An unusual cause of necrosis and nasal septum perforation after septoplasty: *Enterobacter cloacae*

M. Binar[1], F. Arslan[1], H. Tasli[1], O. Karakoc[1], A. Kilic[2] and U. Aydin[1]

1) *Department of Otolaryngology, Head and Neck Surgery and* 2) *Department of Medical Microbiology, Gulhane Military Medical Academy, Ankara, Turkey*

Abstract

A 20-year-old man with nasal obstruction underwent septoplasty due to nasal septal deviation. Nasal packs were inserted at the end of surgery and removed 48 hours after surgery. Twenty-four hours after removal of nasal packs, there was necrosis in both sides of septal mucosa and in bilateral inferior turbinates. Nasal swab culture was performed from both nasal cavities. *Enterobacter cloacae* was isolated from samples. Two weeks after surgery, nasal septum perforation was unavoidable. To our knowledge, this is the first case in literature describing septal mucosal necrosis caused by this pathogen after septoplasty. Mucosal necrosis and perforation as septoplasty complications should be kept in mind, the result of causes both common and, as in the present case, unusual.

Keywords: Antibiotics, *Enterobacter cloacae*, necrosis, septal perforation, septoplasty
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Corresponding author: M. Binar, Department of Otolaryngology, Head and Neck Surgery, Gulhane Military Medical Academy, Etlik 06018, Ankara, Turkey
E-mail: mbinar4@yahoo.com

Introduction

Septoplasty is one of the most performed surgical procedures in rhinology practice, and complications after this surgery are well known. Bleeding, septal hematoma, septal perforation and synechial bands can occur after surgery, although most of these are easy for surgeons to overcome [1,2]. Rare but severe complications such as toxic shock syndrome, endocarditis, osteomyelitis, meningitis and cavernous sinus thrombosis have been described after septoplasty [3,4]. Prophylactic antibiotics are usually sufficient for preventing postoperative infections, but sometimes different pathogens can cause difficult situations for both surgeon and patient. In this report, we present the case of a patient who underwent septoplasty, which was complicated by tissue necrosis and nasal septal perforation by an unusual pathogen, *Enterobacter cloacae*.

Case Report

A 20-year-old man with severe nasal obstruction applied to our Otolaryngology, Head and Neck Surgery Department. After rhinoscopic examination and detailed endoscopic evaluation, septal deviation was diagnosed and a septoplasty procedure offered. The surgery was performed under general anaesthesia following standard sterilization procedures. A Killian incision was preferred for septal deviation, and nasal packs (Merocel standard nasal dressing; Medtronic Xomed, Jacksonville, FL, USA) were inserted into the nasal cavities at the end of surgery. A single dose of 1 g cefazolin iv was administrated on the evening of the day of the operation, and a 2 × 500 mg dose of cefuroxime axetil was provided for the next 7 days. Forty-eight hours after surgery, the Merocel packs were removed. The first thing we observed after the packs' removal was oedema of the nasal mucosa and turbinates, as is routinely seen after nasal septal surgery. No perforation of the nasal septum was observed. Twenty-four hours after removal, there were nasal purulent discharge and color change of mucosa to greyish on both sides of septum and in the inferior turbinates (Fig. 1A, B).

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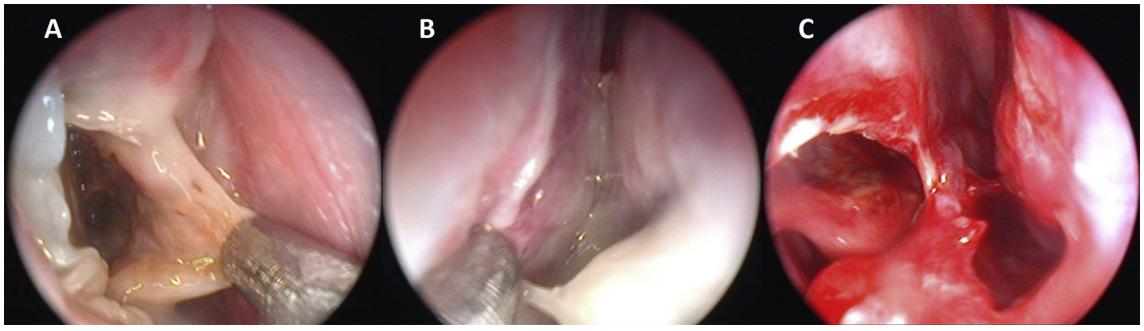

FIG. 1. (A) Necrosis of left septal mucoperichondrial flap. (B) Necrosis of right nasal septal mucosa and inferior turbinate. (C) Nasal septal perforation, left nasal passage, immediately after removal of Doyle splint.

