Case Report

Hidradenitis suppurativa-associated lymphedema: a case and review of the literature

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Abstract

Hidradenitis suppurativa is a chronic inflammatory skin disorder characterized by painful recurring pustules, nodules, abscesses, and sinus tract formation. Secondary lymphedema associated with hidradenitis suppurativa is an uncommon but severe condition, often resulting in significant morbidity. Although the exact link between lymphedema and chronic hidradenitis suppurativa is not fully understood, the chronic inflammatory process with scarring is likely an important factor. Herein, we reported a 52-year-old man with untreated chronic hidradenitis suppurativa, nonalcoholic fatty liver disease-related cirrhosis, and secondary massive scrotal lymphedema, complicated by cellulitis and sepsis. Despite appropriate treatment, the patient's condition deteriorated, and he unfortunately passed away two weeks after hospitalization. Additionally, we reviewed the literature on hidradenitis suppurativa-associated lymphedema, analyzing data from 51 patients. The majority were men with long-standing severe hidradenitis suppurativa. Surgical intervention was identified as the most commonly effective treatment modality, offering substantial improvements in function and appearance. However, some patients experienced adverse postsurgery events. In conclusion, this report highlights the importance of early detection and management of hidradenitis suppurativa and its complications to prevent patients' significant morbidity.

Introduction

Hidradenitis suppurativa (HS) is a chronic and recurrent inflammatory skin condition involving the follicular epithelium and apocrine glands, leading to follicle blockage. It primarily affects the axillae, groin, buttocks, and inframammary regions and is characterized by painful recurring pustules, nodules, abscesses, and sinus tracts.[1] Hidradenitis suppurativa can also result in contractures, scarring, obstruction of lymphatic channels, and an accumulation of lymph in the interstitial space causing lymphedema, predominantly in the genital area.[2] Although the prevalence of HS is reported to be around 1%, cases of lymphedema following HS are relatively uncommon, with only a few published cases.[3] It is important to note that patients with HS already have a significantly reduced quality of life and the presence of lymphedema can further worsen their condition by causing pain, deformity, and impaired functionality, along with various psychosocial complications.[4] Lymphedema can also lead to ulceration, an increased risk of malignancies such as angiosarcoma, and recurrent infections like cellulitis and erysipelas.[5] Considering these potential side effects, clinicians must examine and detect early signs and symptoms of lymphatic obstruction in HS patients and prevent their progression. Herein, we present an advanced case of massive scrotal lymphedema secondary to chronic HS, which was further complicated by cellulitis and sepsis.

Case Synopsis

A 52-year-old man with an 18-year history of HS and a two-year history of nonalcoholic fatty liver disease-related cirrhosis presented to the emergency room with abdominal distention, shortness of breath, orthopnea, and malaise for two weeks. He also complained of progressive swelling in both lower limbs and genitalia. De-

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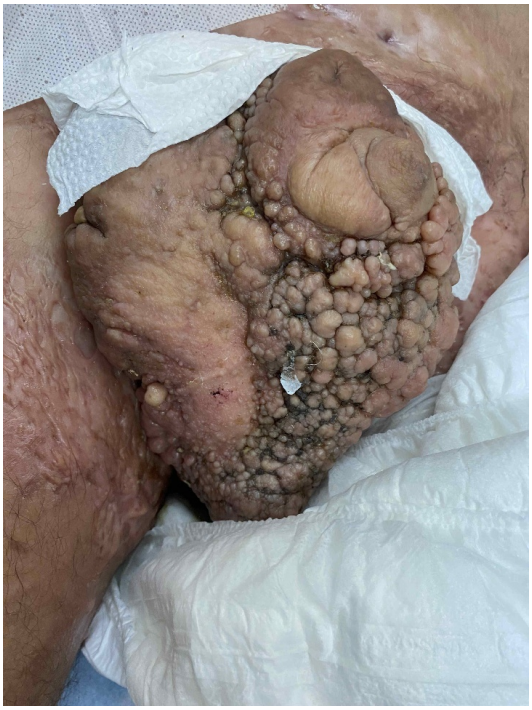

