



New Approaches in Management and Treatment of Hidradenitis Suppurativa

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Abstract

Background / Aim: *Hidradenitis suppurativa* (HS) is a chronic inflammatory disease that most often affects apocrine gland-bearing areas of the skin. The treatment depends on the severity of the clinical presentation. The paper objective was to present new modalities in management and treatment of HS.

Methods: The subjects in this research included the patients suffering from the severe form of HS, who were treated in the University Clinical Centre of the Republic of Srpska for the past three years. The effect of treatment of HS were monitored. In four patients, biologic therapy with adalimumab or adalimumab biosimilars was administered, while four patients received radiotherapy and 17 of them, were treated surgically. Depending on the type of treatment, the effects of therapy were monitored after 6-12 weeks by using clinical examination and by assessing the disease stage according to the Hurley staging. Due to a small number of subjects, especially in patients treated with biologic and radiotherapy, it was not possible to perform any statistical analysis and the results were presented by description, in tables and photographs.

Results: Biologic therapy: Adalimumab was administered subcutaneously 80 mg, twice a month. After 12 weeks, in 4 patients was observed a regression of changes by 60-70 % when compared to previous skin changes. Radiotherapy: the total radiation dose was 5 Gy, distributed in 5 or 10 fractions. After 12 weeks an improvement by 60-70 % was observed. Surgical treatment: after 6-8 weeks, the patients were fully recovered.

Conclusions: Application of biologic and radiotherapy after 12 weeks had similar results, ie it brought to regression of changes by 60-70 %. The best results were achieved after surgical treatment of HS.

Key words: *Hidradenitis suppurativa*; Adalimumab; Radiotherapy; Skin autografting.

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Introduction

Hidradenitis suppurativa (HS) is a chronic, purulent disease with increased inflammatory component and tendency towards fibrosis in apocrine gland-bearing areas of the skin. However it should be pointed out that the HS also occurs in skin areas without apocrine glands. Namely, it was confirmed that the foundation of the disease development is basically folliculitis caused by occlusion of

the follicular epithelium and that apocrine gland involvement was, both clinically and aetiopathogenically, secondary. A small number of patients, in addition to HS, can also have *acne conglobata*, *folliculitis et perifolliculitis capitis* - the so-called 'follicular occlusion triad' or additional pilonidal sinus in case of follicular occlusion tetrad.¹

HS occurs in both sexes, but in males it is mostly localised in the anogenital region. The correlation between obesity and the severity of the clinical presentation has been confirmed, as well as the effect of sex hormones to the disease occurrence and course.²

HS most often occurs in armpits, groin and perianal area. However, the disease can also be confirmed in the areas underneath the breasts, on the stomach, gluteus, scalp and eyelids. According to the clinical presentation, erythematous painful nodules appear first and they usually soften after a few days, after that are formed abscesses and thick purulent, seropurulent and bloody contents are oozing out of them. New nodules appear soon after in the same place or near the previous changes and the process is repeated. This creates sinus tracts between changes that never fully heal. The tendency towards fibrosis changes and scarring is particularly emphasised. Due to the chronic nature of the disease, there is a high risk of complications such as the spread of the disease to the rectum, bladder or urethra with the formation of fistulas. Sepsis is the most serious complication of this disease. Regarding the differential diagnosis of the disease, the following can be considered: carbuncles, lymphadenitis, inflamed cysts, granulomatous diseases and the possibility of skin tuberculosis should be particularly excluded.^{1,2}

HS significantly affects the patients' life quality. Due to the chronic nature of the disease, the appearance of painful nodules and malodorous discharge, patients withdraw from the community because they feel less valuable to other people. The presence of fistulas, scars in the anogenital region also reduces the sexual activity of patients. They sometimes isolate themselves even from their own family members, with the possibility of suffering from severe forms of depression. Due to physical and emotional pain, the patients are sometimes suicidal.³

Hurley staging describes three clinical stages of HS. Stage I is represented by solitary abscess formations, without scarring and sinus tracts. In stage II, recurrent abscesses and lesions with scarring and sinus tracts occur, and in stage III is affected the entire anatomical region with interconnected abscesses and sinus tracts.⁴ Although Hurley staging system is simple, it is not quantitative, so it was modified for the purpose of accuracy of diagnosis and treatment protocol planning: the Modified Hidradenitis Suppurativa Score (HSS score, better known as the Sartorius score),⁵ along with the Hidradenitis Physician Global Assessment Scale (HS-PGA) (Table 1).⁶

Table 1: Hidradenitis suppurativa staging according to the Physician Global Assessment Scale (HS-PGA)

