Single Case

Atypical Clinical Presentation of Hidradenitis Suppurativa in a Patient with Severe Mannose-Binding Lectin Deficiency

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Keywords

Acne inversa · Hidradenitis suppurativa · Mannose-binding lectin deficiency · Aseptic abscess · Immunodeficiency

Abstract

Mannose-binding lectin (MBL) deficiency is associated with recurrent infections, autoimmune and inflammatory skin disease, and vascular complications. MBL deficiency is not a recognized comorbidity in hidradenitis suppurativa (HS); the latter is associated with the group of autoinflammatory disorders. A 32-year-old woman presented with a history of recurrent painful, deep-seated abscesses and pustular lesions since the age of 13 years. Lesions were noted predominantly in HS distribution, i.e., submammary, inguinal, and perianal areas were affected. However, unusual locations (jawlines, neck) were also affected. The patient fulfilled the clinical criteria for HS but the presentation was atypical because lesions were noted in unusual locations, most lesions were in Hurley stage 1 (sparsity of sinus tracts and scarring), and most cultures from abscesses and pustular lesions were negative. The excruciating pain caused by

constantly developing abscesses had a profound impact on the patient's quality of life. Laboratory workup showed an exceptionally low serum MBL level. Treatment was challenging with only a temporary, mild response to oral antibiotic therapy and no response to immunosuppressive and hormonal therapies. This atypical HS presentation may reflect an enhancement of proinflammatory mechanisms. Health care providers should be aware of this clinicopathologic presentation so that the establishment of HS diagnosis is not delayed and the patient receives appropriate counseling.

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Introduction

Mannose-binding lectin (MBL) and MBL-associated serine proteases (MASPs) are an essential component of innate immune response [1]. MBL is a collagen containing C-type lectin protein which helps in the opsonization of pathogens along with the activation of complement and cytokine production that promote chemotaxis and recruitment of inflammatory cells in an antibody-independent fashion [1]. An MBL level of $<0.05 \mu\text{g/mL}$ is considered severe MBL deficiency whereas a level of $0.05\text{--}1 \mu\text{g/mL}$ indicates partial MBL deficiency [2]. MBL deficiency is the most common immunodeficiency in the general population, affecting 5–7% of individuals, although higher figures in Caucasians have been reported [1]. Severe MBL deficiency may occur independently of various primary immunodeficiency disorders, and 10.9% of patients with recurrent infections had MBL deficiency without primary immunodeficiency disorders [3]. Deficiencies of the MBL-MASP pathway are associated with recurrent infections, especially secondary to *Staphylococcus aureus* or *Pseudomonas aeruginosa*, as well as autoimmune and inflammatory skin disease and vascular complications [1]. However, there are very few reports describing dermatological manifestations in patients with MBL deficiency [1]. The reported skin manifestations in patients with MBL deficiency are outlined in Table 1.

Hidradenitis suppurativa (HS) has been associated with a spectrum of conditions, most of which belong to the group of autoinflammatory disorders [4]. MBL deficiency is not a reported comorbidity among hidradenitis patients [4, 5]. We report a case of an atypical clinical presentation of HS in a patient with severe MBL deficiency who presented with recurrent abscesses – predominantly sterile, sterile folliculitis, and lymphadenopathy. Our extensive literature search did not reveal similar cases. Possible pathogenetic mechanisms of this rare clinical presentation are discussed.

Case Presentation

A 32-year-old woman presented with a long history of abscesses and pustular lesions. She first noticed “cysts” over the face, armpits, and groin at the age of 13 years. Since then, she developed numerous painful, deep-seated abscesses predominantly in HS distribution, i.e., submammary, inguinal, and perianal areas (Fig. 1), that required drainage for symptomatic relief. The axillae were less affected. Abscesses in unusual locations, such as the jawlines and neck, were also noted. Most lesions were in Hurley stage 1 because there was a sparsity of well-formed, typical sinus tracts (most lesions were “blind boils”), and scarring was subtle or

absent. Hypertrophic scarring was not noted. Sparse comedones were observed, mostly in the inguinal/pubis area. Recalcitrant folliculitis was invariably noted over the breasts, jawlines, submandibular area/neck, and occasionally the pubic area (Fig. 2). Abscesses were associated with symptomatic, reactive pre-auricular, submandibular, and inguinal lymphadenopathy. Occasional low-grade fever was noted. Skin lesions developed on a weekly basis, thus interfering with the patient's quality of life (QOL). The effect on QOL is also evidenced by the history of depression and anxiety in the patient. Her past medical history also included obesity, polycystic ovary syndrome controlled with a combined oral contraceptive, and acne.

Biopsies of abscesses (Fig. 3) and pustular lesions revealed no pathogenic bacteria or fungi with Brown and Brenn and periodic acid–Schiff stains. Numerous cultures from abscesses and pustules were performed over the years. Most cultures did not yield any pathogen, with only a few cultures showing HS microbial flora (e.g., *Staphylococcus lugdunensis*, *Enterococcus faecalis*, *Peptostreptococcus*). Laboratory workup revealed normal serum levels of C4 complement component and C1 inhibitor protein. The MBL level was exceptionally low at 27 and <0.5 ng/mL on two measurements (reference range: ≥100 ng/mL). Serum IgA and IgG were normal while IgM levels were slightly elevated (287 mg/dL; reference range: 48–271 mg/dL). CRP value was elevated at 18 mg/mL (reference range: <8 mg/mL). An extensive workup by Immunology including, among others, serum protein electrophoresis, lymphocyte subset analysis, serum free light chain ratio, and neutrophil oxidative burst testing did not show any other immunodeficiencies. Procalcitonin value was 0.07 ng/mL (values <0.50 ng/mL are noted in abacterial inflammatory disease) [6].

