Perifolliculitis Capitis Abscedens et Suffodiens Treated with Anti-tumor Necrosis Factor-alpha – Possible New Treatment Option

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ABSTRACT The case of a 26-year-old male patient with perifolliculitis capitis abscedens et suffodiens (PCAS) who later developed hidradenitis suppurativa (HS) and exacerbation of acne is presented. The patient did not respond well to conventional treatment including isotretinoin and oral antibiotics. Quality of life was significantly impaired. After introduction of anti-tumor necrosis factor-alpha (TNF-α) treatment, the patient's clinical picture improved dramatically and quality of life increased. The treatment has been well tolerated by the patient for 15 months at time of writing this report.

KEY WORDS: perifolliculitis capitis abscedens et suffodiens, hidradenitis suppurativa, anti-tumor necrosis factor-alpha, follicular occlusion triad

INTRODUCTION

Perifolliculitis capitis abscedens et suffodiens (PCAS), also known as dissecting cellulitis of the scalp, is a rare, chronic and relapsing inflammatory disease of unknown etiology. It was first described by Spritzer in 1903 and later named by Hoffmann in 1908 (1,2).

The condition is characterized by painful, fluctuant pustules, nodules, abscesses, and sinuses that result in patchy areas of atrophic, hypertrophic, and keloidal scars, as well as alopecia. Lesions are primarily located on the occipital scalp or vertex; however, other sections of the scalp can be affected (3). The disease generally exhibits a chronic course with frequent flare-ups.

Treatment is usually difficult and often unsuccessful, with relapses occurring regularly after discontinuation of treatment. Conventional therapies reported in the literature for the treatment of PCAS include low dose oral zinc, isotretinoin, minocycline, sulfa drugs, tetracyclines, prednisone, intralesional triamcinolone, incision and drainage, dapsone, antiandrogens (in women), topical clindamycin, topical isotretinoin, X-ray epilation and ablation, ablative $C0^2$ lasers, hair removal lasers (800 nm and 694 nm), and surgical excision. Newer treatments reported include tumor necrosis factor inhibitors, quinolones, macrolide antibiotics, rifampin, alitretinoin, metronidazole, and high-dose zinc sulphate (4). Generally, acute flares are best treated with broad-spectrum antibiotics. Good results have been reported in patients subsequently treated with isotretinoin, but the number of reports is small, dosing schedules are variable, and long term follow-up is negligible (3).

PCAS may occur along with hidradenitis suppurativa and acne conglobata, constituting the follicular occlusion triad. Although these diseases occur in different areas of the body, they show the same histologic changes and share a common mechanism of pathogenesis: follicular hyperkeratosis and plugging

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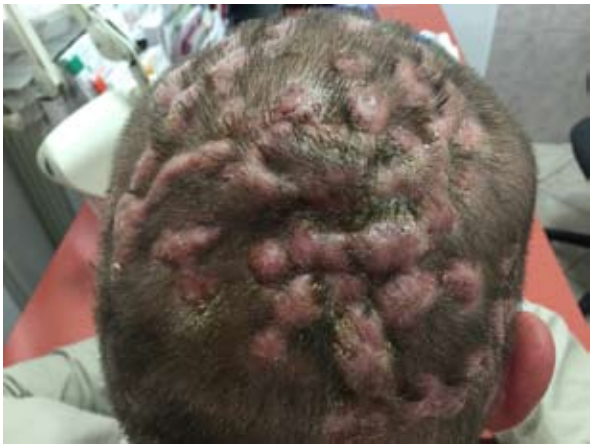

Figure 1. Scalp lesions before initiating therapy with anti-tumor necrosis factor-alpha.

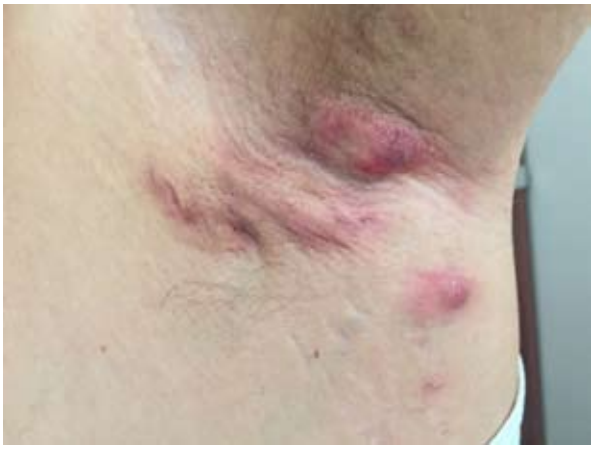

Figure 2. Axillary lesions before initiating therapy with anti-tumor necrosis factor-alpha.

leading to follicular occlusion, dilatation, rupture, and secondary bacterial infection. Infections are most frequently caused by *Staphylococcus aureus* and *Staphylococcus epidermidis*. Keratin and bacteria from ruptured follicles can initiate a neutrophilic and granulomatous response (5).

