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Journal
Dermatology Online Journal, 23(11)

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Publication Date
2017

DOI
10.5070/D32311037275

Vulvar metastatic Crohn disease: clinical, histopathological and ultrasonographic findings

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Abstract

Metastatic Crohn disease (MCD) is an unusual type of cutaneous Crohn disease characterized by skin lesions separated from the lesions of the gastrointestinal tract. The diagnosis of MCD is essentially histological, showing noncaseating granulomas in the dermis and subcutaneous fat tissue. We report a case of MCD with vulvar involvement and clinical, histopathological, and ultrasonographic findings of this disease.

Keywords: metastatic, Crohn, noncaseating granulomas

Introduction

Metastatic Crohn disease (MCD) is an uncommon manifestation of cutaneous Crohn disease characterized by noncaseating granulomas in the skin apart from the lesions of the gastrointestinal tract. Diagnosis of MCD is based on histopathological examination. This entity can be easily mistaken with other clinical manifestations or complications of Crohn disease, so initial clinical suspicion is very important to get the diagnosis. We report a representative case of MCD with vulvar implication as well as its clinical, histopathological and ultrasonographic findings.

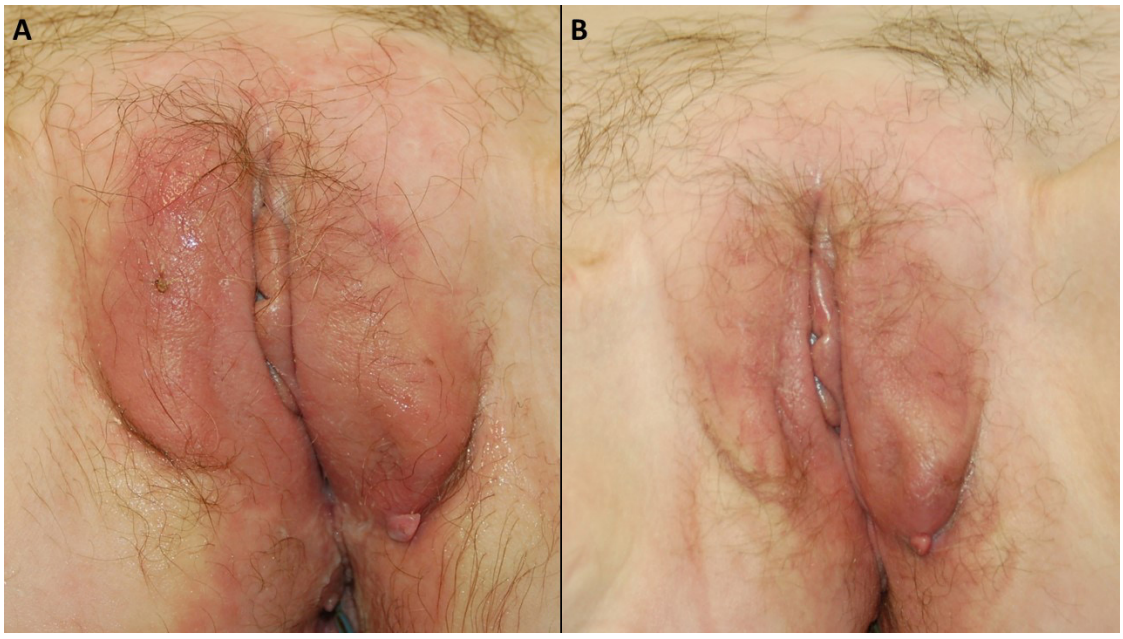

Figure 1. *A) Erythema and edema of the vulvar area as well as a single polyp on her left labium majus. B) Clinical features after 2-week treatment: decreased edema and erythema.*

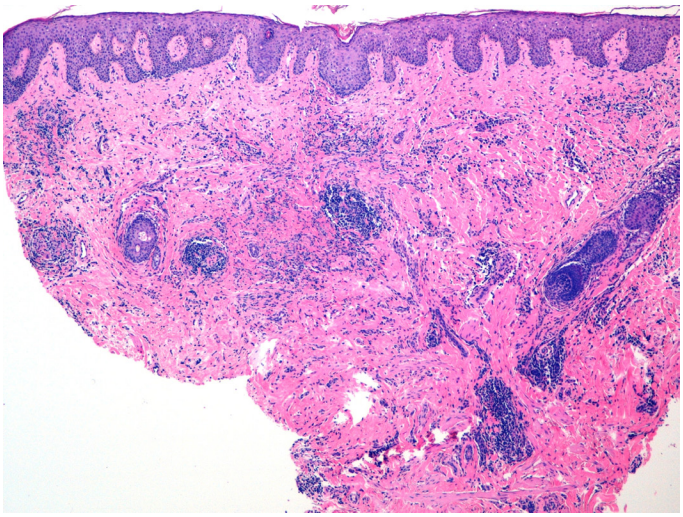

Figure 2. *Histopatologycal findings: diffuse lymphocytic inflammatory infiltrate in dermis as well as noncaseating granulomas. H&E, 4%.*

