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Acne Conglobata

Fatma Pelin Cengiz and Funda Kemeriz

Abstract

Acne conglobata is the severe form of acne, located on the face, back, and chest with large, painful, pus-filled cysts deep in the skin. The abscesses and sinuses result in pain, inflammation, and hypertrophic and atrophic scars. In this chapter, we aimed to clarify the pathways of acne conglobata and review the treatment options based on the literature.

Keywords: acne, nodule, severe, scar, treatment

1. Introduction

Acne conglobata (AC) is a severe chronic inflammatory disorder characterized by the presence of comedones, cysts, and scars on the face, back, and chest. It affects deep skin tissue and can result in swelling, bleeding, pain, and scarring. The clinical effects of treatment options for acne conglobata are often unsatisfactory because of a long course of therapy, side effects, the high rate of recurrence, and failure to prevent scar formation. Therefore, we aim to discuss the treatment options based on the literature in this chapter.

2. Clinical presentation

Acne conglobata (AC) is the uncommon and severe form of acne, characterized by large, tender nodules; draining sinuses; and interconnecting abscesses with seropurulent discharge. These lesions are generally located on the back, chest, and face. Healing of the nodules, abscesses usually causes hypertrophic and atrophic scars. Besides, chronic scars of AC may result in squamous cell carcinoma [1]. This disease is common in males more than females. The disease affects young adults and adolescents more frequently than elder people.
Acne conglobata may develop owing to acute flare of existing acne, or it may occur as the rebound of acne that has been latent for a long time.

Synovitis, pustulosis, acne conglobata, hyperostosis, and osteitis are clinically specific inflammatory disorders that may be seen barely in the same patient in a syndrome known as SAPHO syndrome [2].

Acne conglobata may also be associated with the PAPA syndrome, which consists of pyogenic arthritis, acne conglobata, and pyoderma gangrenosum [3].

The primary causes of acne conglobata are still unknown. The HLA-A and HLA-B phenotypes were evaluated in six patients with acne conglobata and hidradenitis suppurativa, in four of whom had HLA-B7 cross-reacting antigens and all had HLA-DRw4 [4]. Other causes include using anabolic steroids, withdrawal of testosterone therapy, nutrition or medications that contain bromine or iodine, aromatic hydrocarbons, and adrenal gland tumors which release large amount of androgens [5].

Acne conglobata can be malodorous, and patients may eliminate themselves from community. Severe scarring can lead to psychological problems, such as anxiety, depression, and low self-esteem in many patients.

### 3. Treatment

Isotretinoin (13-cis retinoic acid) is an oral pharmaceutical drug primarily preferred in the treatment of severe nodular acne. The adverse effects are the flare of acne, cheilitis, xerosis, an increased susceptibility to sunburn, muscle aches, myalgias, and headaches. The patients need to be monitored for blood lipids and liver enzymes especially closely. It has an X category for pregnancy.

Isotretinoin, generally combined with prednisone, is the approved therapy for severe acne conglobata. The recommended dosage of isotretinoin is 0.5–1.0 mg/kg/day for at least 4–5 months [6].

Gollnick et al. compared the effectiveness and safety profile of combined azelaic acid cream plus oral minocycline with oral isotretinoin in severe acne. Their study involved 85 patients with nodular papulopustular acne or acne conglobata who were treated for 6 months. AA cream was applied twice daily, and minocycline was taken twice daily in a dose of 50 mg (daily 100 mg). The doses of isotretinoin were 0.8 mg/kg for the first month, 0.7 mg/kg for the second month, 0.5–0.7 mg/kg for the third month, and 0.5 mg/kg for the fourth to sixth months per day [7].

In the 6-month course, 50 patients in the combined therapy group achieved median reduction of facial comedones, 70%; of papules and pustules, 88%; and of deep inflammatory acne lesions, 100%, while 35 patients in the oral isotretinoin group achieved reduction of comedones, 83%; of papules and pustules, 97%; and of deep inflammatory acne lesions, 100%. Overall, oral isotretinoin was more effective than the combined treatment. The local side effects observed under the combination of AA and minocycline were significantly lower than that seen with
isotretinoin (36.5% versus 65.7%). The incidence of systemic side effects was lower under the combined therapy than under isotretinoin (8% versus 14.3%). They suggested that the combination of topical 20% AA cream and oral minocycline is a highly effective treatment in severe forms of acne, and it is better tolerated and associated with fewer risks than oral isotretinoin [7].

