

Methicillin-Resistant *Staphylococcus aureus*-Associated Infections following Septorhinoplasty

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Abstract

Septorhinoplasty is associated with postoperative infection in less than 2% of cases, even without the use of prophylactic antibiotics. However, there is a concern that increasingly prevalent, highly virulent pathogens such as MRSA may predispose to postoperative infections. Over the past several decades, MRSA has emerged as the most important cause of antibiotic-resistant nosocomial infection. MRSA-associated infections related to nasal surgery are underreported in the literature. We present a case of MRSA-associated infection following a routine septorhinoplasty in a health care worker. We discuss the incidence of this complication and contributing risk factors. The classification of MRSA-associated infections into genotypically distinct hospital-acquired and community-acquired subtypes is reviewed, and the associated differences in epidemiology, clinical presentation, and antibiotic susceptibility are discussed. A comprehensive strategy incorporating diagnostic workup, preventative management based upon preoperative risk stratification, and treatment of MRSA-associated soft tissue infections is presented.

Keywords

- ▶ septorhinoplasty
- ▶ rhinoplasty
- ▶ infection
- ▶ MRSA
- ▶ complications

Case Report

A 26-year-old healthy female nurse underwent an uncomplicated open approach septorhinoplasty for nasal obstruction and aesthetic concerns. The procedure consisted of a septoplasty, spreader grafts, cephalic trim, tongue-in-groove displacement of the lower-lateral cartilages, a dome-spanning suture, medial and lateral osteotomies, and bilateral type 2 Weir excisions. As per our standard practice, a single dose of preoperative azithromycin was provided given self-reported allergies to penicillin, cephalosporins, clindamycin, and sulfa-based medications. Postoperatively, the patient was instructed to apply Bacitracin ointment to her incision sites for 3 days followed by petroleum jelly for 3 days. The patient convalesced well but contacted the on-call resident on the fourth postoperative day with concerns of persistent nasal discomfort despite narcotic analgesia. The patient was asked to return to the hospital for evaluation but elected to forgo assessment until her upcoming follow-up appointment. On postoperative day 6, the patient presented to the clinic with

continuing discomfort and a fever of 38°C. Examination revealed inflammation and edema at the base of the caudal septum with some slight erythema at the nasal base. A diagnosis of cellulitis was considered and ciprofloxacin was prescribed. The patient returned to the clinic the following day for reassessment. The caudal septum appeared to be more fluctuant and the area was anesthetized, then incised and explored with a sterile hemostat, resulting in egress of a small amount of pus from a moderately sized pocket between the mucoperichondrial flaps. Aerobic and anaerobic cultures were taken from this early septal abscess. Sterile iodoform gauze was then loosely packed into the cavity and the patient returned the following day for reevaluation.

Cultures revealed methicillin-resistant *Staphylococcus aureus* (MRSA) resistant to ciprofloxacin. The inflammation of the caudal septum appeared slightly improved and the iodoform gauze was removed. Review of the patient's allergy history revealed some uncertainty regarding a reaction to sulfa. Consequently, the patient was prescribed trimethoprim/sulfamethoxazole (TMP/SMX) and topical mupirocin

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ointment. The patient returned for assessment on postoperative day 12 having tolerated the antibiotics without incident. Her low-grade fevers had resolved and her nasal discomfort had completely subsided. Examination revealed well-healed incisions and no visible edema or erythema of the caudal septum. The patient completed her course of antibiotics and was seen again 2 weeks later and at 3 months postoperatively. No evidence of infection or compromised healing was noted on either visit.

Discussion

S. aureus is the most commonly isolated organism from nasal swabs. The anterior nares are considered the primary ecologic reservoir for these bacteria. Up to 60% of the general population are intermittent carriers of methicillin-sensitive *Staphylococcus aureus* (MSSA) with an additional 20% designated as persistent carriers.¹ Presence of MSSA is protective against colonization with MRSA.² Nonetheless, 1.5% of the general population in the United States is colonized with MRSA.³ Displacement of MSSA through the use of broad-spectrum antibiotics facilitates nasal colonization with MRSA.² Indeed, MRSA nasal colonization is established in 4.2% of patients on admission and over 20% after an average-length hospitalization.⁴ Health care workers are at increased risk of MRSA colonization. One recent study identified that 6.7% of health-care workers were colonized with MRSA. Within this cohort, nurses demonstrated the highest MRSA prevalence rates of 10.4% secondary to close, frequent patient contact.³ The prevalence may be even higher among those working in intensive care environments. In one pediatric intensive care unit, 26.2% of health care workers were found to be colonized with MRSA.⁵ Health care workers, children, the elderly, and immunosuppressed individuals may be at increased risk of infectious complications following nasal surgery.

