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Exploring the connection between hidradenitis suppurativa and erythema nodosum: a case report

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Abstract

Background: Erythema nodosum (EN) is inflammation of subcutaneous fat. Etiologies include autoimmune diseases, drugs, infections, pregnancy, malignancy, and idiopathic origins. Case: A 37-year-old female with a history of recurrent cellulitis and type II diabetes presented with worsening swollen lumps on upper extremities for four months during a Hurley Stage III hidradenitis suppurativa (HS) flare. Exam revealed multiple erythematous pustules and warm indurated nodules over diffuse edema on the upper extremities. Lesions were refractory to trimethoprim/sulfamethoxazole, cefalexin, clindamycin and levofloxacin. Routine blood labs, ESR, and ANA were unremarkable. EN was diagnosed. Trimethoprim/sulfamethoxazole, saturated solution potassium iodide (SSKI) and ibuprofen were prescribed. At three week follow-up, EN had completely resolved except for one lesion. Discussion: Literature review revealed one case of EN manifestation in association with HS but was complicated by Beçhet's syndrome. We propose HS as an underlying cause of EN and SSKI an effective treatment for EN and HS.

Introduction

Erythema nodosum (EN) is a painful neutrophilic panniculitis affecting 1-5 per 100,000 people worldwide [1]. EN presents as tender, warm, dense, red subcutaneous nodules, frequently on the pretibial region, distributed bilaterally and symmetrically[2]. Although the 98% of cases are limited to the shins, EN on the arms, forearms, buttocks, trunk, and face have been reported[1]. The diagnosis of EN is mainly clinical, and biopsy is often unnecessary[1].

The pathophysiology of EN is complex as it results from a nonspecific reaction to a variety of antigens[3] . The immune response generated is classified as a Type IV delayed hypersensitivity reaction, and there is a strong association with granuloma forming diseases such as inflammatory bowel disease (IBD)[1] . Immune complexes deposit around vessels in the subcutis and subsequently, neutrophils are recruited to the site and can be seen on biopsy[1, 3]. Known triggers include autoimmune and inflammatory diseases, infection, medications, and malignancy, while up to 50% of cases occur idiopathically[1-3]. Here, we report a case of EN with a unique association to acute-on-chronic hidradenitis suppurativa treated with saturated potassium iodide solution (SSKI).

Case report

A 37 year-old female with a history of recurrent cellulitis, latent tuberculosis, type II diabetes and Hurley Stage III hidradenitis suppurativa (Figure 1) presented to dermatology with new painful nodules for four months duration during an acute-on-chronic HS flare. Physical exam revealed

multiple erythematous pustules and warm indurated nodules over diffuse edema on the upper extremities and on the left ankle. (Figure 1).

Ten months prior, she had an HS flare successfully treated by her infectious disease doctor with trimethoprim/sulfamethoxazole and cefalexin. Five months after this flare, she self-tapered off of adalimumab over concerns about the COVID-19 pandemic and, instead, exclusively focused on utilizing a gluten-free anti-inflammatory diet and daily Ibuprofen. A month after discontinuing adalimumab, she experienced acute-on-chronic flaring of her HS in addition to the appearance of several new types of lesions on her upper and lower extremities. The new lesions, managed by infectious disease, were refractory to trimethoprim/sulfamethoxazole and cefalexin and improved to various degrees with doxycycline, levofloxacin, and clindamycin. She stated that these HS flares and the delayed diagnosis and treatment of the new lesions on her extremities caused her significant distress, reducing her ability to focus and work.

Based on her symptoms, history, and physical exam, a clinical diagnosis of EN was made. Complete blood count, complete metabolic panel, erythrocyte sedimentation rate, thyroid stimulating hormone, and anti-nuclear antibody screen were all normal. At the time of exam, a biopsy was not taken due to prior negative cultures of her HS lesions performed by her infectious disease physician, patient's severity of symptoms, and classic presentation of her new lesions. Because her lesions were refractory to supportive management, NSAIDs, and antibiotics, she was started on SSKI 300 mg TID, in addition to trimethoprim/sulfamethoxazole DS TID and 800 mg Ibuprofen. Supportive measures, such as limb elevation, were also encouraged.

The patient's health insurance covered SSKI with prior authorization; however, the price was too expensive. Therefore, the patient's SSKI treatment was delayed a week in order to identify an affordable price for SSKI while she began trimethoprim-sulfamethoxazole and Ibuprofen in the interim.

Three days into SSKI treatment, the patient messaged the portal indicating the swelling and redness was resolving. However, she was experiencing a metallic aftertaste, a common side effect of SSKI solution. Eight days into SSKI treatment, the patient messaged again confirming that her upper extremities were clear and her left ankle was almost clear, improving with elevation. She also mentioned that new small red dots resembling pimples on her forearm had appeared. She was diagnosed with iododerma (Figure 4), and her SSKI was reduced to 200 mg TID which alleviated the acneiform eruption.

