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Herpes simplex virus of the nose masquerading as invasive fungal sinusitis: A pediatric case series

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ABSTRACT

The management of invasive fungal sinusitis differs greatly from the management of herpes simplex virus (HSV) of the nose in immunocompromised patients. However, the diagnosis may be uncertain and a delay in treatment can lead to mortality. Here we describe the successful medical management of a series of immunocompromised pediatric patients with HSV lesions of the nose with the initial concern for invasive fungal sinusitis. The diagnosis of HSV herpes was supported by positive polymerase chain reaction (PCR) testing of the nasal lesion. To our knowledge, these are the first cases described in the pediatric literature, emphasizing the need to include this entity on the differential.

1. Introduction

Acute invasive fungal sinusitis (IFS) is a rare infection with a mortality rate as high as 50%. IFS has predilection for immunocompromised patients (Fig. 1), when fungi, such as *Aspergillus* or *Mucor*, invade the paranasal sinus mucosa and destroy adjacent structures though angioinvasion [1,2]. Risk factors include hematologic malignancy, bone marrow transplantation, uncontrolled diabetes mellitus, HIV/AIDS, corticosteroid use. Symptoms include fever, pain, congestion, facial swelling, edema, pale nasal mucosa, and necrotic tissue. Treatment of IFS includes systemic antifungal therapy, urgent surgical debridement, and correction of immunosuppression [1].

In immunocompromised patients, aggressive herpetic lesions are IFS mimickers and should be on the differential when managing these patients. The herpes simplex virus (HSV) is a double stranded DNA virus with cutaneous manifestations such as formation of vesicles or ulcers. Classically HSV lesions are distinctly described as grouped vesicles on an erythematous base, with a prodrome of burning, itching, or pain [3]. In immunocompromised individuals, the clinical presentation can be atypical. Additional studies include Tzank smear, viral culture, and PCR testing. Herpes infections can also trigger a dense lymphocytic infiltrate that resembles cutaneous lymphoma. [3] Acyclovir given by continuous intravenous infusion may be beneficial in the treatment of herpes virus infections in immunocompromised patients [4].

Upon Institutional Review Board exemption, we describe the successful medical management of a series of immunocompromised pediatric patients with nasal herpetic lesions with an initial concern for invasive fungal sinusitis.

2. Case 1

A 19-year-old female with stage 4 mature B cell leukemia, intubated for a multifocal pneumonia, presented with a sudden onset epistaxis. She was undergoing treatment per the Children's Onocology Group protocol ANHL01P1 and had multi-organ system failure due to tumor lysis syndrome. Absorbable oxidized regenerated cellulose hemostatic agent was placed bilaterally to control the epistaxis. Over the course of the next 3 days, the patient developed nasal cellulitis and crusting. After debridement of packing, blood clot, and crusting overlying her face, the physical exam revealed a nasal lesion with hemorrhagic crusts and ulceration on an erythematous base involving the nasal columella, ala, base, and upper lip (Fig. 2). At that point she had febrile neutropenia and was receiving neupogen for pancytopenia after completing a course of cytarabine, rituximab, and etoposide chemotherapy. Nasal endoscopy revealed sensate pink mucosa and but slightly pale edema on the left middle turbinate (this was the site of a nasogastric feeding tube). A biopsy was performed at this site and cultures of the debrided crusting were sent. Given the hemorrhagic crusting, a nasal swab was also taken

Abbreviations: HSV, herpes simplex virus; IFS, invasive fungal sinusitis; PCR, polymerase chain reaction