MRSA exists in community-acquired (CA-MRSA) and hospital-acquired (HA-MRSA) forms that are genetically distinct. MRSA obtains resistance to penicillin through mutations in penicillin-binding protein 2A (PBP2A) encoded by the *mecA* gene and residing within a free staphylococcal cassette chromosome *mec* (SCC*mec*). SCC*mec* is involved in modulation of resistance genes. SCC*mec* types I to III are associated with HA-MRSA and type IV with CA-MRSA.⁶ HA-MRSA strains seldom carry the gene for the Panton-Valentine leukocidin (PVL) and are often resistant to many classes of non- β -lactam antibiotics. CA-MRSA isolates are less resistant to non- β -lactam antimicrobials and often harbor PVL genes.⁷ The diagnosis of CA- versus HA-MRSA based on their molecular characteristics and antimicrobial susceptibility profiles is not commonly performed in the clinical setting due to cost and time constraints imposed by treating acute infections.

However, clinical characteristics can help distinguish between CA-MRSA and HA-MRSA infections. CA-MRSA infections tend to involve skin and soft tissue and are, generally, less invasive than their HA-MRSA counterparts. In one study evaluating 1100 MRSA infections, skin and soft tissue infections were found to be significantly more common among CA-MRSA cases (75%) than in HA-MRSA cases (37%).⁶ Further

delineation of MRSA phenotype comes through the Centers for Disease Control (CDC) definition. The CDC defines CA-MRSA infection as any MRSA infection diagnosed within 48 hours of hospitalization or assessment if the patient lacks the following health care-associated risk factors: hemodialysis, surgery, residency in a long-term care facility, hospitalization within the previous year, presence of an indwelling catheter or other percutaneous device, and previous isolation of MRSA from the patient. All other infections are attributed to HA-MRSA, including those associated with persistent exposure to a health care environment as in the case of health care workers.⁷ However, the CDC case definition as applied to patients with MRSA infections is not a reliable proxy for the phenotype of MRSA strain causing the infection. Establishing a clear delineation between CA-MRSA and HA-MRSA has not been possible and, consequently, a third category, "health care-associated, community-onset" (HACO-MRSA), has been utilized. This encompasses cases that would, traditionally, be classed as HA-MRSA secondary to exposure to the health care environment but have onset in the community.⁷ The index case described in this report may well represent a case of HACO-MRSA.

When identified, all suspected MRSA surgical site infections warrant detailed clinical assessment to elucidate severity. The usual signs and symptoms of inflammation—erythema, edema, pain, and warmth—are reliable indicators of soft tissue infection. Additional signs associated with more severe MRSA infections that often necessitate immediate surgical intervention include violaceous bullae, cutaneous hemorrhage, skin sloughing, skin anesthesia, rapidly progressive necrosis, and subcutaneous gas.⁸ These "complicated" soft tissue infections tend to occur in patients with complicating comorbidities such as diabetes, chronic steroid use, chronic renal failure, organ transplantation, HIV infection, or a malnourished state.⁸

Early management of MRSA soft tissue infections entails incision and drainage—as performed in the index case—and, if this is unsuccessful, proceeding to needle aspiration. This often provides purulent material for culture to confirm MRSA infection and, critically, to determine antimicrobial susceptibility. Per CDC guidelines, patients should be started on empiric antibiotics for all cellulitis, coexisting morbidities, immunosuppression, extremes of age, and—of particular relevance in relation to this case report—for all infections involving the central face given the propensity of facial soft tissue infections to cause suppurative phlebitis of vessels draining to the cavernous sinus.⁸ Treatment should be parenteral if there are any signs or symptoms of systemic involvement or rapid progression.⁹

