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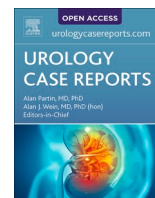
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Inflammation and infection

Herpes simplex virus-2 associated with a large fungating penile mass

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ABSTRACT

A 48-year-old male with HIV/AIDS presented with an enlarging nodular lesion on the base of his penis. Histology revealed changes consistent with chronic viral infection and culture grew herpes simplex virus 2 (HSV-2). The lesion was refractory to valacyclovir and intralesional (IL) cidofovir therapy. Urology excised the mass and the defect was repaired primarily with good cosmetic result. Post-operative pathology confirmed HSV-2 despite the unusual appearance of the lesion consisting of nodular mass without gross ulceration.

Introduction

Classic herpes simplex virus 2 (HSV-2) lesions produce painful genital ulcers. When large, papillary genital masses develop, they are typically caused by human papilloma virus (HPV) serotypes. These lesions have been known to grow to impressive size in those with compromised immune systems, such as in human immunodeficiency virus (HIV) infection. The literature has shown effective treatment of large HPV lesions with intralesional (IL) cidofovir, and otolaryngologists use IL cidofovir in the case of laryngeal papillomatosis with good results.¹ Optimal treatment of verrucous HSV-2 lesions is less well defined in the literature.

Case presentation

We present the case of a 48-year-old male who presented with four months of an enlarging nodular lesion at the base of his penis (Fig. 1). His medical history included HIV/AIDS, alcohol use disorder, anal dysplasia, pulmonary tuberculosis, Pneumocystis pneumonia, and esophagitis. His viral load was undetectable and CD4 count was 98 cell/mm.³ Dermatology initially performed multiple evaluations of the lesion. Biopsy and histology repeatedly revealed changes consistent with chronic viral infection and culture grew herpes simplex virus 2 (HSV-2) sensitive to acyclovir.

He was treated with valacyclovir 1 gram twice daily and topical trifluridine for four months. After continued growth, IL cidofovir 30

milligrams for three total injections was initiated. Despite this, the mass grew larger and he was referred to Urology for excision. Preoperative exam revealed a 4 × 2cm exophytic nodule at the dorsal base of his penis without ulceration and with significant weeping. He was scheduled for surgical excision; at which time the mass had grown to 5.5 × 2.5cm, forty-seven days later. Pathology examination of the excised lesion showed ulcer positive for HSV-2 and dense chronic lymphoplasmacytic infiltrate (Fig. 2). The defect was closed primarily with good cosmetic result.

Discussion

Verrucous, or hypertrophic, HSV lesions represent fewer than 5% of genital herpes lesions.² This presentation is typically associated with acyclovir resistance and occurs almost exclusively in immunocompromised patients. Mechanistically, it has been demonstrated to be due to mutations in the pathways regulating viral thymidine kinase enzyme expression. This enzyme normally functions via intracellular phosphorylation of acyclovir, which is a critical first step in the activation of the drug. Mutations that confer decreased or absent expression of this kinase protein underlie 95% of acyclovir resistance.³

In the rare case of hypertrophic HSV lesions, case reports have demonstrated IL cidofovir therapy to be effective in both acyclovir-sensitive and in acyclovir-resistant infections in HIV positive men.⁴ Moreover, surgical debulking has been shown to be effective for treatment of recalcitrant lesions, but typically is not favored over medical

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Fig. 1. (left) Preoperative depiction of gross lesion and (right) incision at 3 week postoperative check.

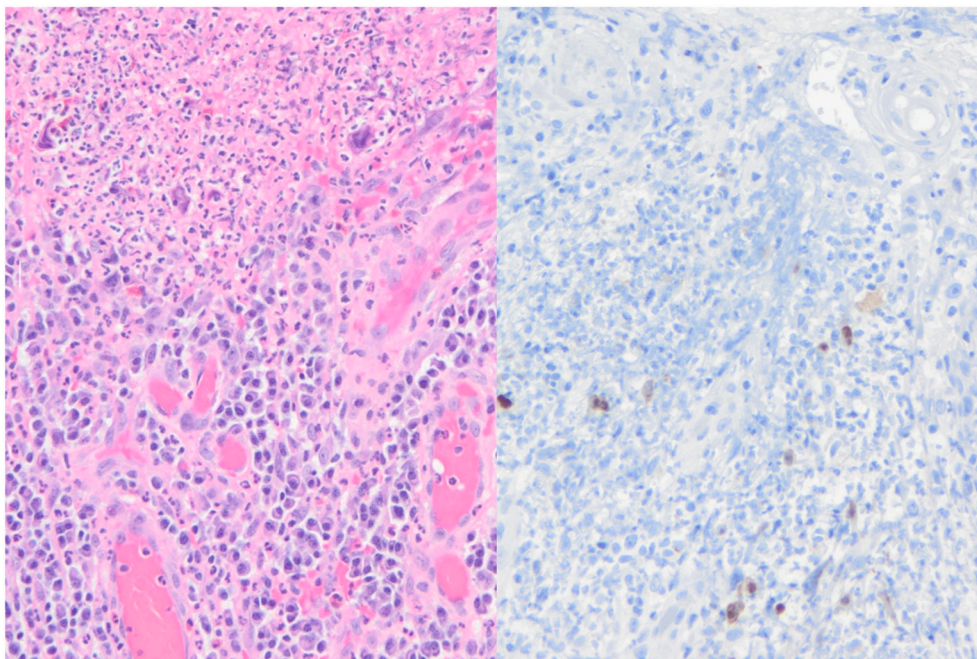


Fig. 2. (left) H&E 20x; Sections show a dense inflammatory infiltrate composed of lymphocytes, plasma cells, eosinophils, and neutrophils. There are several superficial keratinocytes demonstrating nuclear viropathic changes, and there is no evidence of carcinoma and (right) these cells also demonstrate positive nuclear immunohistochemical staining for HSV.

management of genital lesions due to risk of recurrence.⁵ The optimal management of this uncommon pathology is yet to be fully elucidated.

Conclusion

This case demonstrates the importance to consider causes other than HPV in large genital lesions with concomitant HIV or other immunocompromise. Regarding hypertrophic HSV lesions, several aspects of the above presentation are unusual. First, although verrucous HSV has been described in HIV positive patients, it is highly atypical for these lesions

to demonstrate acyclovir-sensitivity. Considering this finding, it is additionally surprising that this lesion continued to grow despite valacyclovir and IL cidofovir treatment. Finally, we have demonstrated that in the event of conservative and medical treatment failure, surgical excision can be a reasonable option with good cosmetic results and substantial improvement in the quality of life of the patient, even in the case of very large lesions.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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