Review paper

Hidradenitis suppurativa – biologic therapy and other available treatment options

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Abstract

Hidradenitis suppurativa (HS) is a chronic recurrent inflammatory skin disease which is characterized by painful, recurrent nodules and abscesses. The overall prevalence of HS is estimated to be 11 per 100 000 individuals in the United States and 4% of the world's population. Women are three times more affected than men, especially patients between 18 and 29 years. Similarly to acne vulgaris, HS is primarily associated with follicular occlusion, which results from a number of biological processes, including follicular epithelial hyperplasia and hyperkeratinization. There are numerous available treatment options for cutaneous lesions in the course of HS. A combination of conservative therapy and appropriate surgical treatment conducted by an experienced surgeon ensures the best possible clinical outcomes. Presently, biologic therapy is the most effective pharmacological treatment in patients with a moderate-to-severe course of the disease. Numerous ongoing clinical trials provide hope for greater availability of new biologic therapy methods.

Key words: hidradenitis suppurativa, dermatology, abscesses, scarring, biologic treatment.

Introduction

Hidradenitis suppurativa (HS) is a chronic recurrent inflammatory skin disease. The condition is characterized by painful, recurrent nodules and abscesses which tend to rupture, thus leading to the formation of sinus tracts and scarring [1, 2]. The affected sites reflect the endogenous distribution of apocrine glands and include the axillae, groin and anogenital region. The core of the disease is not, as it was commonly believed, an inflammatory process affecting the sudoriferous glands. Similarly to acne vulgaris, HS is primarily associated with follicular occlusion, which results from a number of biological processes, including follicular epithelial hyperplasia and hyperkeratinization [3–5]. Population-based studies using routinely collected healthcare data from the USA estimate a prevalence of 0.1%. European studies include undiagnosed patients and typically estimate the prevalence of 1% [6].

According to the statistical reports by the Department of Health Care of the National Health Fund, 367, 373 and 440 new cases of HS were reported in 2014, 2015 and 2016, respectively, thus the mean incidence is estimated to be approximately 0.001% [7].

The disease affects three times as many women as men and most frequently manifests itself in patients aged between 18 and 29 years. There is a large number of treatment options, including biologic therapy, antibiotic therapy, retinoids and topical agents. The latest research indicates the beneficial effect of non-pharmacological interventions including photodynamic therapy and laser therapy. Cutaneous lesions are often associated with pain that may compromise everyday activities [8]. In addition, the presence of disfiguring cutaneous lesions and malodorous purulent discharge has a negative impact on the personal and professional life of the patients [9–11]. Such skin disorders may contribute greatly to the development of depression and pose a greater risk of suicidal thoughts and suicide [12, 13].

Pathogenesis

The exact cause of the disease is not well understood. Disease initiation may be due to, inter alia, genetic

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factors, hormones, smoking, obesity, bacterial infections and antimicrobial peptides (AMPs) which regulate innate immune responses [14]. It is considered that the disease is primarily associated with follicular occlusion observed in histopathology specimens from early-stage lesions [14, 15], which probably results from follicular epithelial hyperplasia and hyperkeratinization and leads to formation of cysts [15–18]. The cysts eventually rupture, releasing their content into the dermis, which induces secretion of proinflammatory mediators and may result in abscess or sinus tract formation as well as scarring in more advanced stages of the process [15–18].

Chronic pain and stigmatization

Patients with HS suffer from acute and chronic pain, which has a significant impact on their overall quality of life. Depression is a risk factor for developing chronic pain and may lead to pain intensification, whereas suppression of the inflammation may contribute to pain reduction [19–21]. An interdisciplinary approach to the patient consisting in implementation of pain assessment and involvement of pain management specialists is crucial [19, 21]. Patients with HS feel stigmatized and have low self-esteem [11, 13, 22–24]. The phenomenon of stigma greatly contributes to developing depression and reduction of quality of life in patients with HS, which may lead to exacerbation of symptoms [11, 13, 22, 23, 25, 26]. Various symptomatic treatment options are available. Topical analgesics such as lidocaine, paracetamol, nonsteroidal anti-inflammatory drugs are preferred in the management of acute pain [27].