The empiric choice of antibacterial agent should be based on prevalence and susceptibility data within the local community. CA-MRSA infections tended to be more susceptible to antimicrobial agents than hospital-associated cases. Suitable agents include clindamycin, tetracyclines, TMP/SMX, rifampin, and linezolid, with the latter reserved for the most severe infections.⁹ In vitro susceptibility testing across six CA-MRSA and six HA-MRSA isolates demonstrated that TMP/SMX is highly effective and more efficacious than other orally

bioavailable agents such as linezolid, rifampin, clindamycin, minocycline, and moxifloxacin.¹⁰ The treatment failure rate associated with the use of TMP/SMX for soft tissue infections is ~10%.⁹ MRSA strains are universally resistant to β -lactam antibiotics including all penicillins and cephalosporins. Fluoroquinolones should be avoided due to inherent resistance to these agents by both CA- and HA-MRSA in vivo despite misleading susceptibility as detected by in vitro laboratory methods.^{6,9} Approximately 90% of HA-MRSA strains are erythromycin-resistant and 80% of isolates show clindamycin resistance. Erythromycin and clindamycin resistances are less common in CA-MRSA strains (56% and 17%, respectively). Thus, in suspected CA-MRSA infections, macrolides should, generally, be avoided; clindamycin can be used effectively. MRSA strains that demonstrate erythromycin resistance often harbor inducible clindamycin resistance, which only becomes apparent on initiation of clindamycin therapy.⁶ Consequently, clindamycin is a suboptimal choice for infection treatment where susceptibility testing indicates erythromycin resistance and, thus, likely inducible clindamycin resistance.

The ideal management strategy in nasal surgery patients is to prevent soft tissue infections altogether. Investigators have studied the relationship between MRSA colonization and risk of subsequent postoperative infection. Approximately half of septorhinoplasty candidates will have *S. aureus* colonization of their nasal cavity prior to surgery. A subset of these patients will be colonized with MRSA, particularly if they are within the aforementioned high-risk categories. A recent study of 157 patients scheduled for endonasal surgery, of whom 26% underwent septoplasty or septorhinoplasty and 57% received endoscopic sinus surgery, found that only 1.3% of patients harbored MRSA preoperatively.¹¹ The only risk factor associated with MRSA colonization was a history of MRSA-associated infection. Hospitalization, previous intranasal surgery, antibiotic use, and health care occupation were not associated with an increased risk of MRSA colonization. Philpott et al retrospectively reviewed 151 endonasal surgery patients and noted that no patients were MRSA carriers preoperatively. Only a single patient had a positive MRSA swab postoperatively. The authors conclude that MRSA colonization is not a significant source of morbidity in nasal surgery patients.²

In essence, there has been no demonstrated correlation between preoperative MRSA in endonasal surgery patients and subsequent infection. This issue continues to receive attention since *S. aureus* has been associated with an infection rate of 3% following nasal and sinus surgery. These infectious complications include cellulitis, sinusitis, cavernous sinus thrombosis, septicemia, brain abscess, and toxic shock syndrome.^{4,12} Yet, there are only two reports in the literature describing MRSA infections following rhinoplasty. Cabouli et al described a case of a culture-proven MRSA abscess developing at the inner canthus of a post-rhinoplasty patient, attributed to infection of the external lateral osteotomy site.¹¹ A similar MRSA-associated infection of the lateral osteotomy site in a rhinoplasty patient with a history of previously treated MRSA-related axillary infection has been reported. Sharma et al postulated that the paucity of reported

cases can be attributed to four factors associated with nasal surgery: (1) a medically fit, middle-aged population; (2) short postoperative hospital course; (3) reduced antibiotic exposure with maintenance of natural nasal flora; and (4) increased vascularity of the nasal mucosa facilitating healing and a robust immune response.⁴

Despite the lack of evidence for MRSA-induced infection in nasal surgery, in the general surgery specialty literature, elimination of nasal *S. aureus* preoperatively results in a 50% reduction in surgical site infections.¹³ This has prompted many practitioners to advocate the prophylactic eradication of nasal MRSA. Three strategies have demonstrated efficacy for preoperative eradication of MRSA: (1) local application of antibiotics or disinfectants, (2) treatment with systemic antibiotics, and (3) bacterial interference using a nonpathogenic *Staphylococcus* strain to competitively inhibit MRSA growth.