We performed debridement of necrotic tissue and took samples from necrotic septal mucosa and left inferior turbinate for histopathologic and microbiologic analysis. During 5 days we continued to apply debridement and cleaning of nasal passages by suction, while also supporting the patient with systemic antibiotic therapy (cefazolin 1 g iv twice a day). Finally, 8 days after surgery (at which time there was still no perforation), we inserted a silicone nasal splint to prevent nasal synechia. The histopathologic analysis of samples was reported as inflammation and necrosis, and *Enterobacter cloacae* was identified by the BD Phoenix automated system (BD Diagnostic Systems, Sparks, MD, USA).

Antibiotic susceptibility was performed by the BD Phoenix automated system and was interpreted according to Clinical Laboratory Standards Institute criteria. *E. cloacae* was susceptible to trimethoprim/sulfamethoxazole (minimum inhibitory concentration (MIC) $\leq$1/19 mg/L), meropenem (MIC $\leq$0.5 mg/L), imipenem (MIC $\leq$1 mg/L), gentamicin (MIC $\leq$2 mg/L), ertapenem (MIC $\leq$0.25 mg/L), ciprofloxacin (MIC $\leq$0.5 mg/L), ceftriaxone (MIC $\leq$1 mg/L), ceftazidime (MIC $\leq$1 mg/L), cefepime (MIC $\leq$1 mg/L) and amikacin (MIC $\leq$8 mg/L) and was resistant to cefoxitin (MIC >16 mg/L), cefazolin (MIC >8 mg/L) and ampicillin-sulbactam (MIC >8/4 mg/L). We thus changed the antibiotic to ciprofloxacin because *Enterobacter* are intrinsically resistant to ampicillin, amoxicillin, amoxicillin-clavulanate, first-generation cephalosporins and cefoxitin owing to the production of constitutive AmpC β-lactamase. After a week we removed the silicon splints and finally observed normal, healthy color of mucosa on inferior turbinates, but unfortunately with perforation of the anterior septum 15 × 10 mm in diameter (Fig. 1C).

Discussion

Because septoplasty is one of the most common surgical procedures in rhinology practice, complications of this surgery are also variable. Surgeon experience, attentive surgery and exact preoperative preparation usually prevent complications. Continuous complaints of subjective nasal obstruction, bleeding, septal hematoma, septal perforation and synechial bands are often present after surgery; most of these are easy to overcome [1,2].

Mucous membranes are traumatized during septoplasty, an invitation to infections and bacteraemia by the vascular route within the nasal mucous membranes [2]. In the study of Makitie *et al.*, the rate of local infection and septal abscess after septoplasty was 12%; on the other hand, Yoder and Weimert showed minor nasal infections only in five patients (0.48%) in a large nasal septal surgery series comprising 1040 patients [3,5]. Rare but severe complications such as toxic shock syndrome, endocarditis, osteomyelitis, meningitis and cavernous sinus thrombosis may also occur after surgery. Most of these serious infections are caused by Staphylococcus aureus, which is found in normal nasal microbial flora in approximately 50% of individuals [3,4,6].

Okur *et al.* investigated the incidence of bacteraemia during septoplasty and septorhinoplasty procedures by analysing the nasal and blood cultures taken preoperatively, intraoperatively and postoperatively [7]. In cultures taken from nasal swabs, coagulase-negative staphylococci were the most frequently isolated bacteria (65%), followed by *S. aureus* with or without other organisms (35%). Even though all preoperative and postoperative blood culture specimens were negative, bacterial growth was observed in five of 60 blood cultures taken intraoperatively, three of which were coagulase-negative staphylococci, one *Escherichia coli* and the other *S. aureus*. They also mentioned that patients with demonstrated bacteraemia from intraoperative blood cultures did not show any clinical sign of focal or systemic infection. In the other study, isolated bacteria from blood cultures taken immediately after surgery and 48 hours after surgery were similar to those that were found in nasal smear cultures except two pathogens,

peptostreptococci and *Candida* spp., which were also isolated from blood cultures [8].

