SAPHO Syndrome with Unusual Cutaneous Manifestations Treated Successfully with Etanercept

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Severe cutaneous manifestations of SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) syndrome are rare, and its treatment remains a therapeutic challenge.

We report here a patient with SAPHO syndrome with impressive cutaneous manifestations in the form of extensive pyoderma vegetans (PV) and follicular occlusion triad with concurrent chronic hepatitis C, who was treated successfully with etanercept.

CASE REPORT

A 47-year-old white male presented with chronic suppurative, malodorous, generalized lesions that impaired his normal well-being and caused him profound psychological distress and social incapacity (Fig. 1a–d). The lesions had first developed 7 years previously as superficial pustules that evolved into suppurative plaques and nodules, eventually healing and leaving scars. New crops of lesions developed periodically, with occasional febricula and chills. Long-term, high doses of oral antimicrobials provided some relief. He had also had acne conglobata on back and nape, hidradenitis suppurativa (Fig. 1e), and perifolliculitis abscedens et suffodiens since his teens, which had been treated with oral antibiotics and isotretinoin with poor results. In addition, 2 years previously the patient had begun to develop progressive polyarticular seronegative arthritis with axial and peripheral manifestations, diagnosed on clinico-radiological grounds, consisting of synovitis of the right wrist and elbow, pain in the sole consistent with enthesopathy and HLA-B27-negative sacroileitis. Articular symptoms correlated with flare-ups of cutaneous manifestations. He was treated with salazopyrin, non-steroidal anti-inflammatory drugs (NSAIDs), and six infusions of pamidronate, with poor results. Finally, he had also had an untreated chronic hepatitis C virus (HCV) infection for an unspecified length of time.

Extensive laboratory evaluations revealed only leukocytosis, raised erythrocyte sedimentation rate (ESR) (72 mm/h, normal 0–20) and raised transaminases (ALT: 178 U/L, normal 5–41; AST 147 U/L, normal 5–38). Notably, iodide and bromide levels were within the normal range and anti-neutrophil cytoplasmic antibodies (ANCAs) were negative. Biopsy of a recent pustular lesion showed a superficial suppurative folliculitis. Biopsy of an evolutionated lesion showed pseudoepitheliomatous and infundibular hyperplasia, multiple abscesses and fistulization. Cultures of repeated purulent discharge disclosed the growth of *Proteus penneri* and *Staphylococcus aureus* in an 18-month follow-up period despite the absence of any form of treatment. Skin biopsy culture, searching for slow-growing microorganisms, was negative.

In view of these features we established a diagnosis of PV (1) in the context of SAPHO syndrome (2). At the time of diagnosis the patient had a high score of 23 on the Dermatology Life Quality Index (DLQI; normal 0–3, maximum 30) (3).

A 12-month cycle of oral cyclosporine produced moderate control of the lesions (DLQI: 15), but was discontinued due to an important flare-up of the disease (DLQI: 23). Finally, he started subcutaneous etanercept at doses of 50 mg twice a week. After 4 weeks the treatment had decreased suppuration, promoted scarring of PV and follicular lesions (Fig. 1f), and improved arthritic symptoms. Cultures became negative, hepatic enzymes decreased to normal levels, HCV quantitative viral charge

