 ml. She had a smooth thyroid swelling but her PBI was 7.5 µg/100 ml and T₄, 7.7 µg/100 ml. During her stay in hospital prednisone 10 mg t.i.d. was substituted for betamethazone with improvement in her joint symptoms but 8 days later she complained of bleeding gums, a subconjunctival haemorrhage in the left eye and haemorrhagic skin lesions. These were petechiae and ecchymoses of varying sizes, predominantly on the limbs. She had a positive Rumpel-Leede test with over twenty petechial lesions in a 2-cm circle. On 12 August she began to pass frequent melaena stools and her Hb fell to 6.9 g/100 ml. An emergency barium meal was normal. Her clotting time was 5

min 8 sec; bleeding time 4 min 44 sec; prothrombin time 14 sec (control 13 sec); platelet count 138,000. She continued to bleed profusely per rectum and was transfused with 9 pints of blood over 5 days. By 17 August the swelling of the gums were most marked on the interdental papillae as seen in scurvy—the so-called scurvy buds (Fig. 1). Prednisone was then immediately stopped and vitamin C 500 mg was given intramuscularly followed by 500 mg on the next day. There was then a prompt cessation of bleeding and the swollen haemorrhagic gums began to subside rapidly. No new crops of

FIG. 1. Swollen, congested, bleeding gums.

ecchymoses appeared and those present began to fade. Vitamin C therapy was continued and she was discharged from hospital a couple of weeks later on Betnelan. X-rays of the ulna, radius, and humerus taken 2 weeks after discharge from hospital showed subperiosteal ballooning and calcification of previous subperiosteal haemorrhages (Fig. 2).

Comment

Haemorrhagic skin lesions are well known complications of steroid therapy. With cortisone, corticotrophin, or hydrocortisone, the incidence of these findings was 2–5% but with prednisone and prednisolone it was considerably higher varying from 18 to 34% (Boland, 1956). Dordick, Sussman & Bernstein (1958) observed this phenomenon in seven of thirty patients (23.3%) given prednisone or prednisolone. All were women in or past the menopause and six were suffering from rheumatoid arthritis. These lesions cleared completely when the dosage of steroid was lowered or terminated or when ascorbic acid (100 mg twice daily) was concomitantly used. Denko & Shroeder (1957) also reported that 20% of a group of seventy-five patients receiving prednisone for a variety of rheumatological disorders developed ecchymotic skin lesions which cleared completely with treatment with ascorbic acid. The alteration in capillary function produced by these steroids, especially prednisone and prednisolone, is difficult to explain. Obviously, some metabolic derangement involving ascorbic acid occurs since

FIG. 2. Subperiosteal calcification of previous haemorrhages.

ascorbic acid resolves the haemorrhagic phenomena. The concentration of ascorbic acid in the adrenal gland has been found to be higher than in any other tissue (Sayers, Sayers & Woodbury, 1948) and it has been shown that following ACTH in the rat and guinea-pig there is a depletion of the adrenal ascorbic acid (Sayers *et al.*, 1949). In addition, observations of increased urinary excretion of ascorbic acid following ACTH have been made by Beck, Browne & McKenzie (1954).

It is interesting that most case reports of haemorrhagic skin manifestations following steroid therapy have been in patients with rheumatoid arthritis. These have occurred as early as 7 days after prednisone therapy (Dordick *et al.*, 1958). Abrams & Sandson (1964) determined the ascorbic acid levels in serum and synovial fluid on patients with rheumatoid arthritis and it was noted that in almost all cases the levels of ascorbic acid were low when compared with normal values. Similar low levels were reported 33 years ago in the serum of patients with rheumatoid arthritis by Rinehart *et al.* (1938) and so there seems to be a fundamental fault in vitamin C metabolism in rheumatoid arthritis. Ascorbic acid is also said to be catabolized excessively in rheumatoid arthritis but frank scurvy has not been reported as a direct complication. However, it appears that in patients with a borderline vitamin C deficiency the addition of prednisone might well precipitate frank scurvy for in the assessment of the nutritional status of this patient for the 6 months prior to her haemorrhagic symptoms it was calculated that her daily intake of vitamin C had been 30 mg which is the minimum acceptable daily allowance for adults recommended by nutritionists (Pearson, 1962).

This case is also unique in that scurvy in the adult has not been seen in this tropical island of Trinidad for many a year. It is known that gastrointestinal haemorrhage may rarely occur in severe scurvy and the subconjunctival haemorrhage, ecchymotic skin lesions, X-ray changes and, above all, the characteristic gum lesions together with the dramatic response to vitamin C all point to the existence of a scorbutic state in this patient. Moreover, the presence of a positive tourniquet test with a normal platelet count is presumptive evidence of a disturbance of normal capillary function or a deficiency of intercellular cement substance as is found in scurvy.

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