Stage (form)	Description
Clear, minimal	No abscesses, fistulas, inflammatory nodules or non-inflammatory nodules
Mild	No abscesses, fistulas, 1-4 inflammatory nodules or 1 abscess and fistula, 0 inflammatory nodules
Moderate	No abscesses, fistulas, but more than 5 inflammatory nodules or 1 abscess and fistula and more than 1 inflammatory nodules or 2-5 abscesses or fistulas and less than 10 inflammatory nodules
Severe	2-5 abscesses or fistulas and more than 10 inflammatory nodules
Very severe	More than 5 abscesses and fistulas

The treatment protocol for HS is determined in accordance with the stage of the disease and the severity of the clinical presentation (Table 2). It is very important to point out the change in the patient's lifestyle: abstinence from smoking, weight loss, change in diet, wound treatment and care for the patient's mental health. Pain is one of the dominant symptoms and therefore it is necessary to use analgesics: lidocaine + diclofenac, topical nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentin and pregabalin, tramadol and ultimately opiates for severe pain that does not stop with NSAIDs.⁷⁻⁹

Table 2: Guidelines in hidradenitis suppurativa treatment according to the clinical severity

Hurley I (PGA mild)	Hurley II (PGA moderate)	Hurley III (PGA severe -very severe)
Topical: 1 % clindamycin lotion for 12 weeks or 15 % resorcinol cream	Clindamycin tbl. 2 x 300 mg + Rifampicin tbl. 2 x 300 mg per day (10 weeks)	Biological: adalimumab 160 mg in the first week, 80 mg for two weeks, then 40 mg a week or 80 mg every two weeks
Tetracycline 2 x 500 mg per day or Doxycycline 2 x 100 mg per day (4 months)	Triamcinolone acetonide (TAC) intralesional injection	Laser therapy
TAC intralesional injection	Laser therapy	Surgical: local or wide excision
Surgical: local excision	Surgical: local or wide excision	

PGA: Physician global assessment scale

In the second line of biologic treatment, it is recommended to administer acitretin (0.25-0.88 mg/kg, 3-12 months), and in the third line it is possible to use dapsone (25-200 mg for 3 months), cyclosporine A (2-6 mg/kg for 6 weeks to 6 months), zinc gluconate (90 mg), isotretinoin (0.5-1.2 mg/kg/day for 4-12 months), hormone therapy and botulinum toxin. In case of hormone imbalance, after the recommendation of the endocrinologist, hormone therapy is included: metformin, cyproterone acetate + ethinyl oestradiol, finasteride, spironolactone.⁸⁻¹⁰

One of the latest trends in treating HS is the use of the monoclonal antibody adalimumab (Humira). Adalimumab has a selective immunosuppressive effect and it reduces the inflammatory process in diseases in which it is used for therapy. The active substance, adalimumab, is a human monoclonal antibody derived from cell culture. Monoclonal antibodies are proteins that recognise and bind to other specific proteins. Adalimumab binds to specific proteins (tumour necrosis factor or TNF α), which is present in increased concentrations in inflammatory diseases. According to the recommendations of the Agency for Medicinal Products and Medical Devices of Bosnia and Herzegovina, it is used for the treatment of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, enthesitis-related arthritis, ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis, psoriatic arthritis, psoriasis, HS, Crohn's disease, ulcerative colitis and non-infectious uveitis affecting the back of the eye. The recommended dosing regimen for adalimumab for adult patients with purulent inflammation of the sweat glands is the initial dose of 160 mg on the first day (given as four 40 mg injections in one day or two 40 mg injections per day for two consecutive days), followed by dose of 80 mg two weeks later, on day 15 (administered in the form of two injections of 40 mg in one day). Two weeks later (day 29), the treatment continues with a dose of 40 mg every week. If necessary, the use of antibiotics can be continued during treatment with adalimumab. It is recommended for the patient to use a local anti-septic solution daily to treat lesions caused by purulent hidradenitis during treatment with adalimumab. In case there is no improvement even after 12 weeks, it is necessary to carefully consider the continuation of the treatment of such a patient. If treatment needs to be temporarily discontinued, adalimumab may later be reintroduced at a dose of 40 mg every week.¹¹

It is necessary to point out the positive effects of radiotherapy, ie of low-dose radiation of the affected region. Although the radiobiological effect of radiation on benign lesions has not been defined yet, there are several assumptions about achieving a favourable therapeutic effect of ionising radiation. It is believed that the effect of ionising radiation in the treatment of HS is based on the destruction of inflammatory cells and the release of mediators, cytokines and proteolytic enzymes. Before starting the treatment, a treatment protocol is established for each patient, which includes precise determination of the target volume, therapeutic dose, number of fractions and total dura-

tion of treatment. According to the protocol, it is necessary to determine the organs at risk (thyroid gland, eyes, gonads, breasts, bone marrow) that need to be protected during radiation.¹²

