

PENILE AND SCROTAL LYMPHEDEMA AS AN UNUSUAL PRESENTATION OF CROHN'S DISEASE: CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Crohn's disease is an inflammatory intestinal disease that primarily causes abdominal pain and diarrhea. We report a male patient who presented with penile and scrotal lymphedema and inguinal fistulas as the first manifestations of Crohn's disease. Extraintestinal or metastatic Crohn's disease initially presenting as genital lymphedema with fistula formation is rare. Skin lesions in extraintestinal Crohn's disease typically show non-caseating, sarcoidal granulomas with numerous foreign body- and Langhans-type multinucleated giant cells, which are separated from intestinal involvement by normal skin. Treatment options are limited and include multi-immunosuppressant medications.

Keywords: Crohn's disease, hidradenitis suppurativa; metastatic Crohn's disease, midline edema, genital edema

Crohn's disease is an ulcerative granulomatous inflammatory disease primarily involving the small and large intestine but may affect any part of the gastrointestinal tract from the mouth to the anus (1).

In addition, several extra-intestinal manifestations can be observed including skin involvement. Patients with Crohn's disease

usually present with abdominal pain or diarrhea; however, initial presentation as genital edema is rare. We present a case of penile and scrotal lymphedema and inguinal fistula formation in a man diagnosed with extensive but undiagnosed Crohn's disease.

CASE REPORT

A 36-year-old male presented with penile and scrotal swelling and pain after a sterilization procedure and circumcision elsewhere. The patient was previously diagnosed with insulin-dependent diabetes mellitus. He had no history of episodic swelling of his genitalia or extremities, or recurrent erysipelas. At physical examination, significant lymphedema of the scrotum and penile shaft was observed by a plastic surgeon. An abdominal computer tomography (CT) scan showed lymphadenopathy in the groin. Cytologic aspiration of the inguinal lymph nodes revealed signs of granulomatous inflammation without malignancy. The patient was diagnosed with decompensated primary lymphedema after minimally invasive surgery. Conservative treatment was initiated to reduce the genital edema and consisted of manual lymph drainage and taping. Because there was no relief of edema and progression of the swelling, the patient underwent scrotal reduction surgery one year later. Impaired



Fig. 1. Top) Scarification of the groin and substantial scrotal swelling divided in two parts by lateral adhesions directed toward the anal region. Lower Left) Fibrosis of the scrotal region and swelling of the penile shaft. Lower Middle) Inguinal and scrotal skin show signs of infection. Lower Right) Skin lesions resembling fistulas are visible around the anus.

wound healing and aggravation of the swelling complicated the recovery period.

Two years later, the patient presented again with unimproved genital edema and development of inflamed and painful skin nodules in the groin and sacrum and was referred to the dermatology department. The diagnosis was extended to include hidradenitis suppurativa. Treatment with minocycline 100 mg daily and local zinc ointment was initiated. The patient denied complaints of abdominal pain or diarrhea, defecation was normal without mucus or blood loss, and his weight remained stable.

One year later, the patient was referred to the expertise center of lympho-vascular medicine for the first time to obtain a second opinion. The genital edema had persisted, and the patient experienced difficulties

walking and sitting, which led to unemployment and relationship problems. Physical examination showed a male with scarification of the groin, fetor and swelling of the scrotum and penile shaft. The substantial scrotal swelling was divided in two parts by lateral adhesions directed toward the anal region (*Fig. 1*). There was moderate pitting edema in the scrotal region with considerable fibrosis, the inguinal, scrotal and perineal skin showed signs of infection, and skin lesions surrounded the anus and resembled fistulas (*Fig. 1*).

A whole body examination revealed no signs of lymphedema elsewhere. Stemmer sign, defined as enlargement of the skin fold above the second toe due to fibrosis and hypertrophy, thereby specific for lymphedema, was negative.

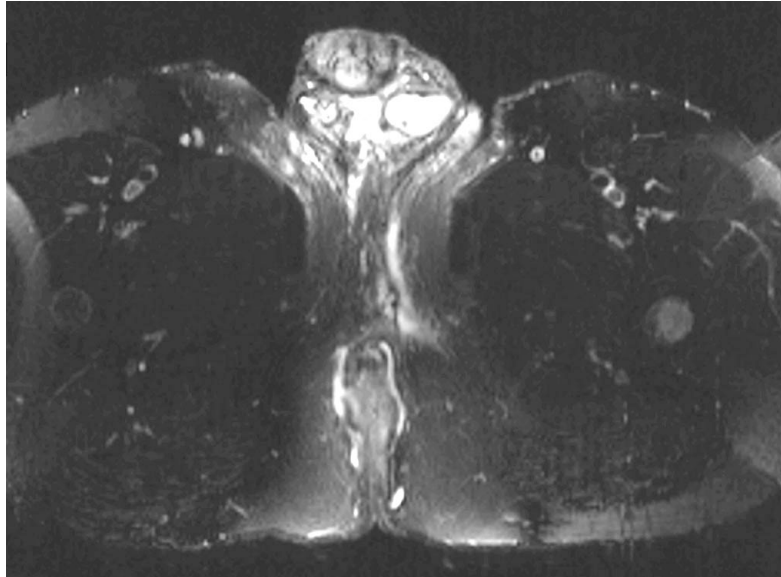


Fig. 2. A pelvic magnetic resonance imaging scan showed lymphadenopathy with extensive perianal fistula formation above the sphincter complex with horizontal branches directed toward the scrotum.

