

Intractable Chronic Furunculosis: Prevention of Recurrences with Pentoxifylline

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A 60-year-old HIV-negative man with known noninsulin-dependent diabetes mellitus and glucose 6-phosphate-dehydrogenase deficiency anemia suffered from chronic recurrent furunculosis since the age of 30. In recent years, his condition had become increasingly severe and the recurrences increasingly frequent. Different measures including continuous therapy with large doses of systemic antibiotics for a period of 6 months failed to prevent the recurrences. Oral treatment with pentoxifylline 400 mg t.i.d. was prescribed, and 2 months later the patient experienced a dramatic and complete remission of his furunculosis. Six months later he was still totally free of lesions while continuing to take the same medication. Pentoxifylline may provide a new and effective approach to the previously difficult and often disappointing problem of the management of patients with chronic recurrent furunculosis.

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Pentoxifylline (PTX) is a hemorrheologically active drug which has profound effects on neutrophil function (1). Although PTX has no direct antibacterial activity when tested alone or in combination with antibiotics in vitro (2), it enhances neutrophil killing of *Staphylococcus aureus* (3). This indirect bactericidal activity of PTX probably also involves a direct effect on neutrophil mobilization in vivo (4). PTX has been shown experimentally to ameliorate the effects of bacterial sepsis in different laboratory animals (5-9) and to increase the survival of mice (6), rabbits (7), pigs (7) and dogs (9) in endotoxic shock.

Chronic recurrent cases of furunculosis often present severe therapeutic problems, as further lesions may develop after the end of each course of antibiotics (10) and prevention of recurrences in such cases is difficult and disappointing (10-12). It was therefore considered worthwhile to try to prevent such recurrences in a patient suffering from severe intractable furunculosis by treating him with PTX,

CASE REPORT

A 60-year-old HIV-negative man with known glucose 6-phosphate-dehydrogenase (G6PD) deficiency suffered from chronic recurrent furunculosis since the age of 30. In 1978, when he was 47 years old, a diagnosis of non-insulin-dependent diabetes mellitus (NIDDM) was made and since then his blood sugar had been under good control with glyburide tablets 5 mg/day or/and a sugar-free diet. However, in spite of good control of his sugar levels, he continued to suffer from recurrent bouts of furunculosis which necessitated the frequent administration of large doses of systemic antibiotics. At this stage, the chemotactic capacity of his neutrophils was evaluated using Boyden chambers and the "lower surface counts" method (13) and was found on

two separate occasions to range between 30% and 50% of control values. He was then treated with clofazimine 300 mg per day for about 18 months. During that period a certain decrease in the frequency of the recurrences as well as in the severity of the lesions was observed; however, he continued to have recurrent lesions which warranted treatment with systemic antibiotics from time to time. Eventually, the administration of clofazimine was stopped because of concern about potentially serious side-effect, as a result of which the frequency and the severity of the lesions increased again. In 1984, an attempt was made to treat his condition with oral isotretinoin. Accutane 0.75 mg per kg per day was prescribed, and 2 months later a partial improvement in his condition was observed. However, 6 months after the beginning of isotretinoin, he still had bouts of furunculosis which necessitated the administration of systemic antibiotics from time to time. The dosage of accutane was gradually increased to 1.5 mg/kg/day and 1 month later the patient experienced a complete remission for the first time in many years. Subsequent attempts to reduce the dosage of isotretinoin, however, resulted in a prompt worsening of his condition with reappearance of lesions. In 1989 after about 4 years of accutane therapy, symptoms and signs of bone toxicity as well as a severe hyperlipidemia occurred and the administration of accutane was stopped. After that, he experienced increasingly severe and increasingly frequent occurrences of furuncles on practically every part of his integument as well as apparent lesions of hydradenitis suppurativa in his axillae and perineum. The patient was instructed to keep his fingernails short, to take a daily shower with an antiseptic soap and to apply a bacitracin ointment 3 times daily to his nares; these measures, however, failed to prevent the recurrence of the lesions. Between December 1990 and June 1991 he was continuously treated with large doses of systemic antibiotics; but even while he was receiving these medications he continued to develop severe lesions. Cultures and sensitivity assays of these lesions were performed and in accordance with the results, he was switched to another antibiotic; but this again failed to prevent the recurrence of new lesions. During that period he was treated alternatively with cloxacillin 3.0 gr per day, cephalixin 3.0 gr per day, augmentin 2.0 gr per day and ciprofloxacin 2.0 gr per day. In June 1991, oral pentoxifylline 400 mg t.i.d. after meals was prescribed; at the same time the patient was told not to stop the previous treatment with oral cephalixin 3.0 gr per day. During the next 2 months, new lesions continued to appear on his left cheek, right axilla, lower abdomen and left gluteus; they were treated with incision and drainage. In August 1991, new lesions stopped to appear and in September 1991 he was instructed to stop taking cephalixin while continuing the treatment with pentoxifylline. To date, 6 months later, the patient remains completely free of furunculosis lesions while continuing to take the same medication. No side effects were observed and repeated blood counts and routine blood biochemistry test remain unchanged.

DISCUSSION

Diabetes, anemia and hypoferrremia may predispose a person to furunculosis (10, 12, 14-15). It is not known from the literature whether G6PD-deficiency *per se* can predispose a person to that condition. The patient presented above had had both NIDDM and G6PD deficiency anemia for many years. The coexistence of at least two separate predisposing factors in the same patient may possible explain the extreme severity and intractability of his condition. The chemotactic capacity of

the patient's neutrophils was extremely low. Decreased chemotaxis together with decreased phagocytosis and bacterial activity are known to occur in diabetes (16). Although it is not known whether G6PD deficiency can cause inhibited chemotaxis, this remains a possibility. Two months after the institution of PTX therapy, the patient experienced a dramatic and complete remission of his furunculosis and to date, 6 months later, he is still totally free of lesions. This remarkable outcome is most probably the result of the therapeutic action of PTX, the possibility of an accidental remission being extremely unlikely. In contrast with isotretinoin therapy, which also completely prevented the recurrence of furunculosis in the same patient, PTX is a relatively non-toxic medication with virtually no serious side-effects even after prolonged administration. To the best of our knowledge, this is the first report of successful prevention of recurrences with PTX in a patient with chronic furunculosis.

PTX increases polymorphonuclear cell chemotaxis, motility and random migration in Boyden chambers (3). It also enhances neutrophil killing of *Staphylococcus aureus* in vitro (18). Neonatal mice have been saved from the lethal effects of staphylococcal injections by pretreatment with PTX (17). The endothelial margination and adherence of PMNs in response to microbial products or endotoxins can be blocked by PTX (3, 9, 18), thus having a direct effect on neutrophil mobilization and increasing the number of circulating PMNs in septic conditions (6–9). These effects of PTX on white blood cells occur at micromolar concentrations (19), 3-logs lower than the millimolar concentrations achieved in the serum by the usual therapeutic doses. Thus, it seems reasonable to assume that the impressive therapeutic effect obtained in our patient is probably the result of the action of PTX on the patient's PMNs.

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