If the patient does not respond to the first-line treatment, use of opioids such as codeine, hydrocodone, morphine should be considered [28].

Tramadol is an opioid-like analgesic and could be used as an alternative to opioids among patients with cardiopulmonary insufficiency [19].

For management of neuropathic pain, anticonvulsants such as pregabalin and gabapentin are preferred [29].

Conventional treatment

Topical treatment

Clindamycin is an antibiotic that shows activity against anaerobic, streptococcal, and staphylococcal species and can lead to decreasing cutaneous inflammation and inhibiting biofilm formation in HS [30, 31].

A double blind trial was conducted to evaluate the effect of topical clindamycin. Effects based on patients' assessment, number of abscesses, inflammatory nodules and pustules was significantly better in the clindamycin group than in the placebo group [32].

Clindamycin (0.1%) is applied topically twice a day for Hurley stage I and stage II HS as the first-line treatment according to guidelines [19, 23, 33–39].

Resorcinol is an organic chemical compound from the group of phenols which has keratolytic and antiseptic properties. Efficiency of topical application of 15% resorcinol twice a day is proven and recommended by the European HS Foundation and Canadian Dermatology Association guidelines as the second-line treatment [40, 41].

Treatment with topical antiseptics can lead to reducing bacterial colonization and inflammation but there are no data comparing their efficacy. North American guidelines mentioned topical antiseptics such as chlorhexidine, benzoyl peroxide, and zinc pyrithione [19]. Triclosan and ammonium bituminosulfonate are cited by Swiss guidelines [39].

Intralesional corticosteroid injections

There are reports on application of direct intralesional triamcinolone injections (10 mg/ml). In one study conducted in a group of 36 patients, a significant decrease in pain intensity was observed 1 day after the injection. Furthermore, a reduction of erythema, oedema, inflammatory infiltration and lesion size was reported 1 week after the injection. However, long-term effects of this therapy are unknown [42].

A prospective cohort study on patients with mild to severe HS and one or more inflammatory lesions was conducted to evaluate the effectiveness of ultrasound-assisted intralesional infiltration of triamcinolone acetonide 40 mg/ml. At week 12, 81.1% (30/37) of nodules, 72.0% (108/150) of abscesses and 53.33% (32/60) of draining fistulas presented complete response versus 69.1% (47/68), 54.3% (38/70) and 35.3% (12/34) respectively for the non-infiltrated lesions. This technique is useful especially for treatment of abscesses and small to medium-size simple draining fistulas [43].

Systemic antibiotic therapy

Clindamycin is an antibiotic that shows activity against *Streptococci*, *Staphylococci,* and anaerobes. Rifampicin on the other hand exhibits activity against Gram-positive and intracellular bacterial species. A combination treatment with clindamycin (300 mg b.i.d.) and rifampicin (300 mg b.i.d.) is recommended as the first-line therapy [44]. Efficacy of antibiotic treatment results from targeted activity against bacterial biofilms, which are an important cause of relapses of the infection. Moreover, antibiotic treatment has an immunomodulatory effect on T-lymphocytes, which participate in the inflammatory cascade [45, 46]. The effectiveness of the therapy has been confirmed in numerous studies as it has been proven to lead to improvement or complete remission of cutaneous lesions. The efficacy of the combination treatment with clindamycin and rifampicin has been evaluated in several major studies, one of which indicates significant improvement or complete remission in 66% of 116 patients [47]. Some minor studies have proven that

the response and complete remission rates in nearly half of the patients are approximately 85% [48, 49]. Monotherapy of rifampicin that is considered to be the basis of this combination treatment could lead to rifampicin resistance. A combination therapy with clindamycin added should aim to limit rifampicin resistance and it is recommended rather than monotherapy [50].

