



The Use of Topical Amphotericin Nasal Packing for Invasive Fungal Sinusitis in an Adolescent Patient

Madelyn N Stevens^{1*}, Kelly C Landeen¹, Sarah Tittman¹ and James Phillips²

¹Department of Otolaryngology-Head and Neck Surgery, Vanderbilt University Medical Center, Nashville, US

²Department of Otolaryngology, Monroe Carrell Jr Children's Hospital, Nashville, US

*Corresponding author: Stevens MN, Department of Otolaryngology-Head and Neck Surgery Vanderbilt University Medical Center, Nashville, US; Tel: 6153226180; E-mail: Madelyn.stevens@vumc.org

Received date: May 18, 2021; Accepted date: June 02, 2021; Published date: June 09, 2021

Abstract

Acute Invasive Fungal Sinusitis (IFS) can be difficult to control, with surgical debridement playing the primary role in treatment. Here we present a novel adjunctive treatment of IFS with topical anti-fungal nasal packing. A 15-year-old female underwent multiple extensive endo nasal debridements with persistent fungal elements. Due to the risk of nasal deformity with further debridement, amphotericin B soaked in dissolvable foam was applied topically within the nose as an adjunct to surgical and intravenous therapy. Pathology after initiation of amphotericin nasal packing was negative for fungal elements on all sites. Patient has not had disease recurrence at 6 months.

Keywords: Invasive fungal sinusitis; Topical antifungal; Topical intranasal

Introduction

Invasive fungal sinusitis (IFS) is notoriously difficult to control, with surgical debridement and Intravenous (IV) antifungals playing the primary role in therapeutic treatment. Even with appropriate management, morbidity and mortality remain high in the pediatric population, highlighting a need for optimization of outcomes [1,2]. The use of topical antifungals, particularly amphotericin B, has been reported as an adjunct treatment in adults with refractory chronic rhinosinusitis, with mixed results [3,4]. Yet there remains a paucity of research on the use of topical antifungals as an adjunct for IFS [5], particularly in the pediatric literature. Here we present a novel treatment of sinonasal IFS with topical anti-fungal nasal packing in an adolescent as an adjunct to surgical debridement and intravenous treatment.

Case Report and Methods

A 14-year-old female undergoing chemotherapeutic treatment for B-cell acute lymphoblastic leukemia at a tertiary academic center had a new finding of epistaxis and black eschar on her right nasal septum. Otolaryngology was consulted and an urgent bedside flexible endoscopic evaluation revealed an insensate black eschar on the right

nasal septum with extension to the nasal floor (Figure 1). Cranial nerve exam was intact other than palatal numbness, and initial Computerized Tomography (CT) scan did not demonstrate bony or soft tissue invasion (Figure 2).

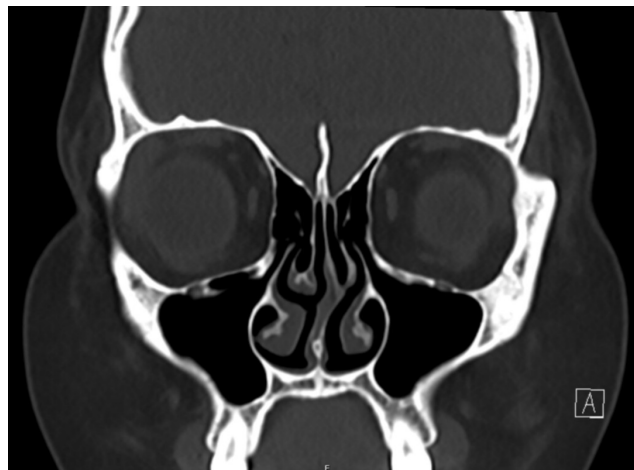


Figure 1: Endoscopic image of right septal eschar at initial presentation.

