ZINC IN THE TREATMENT OF CHRONIC LEG ULCERS OF SYSTEMIC LUPUS ERYTHEMATOSUS

F Wang
B A Adam

Department of Medicine
Faculty of Medicine
University of Malaya
Kuala Lumpur 22-11
Malaysia

F Wang, MBBS, FACP
Professor

B A Adam, MBBS, MRCPE
Associate Professor

SYNOPSIS

Two patients with systemic lupus erythematosus (SLE) had chronic leg ulcers for 4 years and 3 years respectively. All conventional modalities of treatment failed till oral zinc sulphate was used.

INTRODUCTION

Chronic ulcers on the anterior surface of the leg are well known complications of diseases such as hemolytic anaemia, Crohn's disease, ulcerative colitis and rheumatoid arthritis. The ulcers that are usually seen in SLE are acute and they heal as the activity of the disease subsides (1). Chronic ulcers of the leg in SLE, which to our knowledge, has yet to be reported in literature, was seen in two patients and they were resistant to all known modalities of ulcer therapy till zinc sulphate was given.

CASE REPORT

Case 1

A 27 year old Chinese female was admitted to the hospital with arthralgia of the knees and the proximal interphalangeal joints for four years, weight loss and malar rash for six months and non traumatic enlarging ulcer of the legs for six weeks. Physical examination showed low grade fever, anaemia, erythematous rash on the cheeks. There was no evidence of either active arthritis or joint deformity. Each leg showed a clean shallow ulcer above the lateral malleolus, about 4 cm by 5 cm. There was no varicose veins. Investigations: Hb 8.5 Gm%, WBC 4,500 per cmm, Platelets 19,000 per cmm, ANF 1:64 dilution, C_3 40 mg% (normal 66-130 mg/dl) and C_4 47 mg% (normal 20-60 mg/dl). A swab of the ulcer grew no organism. She was diagnosed as SLE and was treated with prednisolone with eusol dressings for the ulcers.

Though both the clinical and serological activity of SLE subsided, the ulcer persisted inspite of enforced bed rest. The ulcers extended peripherally and in depth revealing the ligaments around the ankle joints with restriction of joint movement. The ulcer persisted for about four years and then she was given 750 Gm of zinc sulphate daily in divided doses. After two weeks of therapy, the ulcers showed signs of healing. At the end of two months the ulcer on the right leg healed with scars and hyperpigmentation while the ulcer on the left side shrank to one fourth of its original size (Fig. 1). The patient then failed to turn up for further observation.

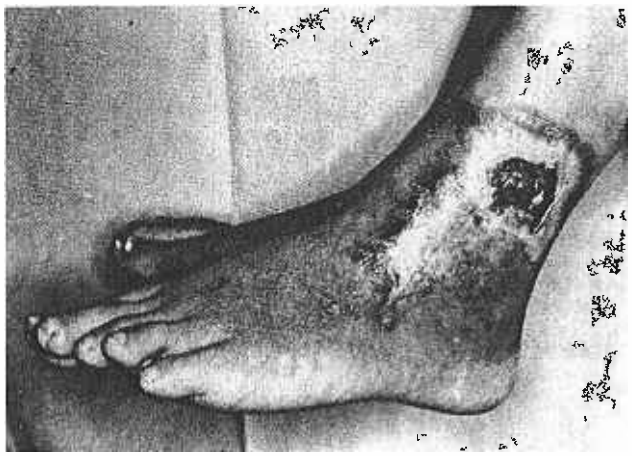

Figure 1 Patient 1. Left leg ulcer – one fourth the original size after 8 weeks treatment.

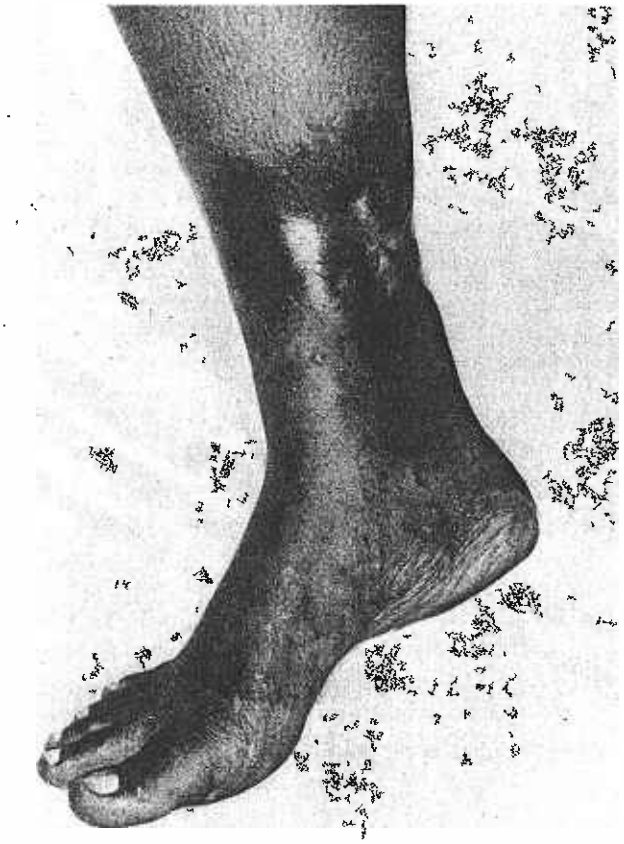

Figure 2 Patient 2. 3-year ulcer right leg healed after 8 weeks oral zinc therapy.