Application of tetracycline (e.g. doxycycline 100 mg b.i.d.) for 12 weeks or longer is recommended in patients with mild-to-moderate HS [19, 33–39, 51].

A prospective, international cohort study was conducted to evaluate the efficiency and tolerability of tetracyclines and clindamycin plus rifampicin.

The study included 135 patients that were treated with oral tetracyclines (500 mg twice daily, doxycycline 100 mg once daily, minocycline 100 mg once daily) and 103 that were treated with clindamycin and rifampicin (clindamycin 300 mg twice daily in combination with rifampicin 600 mg). The Hidradenitis Suppurativa Clinical Response (HiSCR) was achieved in 40.1% and 48.2% of patients, respectively. No significant differences in efficacy were observed between the two treatments [52].

A combination treatment with rifampicin, moxifloxacin, and metronidazole has been proven beneficial as it resulted in remission of cutaneous lesions in 57% of patients after 7 months of therapy [53].

Metronidazole shows activity against anaerobic bacteria. Moxifloxacin on the other hand is effective against Gram-positive, Gram-negative and anaerobic species [53, 54].

Combination treatments reduce the risk of rifampicin resistance and provides broad-spectrum coverage [40, 53].

Ertapenem is a carbapenem antibiotic showing activity against Gram-positive and Gram-negative aerobic and anaerobic species and exhibiting resistance to inactivation by β-lactamases. It can be used as one-time 6-week course of daily intravenous infusion before the surgical intervention or as a course of rescue therapy [19, 40, 53, 55].

The study showed that treatment with 1 g intravenous ertapenem daily led to remission in Hurley stage I/ II disease and significant improvement in quality of life in Hurley stage III patients. Although consolidation treatments are needed to prevent relapses because daily infusions of ertapenem cannot be considered as long-term therapy [40].

Reports on the efficacy of dapsone in patients with HS are inconclusive. In a retrospective study conducted in a group of 24 patients treated with oral dapsone at a dose of 50–200 mg once a day, 38% of them showed clinical improvement. However, none of the patients with Hurley stage III HS responded to the therapy [56].

Systemic corticosteroids

There are little data regarding corticosteroid therapy in patients with HS. Short-term treatment may be applied in exacerbations in order to reduce the inflammation [19]. Long-term corticosteroid therapy at the smallest effective dose may support treatment of patients with severe HS unresponsive to standard therapy [19]. Recurrence of skin lesions was observed after cessation of both short- and long-term treatment.

Hormonal therapy

Androgen receptors are located in apocrine sweat glands. Efficiency of antiandrogen treatment with spironolactone and finasteride has been proven [57–59].

Finasteride is a competitive and selective inhibitor of isoenzyme type II 5α-reductase [60] that blocks conversion of testosterone to dihydrotestosterone (DHT). A dose of finasteride is 1–5 mg/day according to guidelines [47, 51]. The other drug is spironolactone, which blocks the aldosterone receptor.

The other drug is spironolactone, which blocks the aldosterone receptor and can be genuine in female HS patients. It is most frequently used in monotherapy for women with mild-to-moderate HS or as accessory cure in severe HS in North American guidelines and in Brazilian guidelines [19, 51]. Results of clinical trials posted in North American guidelines show that an adequate medicament value oscillates between 100 and 150 mg [40]. Compliance was achieved in 17–20 female HS patients within 3–6 months of treatment and with 11 of the 20 obtain entire disease purification [58]. Moreover described effective and safe long-term alternative for women with HS and there were not any benefits in another treatment with tetracycline or OCP [61].