Figure 1. *The scrotum was massively enlarged and indurated, obscuring the penis. Multiple asymptomatic draining skin-colored papules and nodules were evident on the scrotum.*

spite previous surgical interventions for HS, the disease remained active in the anogenital region, leading to massive scrotal lymphedema over the past few years. He had developed significant swelling in his genitalia with accompanying nodules giving an elephantiasis nostra verrucosa cutis appearance. The lymphedema had been present for the past 8 years, with significant worsening over the last two years, culminating in recurrent infections in the affected area. Approximately 7 months prior to hospitalization, mild generalized edema was detected during clinic visits and gradually worsened over the subsequent months. Over the two weeks prior to hospitalization, an infection in the lymphedematous area caused further deterioration of the patient's condition, including an exacerbation of the generalized edema. In addition to his HS and cirrhosis, he also had hypothyroidism and atrial fibrillation treated with levothyroxine and apixaban, respectively. He had a smoking history of 20 pack years and used oral opium, but he did not report any alcohol consumption.

On physical examination, the patient was ill but conscious and had low blood pressure, symmetric pitting edema in both lower limbs, and abdominal distention. His scrotum was massively enlarged obscuring the penis. He exhibited multiple skin-colored nodules and clear malodorous discharge. Induration and scarring were noted in the axillae and groins, with no active inflammatory lesions (Figure 1). Pulmonary auscultation revealed decreased sounds at the lung bases.

Laboratory tests revealed a markedly elevated leukocyte count (16,500/mm^3; normal range: 4,000-11,000/mm^3), predominately segmented neutrophils, indicating significant inflammation. Platelet count was severely reduced (58,000/mm^3; normal range: 150,000-450,000/mm^3), consistent with advanced portal hypertension and hypersplenism. Hemoglobin was significantly decreased (8.2g/dl; normal range: 13.5-17.5g/dl for men), with a normal mean corpuscular volume of 85fl (normal range: 80-100fl), indicating normocytic anemia likely related to chronic disease and hypersplenism. Renal function tests showed elevated serum creatinine (2.8mg/dl; normal range: 0.6-1.2mg/dl) and blood urea nitrogen (32mg/dl; normal range: 7-20mg/dl).

Liver function tests demonstrated severe impairment, with total bilirubin elevated to 6.5mg/dl (normal range: 0.1-1.2mg/dl) and direct bilirubin at 3.0mg/dl (normal range: 0.0-0.3mg/dl), reflecting pronounced cholestasis. Serum alanine aminotransferase was mildly elevated (50U/l; normal range: 7-56U/l), whereas aspartate aminotransferase was significantly higher (100U/l; normal range: 10-40U/l). The aspartate aminotransferase to alanine aminotransferase ratio remained >2, characteristic of cirrhosis. Alkaline phosphatase was elevated (165U/l; normal range: 44-147U/l). Serum albumin was critically low at 2.0g/dL (normal range: 3.5-5.0g/dl), indicating profoundly impaired hepatic synthetic function. Prothrombin time was prolonged by 8 seconds (normal range: 11-13.5 seconds), corresponding to an international normalized ratio of approximately 2.1, reflecting significant coagulopathy.

Markers of systemic inflammation were notably elevated, with C-reactive protein at 50mg/l (normal range: <10mg/l) and an erythrocyte sedimentation rate of 55mm/hr (normal range: 0-20mm/hr), consistent with advanced liver disease and ongoing systemic inflammation. This profile is indicative of decompensated cirrhosis with a high Child-Pugh score, signifying severe hepatic dysfunction.

Abdominopelvic ultrasonography revealed ascites and subcutaneous fluid accumulation whereas a chest computed tomography scan showed bilateral pleural effusion. Echocardiography indicated normal cardiac ejection fraction despite atrial fibrillation rhythm. A punch biopsy was taken from the scrotal nodules, revealing dilated lymphatic vessels in the dermis, suggesting lymphangiectasis (Figures 2-3). Based on clinical presentation and laboratory findings, the patient was diagnosed with elephantiasis nostra verrucosa cutis resulting from chronic lymphedema secondary to HS, further complicated by ascites. Decompensated liver failure and hepatorenal syndrome complicated by infection, was considered the cause of the exacerbation of peripheral edema, pleural effusion, and ascites. Despite treatment with intravenous fluids, antibiotics, and diuretics, the patient's condition deteriorated, and he unfortunately passed away after two weeks of hospitalization due to sepsis and liver failure.

