20 minutes caused considerable vomiting and passage of some flatus and stool.
44 Phentolamine 180 mg intravenously given over 45 minutes again produced vomiting and passage of flatus and stool. Neostigmine 60 mg then 120 mg daily by mouth with prazosin 1.5 mg daily were given and daily spontaneous defaecation was re-established.
62 Prazosin and metoclopramide were withdrawn, but regular defaecation continued.

The improvement was maintained for a further month but she became steadily weaker as the neoplasm extended. Eventually she developed features of cholinergic overdosage (nausea, miosis, salivation, borborygmi and frequent stools) and the dose of neostigmine was reduced. Seven days later she was again distended and constipated and the previous dose of neostigmine failed to correct this problem. Over the following seven weeks she remained distended and a further infusion of phentolamine, with the addition of metoclopramide 40 mg and prazosin 3 mg rising to 12 mg daily, did not ease the problem. Finally she developed severe abdominal pain and a plain radiograph revealed gas under the diaphragm. At laparotomy a perforation was found at the recto-sigmoid junction and a transverse colostomy was performed, but the patient died soon after surgery.

Discussion

The intestine has both a sympathetic innervation which causes reduced motility and sphincter contraction, and a parasympathetic (cholinergic) innervation which has the opposite effects (Mayer 1980). We consider that our patient's constipation was primarily the result of excess circulating sympathomimetic catecholamines, rather than the effects of the opiates and other analgesics she was given for pain. Large doses of the alpha-adrenoceptor blocking agent phentolamine given intravenously temporarily relieved the constipation but caused unpleasant vomiting. Oral adrenoceptor blocking agents were insufficient to relieve the constipation until a cholinergic drug was added. This restored spontaneous defaecation for a period of six weeks, during which time the opiates were prescribed at their previous dose without adverse effect.

We suggest that the combination of a cholinergic drug with alpha-adrenoceptor blocking agents should be considered in the management of other patients with phaeochromocytomas and constipation unresponsive to adrenoceptor blockade alone.

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Acne fulminans with arthritis in identical twins treated with isotretinoin[1]

C R Darley MB MRCP
H L F Currey MMed FRCP
H Baker MD FRCP
Departments of Dermatology and Rheumatology
The London Hospital, London E1 1BB

Acute febrile ulcerative acne (acne fulminans) is rare. An associated arthralgia or arthritis frequently occurs. It has not previously been reported in twins and we here record the simultaneous onset of acne fulminans in 15-year-old twin boys, both of whom developed arthritis. Response to oral 13-cis-retinoic acid was dramatic.

Case reports

Case 1 (MF): This 15-year-old male Spanish twin from Tenerife developed acute severe acne in July 1982. This steadily worsened, reaching a climax in October 1982. He was severely ill, febrile, anorexic and had painful discharging skin lesions. At this point the knees, ankles, wrists and lumbar spine became painful and he was barely able to move about unaided. There was swelling of the ankles, knees and left wrist. By December 1982 both the skin and joints had begun to subside and the systemic symptoms were less marked. On presentation in the UK in March 1983 he still had severe active acne and troublesome arthralgia. He had lost 8 kg in weight. The only medication he had received had been antibiotics which had not been helpful. There had never been early morning stiffness and the urogenital tract, bowels, eyes and mouth had been unaffected throughout the illness.

On examination there was severe nodulocystic acne with ulceration affecting the face, back and

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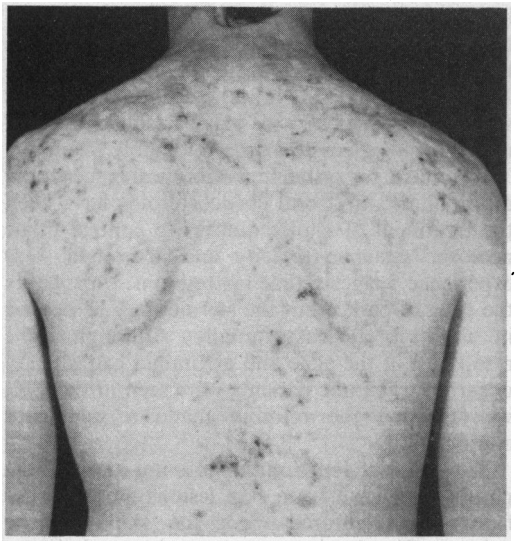

Figure 1. The back of the worst-affected twin (MF) at presentation (March 1983)

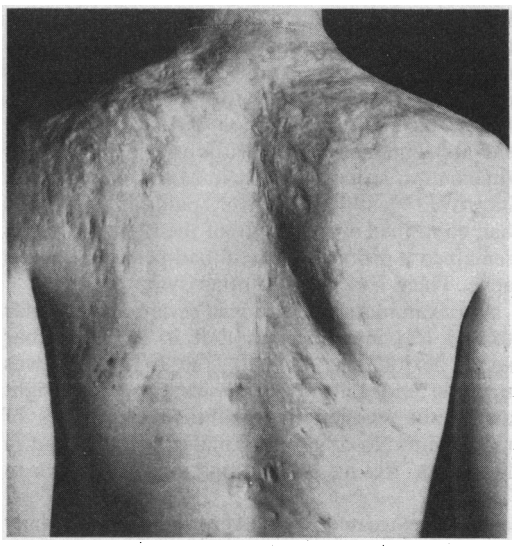

Figure 2. MF four months after treatment with isotretinoin and systemic steroids

chest. Extensive scarring was present (Figure 1). Active joint movements were executed slowly, but there was a full range of passive movements with the exception of lumbar spine flexion which was limited. No evidence of active arthritis was present. The spleen tip was palpable. Table 1 shows the results of investigations