Retinoids

Retinoids affect keratocyte growth and sebaceous glands maturation [57]. Acitretin is a vitamin-A derivative, which has the highest efficacy in the treatment of HS. Therapy with acitretin has been proven to result in reduction of skin lesions [62, 63]. However, there is a well-documented risk of skin lesion recurrence after cessation of treatment [52]. There was a study conducted to investigate the clinical efficacy of acitretin. 53% of the study group consisting of 17 patients finished 9 months' treatment of acitretin at a dose of 0.56 ±0.08 mg/kg daily. Eight patients fulfilled the criteria for response (HSSI ≥ 50% reduction from baseline). 47% of patients have resigned from the study mostly because of drug ineffectiveness and adverse events [63, 64].

Moreover, it should be noted that acitretin poses a high risk of teratogenicity and other adverse effects including depression, dyslipidaemia, headache and skin dryness [57]. The therapeutic effect of isotretinoin is questionable. Studies revealed no response to treatment with isotretinoin in 64.4% of patients [65–70].

Biologic therapy

TNF-α

Biologics are currently the most promising treatment strategy in patients with HS. The most clinical data refer

to TNF-α inhibitors [50]. These agents have shown the greatest efficacy in treatment of patients with Hurley stage III HS by suppressing the inflammation and reducing the amount of purulent discharge as well as the size of sinus tracts. In addition, combined anti-TNF-α and surgical therapy have been proven beneficial. The findings concerned the use of adalimumab, infliximab and etanercept. Adalimumab is the only biologic medication approved by the FDA for this indication. Adalimumab has been proven to decrease cytokine levels, including IL-1β and B- lymphocyte chemoattractant [71].

Two multicentre phase 3 clinical studies (PIONEER I and II) evaluating adalimumab efficacy in HS were conducted. There were 307 patients with moderate-to-severe HS enrolled in PIONEER I and 326 patients enrolled in PIONEER II. In the first 12 weeks (period 1). patients were reassigned to groups receiving adalimumab 40 mg weekly or placebo. In the next 24 weeks (period 2). Patients were receiving placebo or adalimumab 40 mg weekly or every 2 weeks. The primary endpoint was a clinical response at week 12 – Hidradenitis Suppurativa Clinical Response (HiSCR) [72].

HiSCR is defined as at least a 50% reduction from baseline in the abscess and inflammatory-nodule count, with no increase in abscess or draining-fistula counts. 41.8% of patients receiving adalimumab in PIONEER I and 58.9% in PIONEER II have met this primary endpoint at week 12 compared to 26.0% of patients in the placebo group in PIONEER I and 27.6% in PIONEER II [73, 74].

Long-term efficacy of adalimumab in patients with moderate-to-severe HS was evaluated in 3-year phase 3 open-label extension study using PIONEER I and PIONEER II study participants. Patients with partial response to adalimumab defined as 25% improvement in abscesses and inflammatory nodule count were also included in the study [75].

According to the study, 52.3% of patients receiving 40 mg of adalimumab every week and 73.0% of PRRs (partial responders) achieved HiSCR. Moreover, 52.3% of patients who received adalimumab weekly and 57.1% of PRRs maintained achieved HiSCR through week 168 [75].

Recurrence of the disease was observed frequently after cessation of treatment with adalimumab. Moreover, several patients developed tolerance against adalimumab after 3 months of therapy [76].

Infliximab is a chimeric monoclonal antibody against TNF-α. Clinical trials on treatment with infliximab have been conducted as well, revealing a low remission rate and a high partial response rate [57]. Administration of infliximab intravenously at 5 mg/kg at weeks 0, 2, and 6 has been evaluated in an RCT on patients with moderate-to-severe HS. The study revealed no significant difference between the infliximab and placebo group for > 50% improvement in inflammatory nodules. Although the improvement rate of 25–50% was significantly higher for infliximab compared to placebo [77] .

Efficacy of etanercept in moderate-to-severe HS was evaluated in randomized, double-blind, placebo-controlled trial on a group of 20 patients [78].

Study participants received 50 mg of etanercept or placebo twice a week for 12 weeks. After that, for the next 12 weeks, every patient received 50 mg of etanercept twice a week. Results show no significant difference in patient global assessment, physician global assessment or QOL (assessed with DLQI) between etanercept and placebo groups at week 12 or 24 [79].