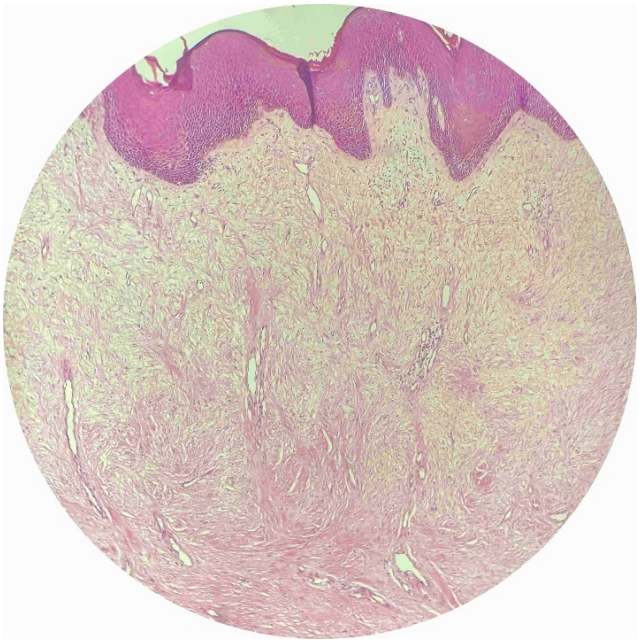

Figure 2. *Histopathologic slide from a punch biopsy of the scrotal nodule. Epidermal acanthosis and multiple ectatic lymphatics were noted in the papillary and middermis surrounded by an edematous stroma with mild infiltration of mononuclear inflammatory cells (hematoxylin-eosin stain; original magnifications, x20).*

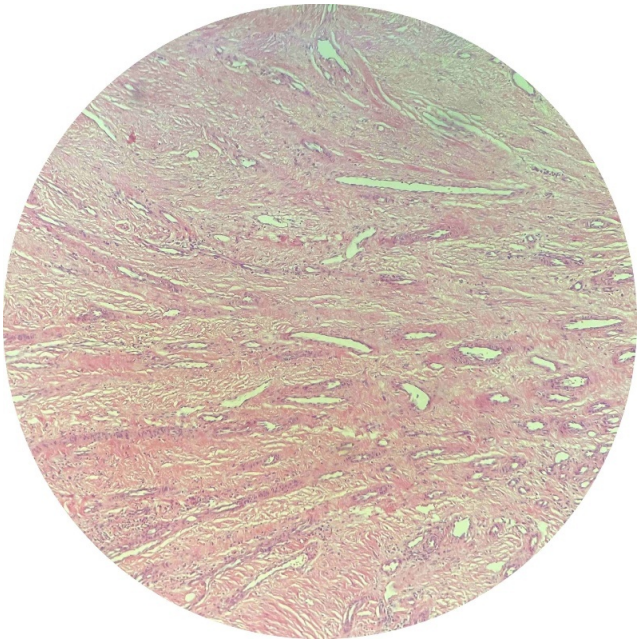

Figure 3. *Histopathologic slide from a punch biopsy of a scrotal nodule showed dilated and angular lymphatic vessels lined by a single layer of endothelial cells within the dermis (hematoxylin & eosin stain; original magnifications, x40).*

Discussion

Lymphedema secondary to HS is uncommon and severely debilitating. In HS, as seen in other diseases chronic, recurrent inflammation and scarring can lead to lymphatic channel blockage, lymphatic malformations, and lymphedema, although the exact mechanism remains unclear.[6,7] The most common site of HS-induced lymphedema is the penoscrotal region. In addition, genital lymphedema typically appears four to 30 years after the onset of chronic HS.[8] Lymphedema can cause recurrent infections, such as erysipelas and skin ulcers, exacerbating the HS condition and creating a vicious cycle.[5]

We present a patient with severe, neglected HS resulting in penoscrotal chronic lymphedema and lymphangiectasis, which had been a longstanding complication of HS for eight years and progressed to an elephantiasis nostra verrucosa cutis appearance over the last two years. The patient had discontinued treatment for several years owing to discouragement over the chronic nature of the disease and the limited effectiveness of prior therapies. Additionally, his cirrhosis contributed to generalized edema, which became more prominent in the last seven months prior to hospitalization. The combination of chronic lymphedema and cirrhosis-associated edema created a complex clinical picture. An acute infection in the lymphedematous area triggered a cascade of events, including exacerbation of generalized edema, the onset of hepatorenal syndrome, and sepsis, ultimately resulting in rapid deterioration and death.

