Genital lymphedema associated with hidradenitis suppurativa unresponsive to adalimumab treatment

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Key words: adalimumab; genital; hidradenitis suppurativa; lymphedema; surgery.

INTRODUCTION

Lymphedema is a disorder clinically characterized by swelling of the soft tissue caused by a blockade or destruction of local lymph drainage routes, resulting from chronic and recurrent episodes of inflammation and scarring. It may be idiopathic or secondary to filariasis, various types of cancer, radiotherapy, hydroelectrolytic imbalance, and inflammatory/granulomatous processes. Lymphedema usually affects the limbs but may be observed in any part of the body, including the genital area.[1] In this anatomic site, genital lymphedema (GL) is an uncommon, debilitating and probably underrecognized complication of long-standing and severe hidradenitis suppurativa (HS).[2] In a systematic review of 27 patients (mean age, 46 years; range, 38-58 years) presenting with GL secondary to HS, men were more affected, and the clinical presentation varied from soft to hard swelling of the penis and of the scrotum to induration and/or verrucous papules or nodules.[2] Complications of GL include lymphangiectasias, lymphangioma circumscriptum, infections, and neoplasms, such as lymphangiosarcoma and squamous cell carcinoma.[3] GL may also have a profound negative sexual, functional, and aesthetic impact in affected patients also impairing their quality of life. Finally, it can be therapeutically challenging, as surgery is usually effective with good functional but variable cosmetic results.[2] Recent reports, however, highlight the beneficial effects of tumor necrosis factor-α inhibitors on limb lymphedema associated with psoriatic arthritis,[4,5] rheumatoid arthritis,[6] and ankylosing spondylitis.[7] We report a case of a patient affected by HS whose GL was unresponsive to biologic therapy.

Abbreviations used:

HS: hidradenitis suppurativa
GL: genital lymphedema

CASE REPORT

A 24-year-old male patient, smoker, with a body mass index of 30 kg/m^2, affected by HS since puberty, presented with typical multiple inflammatory nodules, abscesses, and scars in the axillary regions. He also had moderate lymphedema of pubic and inguinal areas with multiple superficial and deep violaceous nodules of 0.5- to 2-cm diameter extending to the periumbilical region along with areas of sero-purulent drainage from multiple sinus tracts and diffuse hypertrophic scars. The scrotal area was spared (Fig 1). Ultrasound examination of the genital area (MyLab Touch, Esaote SpA, Genova, Italy, 15-18 MHz) found the presence of multiple fluid collections (abscesses and fistulae) and pseudocysts. Based on the clinical presentation and ultrasound features, HS severity was rated as Hurley 3.[8] The patient also complained of difficulty in micturition. Anamnestic data were negative for other notable diseases, and Crohn's disease was excluded by laboratory tests and by colonoscopy. The patient was previously treated with various topical and systemic antibiotics for several years with limited results. Treatment with subcutaneous administration

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Funding sources: None.
Conflicts of interest: Dr Musumeci Maria Letizia has received speaker fees from Eli Lilly and AbbVie. The rest of the authors have no conflicts to disclose.
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JAAD Case Reports 2019;5:326-8.
2352-5126

https://doi.org/10.1016/j.jdcr.2019.01.019

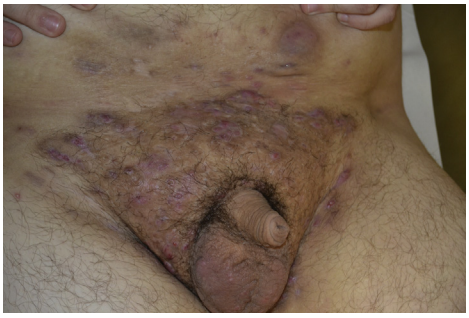

Fig 1. HS at baseline. Multiple superficial and deep violaceous nodules of 0.5 to 2 cm diameter with seropurulent drainage from multiple sinus tracts and diffuse hypertrophic erythematosus scars affecting the pubic area are present. Swelling of pubic and inguinal areas is evident.

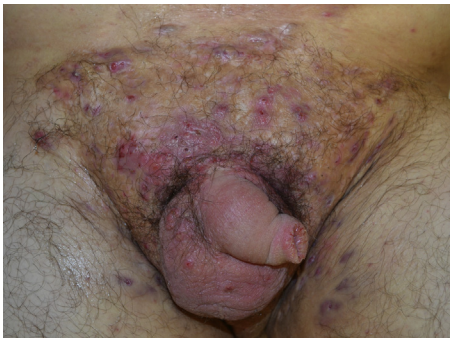

Fig 2. HS after 3 months of adalimumab therapy. The genital lymphedema had progressed with massive extension of the swelling in the pubic and scrotal areas. The involvement of the entire shaft eventually resulted in phimosis.

of adalimumab was started with an induction dose of 160 mg at baseline and 80 mg after 2 weeks followed by a standard dose of 40 mg once a week. After 3 months, the nodules, the abscesses, and the sinus drainage of the axillary, inguinal, and periumbilical areas progressively improved at clinical and ultrasound evaluations, whereas lymphedema worsened, resulting in a massive swelling of the pubic and scrotal areas involving the shaft, which after 1 week resulted in a severe phimotic stage (Fig 2). Because of the critical clinical presentation, the patient was sent for a surgical consultation and subsequently underwent circumcision resulting in significant improvement with decrease of shaft lymphedema and resolution of the micturition dysfunction. We advised the patient that if lymphedema worsened, a further surgical approach would be necessary.

DISCUSSION

Management of HS should consider disease severity, possible complications, patient's discomfort, and quality of life,[9] Adalimumab is the only biologic approved by the US Food and Drug Administration available for the treatment of HS in adult patients with an inadequate response to conventional systemic therapy. Several clinical trials on active and inflammatory lesions of HS have shown a significant response of adalimumab versus controls, even if the treatment dosage varied among different trials and no data were provided regarding long-term efficacy. In general, noninflammatory lesions such as scars and fibrotic tissue were unresponsive to adalimumab, thus requiring a surgical approach.[9] In our patient, adalimumab was able to control and improve inflammatory lesions but not GL,[4] and this could be explained with the presence of extensive scarring and fibrotic tissue in the genital area that may have hampered overall adalimumab efficacy.[9] Patients with HS presenting with mild genital lymphedema should be informed that adalimumab may be not effective and, if lymphedema progresses, surgery should then be considered. In case of severe GL at baseline, a prompt surgical approach should be suggested before starting adalimumab treatment. The presence of scar and fibrotic tissue that may affect treatment response should be carefully evaluated. However, further evidence is necessary to better define the role of adalimumab on HS-associated GL. Our case confirms that the treatment approach in patients affected by advanced HS and progressive lymphedema needs to be individualized based on the association of biologic therapy and surgery to restore normal anatomy and function of the organ involved.[2] However, timing needs to be better defined, and clinical trials evaluating effectiveness of biological agents combined with surgery are needed.[10] Early detection of HS-associated lymphedema is crucial, and a multidisciplinary approach is fundamental.[2]

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