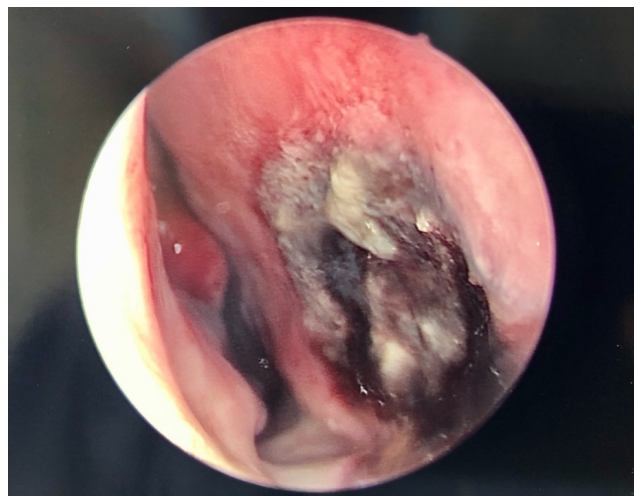


Figure 2: Non-contrasted sinus Computerized Tomography (CT) scan without bony or soft tissue invasion consistent with invasive fungal disease.

Due to high suspicion for IFS, the patient was promptly taken to the operating room for interventions that included biopsies, a partial septectomy, and debridement of the inferior and middle turbinate's and nasal floor. Initial biopsies were positive for bipolar is fungal species. Patient was also urgently started on a course of intravenous amphotericin B. Debridement was repeated on Post-Operative Days (POD) 2 and 7 from initial surgery due to positive biopsies at the margins of debridement. On POD 6 she was also started on oral posaconazole. Biopsies obtained on POD 13 were persistently positive for fungal elements, and there was concern for possible pulmonary involvement despite negative bronchoalveolar lavage. On POD 14, IV amphotericin was switched to IV micafungin. She was also started on a neutrophil-sparing chemotherapy regimen due to ongoing neutropenia. With successive trips to the operating room after initial

debridement the tissue appeared grossly healthy, but biopsies and debridement continued to be positive, particularly towards the anterior caudal margin of the septum towards the columella.

Treatment with topical amphotericin B packing was initiated on POD 16 from initial diagnosis and debridement in an effort to obtain source control while sparing the patient from further surgical debridements. Topical nasal packing consisted of dissolvable foam (surgifoam/surgiflo) soaked in amphotericin B concentration 50 mg/200 ml, which was instilled into the nasal cavity. Packing was changed daily at bedside to ensure ongoing adequate instillation of antifungal treatment, which continued for a total of 7 days.

Pathology specimens from final biopsy after initiation of amphotericin nasal packing were negative for live fungal elements at all sites, and no further surgical debridement was needed. IV micafungin was discontinued on POD 27. The patient was continued on a prolonged course of oral posaconazole throughout her chemotherapy treatments. She did not have disease recurrence identified on repeat nasal endoscopy at 6 months.

Discussion

Here we present a novel treatment of invasive fungal sinusitis with topical amphotericin B nasal packing as an adjunct to established therapies in an adolescent patient. Despite no CT evidence of invasive disease or bony erosion, she had an obvious eschar on endoscopy that required urgent debridement, highlighting the importance of clinical exam in diagnosing IFS. Surgical debridement plays the primary role in treatment of IFS due to the aggressive nature of the disease and was the initial treatment of choice in this case, along with intravenous and oral antifungal therapy [1,2]. The patient underwent three surgical debridements and a course of intravenous amphotericin B and micafungin, as well as oral posaconazole. Despite these interventions, she had persistently positive fungal elements identified after the fourth biopsy after implementing instillation of topical amphotericin B nasal packing, biopsies no longer showed evidence of live fungal elements and further surgical interventions were not needed.

The use of topical medications has been efficacious in treating other rhinologic diseases due to ease of access to the nasal cavity and uptake of medications through the nasal mucosa. Topical intranasal steroids, either alone or with nasal saline irrigation, is the standard of care for chronic rhinosinusitis [6-8]. Research is ongoing into other topical treatment therapies including intranasal antibiotics [9]. Topical steroid treatment has also been investigated in patients with cystic fibrosis with mixed results [10]. The success of prior directed intranasal therapies suggested that a topical approach as an adjunct in this case may be of benefit.

Topical treatments were a particular consideration in this patient due to the importance of preserving nasal form and function. Nasal soft tissues continue to grow throughout adolescence, and some studies even suggest that growth continues into early adulthood [11]. As one of the major support mechanisms for the nasal dorsum, the septum especially helps to provide structure to the nose. Pediatric patients who have experienced nasal trauma, especially septal hematoma or abscess with subsequent necrosis and septal loss, at are increased risk of developing significant deformity such as a saddle nose, diminished anterior or vertical growth, and maxillary hypoplasia [12-14]. For these reasons, thoughtful attention must be paid to the extent of nasal debridement in the pediatric population.