Surgical treatment may include incision and drainage of individual changes, superficial excision or wide excision, depending on the clinical severity. Incision and drainage are applied with minor changes but are avoided due to frequent recurrences. Superficial excision does not require general anaesthesia, the appearance of a scar is acceptable and there is a small number of recurrences. Wide excision is used in long-term and severe cases of Hurley III. It is recommended to apply the coverage with a skin autograft, and it is significant there is a possibility of local flaps in inaccessible regions.^{13,14}

The paper objective was to present new modalities in management and treatment of HS.

Methods

The subjects in this research included the patients who were treated in the University Clinical Centre of the Republic of Srpska (UCC) for the past three years. The subjects were treated with various topical, systemic antibiotics and retinoids.

Due to the duration of the disease and the failure of the therapy used, specialists in dermatovene-reology suggested further treatment with biolog-

Table 3: The Modified Hidradenitis Suppurativa Score as modified by Sartorius, HSS score

Analysed factors	Manner of calculation
Anatomic region involved (armpit, pectoral, inguinal, perianal, perineal)	Number of regions involved x 3
Type of lesions	Number of fistulas x 4 Number of nodules x 2 Number of abscesses x 1 Number of scars x 1 Other changes (folliculitis, pustules) x 0.5
Total skin surface affected with lesions Distance between lesions or Size of the lesion, if only one lesion is present in the region	Number of regions with the distance of less than 5 cm between two lesions x 2 Number of regions with the distance from 5 to 10 cm between two lesions x 4 Number of regions with the distance of more than 10 cm between two lesions x 8
Are all lesions clearly separated by normal skin?	Yes - 0 points No - 6 points

Table 4: Severity Assessment of Hidradenitis Suppurativa, SAHS score

Score / Category	Number of regions involved	Number of inflamed and/or painful lesions besides fistulas	Number of fistulas	Number of new or extended existing abscesses during the last 4 weeks	Pain Rating (NRS 11)
0	0	0	0	0	0 - 1
1	1 - 2	1 - 4	1 - 2	1 - 2	2 - 4
2	3 - 4	5 - 9	3	3 - 4	5 - 6
3	≥ 5	≥ 10	≥ 4	≥ 5	≥ 7

NRS 11: The Numeric Rating Scale;

ic therapy, surgical therapy or, more recently, the use of radiotherapy in the treatment of HS.

The effects of treatment of HS were monitored:

- by applying biologic therapy with adalimumab or adalimumab biosimilars in 4 patients treated at the Clinic for Skin and Venereal Diseases UCC,
- using radiotherapy in 4 patients treated at the Affidea Radiotherapy Centre in Banja Luka, and
- using surgical therapies (skin autografting and reconstruction of the defect with local lobes) in 17 patients treated at the Clinic for Plastic and Reconstructive Surgery UCC.

All subjects had a severe form of HS (Hurley II/III).

To evaluate the effectiveness of biologic therapy, the Hidradenitis Suppurativa Clinical Response Score (HiSCR) was used, which implies a positive effect of treatment-regression of more than 50 % of changes (abscesses and nodules), without the occurrence of new abscesses and fistulas.

The Sartorius score is more dynamic and it provides a more detailed evaluation of HS. The score takes into account: the region of the body involved, the number and types of lesions, the longest distance between two lesions, whether all lesions are clearly separated by normal unaffected skin. Three points are given in each category to give a regional and overall score (Table 3). The Sartorius score is used primarily for research purposes, whereas the Hurley staging is more commonly used in clinical settings.⁵

The criteria for monitoring the clinical severity of HS should be simple to use in clinical practice, dynamic (able to measure the chronic recurrent nature of the disease), sensitive enough to measure treatment outcomes and time-efficient. Based on these, the new scoring system - Severity Assessment of Hidradenitis Suppurativa (SAHS) score has been designed (Table 4).¹⁵

Each item is scored accordingly and calculated for an overall SAHS score with an upper limit of 15. Mild form of the disease is considered for the SAHS score of 4 or less, moderate form of the disease is considered for the SAHS score of 5 to 8 and severe form of the disease is considered for the SAHS score of 9 or higher.

Due to a small number of subjects, especially in patients treated with biologic and radiotherapy, it was not possible to perform any statistical analysis and therefore the results were presented by description, in tables and photographs.