Local application of antibiotics has gained acceptance due to the low-cost, noninvasive, and efficacious nature of this intervention. Mupirocin is often used as intranasal topical agent for MRSA decolonization. Mupirocin acts by binding bacterial isoleucyl tRNA synthetase, thereby inhibiting protein synthesis.⁷ Mupirocin applied topically twice a day for five consecutive days resulted in elimination of *S. aureus*, both MSSA and MRSA variants, in the nasal passages of between 91% and 97% of healthy patients.^{1,12} High-level resistance to mupirocin can rapidly emerge through the presence of the *mupA* gene, which is carried on a plasmid and encodes for a mutant isoleucyl tRNA synthetase, which does not bind mupirocin.⁷ Mupirocin use has been correlated with increased levels of resistance among MRSA isolates, although this has been an inconsistent finding with other investigators noting unchanged levels of resistance despite extensive usage of mupirocin. Mupirocin remains a mainstay of MRSA eradication protocols in most health care facilities in the United States.

No studies have demonstrated a significant reduction in *S. aureus*-related infection following septoplasty or septorhinoplasty in patients receiving prophylactic antibiotics. Weimert and Yoder in a study of 1040 patients undergoing either septoplasty or septorhinoplasty via an endonasal approach, without the use of any preoperative antimicrobials, reported that only five patients (0.48%) developed infections, which resolved with a short course of oral antibiotics.¹⁴ In a study by the same investigators, 174 patients undergoing either septoplasty or septorhinoplasty were, first, treated with bacitracin-impregnated nasal packing and then randomized to a non-treatment group or administration of a preoperative antibiotic dose followed by 5 days of postoperative antibiotics. The incidence of infection (2.4%) was identical in both groups, arguing against the routine use of prophylactic antibiotics.¹⁵ In fact, a protracted course of preoperative systemic antibiotics may facilitate *S. aureus* overgrowth. Jiang and coworkers, in a study of 358 patients undergoing endoscopic sinus surgery, found that preoperative MRSA carriage rate was in the region of 21% with 5% of patients developing postoperative MRSA infections. Critically, all patients received at least 2 weeks of preoperative prophylactic antibiotics. This may have inadvertently selected for MRSA overgrowth, although the authors

conclude that their findings are related to a relatively lengthy postoperative hospital stay of 5 days.¹⁶ The only scenario in which prophylactic antibiotics have been moderately beneficial is in revision rhinoplasty. Pirsig and Schafer in their prospective evaluation of complex revision rhinoplasty cases—75% of which necessitated some form of free tissue transfer—randomized 100 patients to postoperative antistaphylococcal antibiotics or placebo. They found that 18% of patients developed postoperative infections, of which 78% were in the placebo group.¹⁷

Conclusion

Given the absence of randomized clinical trials investigating the use of perioperative antimicrobials in the prevention of MRSA-associated infections following nasal surgery, our recommendations are largely empirical. Healthy patients undergoing septoplasty or septorhinoplasty do not require perioperative topical or systemic antibiotics as the incidence of infection in these patients is exceedingly low. In patients belonging to high-risk groups—such as hospital care workers, the immunocompromised, and the elderly—we recommend administration of a standard 5-day course of twice-daily intranasal mupirocin ointment applied preoperatively. Finally, in high-risk patients who are undergoing revision rhinoplasty or who have a known history of MRSA infections, we suggest administering both preoperative nasal mupirocin and perioperative systemic antibiotics directed against MRSA. The judicious use of mupirocin is critical, as significant increases in MRSA resistance have been associated with extensive use of this otherwise effective agent. Similarly, widespread use of systemic antibiotics will contribute to the increasing problem of antibiotic resistance while concurrently eliminating the physiologic antimicrobial protection afforded by the natural flora of the nasal cavity. Once established, soft tissue infections of the face following nasal surgery should be managed aggressively. Incision and drainage should be performed and the resulting purulent material sent for culture and sensitivity. Empiric antibiotic therapy should be initiated with TMP/SMX as a first-line agent. In patients who are sulfa allergic, clindamycin can be utilized as a second-line agent until antibiotic susceptibility results become available. Progression of the infection or the development of systemic features should prompt hospitalization, aggressive surgical debridement and administration of parenteral antibiotics.

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