He was started on isotretinoin (Ro-accutane, Roche) 60 mg daily. Within three months the active acne lesions had virtually cleared and after four months' treatment no inflammatory lesions were present and only severe scarring remained (Figure 2). The dose of isotretinoin was reduced to 50 mg daily after two months because of recurrent epistaxes. He also developed paronychia towards the end of the treatment course. Apart from cheilitis, other side effects were minor. Serum lipids were normal throughout treatment, and liver function tests were normal. He was also treated with prednisolone 20 mg daily. All joint pains settled within six weeks and the steroid dose was progressively reduced to zero over three months. By August 1983 all treatment had been stopped; the WBC was normal and the ESR was 40 mm in one hour.

Case 2 (AF): The identical twin of MF developed acute severe acne in September 1982. His disease followed exactly the same course as

Table 1. Investigations in identical twins with acne fulminans at the time of presentation (March 1983)

	MF	AF
Haemoglobin	12.1 g/dl	11.8 g/dl
WBC	$15\,900 \times 10^9$/l	$14\,100 \times 10^9$/l
Neutrophils	73%	76%
Lymphocytes	15%	16%
Monocytes	6%	6%
Eosinophils	6%	2%
ESR	95 mm/h	104 mm/h
Latex test	Negative	Negative
Antinuclear antibodies	Negative	Negative
C1q binding assay	Negative	Negative
C3, C4	Normal	Normal
Skin swab	*Staph. epidermidis*	Not done
X-rays hands, feet and lumbosacral spine	Normal	Normal
HLA typing	A/2, A26/BW38, BW55/CW3, -/BW4/6, DRW8, MB1, MT2, DR6 by antigen association	

his brother's. Arthritis began when the illness was at its peak in December 1982, and involved the ankles, knees, hips and lower back. Systemic disturbance was severe with anorexia, dysphagia for six days and weight loss of 10 kg. Antibiotic therapy had been tried without benefit. By the time he was seen in the UK in March 1983 he had improved steadily. However, pains in the joints had continued and swelling of the right ankle had remained a problem. He still had persistent active acne. There had been no other symptoms.

On examination, there was severe acne similar to but less marked than that of MF. Lumbar spine flexion was limited. The right knee was irritable and 15° of flexion was lost. The right ankle was swollen and painful at extremes of movement. No other abnormalities were found in the joints. Results of investigations are shown in Table 1.

He was treated with isotretinoin 30 mg daily for two weeks, increasing to 50 mg daily. Inflammatory acne lesions and joint symptoms had, to a large extent, settled within two months but treatment was continued for four months. At the end of treatment there was residual scarring only. Prednisolone was not given. No joint discomfort was present but examination showed lumbar spine flexion to be 80% of normal. The WBC had returned to normal and the ESR was 29 mm in one hour. Cheilitis was present throughout treatment and paronychia developed after about three months. Serum lipids remained normal throughout treatment, and liver function tests were normal.

Discussion

These twin boys demonstrate all the features of acne fulminans (Goldschmidt *et al.* 1977), first described by Burns & Colville in 1959. It is a disease of male adolescents which presents acutely as a fulminating, inflammatory, tender, ulcerative acne of the face, neck and upper trunk. At the height of the disease there is fever, malaise and weight loss. This occurs some months after the onset of the acne. Arthralgia occurred in 13 of 21 cases reviewed by Goldschmidt *et al.* (1977). Polyarthralgia, asymmetrical, self-limiting, non-deforming peripheral arthritis and destructive but self-limited arthritis have all been described (Lane *et al.* 1976, Hunter & Hensinger 1980, Cros *et al.* 1981, Davis *et al.* 1981, Statham *et al.* 1983). Myalgia is also frequently present (Davis *et al.* 1981). Anaemia is variable but leukocytosis is a constant finding; the sedimentation rate is markedly elevated. Microscopic haematuria has been reported (Lane *et al.* 1976). The arthralgia and other systemic symptoms settle spontaneously to leave residual inflammatory acne. Gross scarring invariably results.

Response to systemic antibiotics is generally disappointing and oral corticosteroids have been the treatment of choice quickly to control tissue necrosis, systemic toxicity and arthralgia. Our experience suggests that isotretinoin is probably the drug of choice but the steroid may be needed in addition, at least initially. Although some resolution of the acne and arthralgia had already occurred when our patients were seen in the UK, we felt that the retinoid made a significant contribution.

The cause of acne fulminans is not known. The pathogens grown from skin lesions do not differ from those cultured from the skin in acne vulgaris. Blood cultures are negative, excluding a septic cause for the arthritis (Lane *et al.* 1976, Goldschmidt *et al.* 1977). No consistent defect in immune function has been recognized.

Arthritis always follows the acne, suggesting that a heavy antigen load from the skin necrosis could be the precipitating factor. Immune complexes have not been found in our patients or in another recent case (Statham *et al.* 1983), but reported associations with microscopic haematuria and low complement levels (Lane *et al.* 1976), and with erythema nodosum (Williamson *et al.* 1977), suggest an immune complex-mediated process.

The almost simultaneous occurrence in our identical twins suggests that a genetic factor is operating in the aetiology of acne fulminans and also possibly in the predisposition to arthritis.

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