Results

Patients treated with biologic therapy

Biologic therapy with adalimumab or adalimumab biosimilars was administered to 4 patients suffering from HS at the Clinic for Skin and Venereal Diseases of the UCC. Adalimumab was administered subcutaneously in two ampules of 40 mg (the total of 80 mg) twice a month. According to the clinical severity, all four patients had Hurley III stage. All patients were male. The youngest patient was 21 and the disease appeared at the age of 14. The oldest patient was 53, and the disease appeared at the age of 34 and in two patients between the ages of 20 and 30. In terms of localisation, the changes in all patients were extensive and involved multiple regions: axillary, submammary, lumbosacral, scrotum and groin and gluteal (Figures 1a, 2a). All four patients had a negative family history of HS and they were all smokers. The most common comorbidities included obesity, arterial hypertension, ulcerative colitis, acne conglobata, fistula perianalis complexa, pilonidal sinus, anxiety and depression. Regression of changes by 60-70 % in all 4 patients was observed in the 12th week from the beginning of the therapy (Figure 1b, 2b).



Figure 1-a: Hidradenitis suppurativa of the inguinal region before the therapy with adalimumab



Figure 2-a: Hidradenitis suppurativa of the axillary region before the therapy with adalimumab



Figure 1-b: Hidradenitis suppurativa after 12 weeks of the therapy with adalimumab



Figure 2-b: Hidradenitis suppurativa of the axillary region after 12 weeks of therapy with adalimumab

Patients treated with radiotherapy

For the past two years, four patients with HS were treated at the Affidea Radiotherapy Centre in Banja Luka. They were all men and their average age was 33. Table 5 shows the data on the localisation of changes, as well as the total dose and number of fractions in patients treated with radiotherapy.

The patients were examined by a dermatologist one month and three months after applying the last dose of radiation, noticing the improvement and regression of changes by 60-70 % compared to the examination before applying radiotherapy (Figure 3a, 3b, 3c).

Surgical treatment

For the past three years, 17 patients with HS have

Table 5: Overview of patients treated with radiotherapy regarding age, sex, localisation of changes and dose/number of fractions received by the patient

Age	Sex	Localisation	Dose (Gy) / number of fractions
59	Male	Gluteus	5 Gy / 5 fractions
21	Male	Gluteus	5 Gy / 10 fractions
28	Male	Abdominal wall	5 Gy / 5 fractions
25	Male	Axillae, on both sides	5 Gy / 10 fractions

*Gy (Gray)

been treated at the Clinic for Plastic and Reconstructive Surgery of the UCC (Table 6).

The average age of patients was 43 years. The oldest patient was 74 years old and the youngest was 17 years old. The patients were mostly male, 13 of them and 4 patients were female. According to the



Figure 3-a: Hidradenitis suppurativa of the gluteal region before applying radiotherapy



Figure 3-b: Hidradenitis suppurativa one month after applying the last dose of ionising radiation



Figure 3-c: Hidradenitis suppurativa three months after applying the last dose of ionising radiation

Table 6: Overview of patients treated with surgical therapy with regard to age, sex, localisation of changes, type of surgery and duration of treatment

Age	Sex	Localisation	Type of surgery	Duration of treatment / day
44	Male	Axillae, on both sides	Skin autografting	12
52	Male	Scrotum and pubic area	Skin autografting	15
74	Male	Gluteal, on both sides	Skin autografting	13
27	Male	Axillae, on both sides	Skin autografting	14
42	Male	Axilla, on one side	Defect reconstruction with a local flap	4
43	Male	Scrotum	Skin autografting	17
32	Male	Axilla, on one side	Defect reconstruction with a local flap	4
39	Male	Axilla, on one side	Defect reconstruction with a local flap	5
50	Female	Axillae, on both sides	Defect reconstruction with a local flap	4
21	Female	Axilla, on one side	Skin autografting	9
50	Male	Axillae, on both sides	Skin autografting	10
31	Male	Axillae, on both sides	Skin autografting	12
43	Male	Axillae, on both sides	Skin autografting	12
17	Female	Axillae, on both sides	Skin autografting	12
45	Male	Axillae, on both sides	Skin autografting	17
43	Male	Scrotum	Skin autografting	13
73	Female	Axillae, on both sides	Skin autografting	12

localisation in 13 patients the changes involved the axillary region, in three patients hidradenitis affected the scrotum and in one patient it involved the gluteal region.