Hidradenitis suppurativa may also occur in other rare syndromes (e.g. Bazex-Dupré-Christol syndrome, Dowling-Degos disease, keratitis, ichthyosis, and deafness (KID) syndrome) which require different management; however, our patient revealed no typical symptoms or signs that can be associated with another syndrome (6).

Conditions to consider in the differential diagnosis of PCAS include pseudopelade of Brocq, inflammatory tinea capitis, folliculotropic mycosis fungoides, and central centrifugal scarring alopecia (7).

CASE REPORT

A 26-year-old male patient presented with patchy hair loss overlying inflammatory papules, pustules, yellow crusts, and tender, fluctuant, suppurative nodules on the frontal scalp. Several nodules formed confluent conglomerates, which discharged purulent secretion when pressed not only in close proximity but also from more distant areas. This presentation indicated the presence of fistulae and interconnecting sinuses. The findings progressively worsened over the course of 2 months with an increase in the number of nodules and affected areas of the scalp, along with swelling of regional lymph nodes.

Skin biopsy taken from the scalp revealed an epidermis with 3 hair follicles showing dilated infundibulums containing keratin, and an infiltrate of mononuclear cells surrounding vessels within the dermis. No abscess was found. Potassium hydroxide smears did not show any fungal elements, and culture of the material was also sterile. Bacterial analysis of the scalp swab revealed only saprophytic bacteria. The patient's overall physical examination was normal. Routine laboratory tests showed increased erythrocyte sedimentation rate (ESR), leukocytosis, dyslipidemia, and

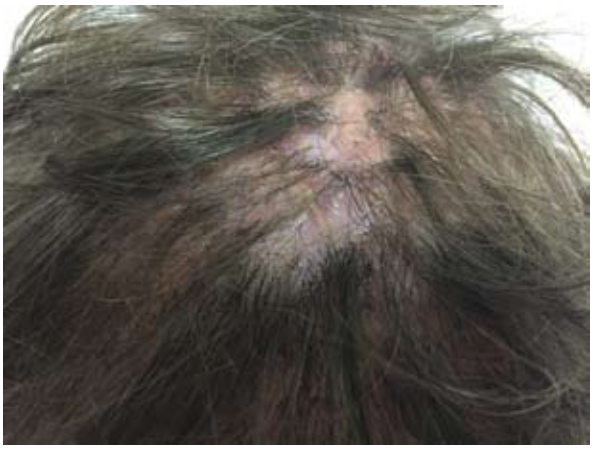

Figure 3. Scalp – 6 months following initiation of anti-tumor necrosis factor-alpha.

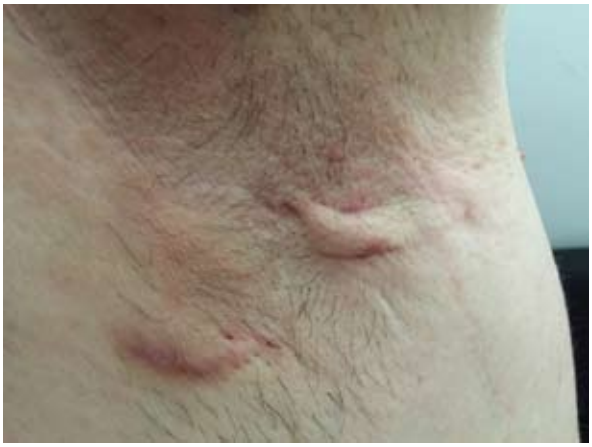

Figure 4. Axilla – 8 months following initiation of anti-tumor necrosis factor-alpha.

Table 1. Cases of perifolliculitis capitis abscedens et suffodiens (PCAS) treated with anti-tumor necrosis factor-alpha (TNF-α) inhibitors