IL-12/IL-23

Ustekinumab is a monoclonal antibody directed against IL-12 and IL-23. Several studies regarding the efficacy of ustekinumab have been published. One study performed in a group of 17 patients revealed that 1 patient achieved complete remission of cutaneous lesions after a lack of response to prior treatment with infliximab and adalimumab, whereas approximately half of the patients achieved a 50% reduction of skin [8]. In 1 study conducted in a group of 3 patients, a 100% response rate was observed, including a complete remission in 1 patient after 6 months of treatment [80]. An open-label study on the group of 17 patients with HS was performed. Patients were treated with 45 or 90 mg (> 100 kg weight) ustekinumab at weeks 0, 4, 16 and 28. At week 40, only 47% of patients achieved HiSCR but 82% achieved at least a 25% improvement in modified Sartorius score [64, 81].

IL-23

Guselkumab is a monoclonal antibody directed against IL-23. Currently there is an ongoing phase II clinical trial of guselkumab in the treatment of moderate-to-severe acne inversa. The use of this agent was described in a group of 4 patients, two of whom achieved a significant reduction of skin lesions. Exacerbation of the primary disease was observed in 1 patient [82].

Risankizumab is a monoclonal antibody targeting IL-23A. Presently there is ongoing recruitment into a phase 2 clinical trial assessing the efficacy of risankizumab in patients with moderate-to-severe HS [82].

IL-17

Secukinumab is an anti-IL-17 antibody. Several case reports of patients with HS treated with secukinumab have been published [12, 83, 84]. Currently there are three ongoing clinical trials of this agent. The results of thus far unpublished studies that were presented at the latest congress of the European Academy of Dermatology and Venerology indicate that 14 out of 18 studied patients achieved Hidradenitis Suppurativa Clinical Response (HiSCR) [85]. The official results are yet to be announced.

Bimekizumab is a humanized antibody directed against IL-17A and IL-17F. A phase II clinical trial of this

agent is complete, thus far the official results have not been published [86]. There is ongoing recruitment into two clinical studies which aim to evaluate the efficacy of bimekizumab in the treatment of moderate-to-severe HS [87, 88].

CJM112 is a human monoclonal antibody targeting IL-17A. The results of a phase II clinical trial of this agent have not been published yet [89].

Brodalumab is a monoclonal antibody directed against the IL-17 receptor, which early phase I clinical trial has already been conducted in a group of 10 patients [90]. All patients achieved HiSCR, whereas 80% of patients achieved an IHS4 improvement in week 12. A significant decrease in pain and pruritus intensity was observed, as well as an increase in the quality of life [91]. Recruitment of patients into another clinical trial is soon to begin [92].

IL-1

Anti-IL-1 antibodies are another drug class used in the therapy of HS. Anakinra is a recombinant human IL-1 receptor antagonist. It blocks the biologic activity of IL-1α and IL-1β by competitively inhibiting IL-1 binding to the IL-1 receptor. The concentration of IL-1 is elevated in patients with HS, both in cutaneous lesions and the adjacent skin areas. A clinical study in a group of 20 patients (19 of whom completed the study) indicated that the activity rate decreased at the end of treatment by 67% in patients treated with anakinra compared to 20% in patients receiving placebo [49]. Recurrence of the disease was observed after cessation of the therapy, though it was slower in patients treated with anakinra than in the placebo group [93]. Another study in a group of 6 patients treated with anakinra for 8 weeks (5 of whom completed the study) showed significant improvement in the Sartorius score, DLQI as well as in clinical assessment conducted by the physician and the patient. The patients were followed up for 8 weeks after cessation of treatment and recurrence of disease activity levels from before treatment was observed [94]. There are several case reports of no response to treatment or increased disease activity in patients undergoing therapy with anakinra [95, 96].