Regarding the type of surgery, 13 patients underwent skin autografting (Figure 4a) and in 4



Figure 4-a: Hidradenitis suppurativa after surgical therapy – skin autografting



Figure 4-b: *Hidradenitis suppurativa, completed recovery after the surgical procedure*

patients defect reconstruction with a local flap. The duration of the hospitalisation was from 4 to 17 days, 11 days on average. Complete recovery of the patient did not occur immediately after the end of hospitalisation, because complete healing and adaptation of the autograft is necessary. The positive effects of surgery are usually observed 15 days after the end of hospitalisation in case there are no postoperative complications and there is a proper wound healing and removal of sutures (Figure 4b). After a period of 6-8 weeks, in most cases the patient can return to his normal work commitments.

It should be mentioned that during the last two years, the number of surgeries, including the surgical treatment of patients with HS, was significantly lower due to the COVID-19 pandemic. Namely, there were occasional suspensions of surgeries or only surgeries involving acute diseases and malignancies were performed.

Discussion

HS is a chronic disease that most often affects apocrine gland-bearing areas of the skin. According to the information referred to in literature, it is more common in female, which is not in accordance with results in this study since the majority of subjects were male. The youngest subject was 17 and the oldest one was 74 years old. In most of presented subjects, the disease appeared immediately after puberty, which is in line with the previous research.^{2, 16} Lifestyle, obesity and smoking are in

direct correlation with the clinical severity of HS. The effect of sex hormones to occurrence and the course of the disease has been confirmed.¹⁷

Skin changes in the form of erythematous nodules, fistulas and scars are most often located in the armpits, groin, genital and gluteal region. Most of analysed subjects had axillary and gluteal changes and on the scrotum. In one subject, skin changes were located on the anterior abdominal wall and in the other below the breast (submammary on both sides). HS can also occur in both the occipital and retroauricular regions and on the eyelids.^{18, 19}

The treatment of severe forms of hidradenitis (Hurley II/III) (Hurley II and Hurley III) starts with the application of the systemic antibiotic therapy. According to the previous research, the best effect is achieved by using the combination of rifampicin and clindamycin in the daily dose of 600 mg for four months. Acitretin, which is recommended in treatment of mild to moderate forms of HS, may be used as the continuation of therapy in treating the severe forms of HS after achieving a good therapy response by using systemic antibiotics, since it decreases the inflammatory component in the dermis by inhibiting the chemotaxis of polymorphonuclear with a consequential decrease in production of inflammatory cytokines, particularly interleukin 6 (IL-6). Biologic therapy with monoclonal antibody adalimumab, which is the only approved biologic medicine for HS treatment, is the first line of treatment in moderate and severe forms of HS that had no response or tolerance to antibiotic therapy.²⁰⁻²³ The application of adalimumab in subjects resulted in regression of changes and improvement by 60-70 %.

Recently, Radiotherapy Centre Affidea started using ionising radiation for HS treatment. It is believed that the effect of ionising radiation in the HS treatment is based on the destruction of inflammatory cells and the release of mediators, cytokines and proteolytic enzymes. Radiation in small doses has the best effect in the early phase of inflammation when vasodilation, oedema and leukocyte accumulation are present. Endothelial cells have an important role in the further spread of inflammation.¹² After applying the dose of 5 Gy in 5 or 10 fractions, subjects had an improvement and regression of changes by 60-70 %. In addition to the treatment of HS, a positive effect was observed in the treatment of other benign diseases such as keloids, pterygium, endocrine orbitopathy, haemangiomas, gynaecomastia, endometrial

hyperplasia and other benign tumours of the central nervous system, soft tissues, bones and locomotor system.²⁴⁻²⁶

If we compared the effects of applying the biologic therapy and radiotherapy in treating severe forms of HS, we could conclude that they both brought significant regression of changes and improvement. During the research, we had a small number of subjects treated with biologic and radiotherapy, so this conclusion should be taken with a reserve. Also, when selecting the therapy, it should be taken into consideration that the costs of biologic therapy are significantly higher compared to the cost of radiotherapy.

Subjects from this study achieved the best results after surgical therapy, ie after skin autografting and reconstruction of the defect with a local flap. They were able to return to their normal life activities after a period of 6-8 weeks. Data from the literature confirm that surgical therapy has the best results in treating severe forms of HS. Surgical therapy is applied in case all previous protocols did not give satisfactory results.^{13, 14, 27}

Conclusion

The recommended therapies for treatment of severe forms of HS include the application of biological therapy, radiotherapy and surgical therapy. The application of biological and radiotherapy both provide similar results after the 12 weeks of treatment, bringing the regression of changes by 60-70 %. The best results in HS treatment were achieved using surgical therapy.

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None.

Conflict of interest

None.

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