TNF-α is one of the important cytokines involved in the pathogenesis of acne conglobata. Graham et al. found that Propionibacterium acnes stimulated keratinocytes to produce interleukin (IL)-1α, IL-8, and TNF-α [8]. Caillon et al. showed that levels of TNF-α and IL-8 secretion in peripheral blood mononuclear cells were significantly higher than in patients with acne vulgaris than controls [9].

As a result of the role of the TNF-α in proliferation of the immune response with the inflammatory infiltrate including neutrophils, lymphocytes, and histiocytes, it was hypothesized that acne conglobata might benefit from anti-inflammatory therapy. Notable results with adalimumab have been reported for the treatment of dissecting cellulitis of the scalp and hidradenitis suppurativa [10, 11].

On the other hand, anti-TNF therapy can stimulate paradoxical inflammatory skin conditions, of which the most frequent is a psoriasiform eruption. There have been three patients with Crohn’s disease, psoriasis vulgaris, and rheumatoid arthritis who were treated with adalimumab in the literature. As a result of adalimumab therapy, acniform eruptions were occurred in these cases [12]. It was suggested that genetic predisposition and overlap with the primary inflammatory disease and autoimmune sensitivity induced interferon-α and cytokine imbalance [13].

Given the previous success reported with hidradenitis suppurativa, Shirakawa et al. considered infliximab therapy in a patient with acne conglobata and rheumatoid arthritis. The patient had experienced flares of the acne conglobata and side effects of oral isotretinoin. The patient was started on the 300 mg (3 mg/kg) of infliximab for the treatment of rheumatoid arthritis. The same dose was repeated at weeks 2 and 6. They observed a significant improvement in the size and number of his cystic lesions after the third dose. Subsequently, the same doses were repeated every 8 weeks and continued for at least 6 months. The patient had achieved a decrease in the number of lesions and pain symptoms [14].

Yiu et al. reported a patient with recalcitrant acne conglobata, who was commenced on subcutaneous adalimumab at 80 mg loading dose, followed by 40 mg every other week, in combination with 15 mg prednisolone. Most of the inflammatory nodules resolved within 4 weeks of commencing treatment with adalimumab, and this response was maintained at the 12-week follow-up [15].

Sand et al. reported another unresponsive patient to doxycycline, oral isotretinoin, combination of prednisolone and isotretinoin, and combination of isotretinoin and dapsone. They initiated monotherapy with adalimumab using an initial loading dose of 80 mg, followed by 40 mg monthly twice. They observed a significant decrease in the size and degree of inflammation of the nodular lesions 4 weeks after initial treatment and disappearance of all nodular lesions after 12 weeks of therapy. The patient had received continuous monotherapy with adalimumab, 40 mg, twice monthly for a total of 12 months, and no recurrence of acne lesions had appeared [16].
Vega et al. reported a 14-year-old adolescent with recalcitrant acne conglobata on the face, neck, and upper chest. That patient had experienced acne fulminans and flares of severe acne while on the isotretinoin and prednisone therapies. Then, twice weekly injections of etanercept 50 mg combined with oral isotretinoin 40 mg/d were started. They observed a clear improvement after 2 months of treatment. The patient had completed the isotretinoin cycle of 9600 mg over 8 months. They continued etanercept (50 mg/wk) 3 months more, and the treatment was completed after 1 year. The patient had experienced no relapse [17].

Schuttealaar et al. reported another young patient with severe acne unresponsive to other treatments. They started him on infliximab 5 mg/kg intravenously at 8-week interval. A total of eight infusions were administered. After three infusions, they did not observe neither new lesions nor activation of the old lesions. After 4 months, they successfully treated negligible relapse of the acne with intralesional corticosteroids. No relapse was occurred at 1-year follow-up [18].

Electron beam processing has the ability to break the chains of DNA in living organisms and results in local destruction of cells. [19, 20]. The electron beam therapy delivers radiation primarily to the superficial skin lesions and spares the deeper tissues from radiation. Electron beam radiation has been used in the treatment of mycosis fungoides, basal cell carcinoma, squamous cell carcinoma, and AIDS-related molluscum contagiosum lesions and Kaposi’s sarcoma [19–23]. The acute side effects of electron beam radiation are fatigue, itching, tanning, and burns. Long-term side effects include dry skin, decreased sweating, skin color changes, loss of scalp hair, and the development of dilated blood vessels [24].

