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Granulomatous Inflammation of the Penis and Scrotum Following Application of Topical Cream

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Abstract
Granulomas are collections of histiocytes that develop as an inflammatory response to bacterial and fungal infections, as well as foreign substances. We discuss here the case of a 49-year-old male who presented with a penile and scrotal mass with granulomatous inflammation, after application of a topical cream for enhancement of erectile function. While granuloma formation can often be seen with penile injections, this case presents the rare development of a foreign body granuloma after topical cream application on the penis and scrotum.

Introduction
The immune system uses a variety of methods to combat pathogens and infections. Granuloma formation is a method by which macrophages wall off certain bacteria, fungi, and foreign substances. Acute inflammation begins with the entry of a foreign substance, and chronic inflammation continues as neutrophils and then macrophages fail to eliminate and begin to isolate the pathogen or substance. Granuloma formation is often evident in diseases such as tuberculosis, sarcoidosis, and vasculitides, particularly in the lungs. However, granuloma formation can also present cutaneously in cases of foreign bodies. With respect to the male genitalia, granulomatous inflammation has been previously observed in rare cases of sarcoidosis and, more commonly, in patients using injectable fillers into the penis for cosmetic purposes. Materials such as mineral oil, silicone, collagen, and hyaluronic acid have all been documented as leading to granuloma formation within the male genitalia. In addition, topical administration of talc has been shown to be involved in foreign-body granuloma formation. However, review of the literature shows no reports of granulomatous inflammation following administration of a topical cream on the male genitalia, as seen in our case.

Case presentation
A 49-year-old Cambodian male visited our clinic with concern for a penile and scrotal mass growing in size for the past 3 months. The patient was asymptomatic and denied fevers, chills, weight loss, pain, obstructive or irritative lower urinary tract symptoms, and hematuria. Family and social histories were unremarkable. The patient initially denied any new medications, supplements, or chemicals but later admitted to using a topical cream, purchased on the internet, for enhancement of erectile function. He denied any injections into his genitalia.

The patient's vital signs were within normal limits. On exam, the spermatic cord was palpable and non-tender, with no hernia noted. The penis was circumcised, with a firm mass at the midline mons pubis extending circumferentially around the base of the penis and superior scrotum. No discharge was noted. The testes were symmetric, firm, and non-tender, with normal, non-tender epididymis and no testicular masses or palpable nodules. Urethral meatus, urethra, and urothelium were unremarkable.

The patient brought with him a CT abdomen and pelvis from his primary physician's office, which demonstrated a 5 × 6.5 × 5 cm...
region of abnormally enhancing subcutaneous tissue superior to the penis and anterior to the pubic symphysis, along with mildly prominent enhancing bilateral inguinal lymphadenopathy (Fig. 1). CT imaging was otherwise unremarkable. The patient then underwent examination under anesthesia (EUA), scrotal biopsy, and cystourethroscopy. EUA revealed the firm, circumferential mass at the mons pubis and superior scrotum, extending along the median raphe toward the perineum but without perineal involvement. No lymphadenopathy was noted, and cystourethroscopic exam was unremarkable. An excision of the scrotal mass (2 × 2 × 2 cm) and overlying skin was obtained via midline incision of the superior aspect of the ventral scrotum at the median raphe and was sent to pathology. Pathology results revealed homogenous, dense and white fibrous tissue containing non-caseating granulomatous inflammation, giant cell reaction, and fibrosis (Fig. 2). The sample of overlying skin showed non-caseating granulomatous inflammation of the dermis, as well as fibrosis and chronic inflammation of the epidermis. Polarizable foreign material within the giant cell reaction was noted in the dermis (Fig. 3). Grocott’s methenamine silver (GMS) stain for fungi and an acid-fast bacilli (AFB) stain were both

Figure 1. Coronal and sagittal CT of the abdomen and pelvis (left) demonstrating a 5 cm infiltrative mass within the subcutaneous tissues of the mons pubis. Derms was relatively spared, with no associated abscess. Axial CT contrast of the pelvis (right) demonstrating an inflammatory soft tissue mass in the mons pubis, not extending into the inguinal canals or involving the pubic bones.

Figure 2. Granulomatous inflammation with multiple foreign body giant cells (medium power at 10×, H&E stain).

Figure 3. Giant cell engulfing a polarizable, crystallloid-type object (high power at 40×, H&E stain).
negative. The biopsy results were discussed with the patient at his follow-up appointment, and he was advised to refrain from further use of the topical cream.

Discussion

Granulomas are a macrophage-driven inflammatory response to isolate foreign pathogens and substances. While common in tuberculoid and sarcoid presentations in the lungs, granulomas can also be seen cutaneously with administration of foreign substances. Granuloma formation in the male genitalia has been well-documented in the case of permanent, injectable fillers for cosmetic purposes, yet there is no report of granuloma formation following topical cream administration. Topical usage of talc has been demonstrated to result in cutaneous foreign-body granulomas, but this has not been documented as presenting in the male genitalia.\(^4\) The topical product used by the patient was found to be a cream called MAX Size. The active ingredient in the product was a natural phosphodiesterase type 5 inhibitor used to block the degradative action of cGMP-specific phosphodiesterase type 5 (PDE5) on cyclic GMP in the smooth muscle cells lining the blood vessels supplying the corpora cavernosa of the penis.

While our patient was hesitant to report his topical cream use, he denied using any injections into his genitalia. While the differential included etiologies such as sarcoidosis, tuberculosis, and vasculitides, the clinical presentation, along with the history and pathology, supported foreign-body granulomas in response to topical cream administration.\(^1\) This case thus demonstrates the rare presentation of subcutaneous and dermal granulomatous inflammation and giant cell reaction of the penis and scrotum following topical cream usage.

Conclusion

A rare granulomatous inflammation and giant cell reaction in the genitalia can result from the use of topical cream administration for enhancement of erectile function. A thorough history of genitourinary exposure to exogenous substances is warranted in cases of penile and scrotal masses. It remains unclear how this topical cream led to such a granulomatous reaction. Further work needs to be done to document and evaluate the potential causes of granulomatous formation in the male genitalia.

Conflict of interest statement

The authors have no conflicts of interest.

References