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Case Report

Adalimumab for the Treatment of Periodontitis in a 35-Year-Old Woman with Hidradenitis Suppurativa

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Adalimumab · Hidradenitis suppurativa · Inflammation · Periodontitis

Abstract
Increasing evidence suggests an association between chronic inflammatory conditions and oral health. Herein, we present a case of a 35-year-old woman with concomitant hidradenitis suppurativa (HS) and periodontitis, who was treated successfully with adalimumab. After 3 months of treatment, a marked improvement was observed in her clinical scores of HS, quality of life, as well as her gingival pain and signs of inflammation. This finding calls for a closer collaboration between dermatologists and dentists to further explore the possible beneficial role of biologic therapy for chronic inflammatory skin conditions as well as periodontitis.

Introduction

A link between chronic inflammatory conditions and oral health has been established. Hidradenitis suppurativa (HS) is a chronic, inflammatory skin disease of the hair follicle defined by recurrent nodules, tunnels, and scarring involving the intertriginous regions. HS and periodontitis, an inflammatory oral disease characterized by connective tissue damage and alveolar bone loss, share many common clinical and pathologic features. Although the pathogenesis of HS and periodontitis remains enigmatic, it is thought to involve immune

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dysregulation. Particularly, tumor necrosis factor (TNF) has been implicated in the pathogenesis of both diseases [1, 2]. Moreover, recent studies indicate the involvement of specific anaerobic Gram-negative bacteria (*Prevotella* spp. and *Porphyromonas* spp.) in both early and mature HS lesions [3, 4], which are also well-known pathogens in periodontitis. Furthermore, both periodontitis and HS share several risk factors, including smoking, obesity, and diabetes mellitus. However, although periodontitis is well described in other chronic inflammatory skin diseases, no previous studies have described a potential association between HS and periodontitis.

Adalimumab (TNF inhibitor) is currently the only FDA-approved biologic treatment for HS. While not approved for the treatment of periodontitis, a beneficial effect of adalimumab has previously been suggested [5]. In this report, we present a case of improved periodontitis in a patient with HS treated with adalimumab. The CARE Checklist has been completed by the authors for this case report, attached as supplementary material (available at www.karger.com/doi/10.1159/000528139).

Case Report

A 35-year-old woman, who was otherwise healthy, was referred to our department due to frequent HS flares since puberty. Upon physical examination, the patient had a total of nine inflammatory nodules and excessive scarring distributed bilaterally in the axillary and inguinal regions, as well as the left gluteal, inframammary, and abdominal regions with no abscesses or fistulae, corresponding to Hurley stage II (Hidradenitis Suppurativa Score [HSS] = 61 and the International Hidradenitis Suppurativa Score [IHS4] = 9). Dermatology Life Quality Index (DLQI) was 15, and overall disease bother score and overall disease-related pain score on a visual analog scale (VAS) was 6.6 and 10 out of 10, respectively. She had a BMI of 43.0 kg/m^2, a smoking history of 16 pack years, and her blood samples showed elevated leukocytes, neutrophils, and total cholesterol, with normal liver and kidney function. The patient had previously been treated with topical azelaic acid – and clindamycin without satisfactory results. Further, the patient had been treated with systemic lymecycline 300 mg twice daily for 3 months with insufficient effect and for 9 months with adalimumab as part of a clinical trial. The patient's HS greatly improved during this period and was manageable by topical clindamycin as monotherapy at the end of the study.

When evaluated at our department, she experienced gradual relapse of HS and was also diagnosed with periodontitis, reporting severe gingival irritation and bleeding in relation to dental care, i.e., tooth brushing and dental flossing as shown in Figure 1 (left image). The patient had suffered from these oral symptoms for several years and was also examined by a dentist. Unfortunately, no specific treatments were initiated by the dentist. Possible surgery was also discussed with her dentist. Due to the previous efficacy of adalimumab, we initiated treatment with biosimilar adalimumab at a dose of 160 mg at day 0, followed by 80 mg at day 14, and 40 mg weekly from day 28 onward. After 3 months of treatment, the patient reported markedly improved control of HS (HSS = 8 and IHS4 = 4) and better quality of life (DLQI = 6); overall disease bother score and overall pain score decreased to 4.6 and 4.7 out of 10, respectively. There was also a substantial amelioration of the patient's periodontitis as she was able to perform oral hygiene with less pain and bleeding; thus, possible surgery was put on hold. A comparison of the images before and after adalimumab treatment of the patient's teeth revealed fewer dental plaques, less discoloration, and reduced gingival inflammation as shown in Figure 1 (right panel).