Bermekimab (MABp1) belongs to a group of drugs with anti-IL-1α activity [97–99]. In a clinical trial conducted in a group of 20 patients, 60% of patients treated with bermekimab achieved a positive HiSCR score compared to 10% of patients receiving placebo [97]. Recruitment into a clinical trial aiming to evaluate the efficacy of bermekimab in two subgroups of patients (patients with prior exposure to anti-TNF drugs and patients with no such exposure) has been completed [100].

Other biologic agents

Efalizumab is a humanized monoclonal antibody that inhibits the binding of leukocytes to intercellular adhesion molecule-1 (ICAM-1). One clinical trial was conducted in a group of 5 patients, 2 of whom experienced disease exacerbation. No clinical benefit from the therapy was observed [83, 84]. The agent was withdrawn in 2009 due to four reported cases of progressive multifocal leukoencephalopathy (PML) [101].

IFX-1 is a monoclonal antibody which binds to complement component C5a. In a clinical study aiming to evaluate its therapeutic efficacy performed in a group of 12 patients, 75% of patients achieved HiSCR within 50 days of treatment [102]. The randomized, double-blind, placebo-controlled, multicentre study enrolled a total of 179 patients in four active dose arms and a placebo arm at over 40 sites in 9 countries in North America and Europe. The primary endpoint of the trial was a dose response signal, assessed by the Hidradenitis Suppurativa Clinical Response (HiSCR) score at week 16. The primary statistical analysis by multiple-comparison procedure modelling (MCP-mod) showed no significant dose response for the IFX-1 treatment [103].

CFZ533 is a monoclonal antibody which has anti-CD40 activity. CD40 is found on B-lymphocytes and antigen-presenting cells and triggers numerous inflammatory responses by binding to its ligand. Presently there is ongoing recruitment into a phase II clinical trial aiming to assess the efficacy of CFZ533 in the treatment of HS [92].

Photodynamic therapy

Photodynamic therapy has been proven effective in the treatment of acne vulgaris [57]. First, a cream containing a photosensitizing agent is applied on the cutaneous lesions, the affected skin area is subsequently exposed to red light. Several studies regarding the use of superficial and intralesional photodynamic therapy with 5-aminolevulinic acid (5-ALA) or methylene blue (MB) in patients with HS have been published [104]. Injection of 5-ALA or MB and subsequent irradiation with a fibre-optic sensor positioned within the lesion appears to be a more beneficial treatment option [105]. The study revealed a 96% response rate and significant improvement or remission in 78% of patients [106]. It seems that photodynamic therapy applied in combination with other treatment methods may improve outcomes in patients who want to avoid surgery [80].

Laser therapy

Treatment with laser therapy for patients with HS was described by Dalrymple *et al.* in 1987 [107]. Lasers work in two major pathways – selective and ablative. Two types of laser intervention have been evaluated for the therapy of HS, including long-pulse Nd:YAG and CO_2 laser excision of cutaneous lesions [80]. The CO_2 laser allows thermal ablation of the lesion [57]. Multiple studies have indicated high treatment efficacy and low recurrence

rates [108]. Long-pulse Nd:YAG laser acts by destroying pilosebaceous units [80].

Neodymium-doped yttrium aluminium garnet (ND:YAG) is helpful in Hurley stage I or II. It can lead to reduce the number of hair follicles and sebaceous glands. Ablative CO_2 laser is useful in Hurley stage II and III [109]. One study showed reduction of disease activity after 4 months of laser therapy cycles, which was maintained for 2 months after cessation of treatment. The improvement rate averaged for all anatomical areas was 72.2% in the laser therapy group compared to 22.9% in the control group ($p < 0.05$) [110].

There are specific procedures based on laser therapy e.g. Fistula-tract Laser Closure (FiLaC, Biolitec, Germany). FiLaC is the new treatment technique used to close the fistulas in-ano and pilonidal sinus. It is based on cauterization of the fistula tract by a laser probe to eliminate a chronically inflamed centre of the tissue [111]. Long-term follow-up shows that this kind of procedure gives good therapeutical effects and suggest using FiLaC as the first-line treatment [111]. In a clinical trial, Dessily *et al*. applied the FiLaC technique on 40 patients with pilonidal sinus and noticed better clinical response of 87.5% (35/40 patients) with only one recurrence during follow-up [111].