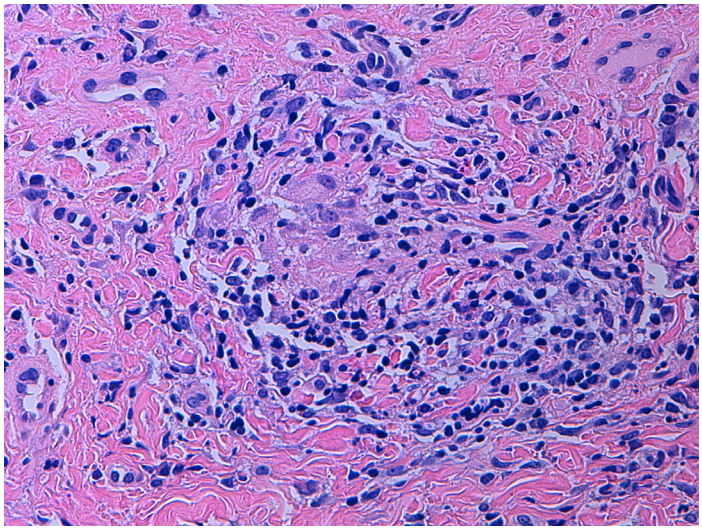

Figure 3. *Histopatologycal detail of noncaseating granulomas. H&E, 20%.*

Case Synopsis

A 35-year-old woman with stenotic Crohn disease (for the past 15 years) underwent two intestinal surgeries and two anti-TNF drug treatment regimen trials to no avail. In addition, she developed perianal involvement of Crohn disease, which also required surgical treatment. For six month prior to presentation the patient was treated with vedolizumab without improvement of symptoms.

The patient was referred owing to ongoing painful erythema and swelling of the vulvar area during the previous four months. Skin examination showed a diffuse, non-ulcerated, symmetric erythema and edema of the genital area as well as a single pedunculated polyp of approximately 5 mm size located on her left labium majus (**Figure 1**A).

A biopsy from the skin of her right labium majus was made and the histopathological examination demonstrated a diffuse lymphocytic inflammatory infiltration in dermis with multiple noncaseating granulomas. Acid-fast stain was negative and no foreign-body material was detected under polarized light (**Figure 2**, 3).

Furthermore, skin ultrasonography of the area was performed with a 10-18 MHz linear probe by using grey-scale and color Doppler techniques during sonographic examinations (PRF 750 KHz and gain color immediately before the noise artefact). It showed a diffuse hypoechogenicity and increased dermal thickness as well as an alteration of the subcutaneous fat. Fistulas or abscesses were not demonstrated. Color Doppler signal was diffusely elevated by local inflammation (**Figure 4**).

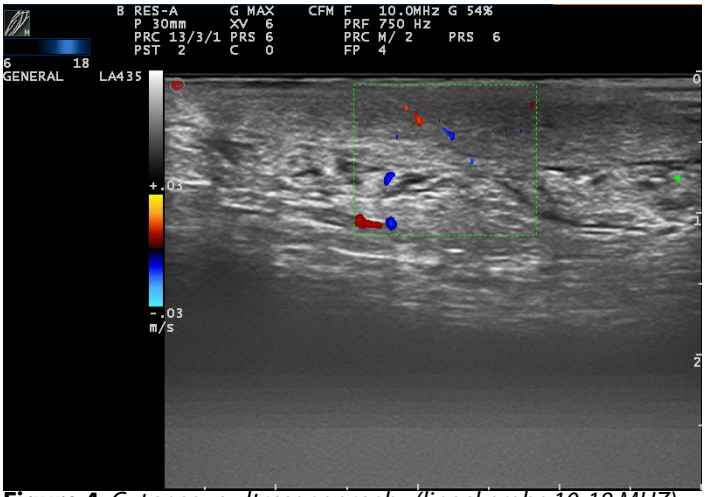

Figure 4. *Cutaneous ultrasonography (lineal probe 10-18 MHZ): difuse hypoechogenicity and increased dermal thickness with a intensify color Doppler. The presence of fistulas or abscesses was rejected.*

