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Acne Fulminans with Bone Lesions

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We present 5 young men who developed acne fulminans. During the acute, febrile illness, all had musculoskeletal symptoms, and X-ray and bone scan examinations revealed that 4 of the patients had osteolytic bone lesions. The disease was resistant to various antibiotics and one patient needed surgical trepanation of the sternum. No evidence of sepsis or bacterial osteomyelitis was found, as all bacteriological cultures proved negative and the tissue reaction was unspecific. The dermatopathogenetic origin of bone lesions in the present patients seems evident, but speculation that the etiology depends on immune mechanisms remains open. (Received December 28, 1988.)

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Several cases of acute, ulcerative acne associated with systemic symptoms such as septic fever, and musculoskeletal pain have been described and termed either acute febrile ulcerative conglobate acne with polyarthralgia (1), with leukemoid reaction (2), or simply acne fulminans (3). This rare form of acne usually affects young men whose mild acne rapidly develops into ulcerative lesions. The patients are febrile, with leukocytosis and increased ESR. Septic infection is often suspected but the disease is very resistant to antibiotic treatment. Polyarthralgia occurs in half of the cases (4, 5) and recently a few acne fulminans cases have been reported in association with osteolytic bone lesions (6–10).

In the present study we describe 5 acne fulminans patients with musculoskeletal symptoms, and in 4 we found evidence of bone lesions, showing that such lesions are not uncommon in acne fulminans.

PATIENTS

During the past 10 years we have examined 5 patients with clinical characteristics of acne fulminans. All were young males and their main clinical and laboratory findings are given in Table I. Two of the patients are described in greater detail.

Case 1 was a 15-year-old male with mild papulopustular acne on his face and chest. He used only topical treatment but when acne worsened, oral tetracycline (2 g/day) was started. After one week, acne lesions rapidly became painful, a fever developed and the patient was admitted to the Department of Dermatology, University Central Hospital, Helsinki. At the examination he had crusting, ulcerative acne lesions on his face and chest. Erythromycin (2 g/day) was started. He became afebrile but experienced severe pain in the left shoulder and in both knees, which were swollen. After 2 weeks he had a new febrile attack and X-ray examination revealed an osteolytic lesion in the left acromion (Fig. 1) but the knees were normal. He was given clindamycin (600 mg/day), then cloxacillin (4 g–2 g/day) and then at first he again became afebrile. However, the acne lesions and musculoskeletal pain abated very slowly. An orthopaedic surgeon was consulted. The function of the upper limb was normal; X-rays showed new bone formation in acromion and no biopsy was performed. After one month in a hospital he was discharged with oral tetracycline (1 g/day) treatment. One month later, acne was inactive and the tetracycline was withdrawn. A deterioration occurred after one year but it was again controlled with a one-month course of tetracycline.

Fig. 1. X-ray of an osteolytic lesion (*arrows*) in left acromion in a patient with acne fulminans.

Case 2 was a 16-year-old male who had a history of mild acne for one year. When his acne became worse he was treated first with tetracycline (1–0.5 g/day). At first the response was good but after 2 months rapidly multiple, confluent, ulcerative acne lesions appeared on his face, and a few lesions developed on his chest and back. When he was admitted to the Department of Dermatology, University Central Hospital, Tampere, he was febrile, and oral sulphathrimethoprim with debriding topical treatment was started. No response was achieved and one week later pain had developed in his chest and he had difficulty in rising from his bed. The upper part of the sternum was tender and swollen and he was then treated with dicloxacillin (1.5 g/day). After one week there was no improvement and roentgenography demonstrated an osteolytic defect and tumorous thickening in soft tissues over the corpus sterni. Bone scan revealed an increased uptake in this area (Fig. 2). An explorative operation revealed a tumorous mass with no purulent material. Histological specimens showed unspecific, inflammatory tissue reaction and the bacterial cultures were negative.

At the operation he received first cephuroxim (4.5 g/day) and then cephexin (2 g/day) for 10 days. After a few days he was much better and the acne lesions started to heal. After 2 weeks the sternum was painless and he was discharged after being in hospital for a total of 1 1/2 months. During the next 2 years, three courses of erythromycin were given because the acne reappeared but these bouts were not associated with musculoskeletal symptoms. Four years later no active acne lesions were found but some scars remained on the patient's chest and face. Control X-rays revealed no active changes in the sternum.

Table I. *Clinical and laboratory findings in 5 patients with acne fulminans*

Patient	Age/ sex	Fever (°C)	Leukocyte count ($\times 10^9$/l)	ESR (mm/h)	Musculoskeletal symptoms	Findings in X-ray or bone scan	Biopsy or exploration
1	15/M	38.6[a]	13.6 (9.7)[b]	83	Pain in left shoulder, swollen knees	Osteolytic defect in left acromion	Not done
2	16/M	38.0	10.7 (5.4)	98	Chest pain and swelling in sternum	Osteolytic defect and increased uptake in sternum	Tumorous mass in corpus sterni
3	14/M	38.6	17.3 (13.8)	80	Pain in both legs and right hip	Osteolytic defect in left fibula, increased uptake in fibula and left clavicula	Inflammatory material in clavicula
4	16/M	39.6	20.1 (14.9)	80	Pain in lower back, redness in right leg	Normal tibia	No abnormal tissue
5	16/M	38.0	14.7 (9.8)	70	Pain in chest and lower back	Osteolytic defect and increased uptake in sternum	Not done

[a] Highest temperature measured during the hospital stay.
[b] Polymorphonuclear count in parentheses.