Moreover, there is also LAight® therapy (LENICURA, Wiesbaden, Germany), which is non-invasive procedure using intense pulsed light (IPL) and radiofrequency (RF).

After 10 treatment sessions inflammation was significantly decreased, the Dermatology Life Quality Index (DLQI) was reduced to 4 points, but pain intensity remained similar. After 24 sessions – inflammatory lesions were nearly healed, DLQI was reduced to 2 points and pain perception decreased to 3 points. Unfortunately, this procedure did not cause any improvement of the scars [112].

Botulinum toxin

There are published case reports of 5 HS patients treated with type A botulinum toxin who showed good response to treatment (3 patients achieved skin lesions remission) [113–117]. The described cases were meticulously analysed in a prospective study aiming to assess the influence of hyperhidrosis on quality of life of patients with HS. The study revealed neither an objective clinical improvement nor a significant decrease in the number of active nodular lesions, nor a reduction in pain intensity. However, a reduction of hyperhidrosis and improvement in the quality of life were observed in the patient group [118]. A randomized double-blind placebo-controlled clinical trial was conducted in a group of 20 HS patients treated with type B botulinum toxin. Improvement in the quality of life (DLQI), as well as a subjective reduction of symptoms experienced by the patients and a decrease in the number of cutaneous lesions was observed. In addition, 55% of patients reported a reduction of hyperhidrosis [119]. It appears that reduction of hyperhidrosis may have a significant positive impact on the quality of life of HS patients.

Surgical treatment

Every surgical intervention requires an individual approach and personalisation of treatment. In the case of HS, meticulous qualification for the procedure is essential and possible due to a multidisciplinary approach as well as strict cooperation between the surgeon and the dermatologist [120]. Despite numerous novel conservative therapy methods, surgical intervention in acne inversa remains the most effective, but under the condition that it is complemented by optimal non-invasive treatment [121].

If the decision is made to perform surgery, available options include skin-tissue sparing excision of the lesion as well as radical excision with primary wound closure, secondary wound closure after granulation tissue formation or wound closure with the use of full- or partial-thickness skin grafts.

An additional treatment method that ensures maximal sparing of the surrounding tissues is the deroofing technique which involves loop electrosurgical excision of the lesion and the interconnected sinus tracts with secondary wound closure after granulation tissue formation. It is the treatment of choice in Hurley stage I/II [38].

The initial choice of the optimal surgical technique is dependent on the clinical stage of the disease as well as on the affected skin area [38].

Patients with Hurley stage I/II HS do not require mandatory surgical treatment [122]. In acute situations, in the event of abscess formation, urgent incision and drainage must be performed, which should be followed by subsequent pharmacological treatment due to a high recurrence risk [123].

In case of solitary lesions or recurrent lesions at fixed locations, available treatment options include skin-tissue sparing excision with electrosurgical peeling (STEEP), deroofing and electrosurgical excision with secondary wound closure after granulation tissue formation [123]. STEEP and deroofing are recommended in patients with Hurley II or III HS.

During the deroofing technique the double-ended fistula probe is used to localize all the fistulas in the area of the HS skin changes. After visualization of the fistulas, the tissue overlying the sinus is removed to create bevelled edges.

STEEP is a technique in which the electrosurgical wire loop is passed over the sinuses to remove all scars and lesional tissue till the epithelialized floor of fistulas and subcutaneous fat [124, 125].