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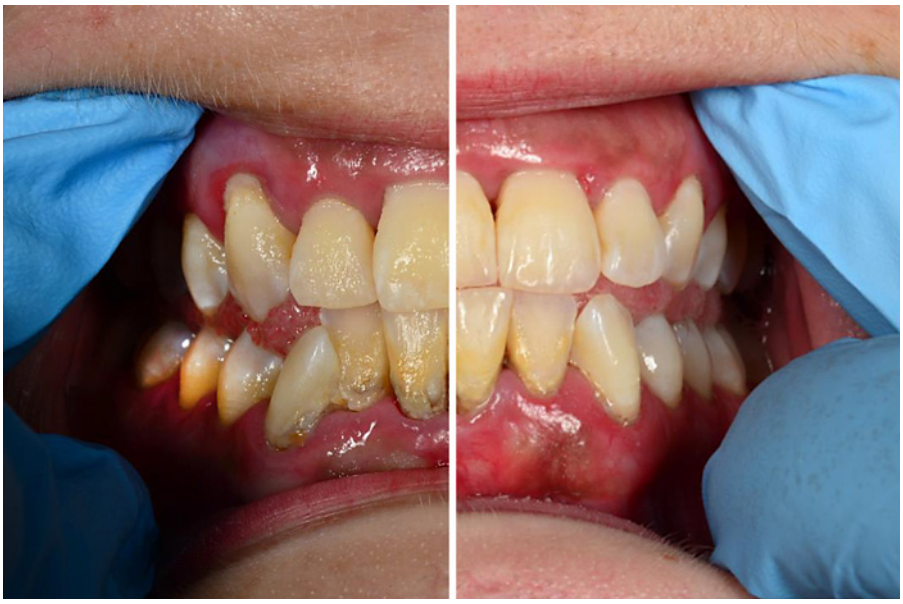

Fig. 1. Photo demonstrating the clinical efficacy of 3-month adalimumab therapy on periodontitis; before treatment (left image) and after treatment (right image). Visible changes: (1) reduced inflammation of upper gingiva, particularly evident as less purplish coloration adjacently to the upper canine tooth, (2) reduction of desquamation of mucosal surface in upper and lower gingiva exemplified by restoration of natural shiny mucosa with post-inflammatory hyperpigmented spots instead of superficial ulcerations, and (3) considerable pan-oral reduction in dental plaque formation.

Discussion

Herein, we report a case of concomitant periodontitis and HS in a 35-year-old woman treated with adalimumab. The patient experienced marked improvement in both conditions after 3 months of treatment.

In rat models, TNF protein levels were increased in cases of induced periodontitis [6], and treatment of induced periodontitis with etanercept, another anti-TNF agent, significantly reduced the degree of periodontal inflammation and tissue injury [7]. The favorable results of anti-TNF therapy with adalimumab in the treatment of periodontitis have also been demonstrated in human patients with concomitant rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis [8, 9], all of which share common pathologic pathways with HS. Interestingly, several studies have previously demonstrated good clinical efficacy by increasing the adalimumab dosage from 40 mg weekly to 80 mg weekly in HS [10]. Considering the intractable and chronic nature of both periodontitis and HS, it may be speculated if such intensification of the weekly adalimumab dosage also may have some justification in HS patients with the co-occurrence of periodontitis.

The association between oral health and chronic inflammatory skin conditions, in particular psoriasis, is well described in the literature [11]. Yet, there is a distinct lack of therapeutic attention to this interrelationship. Despite the quite limited knowledge on periodontal diseases and HS, the available data suggest that patients with HS have increased gingival inflammation which is possibly amplified during acute HS flares [12]. This present report is, to our knowledge, the first case of clinical improvement of concomitant HS and periodontitis treated with adalimumab.

A different, less well-understood perspective is the potential role of bacteria in the pathogenesis in both diseases. Recent studies on the bacterial microbiome of HS suggest

that HS lesions are associated with cutaneous dysbiosis [3, 4]. The studies show that HS lesions are primarily dominated by anaerobic Gram-negative species such as *Prevotella* sp. and *Porphyromonas* sp. Interestingly, both *Prevotella* and *Porphyromonas* are prevalent on mucosal surfaces, e.g., oral cavity and tongue [13]. It could be speculated that adalimumab contributes to the restoration of bacterial homeostasis in both the skin and in the oral cavity, e.g., through the regulation of antimicrobial peptides. Unfortunately, no studies have previously investigated the microbiome of the oral cavity in HS patients.

Currently, the treatment of periodontitis comprises mostly oral antibiotics and sometimes in combination with flap surgery and soft or hard tissue grafting. However, with the improved availability of biologic treatments as a result of the rapid expansion in the number of available biosimilars, this treatment modality is becoming increasingly feasible. In the future, collaboration between dentists and medical doctors is needed to explore the full potential of this new therapeutic domain.

Statement of Ethics

Ethical approval is not required for this study in accordance with national guidelines. This retrospective review of patient data did not require ethical approval in accordance with national guidelines. Written informed consent was obtained from the patient for publication of the details of the medical case and the accompanying images.

Conflict of Interest Statement

Outside the submitted work, Simon Francis Thomsen has been a speaker or advisor for Sanofi, AbbVie, LEO Pharma, Pfizer, Eli Lilly, Novartis, UCB Pharma, Almirall, and Janssen Pharmaceuticals and has received research support from Sanofi, AbbVie, LEO Pharma, Novartis, UCB Pharma, and Janssen Pharmaceuticals.

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Author Contributions

Yiqiu Yao drafted the manuscript; made substantial contributions to the design and the acquisition, analysis, and interpretation of data; revised the manuscript for intellectual content and approved the final version; and is accountable for all aspects of the work. Misbah Noshela Ghazanfar, Astrid-Helene Ravn Jørgensen, and Hans Christian Ring made substantial contributions to the design and the acquisition, analysis, and interpretation of data; revised the manuscript for intellectual content and approved the final version; and is accountable for all aspects of the work. Simon Francis Thomsen initiated the work; made substantial contributions to the design and the acquisition, analysis, and interpretation of data; revised the manuscript for intellectual content and approved the final version; and is accountable for all aspects of the work.

Data Availability Statement

Data for the work are stored on file and are not publicly available due to privacy data legislation. All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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