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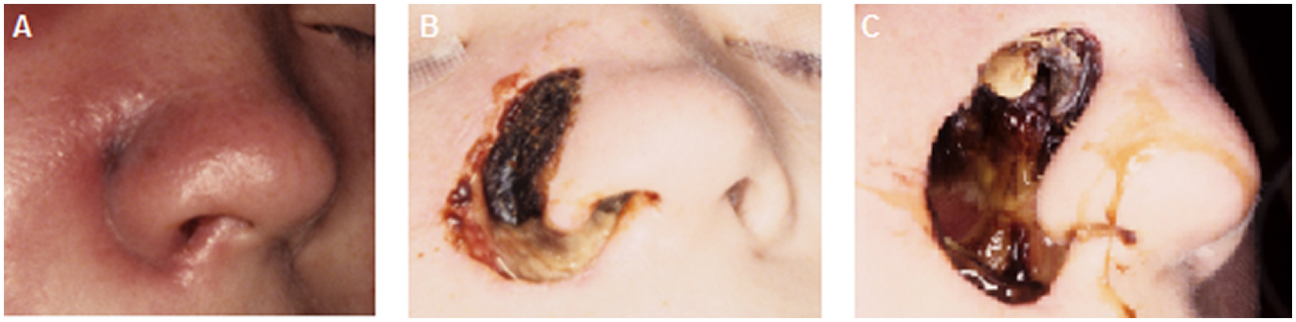

Fig. 1. Invasive fungal sinusitis progression in a 15 year old immunocompromised female on maintenance chemotherapy for leukemia. She presented with fevers, check swelling, and pain. A) Nasal rim erythema/edema. B) Rapidly progressing skin necrosis with a diagnosis confirmed by endonasal biopsy of necrotic turbinate mucosa. C) Necrotic skin demarcated.

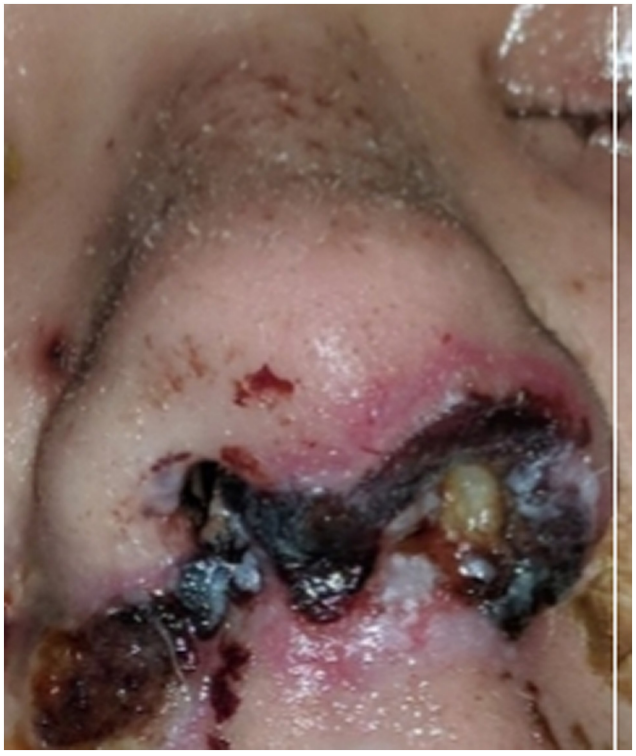

Fig. 2. Nasal herpes in a 15 year old patient. Hemorrhagic crusts are seen on an erythematous base involving the columella and alar rims, and ulceration/crusting on the right nasal base/upper lateral lip subunit.

specifically for HSV PCR testing.

As IFS and HSV were on the differential, the patient's fluconazole prophylaxis was temporarily broadened to amphotericin B and acyclovir was added awaiting culture results. Pathology confirmed no fungal elements and showed only inflamed nasal mucosa and cultures showed no growth. CT imaging revealed mild sinus mucosal thickening but no evidence of erosion or invasion of adjacent fat planes. The amphotericin B was discontinued. HSV viral PCR came back positive for HSV1 and the patient's treatment regimen was narrowed to intravenous acyclovir. The nasal ulcer was also managed with topical mupirocin and the lesion resolved over the course of 2 weeks.