We thoroughly reviewed the literature using "lymphedema" and "HS" as keywords. In total, 51 patients were included, with 28 from individual case reports (Table 1) and 23 from case series (Table 2). The patients ranged from 24 to 67 years old, with most in their early 40s. The majority were men, but 11 (21.5%) were women, showing that HS with lymphedema is more common among men, consistent with the previous studies.[8] The duration of HS among these patients ranged from two years to over 30 years, with many experiencing symptoms since adolescence, highlighting the chronic and persistent nature of HS in developing lymphedema.[8]

Considering HS severity and lymphedema location, all patients except one, had Hurley Stage III HS, indicating severe disease with extensive scarring and fistula formation (Table 3). Lymphedema was most commonly found in the penoscrotal region, although it also affected the inguinal, perineal, abdominal, and pubic areas.[12,27,33] Several patients experienced significant complications as a result of HS and lymphedema, such as micturition dysfunction, impotence, and recurrent infections.[12,14,17]

In general, there is insufficient data to support the effectiveness of medication alone in the treatment of HS lymphedema.[8] Based on the current review, lymphedema was treated exclusively with medication in 11 individuals (21.6%). This treatment included biological agents such as infliximab and adalimumab, as well as other medications like minocycline and isotretinoin. The response to medical treatment varied from no improve-

Table 1. *Overview of Case Reports on Lymphedema in Hidradenitis Suppurativa: Basic Information, Treatment, and Outcomes.*

	Reference	Age/Sex	HS Duration (years)	HS Severity and Lymphedema Location	Treatment Type	Outcome
1	Moosbrugger et al.[9]	33 / F	15	Hurley Stage III, vulvar and perineal	Excision of involved skin, split-thickness skin graft	Excellent results
2	Bains et al.[10]	35 / F	Since adolescence	Hurley Stage III, perineum and pubic region	Isotretinoin, tapering course of prednisolone	Decrease in seropurulent discharge; refused surgery
3	Wrone et al.[11]	41 / F	10	Hurley Stage III, vulva and perineum	Total vulvectomy, split-thickness skin graft, abdominal skin flap	NS
4	Musumeci et al.[12]	24 / M	Since puberty	Hurley Stage III, pubic and penoscrotal	Circumcision	Significant improvement, decreased shaft lymphedema, resolved micturition dysfunction
5	Fernandes et al.[13]	38 / M	NS	Hurley Stage III, penoscrotal elephantiasis	Radical excision of penile and scrotal skin and subcutaneous tissue, partial split-thickness skin graft	Satisfactory cosmetic and functional results
6	Snyder et al. 2020 [18]	39 / M	20	Hurley Stage III, scrotum elephantiasis	Debridement of infected skin, split-thickness skin graft	The surgery site healed well.
7	Fania et al. 2019 ?[30]	39 / M	NS	Hurley Stage III, penoscrotal	NS	NS
8	Smith et al.[14]	40 / M	20	Hurley Stage III, anogenital and inguinal	Excision of inguinal and scrotal disease, split-thickness skin graft	Functional and cosmetic improvement; reduced penile lymphedema
9	de Vasconcelos et al.[15]	40 / M	22	Hurley Stage III, perineal and scrotum	Complete excision of affected tissue, partial-thickness skin graft	Improved quality of life
10	Corder et al.[16]	2 male patients, average age: 40	NS	NS, scrotum, and buried penis lymphedema	Penile excavation, split-thickness skin graft for penile epithelization	Highly satisfied outcomes; significant scrotal edema postoperatively
11	Yu et al.[17]	41 / M	25	Hurley Stage III, scrotum	Excision of interstitial edema tissue of the scrotum, inverted tunica vaginalis fixed, subcutaneous lymphatic tissue flap	Satisfactory cosmetic results; recovery of sexual function
12	Rubaian et al.[18]	42 / M	9	Hurley Stage III, penoscrotal	NS	NS
13	Hazen et al.[19]	43 / M	NS	Hurley Stage III, inguinal, scrotal, and perineal regions	CO2 laser excision of large affected areas	Complete resolution of lymphedema; postoperative Hurley Stage I
14	Konety et al.[20]	46 / M	NS	Hurley Stage III, perineum	Wide excision of scrotum and perineum, split-thickness skin graft, skin flap, secondary intention	Complete resolution of lymphedema; resumed satisfactory sexual function
15	Moschella et al.[21]	46 / M	20	Hurley Stage III, penis and scrotum	Infliximab infusions (5 mg/kg) and minocycline, 100 mg twice daily	Genital hidradenitis sufficiently cleared; referred for surgery
16	Patil et al.[22]	47 / M	2	Hurley Stage III, penoscrotal	Lost to follow-up	NS
17	Kok et al.[23]	49 / M	13	Hurley Stage III, perineum, penoscrotal	Excision of edematous mass, refashioning of remaining skin	Symptom-free, full return to function

