Edema Affecting the Penis and Scrotum

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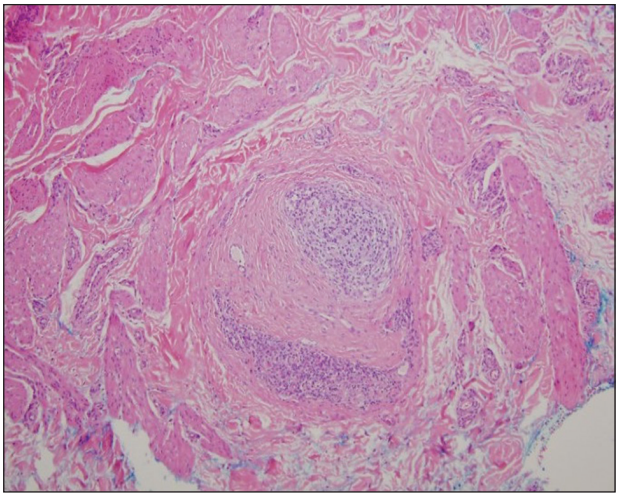

H&E, original magnification ×100.

A 44-year-old man presented for evaluation of self-described "skin ripping" on the penis with penile and scrotal edema of 1 year's duration. He had a history of bowel symptoms and anorectal fistula of 3 years' duration. Purulent penile drainage and inguinal lymphadenopathy were noted on physical examination. Excisional biopsies of the scrotum and penis were performed. Special stains for organisms were negative.

THE BEST **DIAGNOSIS IS:**

a. cutaneous Crohn disease
b. granulomatous mycosis fungoides
c. hidradenitis suppurativa
d. mycobacterial infection
e. sarcoidosis

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THE **DIAGNOSIS:** Cutaneous Crohn Disease

Crohn disease (CD) is an inflammatory bowel disease that can involve any region of the gastrointestinal (GI) tract from the mouth to the anus but most commonly presents in the terminal ileum, colon, or small bowel with transmural inflammation, fistula formation, and knife-cut fissures among the frequently described findings. Extraintestinal manifestations may be found in the liver, eyes, and joints, with cutaneous extraintestinal manifestations occurring in up to one-third of patients.[1]

Crohn disease can be associated with multiple cutaneous findings, including erythema nodosum, pyoderma gangrenosum, aphthous ulcers, pyodermatitis-pyostomatitis vegetans, necrotizing vasculitis, and metastatic Crohn disease (MCD).[2] Typical histopathologic findings seen in MCD such as noncaseating granulomatous inflammation in the papillary and reticular dermis, possibly extending to the subcutaneous fat, are not specific to MCD. Associated genital edema is thought to be a consequence of granulomatous inflammation of lymphatic vessels. In one study reviewing specimens from 10 cases of CD, a mean of 46% of all granulomas identified on the slides (N=264) were located proximal to lymphatic vessels, suggesting a common pathway for development of intestinal disease and genital edema.[3] The differential diagnosis for penile and scrotal swelling is broad, and the diagnosis may be missed if attention is not given to the clinical history of the patient in addition to histopathologic findings.[2]

Skin changes in CD also can be separated into perianal disease and true metastatic disease—the former presents as anal lesions associated with segmental involvement of the GI tract and the latter as ulceration of the skin separated from the GI tract by normal tissue.[1] The term *sarcoidal reaction* often is used to describe histopathologic findings in cutaneous CD, as it refers to the noncaseating granulomas found in approximately 60% of all cases.[4] Ultimately, the location of noncaseating granulomas within the dermis of our patient's biopsy, taken in conjunction with the clinical history and the lack of defining features for other potential etiologies (eg, polarizable material, organisms on special stains), led to the diagnosis of cutaneous CD.