Case 2

A 32 year old Malay female complained of arthralgia for 3 years, scalp hair loss, ulcers in the mouth and weight loss (15 kg.) for six months. Few weeks before admission, she developed pain over the medial malleolus on both legs followed by an ulcer which gradually grew in size. Physical examination showed anaemia, diffuse scalp hair loss, superficial ulcer on the hard palate, and arthralgia of the finger joints. Above each medial malleolus there was an ulcer with a clean base, measuring 3 cm by 4 cm. There was no varicose veins. Investigations: Hb 9.4 Gm%, WBC 3000 per cmm, L.E. Cells present, C_3 85 mg%, C_4 14 mg%. She was diagnosed as SLE. Besides prednisolone therapy, her ulcers were treated with wet dressings and bed rest. As the ulcer did not heal for two years, they were closed with skin graft. A month later, the ulcer on the right leg recurred at the site of the graft and continued to enlarge to a size of 6 cm. by 9 cm. During the next two years though the activity of SLE had few remissions, the ulcer remained indolent with no sign of healing. As the first patient responded to zinc therapy, this patient was given a similar dose of the zinc sulphate. The ulcer healed at the end of 8 weeks of therapy. In a follow up 15 months later, the ulcer has remained healed (Fig. 2).

DISCUSSION

Both patients fulfil the ARA criteria for SLE (2). Since the ulcers developed spontaneously and there was no other systemic or regional predisposing factor, such as varicose veins, it is concluded that these patients' ulcers are part of the many manifestations of SLE. Vasculitis resulting in ischaemic ulcerations of the overlying skin was probably the initial process in the formation of ulcer and one of our patients did have ischaemic pain at the site of ulceration. Physical forces that may operate near a joint may be one of the factors responsible for the persistence of the ulcer.

Myers and Cheng (3) reported that patients deficient in zinc had poor wound healing and Halbrook and Lanner (4) found that zinc deficiency delayed the rate of healing of venous leg ulcers with the restoration to normal healing rate following zinc therapy. Though serum zinc levels were not measured in both patients, significant weight loss probably resulted from deficient intake of food leading to sub-optimal levels of nutrients including zinc. Dramatic healing of the ulcers in our patients following zinc therapy further supports the assumption that they were deficient in zinc. The process that leads to wound healing following zinc therapy in zinc deficient patients, is not clear, though it has been shown in the skin of zinc deficient animals that decreased protein, collagen and deoxyribonucleic acid synthesis occurs (5, 6, 7).

Allen et al (8) suggested that in man reversible T lymphocyte dysfunction could be induced by zinc deficiency. Thus it is tempting to suggest that zinc corrected the T cell dysfunction that is known to exist in SLE and thus contributed to the healing of ulcers. However it must be noted that the ulcer persisted inspite of clinical and serological remission of SLE. Therefore it was probably the disturbed zinc-dependent wound healing function rather than the immuno-

logical function that was repsonsible for the persistence of the ulcer.

ACKNOWLEDGEMENT

We thank Puan Rohani for clerical assistance.

REFERENCES

1. Dubois E L: Lupus erythematosus, 2nd Ed. 255, 411, University of Southern California, 1974.
2. Cohen A S, Reynolds W E, Franklin E C et al: Preliminary criteria for the classification of systemic lupus erythematosus. Bulletin of the Rheumatic Diseases 1971; 21: 643-8.
3. Myers M B and Cheng G: Zinc and the healing of chronic leg ulcers. Am J Surg 1970; 120: 77-81.
4. Hallbrook T and Lanner E: Serum zinc and healing of venous ulcers. Lancet 1972; 2: 780-2.
5. Hsu J M: Decreased in corporation of L-cysteine-^{35}S into skin protein of rats: in newer trace elements in nutrition, 327, Marcel and Dekker, New York, 1971.
6. Hsu J M and Anthony W L: Zinc deficiency and collagen synthesis in rat skin. Trace Substances in Environmental Health 1973; 6: 137-43.
7. Stephen J K and Hsu J M: Effect of zinc deficiency and wounding on DNA synthesis in rat skin. J Nutr 1973; 103: 548-52.
8. Allen J I, Kay N E and McClain C J: Severe zinc deficiency in humans: association with reversible T-lymphocyte dysfunction. Ann Int Med 1981; 95: 154-7.