At 3-week follow-up, the patient's upper extremities were completely clear, and the nodule on the left ankle was reduced to a 1 cm firm, pink nodule. There were approximately 12 pustulopapules across the left and right dorsal upper extremities remaining from the iododerma, and

she was instructed to continue the SSKI for one week until she could restart adalimumab treatment in order to undergo plastic surgery for HS scarring in the pelvic region.

Discussion

EN is caused by many systemic, infectious and inflammatory disorders such as pregnancy, paraneoplastic syndromes and Crohn's disease[1, 2]. Similarly, HS is strongly associated with several autoimmune and inflammatory disorders, such as inflammatory bowel disease, rheumatoid arthritis, diabetes and metabolic syndrome (Table 1)[4-10]. There are several disorders associated with EN and HS that overlap, including Behçet's disease. Review of the literature found only one report of EN in the setting of HS which was complicated by Behçet's syndrome, but there have been no uncomplicated reports of EN occurring in the setting of HS[4]. Our case supports the association of EN and HS because the patient's HS flare preceded the onset of her EN lesions in the absence of an identifiable cause.

Hidradenitis suppurativa is an inflammatory follicular disease caused by hyperkeratosis and follicular plugging[5]. As a result, follicular ducts expand, and antigens leak out of the enlarged plugged pores due to mechanical stress. The pathogenesis of HS is hypothesized to involve the dysregulation of the innate and adaptive immune systems[9]. This immune dysregulation and antigen leakage may increase an individual's vulnerability to developing EN, which is caused by a hypersensitivity reaction to antigens.

Treatment of EN focuses on treating the underlying condition in addition to supportive measures such as rest and compression stockings[1]. Symptomatic management of pain can be achieved with non-steroidal anti-inflammatory drugs. EN that is refractory to other treatments can be treated with potassium iodide, which may increase expression of IL-10, an anti-inflammatory interleukin, or in serious cases be treated with steroids[11]. Potassium iodide is an inexpensive salt which can be easily formulated into SSKI. Her treatment was complicated by side effects, so the dose was reduced from 300mg to 200mg TID which effectively resolved the iododerma and her EN.

Conclusions

Erythema nodosum is typically a painful, idiopathic, neutrophilic panniculitis associated with a plethora of infectious and inflammatory conditions. Hidradenitis suppurativa is an inflammatory follicular disease which has also been associated with a variety of infectious and inflammatory conditions. The present case demonstrates a possible association between EN and HS and establishes a role for SSKI in treating refractory EN in the setting of HS.

References

1. Leung, A.K.C., K.F. Leong, and J.M. Lam, Erythema nodosum. World J Pediatr, 2018. 14(6): p. 548-554.
2. Perez-Garza, D.M., et al., Erythema Nodosum: A Practical Approach and Diagnostic Algorithm. Am J Clin Dermatol, 2021. 22(3): p. 367-378.
3. Schwartz, R.A. and S.J. Nervi, Erythema nodosum: a sign of systemic disease. Am Fam Physician, 2007. 75(5): p. 695-700.
4. Scheinfeld, N., Diseases associated with hidranitis suppurativa: part 2 of a series on hidradenitis. Dermatol Online J, 2013. 19(6): p. 18558.
5. Kurzen, H., et al., What causes hidradenitis suppurativa? Exp Dermatol, 2008. 17(5): p. 455-6; discussion 457-72.
6. Cartron, A. and M.S. Driscoll, Comorbidities of hidradenitis suppurativa: A review of the literature. Int J Womens Dermatol, 2019. 5(5): p. 330-334.
7. Shalom, G., et al., Hidradenitis suppurativa and metabolic syndrome: a comparative cross-sectional study of 3207 patients. Br J Dermatol, 2015. 173(2): p. 464-70.
8. Fimmel, S. and C.C. Zouboulis, Comorbidities of hidradenitis suppurativa (acne inversa). Dermatoendocrinol, 2010. 2(1): p. 9-16.
9. Scala, E., et al., Hidradenitis Suppurativa: Where We Are and Where We Are Going. Cells, 2021. 10(8).
10. Guet-Revillet, H., et al., Bacterial pathogens associated with hidradenitis suppurativa, France. Emerg Infect Dis, 2014. 20(12): p. 1990-8.
11. Hayashi, S., et al., Anti-Inflammatory Effects of Potassium Iodide on SDS-Induced Murine Skin Inflammation. J Invest Dermatol, 2020. 140(10): p. 2001-2008.

