

Haemolytic streptococcal gangrene and non-steroidal anti-inflammatory drugs

All patients with necrotising fasciitis seen at this hospital over 10 years were reviewed. Six cases were found in which non-steroidal anti-inflammatory drugs were suspected of having contributed to the infection; these cases are reported below.

Patients, methods, and results

The records of all 31 patients seen at this hospital during 1972-82 with a discharge diagnosis of necrotising fasciitis were reviewed. We considered for analysis only those who fulfilled strict criteria for acute dermal gangrene¹—that is, with a history of rapidly spreading cutaneous infection and evidence of extensive subcutaneous necrosis and oedema but sparing of underlying muscle. To select patients who had not had a predisposing condition we excluded those with postoperative necrotising fasciitis or suprainfection of chronic venous or arterial leg ulcers and those with any debilitating underlying disease that could have affected normal defence mechanisms. Thus six previously healthy patients in whom severe necrotising fasciitis had developed apparently spontaneously or after minor trauma remained for analysis.

A history of recent minor trauma was noted in four of the six patients (table). When the initial symptoms arose non-specific inflammation or superficial phlebitis was diagnosed in all six cases and therapeutic dosages of non-steroidal anti-inflammatory drugs prescribed. Two patients were subsequently given steroids because of continued inflammation. Four patients received more than one anti-inflammatory agent, of whom two received a combination of three drugs including aspirin. Four to 10 days elapsed between the initial symptoms and referral to hospital, when extensive necrotising fasciitis was diagnosed.

In all patients except one (case 1), to whom benzylpenicillin had been given for 24 hours before admission, a Lancefield's group A β -haemolytic streptococcus was recovered from cultures of the blisters or from areas of necrosis; blood cultures in two cases also yielded this organism. Treatment included intravenous administration of aqueous benzylpenicillin in high doses (12-20 MU/day), fluid replacement, and early surgery. One patient (case 5), with necrotising fasciitis extending to the lateral chest wall, died of septic shock within 24 hours after admission despite immediate surgery and aggressive supportive therapy. The five other patients survived after a prolonged stay in hospital that entailed multiple re-explorations of infected areas, excision of necrotic tissue, and eventual skin grafting in four cases.

Comment

Necrotising fasciitis is a potentially fatal infection of soft tissue that usually occurs after trauma or surgery.^{1,2} The group A β -haemolytic streptococcus (*Streptococcus pyogenes*) has long been recognised as an agent of this infection and still accounts for many cases.³ Patients with the infection often have serious underlying diseases, including diabetes mellitus, severe cardiovascular disease, hepatic cirrhosis, and conditions requiring long term treatment with steroids.¹⁻³ No underlying disease was present in our patients, but all had been given non-steroidal anti-inflammatory drugs. The sequence of events suggested that these compounds affected the development or extension of the disease in our patients as no other drugs were given. Activation of latent infections in debilitated patients treated with non-steroidal anti-inflammatory drugs was suspected by Solomon.⁴ In vitro studies support this hypothesis by suggesting that functions

mediated by granulocytes, which are critical in the early stages of host defence against infection, may be impaired by non-steroidal anti-inflammatory drugs. In vitro chemotaxis, phagocytosis, and bactericidal activity of granulocytes are reduced by these drugs. Solberg *et al* observed reduced in vitro killing of *Staphylococcus aureus* and streptococcus group B by granulocytes incubated with phenylbutazone.⁵ Whether these effects occur in vivo in patients given non-steroidal anti-inflammatory drugs remains to be determined.

Our observations suggest that non-steroidal anti-inflammatory drugs should be used cautiously when infection is suspected in a patient with an apparently benign "non-specific" inflammatory lesion of the skin.

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- 2 Ledingham IMcA, Tehrani MA. Diagnosis, clinical course, and treatment of acute dermal gangrene. *Br J Surg* 1975;62:364-72.
- 3 Aitken DR, Mackett T, Smith LL. The changing pattern of hemolytic streptococcal gangrene. *Arch Surg* 1982;117:561-7.
- 4 Solomon L. Activation of latent infection by indomethacin: a report of three cases. *Br Med J* 1966;i:961-2.
- 5 Solberg CO, Allred CD, Hill HR. Influence of phenylbutazone on leucocytes chemiluminescence and function. *Acta Pathol Microbiol Immunol Scand* 1978; 86:165-71.

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Smoking, sugar, and inflammatory bowel disease

Previous studies have suggested that an association exists between smoking habit and both ulcerative colitis^{1,2} and Crohn's disease.³ We reported studies of the diets before illness of patients who developed both types of inflammatory bowel disease^{4,5}: the patients who developed Crohn's disease had a high intake of refined sugar and a low intake of fibre from fruit. We now report the smoking behaviour of these patients and relate it to their dietary habits.

Subjects, methods, and results

We studied 30 consecutive patients with ulcerative colitis and 30 consecutive patients with Crohn's disease. All were interviewed within three months of diagnosis. The two groups of control subjects had recently attended a fracture clinic but were otherwise healthy. They were matched for age (to

Clinical presentation of patients with necrotising fasciitis associated with non-steroidal anti-inflammatory drugs

Case No	Age/sex	Triggering event	Initial diagnosis	Drugs administered	Delay* (days)	Extent of necrotising fasciitis	Culture for group A streptococcus (skin/blood)	Complications	Outcome
1	34/F	Heel graze	Phlebitis	Indomethacin, phenylbutazone	8	Right calf and foot	-/-	Shock	Survived
2	55/F	Unknown	Phlebitis	Diclofenac	6	Left calf and thigh	+/-	Renal failure, thrombocytopenia	Survived
3	47/F	Foot scar	Phlebitis	Indomethacin, oxyphenbutazone	6	Right calf, foot, and thigh	+/+	Renal failure	Survived
4	63/F	Rose thorn scratch	Non-specific inflammation	Indomethacin, aspirin, prednisone 30 mg/day	4	Left arm and forearm	+/+	Shock	Survived
5	70/M	Unknown	Non-specific inflammation	Indomethacin	4	Upper right arm and lateral chest wall	+/-	Shock	Died
6	43/F	Insect bite	Non-specific inflammation	Phenylbutazone, aspirin, oxyphenbutazone, then methylpredisolone	10	Left calf	+/-+		Survived

*Delay from triggering event to overt necrotising fasciitis and referral to hospital.
†*Staphylococcus aureus* also isolated from cultures of skin blisters in this patient.