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Letters to the Editor

USE OF COLCHICINE IN THE MANAGEMENT OF ERYTHEMA NODOSUM LEPROSUM (ENL)

Sir,

Erythema nodosum leprosum (ENL) has classically been thought of as a clinical manifestation of the Arthus phenomenon.[1] Recently, however, this concept has been challenged[2, 3] and many immunological differences have been noted in patients with ENL compared to those without ENL.[4–7] The understanding of the pathogenesis of this complication will, it is hoped, allow the formulation of a rational management of ENL.

Since 1965, the superiority of thalidomide in the treatment of ENL has been well documented.[8–11] Due to teratogenicity, however, this drug is not easily available. Clofazimine (lamprene) has also been shown to be useful, especially in patients with chronic or recurrent ENL attacks.[12–14] Other drugs, including steroids, have also been used with varying efficacy in the management of ENL. The exact mechanisms by which these drugs produce their effects are not known.

Recently it has been shown that colchicine is able to suppress the Arthus reaction in rabbits despite deposition of immune complexes.[15] This effect was thought to be due to suppression of polymorphonuclear leukocyte directional chemotaxis by colchicine. This drug is expected, therefore, to have a beneficial effect in diseases thought to have a pathogenetic mechanism similar to the Arthus phenomenon. Indeed colchicine has been used successfully in the treatment of Behçet's syndrome[16–18] and cutaneous lesions of necrotizing vasculitis.[19] If ENL really is a clinical manifestation of the Arthus phenomenon, then colchicine could be expected to have a beneficial effect. Immunoregulatory disturbances occurring during ENL have been documented[4–7] and one of the outstanding features is a decrease in thymus-dependent lymphocytes (T-cells) carrying a suppressor/cytotoxic phenotype:[4–6] this has been shown to revert to pre-ENL levels after clinical improvement of ENL.[6] It is interesting to note that patients with familial Mediterranean fever (FMF) can develop skin eruptions accompanied by fever, and this has been shown to be associated with a decrease of suppressor T-cells:[20–2] colchicine has been used in this disease to prevent amyloidosis[23–5] as well as the recurrent skin eruptions. Interestingly, colchicine has been shown to be able to restore the T-cell balance[26] and may thus have immunoregulatory effects. If ENL is precipitated by an imbalance of immunoregulatory T-cells,[3–5] colchicine would be expected, therefore, to be of value in its management.

Based on these observations we have treated 10 male adult patients with recurrent or chronic ENL with colchicine, 1·5–2·0 mg daily given in divided doses. All drugs known to affect ENL namely, thalidomide, clofazimine, steroids, chloroquine and analgesics were withdrawn prior to the administration of colchicine. Patients were thus receiving dapsone and colchicine alone during the entire period of the pilot study. All patients were taken into the study when they had clear evidence of ENL and were observed for 3 months. After clinical improvement had been achieved, patients were given a maintenance dose of of 1 mg colchicine daily. Two of the patients have had several attacks of ENL in the past despite concurrent use of clofazimine, steroids and thalidomide.

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Twenty-four hours after initiation of colchicine the fever had gone down in all patients, and in 8 hours ENL lesions had begun to resolve. During this time too, the leukocytosis and raised ESR had been considerably reduced. By the end of the second day most of the lesions had disappeared and no new nodular eruptions had occurred. During the whole follow-up period none of these patients have developed new ENL attacks while using a maintenance dose of colchicine. In one patient colchicine was withdrawn after the patient had improved from the ENL attack. Two days after withdrawal of colchicine, the patient developed fever and a substantial number of ENL nodules on the forearms and thighs. Colchicine was then reinstituted and within 24 hours the lesions had started to disappear and the fever had gone down. We have thus noted a dramatic effect of colchicine in the management of acute ENL attacks. Furthermore, a maintenance dose of 1 mg daily seemed to prevent recurrent ENL attacks. The fact that these lesions started to resolve within 24 hours, and that in one patient withdrawal of colchicine led to eruption of new nodules which were subsequently controlled by colchicine, would indicate that colchicine has a direct beneficial effect in the management of ENL. Colchicine can be used for prolonged periods without major side effects as has been shown in FMF.[23–5, 27] Furthermore, the risks incurred seem to be less than those of using steroids or thalidomide for a prolonged time.

Since this was not a controlled double blind study we cannot draw any hard conclusions. However, we feel that a controlled double blind study to evaluate the use of colchicine in the management of ENL is now warranted.

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