After multiple resections including a near-complete anterior septectomy, there was concern that further aggressive debridement's in this patient would cause nasal deformity that could be functionally and cosmetically deleterious. Shared decision making was utilized with the patient and her guardians regarding morbidity associated with continued aggressive resections, balanced against the risk of not obtaining source control of her persistent fungal disease. In this case, the decision was made to attempt to obtain negative biopsies with topical treatment before performing additional surgical resections that could result in significant deformity.

Utilizing adjunct treatments such as topical antifungals may help to obtain source control and mitigate the need for aggressive surgical resection that can lead to nasal deformity in a child. The authors encourage the consideration of these methods in pediatric patients who will tolerate such treatment, as it may lead to improved rhinologic and aesthetic outcomes.

Limitations of this report include that it is a single case and further investigation is warranted to evaluate the use of topical medications in children to support its implementation into treatment algorithms for acute IFS. Of note, however, topical antifungals were not used as a single modality in this case—nor would it be appropriate to do so. The heterogenous nature as well as the rarity of individual cases of IFS makes it difficult to standardize treatment. However, we propose that topical antifungal application presents a low-risk adjunct that may expedite clearance of disease and help patients to avoid extensive surgical interventions.

Conclusion

Nasal packing with amphotericin B soaked in a dissolvable matrix was used as an effective adjunct to surgical debridement for treatment of acute IFS in this adolescent patient. This helped minimize the need for aggressive surgical resection, which could have caused significant nasal deformity in a young, developing nose. Future cases could benefit from earlier utilization of topical amphotericin B, and additional study is warranted into the efficacy of topical antifungals against various fungal species.

References

1. Hanba C, Svider PF, Lai W, Raza SN, Sheyn A, et al. (2017) An investigation of operative outcomes: Pediatric invasive fungal sinusitis. *Int J Pediatr Otorhinolaryngol* 102: 142-147.
2. Alejandro A, González C, Edgar M, Perla V (2020) Factors associated with all-cause mortality in pediatric invasive fungal rhinosinusitis. *Int J Pediatr Otorhinolaryngol* 129.
3. Wang T, Su J, Feng Y (2015) The effectiveness topical amphotericin B in the management of chronic rhinosinusitis: A meta-analysis. *Eur Arch Otorhinolaryngol* 272:1923-9.
4. Shirazi MA, Stankiewicz JA, Kammeyer P (2007) Activity of nasal amphotericin B irrigation against fungal organisms *in vitro*. *Am J Rhinol* 21:145-8.
5. Galvez AF, Lipka OL, Haith LR, Scantling D, Kaplan MA, et al. (2017) Treatment of invasive mucormycosis with intravenous isavuconazonium and topical amphotericin B in a renal-impaired patient: case report and review of the literature. *Surg Infect Case Rep* 2:40-45.

6. Chong LY, Head K, Hopkins C, Philpott C, Burton MJ, et al. (2016) Different types of intranasal steroids for chronic rhinosinusitis. *Cochrane Database Syst Rev* 26: 4.
7. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, Brook I, Ashok KK, et al. (2015) Clinical practice guideline (update): Adult sinusitis. *Otolaryngol Head Neck Surg* 152.
8. Tan NCW, Psaltis AJ (2020) Latest developments on topical therapies in chronic rhinosinusitis. *Curr Opin Otolaryngol Head Neck Surg* 28:25-30.
9. Carlton DA, Beahm DD, Chiu AG (2019) Topical antibiotic therapy in chronic rhinosinusitis: an update. *Int Forum Allergy Rhinol* 9:S27-S31.
10. Beer H, Southern KW, Swift AC (2015) Topical nasal steroids for treating nasal polyposis in people with cystic fibrosis. *Cochrane Database Syst Rev*.
11. Sharma P, Arora A, Valiathan A (2014) Age changes of jaws and soft tissue profile. *Sci World J* 2014.
12. Olsen KD, Carpenter RJ III, Kern EB (1980) Nasal septal injury in children: Diagnosis and management. *Arch Otolaryngol* 106: 317-320.
13. Rohrich RJ, Adams Jr WP (2000) Nasal fracture management: minimizing secondary nasal deformities. *Plast Reconstr Surg* 106: 266-273.
14. Grymer LF, Bosch C (1997) The nasal septum and the development of the midface. A longitudinal study of a pair of monozygotic twins. *Rhinology* 35:6-10.