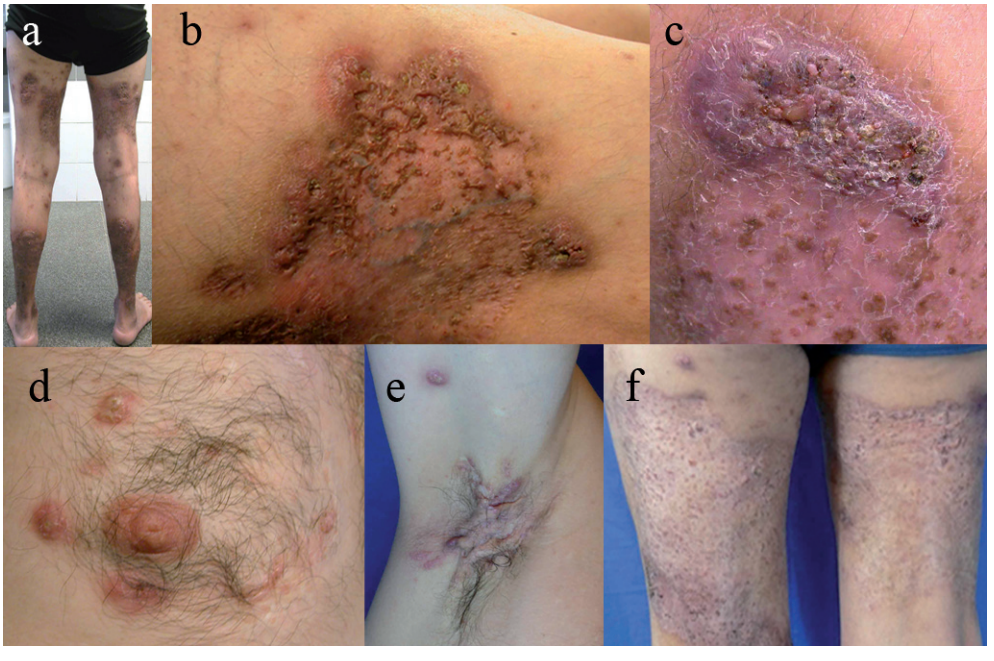

Fig. 1. Clinical aspect of a patient with pyoderma vegetans, follicular occlusion triad, seronegative arthritis rheumatoid and chronic hepatitis C infection (DLQI: 24). (a) Generalized malodorous lesions were more prominent on the legs, abdomen and thighs, although there were also isolated lesions on the trunk, pubis and face. (b) External side of thigh. Suppurative confluent brown-to-violaceous plaques with raised borders without ulceration. Some lesions had a crusted border. Note atrophic cribiform scarring as a result of auto-involution. (c) Posterior thigh. Palpation of lesions showed fluctuation and drainage of purulent material through multiple fistulous holes. (d) Isolated new pustular lesions, like these in the periareolar area, were also seen elsewhere. (e) Hidradenitis suppurative lesions in the axillae and groin. (f) Clinical aspect of the patient after successful treatment with etanercept (DLQI: 5).

decreased to 1,880,000 IU/ml and DLQI decreased to 5. Three months later, he experienced one flare-up with skin ulceration (DLQI: 22), severe arthralgia and growth of *Pseudomonas aeruginosa*, *S. aureus* and *Streptococcus pyogenes* in cultures. Treatment with an additional cycle of oral ciprofloxacin without stopping etanercept led to gradual improvement. Thirty-two months later, the patient remained under treatment, with good control (DLQI: 1).

DISCUSSION

Extensive cutaneous affectation in SAPHO syndrome is unusual (2). Our patient presented with PV, a rare, extensive, suppurative vegetating disease that had been observed in association with other inflammatory, immunodeficiency, autoimmune and malignant pathologies (4). The aetiology of PV is unknown, but it is regarded as an unusual vegetating tissue reaction in patients with low resistance to secondary bacterial infection (4). The question that PV may be a form of pyoderma gangrenosa (PG) with vegetating prominent features, or is an entity in itself, is under discussion (5). Our patient fulfilled the five criteria proposed for diagnosis of PV (2), but there is considerable overlap with PG and the diagnosis rests on clinical features only. There are occasional reports of association of PV with hidradenitis suppurativa, severe acne, and psoriatic arthritis (4) and of SAPHO associated with PG (6). However, we have not found PV described as part of SAPHO syndrome elsewhere.

Treatment of this patient was challenging. Many treatments have been used in SAPHO and PV, with limited success. Some authors have proposed that SAPHO syndrome may be a reactive infectious osteitis due to *Propionibacterium acnes* in genetically predisposed subjects, although this has not yet been demonstrated (7). However, the initial efficacy of antibiotics is lost after discontinuation (9). Pamidronate appears to be very successful in controlling articular symptoms, but is less successful for cutaneous symptoms (10). However, it was not useful in our patient. Successful treatment with oral bisphosphonate has also been reported (11). The use of anti-tumour necrosis factor (TNF)-alpha therapies in refractory SAPHO is increasing (12). Infliximab is usually used (12), but some authors find a poorer response of cutaneous manifestations than articular ones to this drug (13). In addition, a case of SAPHO that developed after the treatment of ulcerative colitis with infliximab has been reported (14).

We chose etanercept for treatment of our patient because it appeared to be useful in treating all the manifestations he displayed. There are some published reports of cases of SAPHO treated successfully with etanercept (8, 12). In addition, there is one report of a case of PV treated successfully with etanercept (4). Finally, the use of TNF-alpha blockers seems to be safe in the presence of concurrent infection with HCV (15). In view of the present case, we conclude that etanercept is a useful treatment for this type of SAPHO patient, although more observations are necessary to confirm this conclusion.

The authors declare no conflict of interest.

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