The patient did not tolerate oral antibiotics, including tetracyclines, amoxicillin clavulanate, and clindamycin +/- rifampin, which, when tried, provided only mild temporary relief. Also, immunosuppressive agents including prednisone and cyclosporine, and hormonal treatment with spironolactone were ineffective. Furthermore, MBL replacement therapy was not an option because the twice-a-week infusion schedule was not possible for the patient [7]. The above made the patient dependent upon intralesional steroid (triamcinolone) injections and drainage of abscesses and tender pustules. Two recalcitrant abscesses required excision.

Discussion

The role of the MBL-MASP pathway in dermatological disease has not been adequately studied. A study reported 6 patients with recurrent inflammatory or infectious skin conditions with severely low MBL levels [1]. Deficiency of MBL-2 gene has been associated with autoimmune disease [8]. MBL plays an important role in the clearance of immune complexes and apoptotic cells, the accumulation of which can favor autoimmunity. A similar mechanism may underlie the reported association of MBL with Behcet disease [1]. It was suggested that impaired clearance of polymorphonuclear cells, after they undergo apoptosis, can precipitate the immune response in Behcet disease. Low MBL levels also allow a more constant pathogenic stimulation, leading to immune cell infiltration and a Th1-type cytokine profile [9]. This may enhance the pro-inflammatory processes in conditions known to display a Th1-type profile, such as HS, and can be relevant to the severity of the clinical presentation in our case. It would be worth investigating the prevalence of MBL among HS patients and further study the features of HS in the subgroup of patients with MBL deficiency.

Our patient satisfied the clinical criteria for diagnosis of HS (characteristic lesions, predilection for flexural areas, lesion recurrence) [5]. However, the clinical presentation was atypical, evidenced by the presence of lesions on the lower face/neck, predominance of aseptic abscesses, and relative sparsity of draining sinuses. The predominance of abacterial abscesses in our case is unusual and may indicate enhancement of proinflammatory mechanisms in HS. An autoinflammatory pathway in HS is supported by studies showing upregulated TNF- α , IL-1 β and IL-10, and inflammasome NLRP3 in lesional skin in HS [10, 11]. Some authors support an overall “altered” immune response to bacteria on the skin leading to chronic inflammation in HS [12], and a theory of immune overactivity has been proposed [13].

Our case shows some clinical similarities with aseptic abscesses disorder that is included in the spectrum of autoinflammatory diseases [14]. Like HS, aseptic abscesses have been associated with underlying inflammatory bowel disease and/or neutrophilic dermatoses such as pyoderma gangrenosum, Sweet’s, and PAPA (pyogenic sterile arthritis, pyoderma gangrenosum and acne) syndromes [14]. Like aseptic abscesses syndrome patients, our patient developed numerous deep-seated sterile neutrophilic abscesses that were occasionally associated with low-grade fever and did not respond to oral antibiotics. Unlike aseptic abscesses that respond dramatically to systemic corticosteroids, our patient did not respond to prednisone.

Conclusions

This case indicates that patients with concomitant HS and MBL deficiency can develop very symptomatic, recurrent, aseptic abscesses and folliculitis that present a therapeutic challenge. This severe, atypical HS presentation affects QOL profoundly. MBL deficiency may enhance proinflammatory processes in HS. Health care providers should be familiar with this clinicopathologic presentation so that the establishment of HS diagnosis is not delayed and the patient receives appropriate counseling.

Statement of Ethics

Written Informed consent was obtained from the patient for the publication of this case report and any accompanying images. This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki (<https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>).

Disclosure Statement

The authors declare that they have no competing interests.

Funding Sources

The authors have no funding sources to declare in relation to this publication.

Author Contributions

S.B. was involved in analyzing the pathology and laboratory findings, reviewing the literature, and drafting the manuscript. N.B. was involved in the pathology of the case and relevant section in the paper. G.K. was involved in direct management of the patient, and critically reviewed the manuscript. All authors read and approved the final manuscript.

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Fig. 1. Tender sterile abscess is shown on the right medial buttock extending onto the midgluteal fold.

Fig. 2. Folliculitis on the left lower breast and submammary area.

Fig. 3. Histologic features of abscess on the right medial buttock (Fig. 1). Top: a dermal abscess with focal embedded squamous epithelium and surrounding fibrosis. Hematoxylin eosin stain. ×40. Bottom: dense neutrophilic infiltrate without identifiable bacterial organisms. Hematoxylin eosin stain. ×400.

Table 1. Skin manifestations in patients with MBL deficiency [1, 5, 7, 8]

Recurrent folliculitis
Recurrent furunculosis/abscesses
MRSA infection
Vulvar infection with abscess formation
Postoperative infections
Pustular eruption
Cellulitis and ulcers
Viral (e.g., erythema multiforme with HSV reactivation)
Fungal infections
Atopic dermatitis/other eruption
Systemic lupus manifestations
Grover disease
Orogenital ulcerations (forme fruste of BD)
Hidradenitis suppurativa (present case)

BD, Behcet disease; HSV, herpes simplex virus; MRSA, methicillin-resistant *Staphylococcus aureus*.