3. Case 2

An 8 year old boy with relapse of pre-B acute lymphoblastic leukemia (ALL) undergoing chemotherapy per Children's Oncology Group AALL0932 protocol, presented with fever, thrombocytopenia and eye swelling. CT scan of orbits revealed periorbital cellulitis. He began re-induction chemotherapy, consisting of Dexamethasone, Vincristine, Pegaspargase, Mitoxantrone and intrathecal Methotrexate. The periorbital cellulitis fully resolved after treatment with Cefepime and Vancomycin. Despite resolution of the periorbital cellulitis, the patient remained neutropenic with persistent fevers. Antibiotics were broadened to Meropenem, Vancomycin and Amikacin; Amikacin was discontinued after blood cultures were negative for 48 h. At that time, he developed an erythematous, slightly cystic nasal lesion involving the right alar rim (Fig. 3). CT imaging revealed mild sinus mucosal thickening but no evidence of erosion or invasion of adjacent fat planes. Nasal endoscopy revealed normal, sensate mucosa therefore a biopsy was not performed. Given the erythematous base of the lesion, and a high degree of suspicion for a viral herpes infection, a nasal swab was also taken specifically for HSV PCR testing. There was low clinical suspicion for an invasive fungal infection, but given persistent fevers, Voriconazole was added until the PCR testing came back the following day. HSV viral PCR resulted positive for HSV1 and the patient was treated with intravenous Acyclovir for a nasal HSV infection. The lesion crusted over and resolved over the course of one week on Acyclovir.

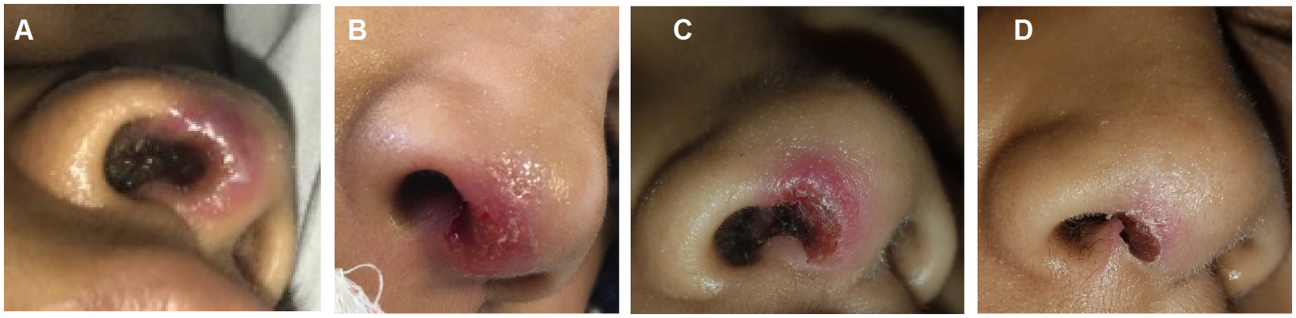

Fig. 3. Nasal herpes in an immunocompromised patient A) nasal lesion at presentation B) nasal lesion after 1 day C) nasal lesion after 2 days D) nasal lesion after 6 days.

4. Discussion

The nasal lesions described here fit many of the classic findings of HSV infection in terms of ulceration and crusting on an erythematous base but the lack of characteristic vesicles in the presence of aggressive hemorrhagic lesions make the diagnosis misleading. When differentiating between nasal HSV and IFS, cultures and a biopsy should be performed if there are any suspicious nasal findings as a missed IFS is rapidly fatal. The site specific diagnosis of nasal herpes can also be rapidly corroborated with a nasal HSV viral PCR swab. The results may be available within 24 h. In immunocompromised patients, the management of invasive fungal sinusitis involves surgical debridement and antifungal therapy whereas nasal herpes is managed with intravenous acyclovir and wound care. For this reason, it is important to keep HSV nasal infection in mind for the differential when managing immunocompromised patients with nasal findings.

5. Conclusion

Reported here are the first descriptions of pediatric nasal HSV infection in immunocompromised patients with an initial concern for invasive fungal sinusitis. The diagnosis of HSV was confirmed with PCR testing and the disease was successfully management medically with intravenous acyclovir.

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IRB

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Declaration of Competing Interest

The authors have no conflicts of interest relevant to this article to disclose.

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