Laboratory investigations of blood showed leukocytes of $19.4 \times 10^9/l$ ($N = 2.00-7.20 \times 10^9/l$) and a C-reactive protein level of 73 mg/L ($N < 2.5$). Blood glucose was found to be elevated with 21.4 mmol/l with an HbA1c of 6.6%. Full blood count, electrolytes, liver and kidney function tests remained unremarkable. Lymphoscintigraphy of both arms and legs did not reveal lymphatic impairment. Chest X-ray and serum angiotensin-converting enzyme were normal. A 3-mm skin biopsy was taken from a lesion on the left groin. A pelvic magnetic resonance imaging scan showed lymphadenopathy with extensive perianal fistula formation above the sphincter complex with horizontal branches directed toward the scrotum (*Fig. 2*).

Differential diagnosis of penile/scrotal lymphedema and inguinal fistula formation included idiopathic chronic genital lymphedema and hidradenitis suppurativa, granulomatous lymphangitis, and extraintestinal or metastatic Crohn's disease.

Histopathology revealed non-caseating epithelioid granulomas in the dermis with adjacent Langhans giant cells. Necrosis was

absent and no foreign material was found. Subsequently, the patient was referred to a gastroenterologist with suspected extraintestinal Crohn's disease. A colonoscopy was performed and showed inflammation and ulceration of the terminal ileum, multiple aphtheous ulcerations, and nonspecific erosions located in the cecum and rectum. Histopathology of the lesional biopsies showed nonspecific chronic transmural inflammation with granulomas. The patient was diagnosed with extraintestinal Crohn's disease manifesting as inguinal fistula formation and secondary penile/scrotal edema.

Treatment initially focused on Crohn's disease in accordance with the gastroenterologist. Anti-inflammatory treatment with adalimumab subcutaneously at 40 mg once per two weeks was combined with prednisolone 30 mg daily and azathioprine 100 mg daily. Subsequently, scrotal reconstruction and reduction surgery were performed. Dermatologic treatment involved compression therapy, manual lymph drainage and intravenous antibiotics. Within 6 months, the edema resolved, and the inguinal skin

healed. The patient achieved a satisfactory result and refused reconstructive surgery.

DISCUSSION

Extraintestinal and Metastatic Crohn's Disease

Signs of extraintestinal Crohn's disease occur in 10% to 44% of patients with enteral Crohn's disease (2). Skin lesions are the second most common extraintestinal manifestation of Crohn's disease after musculoskeletal involvement (3) and can be subdivided into contiguous and non-contiguous skin lesions. Direct contiguous extension from the involved bowel may lead to perineal ulceration, fistulas and abscesses (2,4). Non-contiguous skin involvement, also referred to as metastatic Crohn's disease, presents as skin lesions at sites that are separated from the gastrointestinal tract by normal tissue (5,6).

Genital Metastatic Crohn's Disease

Although genital metastatic Crohn's disease has been reported (5,7-10), cases of patients presenting with penile and/or scrotal swelling as the initial manifestation of Crohn's disease are less common. The lower legs are most commonly affected by metastatic Crohn's disease but involvement of the face, axilla, trunk and groin are also observed (2). Possible dermatological lesions of metastatic Crohn's disease are tender nodules, plaques with or without ulceration on the extremities and genital ulcers, and in young patients, genital swelling is a most frequent presentation (2,6).

In one-third of adult patients with metastatic Crohn's disease, concomitant gastrointestinal symptoms are present (6). However, in 70% of the cases, metastatic Crohn's disease appears long after the initial diagnosis of Crohn's disease (6). It is generally considered that there is no correlation between intestinal disease activity and the appearance of skin manifestations (11).

The clinical differential diagnosis of genital lymphedema includes hidradenitis suppurativa, infection, amyloidosis, sarcoidosis, malignancy, trauma, and iatrogenic and congenital causes. Chronic idiopathic genital lymphedema may be caused by primary hypoplastic lymphatic channels or intercurrent unidentified infections with or without a coexisting dermatosis (12).

Etiology

The etiology of metastatic Crohn's disease is poorly understood. Two different pathogenic mechanisms have been postulated. The first suggesting deposition of immune complexes within the skin as responsible for the development of extraintestinal granulomas. The second proposes a T-lymphocyte-mediated type IV hypersensitivity reaction leading to granuloma formation and vascular damage (6). Genital lymphedema in Crohn's patients is thought to be caused by disruption of lymphatic vessels by scarring and sinus formation (13). Additionally, an impaired mesenteric lymphatic pump function during inflammation may contribute to edema and granuloma formation in Crohn's disease (14).

Histopathological Diagnosis

Histopathologically, metastatic Crohn's disease is characterized by deep and superficial non-caseating, sarcoidal granulomas with numerous foreign body- and Langhans-type multinucleated giant cells (15). A dense infiltrate of lymphocytes around the vessels and granulomas is also present (2). Differential diagnosis should encompass sarcoidal granulomatous inflammation of genital skin, including sarcoidosis, mycobacterial infection, rheumatoid arthritis and leprosy, and the granulomatous infiltrate with certain exogenous materials, such as silica, beryllium and tattoo pigments (2).

Treatment

Treatment options for Crohn's disease are limited to controlling symptoms, maintaining remission and preventing relapse. Therapy for genital metastatic Crohn's disease often involves multi-immunosuppressant therapies, such as systemic steroids, sulfasalazine, metronidazole, azathioprine and biological agents including infliximab. Treatment is similar for both children and adults with metastatic Crohn's disease (3,16).

CONCLUSION

We report a male patient who presented with penile and scrotal edema and inguinal fistula formation in the absence of gastrointestinal complaints and was ultimately diagnosed with Crohn's disease. Although this type of initial disease presentation is rare, gastroenterological assessment with colonoscopy might be recommended for patients with persistent genital edema and inguinal fistulas from an unknown cause. Chronic idiopathic genital lymphedema can be due to metastatic Crohn's disease. Proper diagnosis of genital swelling and lymphedema is important before commencing treatment.

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