Cutaneous manifestations of sarcoidosis most commonly occur as papules, plaques, and subcutaneous nodules predominantly on the face, upper back, arms, and legs. Although the histologic features of sarcoidosis are characterized by lymphocyte-poor noncaseating granulomas (Figure 1), these findings also can be seen as a consequence of multiple granulomatous causes.[5,6] In a review of 48 cutaneous specimens from patients with sarcoidosis, the granulomas were found most frequently in the deep dermis (34/48 [70.8%]), with superficial dermis (21/48) and subcutaneous fat granulomas (20/48) each present in less than 50% of biopsies.[5] Although less typical, cutaneous sarcoidosis also has been noted in the literature to present in the perianal and gluteal regions, demonstrating dermal noncaseating granulomas on biopsy.[7] One distinction in particular to be noted between sarcoidosis and CD is that sarcoid lesions in the skin rarely ulcerate, while the lesions of cutaneous CD often are ulcerated.[4,6]

Lesions including abscesses in the groin may raise concern for hidradenitis suppurativa (HS), a disease of apocrine gland–bearing skin. Typical lesions are tender, subcutaneous, erythematous nodules, cysts, and comedones that develop rapidly and may rupture to drain suppurative bloody discharge, subsequently healing with an atrophic scar.[8] More persistent inflammation and rupture of nodules into the dermis may lead to formation of dermal tunnels with palpable cords and sinus tracts.[8] Typical areas of disease involvement are in the axillae, inframammary folds, groin, or perigenital or perineal regions, with diagnosis based on a combination of lesion morphology, location, and progression/recurrence frequency.[9] Histologic examination of HS specimens can demonstrate a perifollicular lymphocytic infiltrate, with more advanced disease characterized by increased inflammatory cells, predominantly neutrophils, monocytes, and mast cells (Figure 2). The presence of granulomas in HS most often is of the foreign body type.[9] Epithelioid granulomas noted in an area separate from

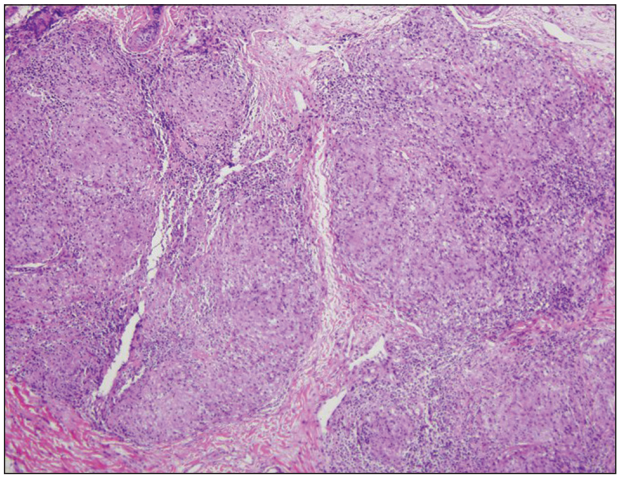

FIGURE 1. Sarcoidosis. Noncaseating granulomas composed of epithelioid histiocytes and multinucleated giant cells (H&E, original magnification ×100).

inflammation in a patient with HS serve as a clue to be alert for systemic granulomatous disease.[10]

Mycosis fungoides is the most common primary cutaneous lymphoma to show a granulomatous infiltrate; the granuloma generally is sarcoidal, though other forms have been described (Figure 3).[11] Beyond these granulomatous foci, the key histopathologic feature of granulomatous mycosis fungoides (GMF) is diffuse dermal infiltration by atypical lymphoid cells. Epidermotropism and sparing of dermal nerves is the most critical finding in the diagnosis of GMF, especially in geographic regions where leprosy is endemic and high on the differential, as the conditions have histopathologic similarities.[11,12] At the same time, lack of epidermotropism does not exclude the diagnosis of GMF.[13] Clinically, GMF presentation is variable, but common findings include erythematous and hyperpigmented patches and plaques. Given the lack of clear clinical criteria, the diagnosis relies primarily on histopathologic features.[11]