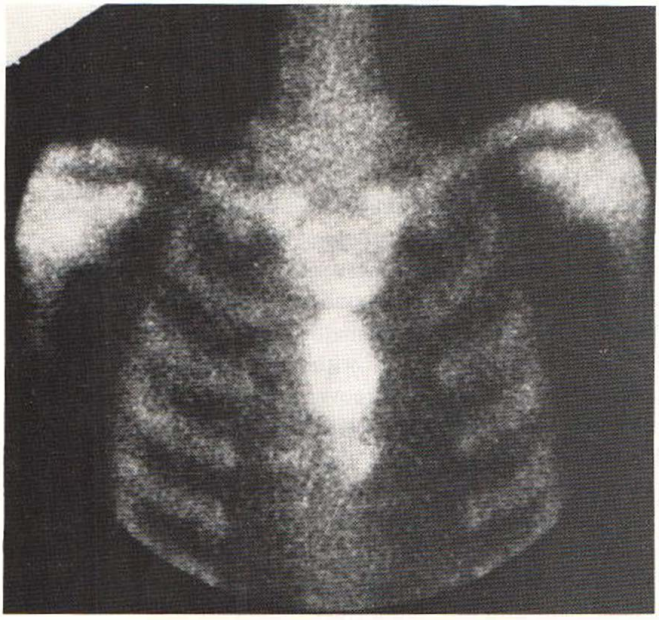

Fig. 2. A bone scan showing increased uptake in the sternum in a patient with acne fulminans.

Laboratory studies

During the admission, all 5 patients had leukocytosis and ESR increased during the first week in hospital (Table I). Several blood cultures were taken during the septic attacks but all proved negative. Skin cultures were negative or showed either normal flora or one isolate of *S. aureus* and one of Gram-negative bacteria. None of the patients developed increased antistaphylococcal antibody titres, and the immunoglobulin and complement (C3, C4) levels showed no marked alterations. The Mantoux-test with 100 tuberculin units proved negative in 2 patients and in vitro stimulation tests (11) showed that both had normal lymphocyte responses to purified protein derivate (PPD).

DISCUSSION

Our 5 patients had the typical clinical picture of acne fulminans. All were young men who during the acute attacks were febrile, had leukocytosis, increased ESR and characteristic ulcerative, crusting acne lesions which developed during tetracycline, erythromycin or isotretinoin treatment. They all had various musculoskeletal symptoms, including clearly swollen knees in one patient. Moreover, osteolytic lesions developed in 4 patients. A trepanation of the sternum and two surgical bone explorations were performed. No purulent material was found and all bacteriological specimens were negative.

A few similar acne fulminans cases associated with osteolytic bone lesions have recently been described (6–10). Because the patients have usually received antibiotic treatment when the bacterial cultures are taken, negative results do not definitely exclude the possible infection in the bone lesions. In our patients, staphylococcal osteomyelitis does not seem likely because the response to antibiotic treatment was not good and antistaphylococcal antibody titres remained normal. Propionibacterium acnes has been isolated from the bone lesion of one acne fulminans patient (7) but the authors did not consider even this finding to be of major importance.

The immunological features of acne have been investigated in many studies (12–15). In acne vulgaris, the delayed skin test reactivity to *Propionibacterium acnes* seems to correlate with the severity of inflammation (14). In contrast, acne conglobata (12) and acne fulminans (16) patients have shown depressed cell mediated immunity to a battery of antigens in skin

tests. We also found 2 anergic patients in the Mantoux-test, but lymphocyte stimulation tests showed that they both had normal PPD responses in peripheral blood. It therefore seems likely that the delayed immunity is altered only secondarily in the skin of acne fulminans patients.

The pathogenesis of the bone lesions associated with acne fulminans remains obscure. No bacterial aetiology has been verified, the response to antibiotic treatment is variable and the patients seem not to have any marked defects in their polymorphonuclear leukocyte or immune system (5, 16). Arthritis can occur in the association with the inflammatory bowel disease (17) and acne fulminans has developed at the onset of Crohn's disease (18). The present 4 patients and some other recently reported acne fulminans cases with bone lesions show also that a dermatologic condition, i.e. acne fulminans, may be an inflammatory source of the arthralgias and bone lesions. These usually develop concomitantly with acne exacerbations unresponsive to antibiotic or isotretinoin treatment (19, 20). Moreover, further studies are needed to show whether a possible explanation is provided by hypersensitivity to a bacterial antigen present in the skin and possibly to a similar antigen in the bone (7). Circulating immune complexes have been considered to be important, and acne fulminans has occurred in association with erythema nodosum (15, 20, 21). Interestingly, previous studies (1, 2, 4, 10) have recorded that the addition of systemic corticosteroids to antibiotic treatment dramatically improves acne fulminans and also assists the control of arthralgia (7, 19). Our experience in 2 patients with acne fulminans is in agreement with this, but further studies are warranted to document the possible effect of corticosteroids on the development of bone lesions.

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