	Reference	Age/Sex	HS Duration (years)	HS Severity and Lymphedema Location	Treatment Type	Outcome
18	Coseriu et al.[24]	50 / M	32	Hurley Stage III, penoscrotal	Wide surgical excision, skin flaps, split-thickness skin graft for the penis	Good cosmetic and functional outcome
19	Jimenez Gomez et al.[25]	52 / M	Since adolescence	Hurley Stage III, penoscrotal	Debridement of affected tissue; adalimumab started after surgery	Persistent pain and suppuration; HS controlled after adalimumab
20	Thomas et al.[26]	52 / M	25	Hurley Stage III, scrotum	Laparoscopic sleeve gastrectomy, acitretin	Lymphedema improved but still present; HS quiescent
21	Caposiena Caro et al.[27]	54 / M	3	Hurley Stage III, inguinal region	Adalimumab	Reduction in tenderness and discharge; no improvement in lymphedema
22	Baughman et al.[28]	55 / M	20	Hurley Stage III, penis	Excision of indurated penile tissue, reconstruction with full-thickness dorsal skin flap from abdominal skin	Minimal recurrent induration; normal sensation, voiding, and erectile function
23	Khan et al.[29]	1: 30 / M, 2: 58 / M	1: 4 2: 15	1: scrotum, inguinal 2: scrotum, perineum	Massive excision of scrotal mass	NS
24	Ghassan et al.[30]	58 / M	15	Hurley Stage III, scrotum	Wide excision of scrotum and perineum with skin flap	NS
25	Good et al.[31]	58 / M	Adult life	Hurley Stage III, scrotum	NS	NS
26	Garcovich et al.[32]	67 / M	7	Hurley Stage III, penoscrotal	NS	NS

Abbreviations: F, female; HS, hidradenitis suppurativa; M, male; NS, not stated.

ment to significant management of the condition using the aforementioned drugs.[10,21,27,33] Although medical therapy is essential for managing the disease's inflammatory component, a combined surgical and medical approach is the best way to treat HS and its complications.[38]

According to our review, surgery was the most frequently reported effective treatment for HS-induced lymphedema. Various surgical techniques have been shown to be effective, including wide surgical excisions, debridement, circumcisions, and carbon dioxide laser excisions.[12,19,24,39] Significant improvements in both functional and cosmetic outcomes following surgical procedures have been documented in numerous studies.[9,13,17,23,24] Despite many successes, some adverse events and incomplete treatment outcomes were reported, for example, in a study by Jimenez Gomez et al.[25] Ongoing pain and suppuration even after debridement and skin grafting were reported. Lelonek et al noted pain in two patients, contracture in one, and infection in another following wide excision and combined surgical techniques.[34] Moreover, wound breakdown, graft loss, and cellulitis were also reported as postsurgery complications.[16,35] Therefore, further research is needed to establish a standardized treatment approach exclusively for lymphedema secondary to HS.