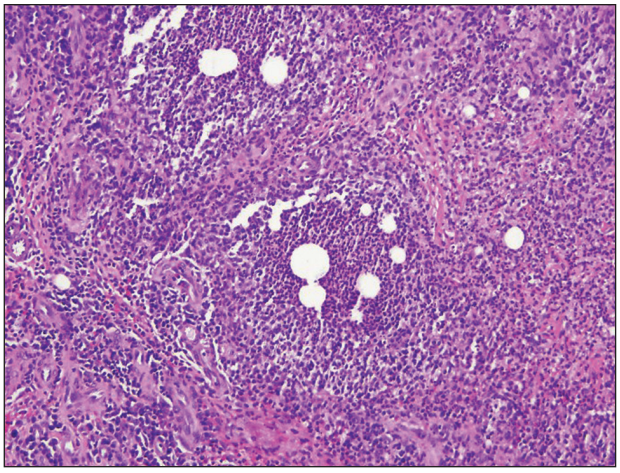

FIGURE 4. Mycobacterial infection. Suppurative granulomatous inflammation with inflammatory cells and multinucleate giant cells (H&E, original magnification ×200).

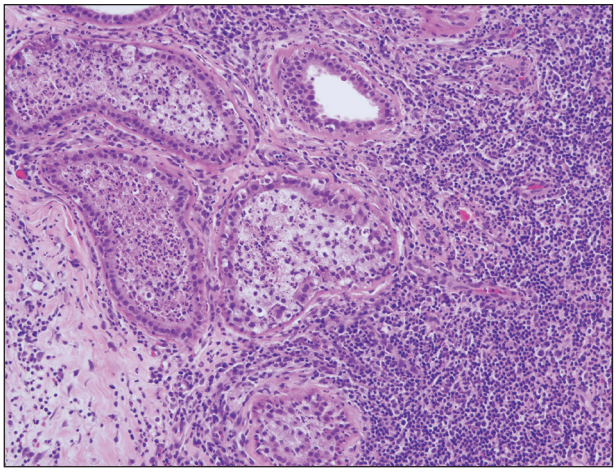

FIGURE 2. Hidradenitis suppurativa. Punch biopsy demonstrating a neutrophil-predominant infiltrate (H&E, original magnification ×200).

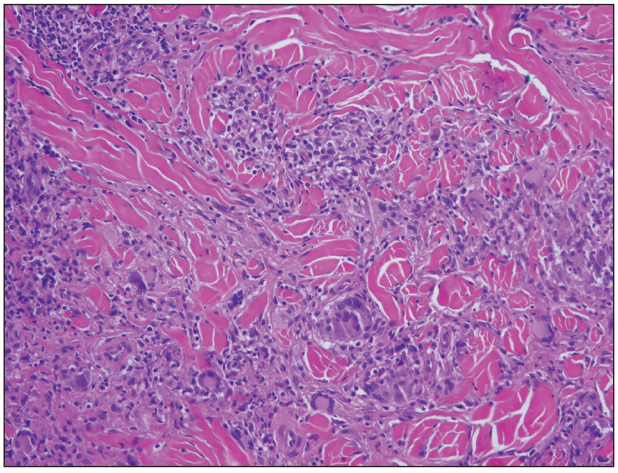

FIGURE 3. Granulomatous mycosis fungoides. Poorly formed granulomas surrounding the follicular unit (H&E, original magnification ×200).

Mycobacterial skin and soft tissue infections may be attributed to both tuberculous and nontuberculous strains (atypical species).[14] Clinical features range from small papules to large deformative plaques and ulcers.[15] Histologic features also distinguish cutaneous tuberculosis (TB) from nontuberculous mycobacterial causes. Cutaneous TB shows caseous granulomas in the upper and mid dermis, while nontuberculous mycobacterial infections have more prominent neutrophil infiltration and interstitial granulomas (Figure 4).[16]

In cutaneous TB specifically, extrapulmonary manifestations may involve the skin in 1% to 1.5% of all TB cases, and although rare, ulcerative skin TB has been noted in one report as a nonhealing perianal ulcer that showed necrotizing granulomas on biopsy.[17] Ultimately, diagnosis of cutaneous mycobacterial infection is confirmed with detection of acid-fast bacilli in the biopsy specimen.[16]

Diagnosis of cutaneous CD requires clinicopathologic correlation, as the clinical and histopathologic differential diagnoses of genital edema and noncaseating granulomas, respectively, are broad. Even though the clinical context was appropriate for cutaneous CD in this case, correct diagnosis required confirmatory histologic findings. Furthermore, taking multiple biopsies is prudent. In our patient, diagnostic findings only were present in the biopsy from the scrotum.