Clinical, ultrasonography and histopathological findings were indicative of MCD. Oral treatment with metronidazole (800 mg per day) and topical medication with betamethasone dipropionate twice per day was prescribed. After a 2-week treatment, clinical improvement with a decrease of edema and erythema was noted (**Figure 1**B). Vulvar Crohn disease has been controlled after 6 months of follow up with occasional flares that are responsive to

topical steroid treatment.

Case Discussion

Crohn disease (CD) is a chronic granulomatous inflammatory bowel disorder. Mucocutaneos involvement is the most frequent extraintestinal manifestation of this disease, with approximately 40% of patients affected [1]. Cutaneous manifestations of CD can be specific or nonspecific. The first group is characterized by noncaseating granulomas, similar to inflammatory bowel lesions. Specific dermatologic manifestations can appear in areas close to gastrointestinal inflammation, such as perianal, perifistular, or periostomal skin; separate metastatic involvement may also occur [2, 3]. MCD is the most uncommon cutaneous manifestation of Crohn disease; only approximately 100 cases have been described in the literature to date. Nonspecific or reactive dermatologic features of CD, including pyoderma gangrenosum, erythema nodosum, or erythema multiforme, lack granulomas and have distinguishing histological findings, in contrast to specific dermatologic manifestations of CD [4].

MCD usually affects young adults, but has also been described in children [5]. This entity could develop prior to or concomitant with intestinal CD. MCD may present as isolated or multiple lesions and often involves the genital area and extremities, but could also appear elsewhere on the body. The most frequent clinical manifestations of vulvar MCD is ulceration, followed by fissures, erythema, and edema. Other uncommon clinical features described are condyloma-like papules and plaques, skin tags, and lymphedema [6]. Our patient presented with vulvar lymphedema and a condyloma-like papule.

The pathogenesis of MCD still remains unclear. Several theories have been postulated, such as the production of skin granulomas related to the deposit of immune complexes stemming from the gastrointestinal tract and autoimmune cross-reactivity, among others [7].

The histological features include the presence of aseptic noncaseating granulomas located primarily in the dermis with occasional spreading into the subcutaneous fat tissue. Ziehl-Neelsen staining is negative. Eosinophil infiltrate and necrobiosis have been also described [8, 9].

The diagnosis of MCD is established with a consistent clinical history and characteristic histopathological study. In some cases, an imaging technique is needed to differentiate between the specific cutaneous manifestations of CD and complications of the disease, such as fistulas or abscesses [10, 11]. For this purpose we have used ultrasonography an affordable, innocuous, rapid, and office-based procedure that can be performed by the dermatologist. Ultrasound was used to exclude fistulae of Crohn disease. Ultrasound has proven to be comparable to the gold standard MRI in the diagnosis of perianal fistulae in Crohn disease [12].

The differential diagnosis of vulvar MCD should include other granulomatous skin diseases, such as sarcoidosis, erythema nodosum, and mycobacterial disease, or foreign body reaction, together with non-specific manifestations of Crohn disease and hidradenitis suppurativa [13].

Owing to the low incidence of MCD, only a small number of cases with their therapeutic results have been gathered. Drew et al. [14] have reported a therapeutic algorithm for MCD. Glucocorticosteroids are considered as the first-line therapy for treating MCD, both topically or systemically. In the case of systemic therapy, the most common effective reported dosage is prednisolone 30mg/d. Oral metronidazole has also been used successfully for MCD treatment, with a recommended dosage between 800 to 1500 mg/d during a 4-month period before treatment failure can be determined. In case of failure, biologic therapies have been prescribed, especially TNF inhibitors such as adalimumab, infliximab, and certolizumab [15]. Alternatively, antibiotics, methotrexate, azathioprine, cyclosporine, and thalidomide had been used with less satisfactory results [16-18].

Conclusion

MCD is an uncommon extraintestinal manifestation of Crohn disease with diverse clinical features. As a consequence, it can be easily confused with other manifestations or complications of Crohn disease. We report a representative case of vulvar MCD as well as the clinical, histopathological, and ultrasonographic

findings.

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