Myers et al. reported a 53-year-old patient with acne conglobata and hidradenitis suppurativa who is unresponsive to oral doxycycline, oral ampicillin, triamcinolone intralesional injections, topical benzoyl peroxide 5% wash, clindamycin phosphate, 1% topical solution, betamethasone valerate 0.1% cream, and cyclosporine 5 mg/kg per day. After these therapies, the patient was started a total of eight treatments of modern external beam radiation over 2 weeks localized to the bilateral mandibular cheeks. Electron energies were 9 MeV. Daily fraction sizes were 2.5 Gy for a total of 20 Gy to each side of the face. Three weeks after radiation, the patient reported subjective improvement in cyst size, cyst drainage, pain, and self-esteem. He had no significant xerosis or pigmentary abnormalities status after radiation. The patient had experienced no relapse at 5-month follow-up [25].

Photodynamic therapy (PDT) is a kind of phototherapy that induces selective cytotoxic destruction by the activation of a nontoxic light-sensitive compound with light. Up-to-date PDT has been used for several dermatologic diseases, such as psoriasis, cutaneous T-cell lymphoma, and warts [26]. PDT with topical 5-ALA damages sebaceous glands, inhibits sebum production, kills Propionibacterium acnes, and obstructs the follicular openings [27]. The advantages of PDT include rapid efficacy, short recovery time, less destruction, and pain. Despite of these advantages, the local side effects of PDT are erythema, skin peeling, pain, burning, stinging, exfoliation, and post-inflammatory hyperpigmentation [27, 28]. It is obligatory to photoprotect after treatment for phototoxicity [29].
Yang et al. investigated the clinical effects of photodynamic therapy with topical 5-aminolevulinic acid for facial acne conglobata. They included 75 patients with facial acne conglobata. They divided the patients into photodynamic therapy (PDT) group with topical 5% aminolevulinic acid and red light for three times in a month and control group (n = 40) with the Chinese herbal medicine mask plus red light once a week. The patients were also administered topical metronidazole, oral doxycycline, viaminate, and zinc gluconate. Efficacy was assessed according to symptom score, cure rate, and response rate, 2 weeks after the final therapy course, and time points for assessment were selected as day 0, day 10, and day 20; day 34 for the treatment group; and day 7, day 14, day 21, and day 35 for the control group. They observed that PDT was more effective for pustules and papules than control group. The PDT group was associated with a higher cure rate, a lower symptom score, and response rate than the control group. They didn’t observe systemic side effects. The erythematous swelling, increased number of cysts, pigmentation, and severe pain were the local side effects which they observed in the treatment group with PDT. They demonstrated that the treatment of acne conglobata with PDT is associated with a high cure rate, short treatment period, few side effects, and reduced scar formation [30].

Hasegawa et al. achieved to treat a case of acne conglobata by CO(2) laser ablation to remove the top of the sinuses and their tracts. After laser ablation, topical tretinoin therapy was also started simultaneously to prevent the appearance of new acne lesions. They proposed the CO(2) laser ablation with topical tretinoin as a powerful treatment option for acne conglobata [31]. They also reported another acne conglobata case, which they successfully treated by fractional laser after CO laser abrassion of cysts combined with topical tretinoin [32].

Liu et al. compared the effectiveness of encircling acupuncture combined with venesection and cupping and oral isotretinoin. A total of 26 acupuncture patients had their acupuncture courses once daily; venesection and cupping were applied twice a week. Patients of isotretinoin group were treated with oral isotretinoin 20 mg/d. The duration of study was 4 weeks. After 4 weeks, in acupuncture group and Western medicine group, 3 (11.5%) and 4 (15.4%) cases experienced remarkable relief in their signs, 14 (53.8%) and 11 (42.3%) had marked improvement, 6 (23.1%) and 7 (26.9%) had improvement, and 3 (11.5%) and 4 (15.4%) failed, with the effective rates being 88.5% and 84.6%, respectively. Overall, they didn’t observe any significant difference between acupuncture and oral isotretinoin (P > 0.05). In terms of lowering serum IL-6 content, acupuncture was found superior than oral isotretinoin (P < 0.05) [33].

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