REFERENCES

1. Hagen JW, Swoger JM, Grandinetti LM. Cutaneous manifestations of Crohn disease. *Dermatol Clin*. 2015;33:417-431.
2. Barrick BJ, Tollefson MM, Schoch JJ, et al. Penile and scrotal swelling: an underrecognized presentation of Crohn's disease. *Pediatr Dermatol*. 2016;33:172-177.
3. Mooney EE, Walker J, Hourihane DO. Relation of granulomas to lymphatic vessels in Crohn's disease. *J Clin Pathol*. 1995;48:335-338.

4. Parks AG, Morson BC, Pegum JS. Crohn's disease with cutaneous involvement. *Proc R Soc Med.* 1965;58:241-242.
5. García-Colmenero L, Sánchez-Schmidt JM, Barranco C, et al. The natural history of cutaneous sarcoidosis: clinical spectrum and histological analysis of 40 cases [published online October 18, 2018]. *Int J Dermatol*. 2019;58:178-184.
6. Yoo SS, Mimouni D, Nikolskaia OV, et al. Clinicopathologic features of ulcerative-atrophic sarcoidosis. *Int J Dermatol.* 2004;43:108-112.
7. Cohen GF, Wolfe CM. Recalcitrant diffuse cutaneous sarcoidosis with perianal involvement responding to adalimumab. *J Drugs Dermatol.* 2017;16:1305-1306.
8. Hoffman LK, Ghias MH, Lowes MA. Pathophysiology of hidradenitis suppurativa. *Semin Cutan Med Surg.* 2017;36:47-54.
9. Saunte DML, Jemec GBE. Hidradenitis suppurativa: advances in diagnosis and treatment. *JAMA.* 2017;318:2019-2032.
10. Attanoos RL, Appleton MA, Hughes LE, et al. Granulomatous hidradenitis suppurativa and cutaneous Crohn's disease. *Histopathology.* 1993;23:111-115.
11. Gutte R, Kharkar V, Mahajan S, et al. Granulomatous mycosis fungoides with hypohydrosis mimicking lepromatous leprosy. *Indian J Dermatol Venerol Leprol*. 2010;76:686-690.
12. Pousa CM, Nery NS, Mann D, et al. Granulomatous mycosis fungoides—a diagnostic challenge. *An Bras Dermatol*. 2015;90:554-556.
13. Kempf W, Ostheeren-Michaelis S, Paulli M, et al. Granulomatous mycosis fungoides and granulomatous slack skin: a multicenter study of the Cutaneous Lymphoma Histopathology Task Force Group of the European Organization for Research and Treatment of Cancer (EORTC). *Arch Dermatol*. 2008;144:1609-1617.
14. van Mechelen M, van der Hilst J, Gyssens IC, et al. Mycobacterial skin and soft tissue infections: TB or not TB? *Neth J Med.* 2018;76:269-274.
15. van Zyl L, du Plessis J, Viljoen J. Cutaneous tuberculosis overview and current treatment regimens. *Tuberculosis (Edinb).* 2015;95:629-638.
16. De Maio F, Trecarichi EM, Visconti E, et al. Understanding cutaneous tuberculosis: two clinical cases. *JMM Case Rep.* 2016;3:E005070.
17. Wu S, Wang W, Chen H, et al. Perianal ulcerative skin tuberculosis: a case report. *Medicine (Baltimore)*. 2018;97:E10836.