Wide radical excision of the entire inflamed area with removal of sinuses, nodules and scar tissue as well as with a 1–2 cm resection margin should be performed in

Hurley stage III to prevent recurrence [109]. It should be noted, however, that radical excision poses an increased risk of postoperative complications including increased pain intensity compared to sparing surgery, wound dehiscence or infection, graft necrosis following wound closure with skin grafting, limitation of joint mobility due to surgical scar tissue, hypertrophic scarring, infection and hematoma [110]. Local administration of gentamicin sponge shortens wound healing time and reduces the incidence of infection [105].

For patients with severe HS which do not fully respond to pharmacological treatment even biologic treatment, adalimumab can be considered as adjunct therapy to surgery. The biologic drug is used to minimize the area required for surgical resection. First results of the trial show that the combination of adalimumab with surgery will help refine the treatment approach for this category of severe HS [16].

Chronic inactive HS lesions that have not shown any sign of inflammation or relapse for a prolonged period of time should be excised to prevent further recurrence [34].

It transpires that clearly visible cutaneous lesions are often much more extensive and advanced below the skin. Ultrasound-based mapping is remarkably useful as it allows for a precise assessment of the extent and advancement of lesions within the dermis, which often infiltrate the subcutaneous tissue, major blood vessels and nerves as well. Only an accurate diagnosis along with preprocedural multidisciplinary consultation allows for effective treatment and reduces the risk of complications after surgery performed under difficult conditions.

The recurrence rate after an urgent surgical intervention such as drainage of abscesses is 100%. In case of lesion excision with a too narrow resection margin, the recurrence rate is 42.7%, whereas it is only 27% in patients who underwent wide radical excision after 6 years of follow-up. Lesion excision with secondary wound closure after granulation tissue formation leads to complete recovery in 83% of patients with a mean follow-up period of 34 months [105]. In addition, skin grafting reduces the risk of disease recurrence compared to primary wound closure with sutures [121].

Choosing the most opportune moment for surgical intervention is crucial as modification of conservative treatment including pharmacotherapy often results in skin lesion reduction, allowing for less extensive surgery and thus improves treatment outcomes and is beneficial for the patient.

Currently there are no clear guidelines regarding surgical therapy in HS, therefore experience of the surgeon is essential in choosing the optimal intervention.

Conclusions

There are numerous available treatment options for cutaneous lesions in the course of HS. The combination of conservative therapy and appropriate surgical treatment conducted by an experienced surgeon ensures the best possible clinical outcomes. Presently, biologic therapy is the most effective pharmacological treatment in patients with a moderate-to-severe course of the disease. The registration of a given drug requires proof of effectiveness and safety in randomized controlled trials (RCTs). However, the exclusion criteria often apply to patients for whom therapy is the most demanding. Such action may distort the picture of the true effectiveness of the drug. Moreover, the inclusion criteria for randomized clinical trials so far included patients with the presence of a scarring component, which excluded patients with Hurley stage I disease. The above-mentioned restrictions on patient inclusion in RCTs have resulted in the collection of real-world data, which can be obtained from a variety of sources that are linked to outcomes in heterogeneous patient populations in real-world settings, such as patient surveys, clinical trials, and observational cohort studies.

Recently, investigators from the European Medicines Agency (EMA) recommended that in order to make novel analytical methods for evaluating real-world and patient-level data acceptable to regulators and other decision makers [126].

Marzano *et al*. present their results of a retrospective and observational study with 389 patients with HS treated with adalimumab in 21 Italian centres in a real-world setting [127].

The study's findings, combined with the inverse correlation between achieved Hidradenitis Suppurativa Clinical Response (HiSCR) and prior immunosuppressive treatment, establish a 'window of opportunity' for adalimumab administration in the early stages of HS. Additionally, this evidence demonstrates unequivocally that using validated outcomes, such as International Hidradenitis Suppurativa Severity Score System (IHS4), to define the entry point for an RCT may be beneficial [128].

Adalimumab remains the only biologic agent approved for the treatment of hidradenitis suppurativa in Poland. Numerous ongoing clinical trials provide hope for greater availability of new biologic therapy methods.

Conflict of interest

The authors declare no conflict of interest.

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