The follow-up durations ranged from three months to three years in different studies.[28,34] Encouragingly, the majority of studies found no relapses during their follow-up periods. For example, Yu et al[17] and Chen et al[35] observed no relapses after their respective procedures. However, longer follow-ups are crucial for evaluating the enduring efficacy of these surgical interventions and tracking any potential recurrences.

The findings of this literature review emphasize the importance of a team approach involving dermatologists, surgeons, and psychiatrists to optimize outcomes. Personalized treatment approaches are required for managing HS-associated lymphedema. The reassuring therapeutic response in many cases indicates that surgical intervention can significantly improve a patient's quality of life. However, persistent complications in some cases highlight the necessity of ongoing care and monitoring. It is essential to educate patients about the chronic nature of HS and the possibility of recurrence to set realistic expectations and ensure adherence to post-operative care as well as psychiatric support. Furthermore, physicians should take lymphedema seriously and encourage patients to seek medical care promptly owing to the probability of severe outcomes such as those reported in this study.

Table 2. *Overview of Case Series on Lymphedema in Hidradenitis Suppurativa: Basic Information, Treatment, Outcomes, and Side Effects.*

	Reference	Age/sex	HS Duration (years)	HS Severity and Lymphedema Location	Treatment type	Outcome	Adverse effect
1	Sanchez-Diaz et al. 2021[33]	1: 30 / F 2: 47 / M 3: 55 / M	1: 12 2: 6.25 3: 2.5	1: Hurley Stage III Groin, Genital 2: Hurley Stage III Groin, Abdomen 3: Hurley Stage II, Perianal,	1,2: biologic and other medication 3: Surgical excision and reconstruction with skin graft	1,2: moderate control of the disease 3: improvement of the disease in the genital area	NS
2	Lelonek et al. 2021[34]	4 male, 3 female, Mean age: 41.0 ± 8.6	Mean disease duration: 14 ± 7.3	Hurley Stage III Genital elephantiasis	Wide excision of affected genital areas, partial suture with secondary intention healing, graft, local flap techniques	Good cosmetic and functional effect	Pain (2 patients), contracture (1 patient), infection (1 patient)
3	Chen et al. 2014[35]	6 patients, average age: 49 (41–66), 2/6 lymphedema	NS	Scrotal involvement in all, perineal involvement in 3	Radical excision, split-thickness skin graft	Excellent cosmetic results	Penile edema (1), small wound breakdown with no infection (2), wound breakdown with cellulitis (1)
4	Chu et al. 2013[36]	1: 43 / F 2: 44 / F 3: 55 / F 4: 58 / F 5: 55 / M	1: 25 2: 20 3: 15 4: NS 5: 30	1: Hurley Stage III, buttocks, 2: Hurley Stage III, labia majora 3: Hurley Stage III, buttocks 4: Hurley Stage III, abdomen 5: Hurley Stage III, buttocks and perineum	NS	NS	NS
5	Moriarty et al. 2014[37]	7 males, 6/7 had lymphedema	14–34	Hurley Stage III, Scrotum	biological therapies (five infliximab, two adalimumab), in combination with incision and drainage of lesions	NS	NS

Abbreviations: F, female; HS, hidradenitis suppurativa; M, male; NS, not stated.

Table 3. *Hurley Staging System for Hidradenitis Suppurativa.*

Hurley Stage	**Clinical Description**
Stage I	This stage is characterized by isolated or multiple abscesses that do not develop sinus tracts or result in scarring.
Stage II	In this stage, there are recurring abscesses accompanied by sinus tracts and scarring. These lesions are typically spread across multiple, distinct areas.
Stage III	This is the most severe stage, involving extensive or widespread areas with multiple interconnected sinus tracts and abscesses, leading to significant tissue damage and scarring.

Conclusion

This case report and literature review explain the severe consequences of untreated HS-related lymphedema, including life-threatening complications such as sepsis. It highlights the importance of early intervention, multidisciplinary care, and patient education to manage HS complications effectively. Further research is needed to develop standardized treatment protocols for lymphedema secondary to HS.

Potential conflicts of interest

The authors declare no conflicts of interest.

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