REFERENCE	AGE/ GENDER	PREVIOUS TREATMENTS	TREATMENT	OUTCOME
Badaoui *et al.* (13)	1 patient	NA	infliximab	no improvement
Brandt *et al.* (14)	24/male	dapsone, doxycycline, ciprofloxacine, isotretinoin	infliximab 5 mg/kg at 8-week intervals for 12 months	hair beginning to regrow after second treatment; 1 year after discontinuing treatment no signs of relapse
Mansouri *et al.* (11)	1. 48/male 2. 27/male	1. multiple antibiotics, zinc sulfate, dapsone, isotretinoin, systemic CS, surgical excision and drainage 2. topical and systemic CS, antibiotics including dapsone, isotretinoin	1. adalimumab 80 mg on day 0, 40 mg on day 7, 40 mg every other week thereafter 2. infliximab 5 mg/kg at weeks 0, 2, 6 followed by 8 week intervals (20 months and continuing)	1. after 1 month –improvement; at 5 months DLQI from 21 to 10 2. reduction of symptoms, inflammation and odor within 3 months, continuous improvement; DLQI 18 to 6 within 12 months
Martín-García & Rullán (15)	30/male	intralesional CS (triamcinolone), antibiotics (doxycycline, ciprofloxacine), isotretinoin	adalimumab 80 mg on day 0, 40 mg on day 7, 40 mg every other week thereafter (2 years and continuing)	after 1 month significant improvement; after 7 months complete clearance of inflammatory lesions
Navarini & Trüeb (16)	1. 27/male 2. 29/male 3. 30/male	1. antibiotics 2. antibiotics, tetracyclines, isotretinoin 3. antibiotics, tetracyclines, levofloxacin, isotretinoin	1., 2., 3. adalimumab 80 mg on day 0, 40 mg on day 7, 40 mg every other week thereafter	1., 2., 3. clinical symptoms subsided within 8 weeks of treatment; after 3 months clinical activity and subjective symptoms were reduced 3. after 4 months of successful treatment, disease returned within 4 weeks
Sand & Thomsen (17)	1. elderly male 2. young male	isotretinoin, dapsone, triamcinolone	adalimumab	1. total clearance of disease within 3 months 2. did not respond to 6 months of therapy
Sjerobabski & Franceschi	26/male	isotretinoin, antibiotics	adalimumab 80 mg on day 0, 1, 14, 40 mg on day 28, 40 mg every week thereafter	excellent response after only 10 weeks, DLQI 27 to 1
Sukhatme *et al.* (18)	39/male	antibiotics, intralesional triamcinolone, surgery, isotretinoin	adalimumab 40 mg ×2 week 1, 40 mg week 2, 40 mg every other week	pain and purulent discharge stopped within 1 month; at 5-month follow up lesions had cleared, hair was growing back
Wollina *et al.* (19)	30/male	rifampicin, prednisolone, isotretinoin, minor surgery	infliximab 5 mg/kg at weeks 0, 2, and 6	reduction of inflammation, secretion, pain and nodules even after first treatment; nearly complete remission at 3-month follow up

CS: corticosteroid; NA: not available

increased serum gamma-glutamyltransferase levels. Patient body mass index was 35.8. Patient history revealed he was a smoker.

Quality of life, measured using the Dermatology Life Quality Index (DLQI), was significantly reduced.

Initially, the patient was treated with a systemic retinoid, isotretinoin, at a dose of 0.64 mg/kg over 10 months, achieving a cumulative dose of 150 mg/kg. After 3 months of treatment with isotretinoin, the lesions on the scalp slightly improved, no new nodules were present, and secretion was milder in extent. However, the patient developed hidradenitis suppurativa, manifesting as painful furuncles in the left axilla and later in the right axilla, inguinum, and lower abdomen, at places forming interconnecting sinuses, and partially healing with atrophic or hypertrophic livid scars. These findings classified as Hurley stage 2 hidradenitis suppurativa (8).

The patient additionally developed exacerbation of facial acne during treatment. After 10 months of therapy, the inflammation and secretions on the scalp subsided, while lesions in the inguinum and axillary area worsened and facial acne also persisted. After failure of isotretinoin therapy, treatment with multiple antibiotics was started over a course of 12 weeks; however, no significant improvement was achieved.

Tumor necrosis factor alpha (TNF-α) inhibitors have been shown to be successful in treating hidradenitis suppurativa; thus, treatment with adalimumab was considered (9). The patient was tested for tuberculosis, HIV, and hepatitis B and C, with all results coming back negative. The patient was then initiated on adalimumab 80 mg on days 0, 1, and 14 followed by 40 mg on day 28 and every week thereafter (10). Response to treatment was excellent after only 10 weeks of therapy. A significant improvement of all symptoms was observed, with reduced secretion, pain, and inflammatory changes on the scalp, absence of new nodules and sinus tracts in the bilateral axilla, inguinum, and pubic region, as well as clearing of facial acne. The patient's DLQI had also reduced significantly from 27 to 1. As if this writing, the treatment has been well tolerated by the patient for 15 months, with the patient receiving adalimumab 40 mg injections every week.

DISCUSSION

Treatment of perifolliculitis capitis abscedens et suffodiens and hidradenitis suppurativa is difficult, often disappointing, and unpredictable. PCAS often persists or recurs despite different treatment modalities including topical and oral antibiotics, isotretinoin, topical, intralesional and systemic steroids, incision and drainage, zinc sulfate, and procedural therapies including laser-assisted epilation, carbon dioxide laser ablation, and wide surgical excision with skin grafting (4).

Treatment with TNF-α inhibitors has been reported in recent literature (Table 1) as a new approach in the treatment of PCAS (11). Adalimumab is a monoclonal antibody that binds to TNF-α, a pro-inflammatory cytokine that is thought to play an important role in the pathogenesis of follicular occlusion disorders. In July 2015, the European Medicines Agency (EMA) approved the use of adalimumab for treatment of active moderate to severe hidradenitis suppurativa in patients older than 12 years of age with inadequate response to conventional systemic hidradenitis therapy (12). Since PCAS and HS are believed to exhibit the same pathogenesis and frequently occur in the same patient, TNF-α inhibitors may be an effective option in the management of PCAS, as was demonstrated in our patient.

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