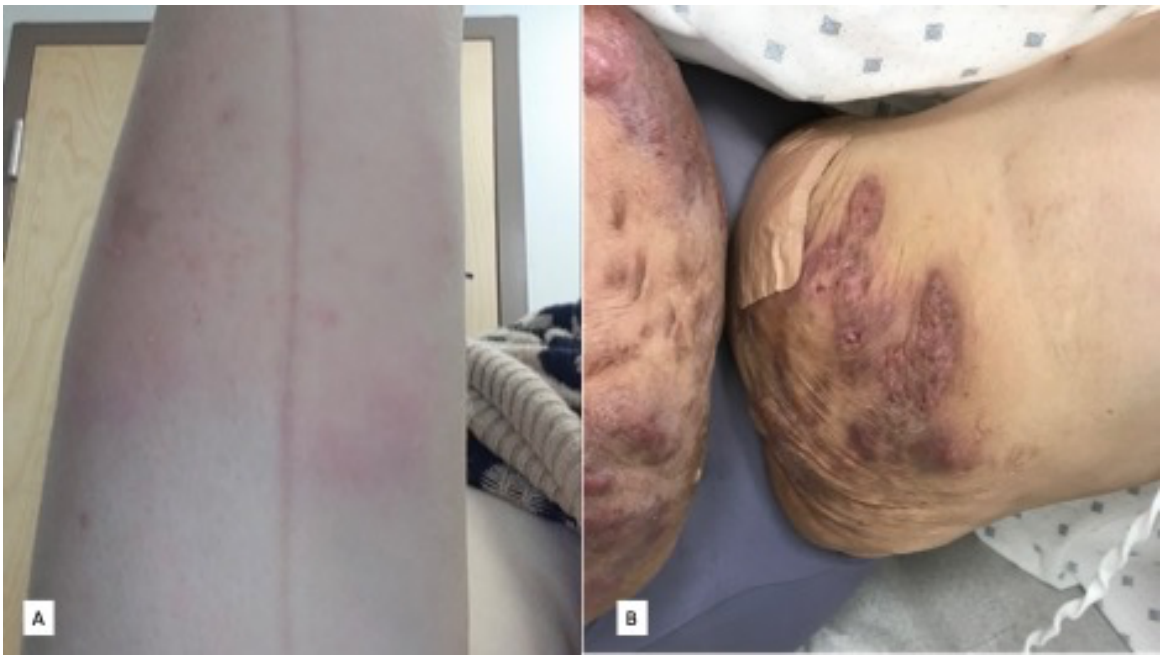

Figure 1. Clinical presentation of the patient. A) erythema nodosum on the right forearm; B) hurley stage III hidrantitis suppurativa in the groin.

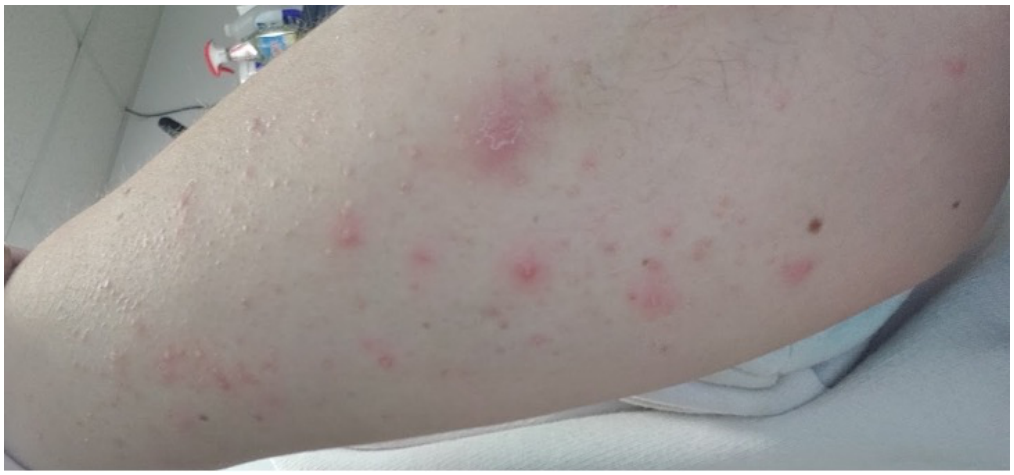

Figure 2. Iododerma eight days into supersaturated potassium iodide treatment.

Table 1. Associated diseases of erythema nodosum, hidranenitis suppurativa, or both.

	Associated Diseases of Erythema Nodosum	Associated Diseases of Hidradenitis suppurativa	Associated Diseases of Both EN and HS
Autoimmune/Inflammatory Disorders	Sweet Syndrome Sarcoidosis	Metabolic syndrome Pyoderma gangrenosum Acne conglobata Rheumatoid arthritis	Crohn's disease Ulcerative Colitis Behçet's disease
Infectious Causes	Tuberculosis Fungal- blastomycosis, histoplasmosis Viral- hepatitis B, infectious mononucleosis	Anaerobes Enterococcus	Staphylococcus Streptococcus