The use of prophylactic antibiotics in rhinologic surgery is preferred by most physicians. However, the most recent studies have demonstrated that there is still not strong evidence to use antibiotics for every septal surgery. Caniello *et al*. did not observe significant differences in the their study groups—patients who did or did not receive antibiotics after surgery—for fever, purulent secretion and infections; therefore, they suggested that nasal surgeries are clean contaminated and do not need antibiotic prophylaxis because of low infection risk [9]. The study of Ricci and D'Ascanio, consisting of 630 patients, showed that septoplasty procedures that used antibiotics did not differ from those that did not in terms of infection development [10].

Antibiotics are usually sufficient for preventing infections, but sometimes different pathogens can cause difficult situations for both surgeon and patient. *E. cloacae* is a facultative Gram-negative proteobacterium belonging to the *Enterobacteriaceae* family [11]. Bacteria of the *Enterobacter* genus are widely found in nature; they are saprophytic in the environment, as they are found in soil and sewage, and are also part of the commensal enteric flora of the human gastrointestinal tract. *Enterobacter cloacae, Enterobacter agglomerans* and *Enterobacter aerogenes* have been found to multiply faster in 5% dextrose than *Escherichia coli, Pseudomonas aeruginosa, Proteus* spp. and *Staphylococcus* spp. *Enterobacter* spp. now pose a much broader nosocomial problem, causing a wide variety of infections. Overviews of *Enterobacter* infections suggest that common reservoirs for the organism include the urinary, respiratory and gastrointestinal tracts, in addition to surgical and burn wounds [12,13].

In the study of Hulterstrom *et al*., the most prevalent finding in nasal septal mucosa was aerobic irregular Gram-positive rods suggestive of *Corynebacterium* (58%); coagulase-negative staphylococci colonization was 53%, *S. aureus* 13% and *Enterobacteriaceae* 3% [14]. The study of Frank *et al*. showed that *Proteobacteria* (e.g. *Enterobacter* spp.) was 4% in anterior nares swabs in healthy adults [15].

Yoo *et al*. performed a retrospective review of 363 consecutive adult patients who underwent preoperative nasal swab testing and rhinoplasty or septorhinoplasty (174 primary rhinoplasty, 189 revision rhinoplasty). In the study design, first they identified endogenous nasal flora preoperatively, then pathogenic bacteria treated with culture-directed antibiotics. They found that 78.2% of patients had normal flora; 10.7% had *S. aureus*; and 0.28% had methicillin-resistant *S. aureus*. In 7.4% of patients, faecal coliforms including *Escherichia coli, Enterobacter* spp., and *Citrobacter* spp. were found. They stated that age, sex, smoking, the use of oral contraceptives and the presence of seasonal allergies did not significantly change the nasal flora or the postoperative infection rate. Patients with adult acne were found to have an increased incidence of colonization with faecal coliforms (43.8%; $p < 0.001$) [16].

We did not assess patients' nasal flora before surgery, so we did not perform any tests learn whether *E. cloacae* was a member of patient's nasal flora. Nevertheless, we cannot exclude the possibility that the infection might have developed by means of horizontal transmission. In the prospective epidemiologic study of Flynn *et al*. on patients undergoing one type of surgery, most *Enterobacter* infections developed in patients who already had *Enterobacter* spp. as part of their endogenous flora. Horizontal transmission was responsible for only two of 12 *Enterobacter* infections [17].

To our knowledge, the present case is the first in the literature to describe *E. cloacae* as a cause of necrosis of the nasal septal mucosa. We could not achieve progress by using antibiotics (single-dose cefazolin iv on the surgery day and cefuroxime axetil po on the following days), which many physicians usually prefer after septoplasty. After isolation of *Enterobacter* infection, we changed the antibiotic to ciprofloxacin because the bacterium has an intrinsic resistance to ampicillin, amoxicillin and cephalosporins [18]. Many intensive care physicians would agree that the excessive use of broad-spectrum antibiotics, especially cephalosporin agents, has contributed to the emerging prominence of *Enterobacter* spp. as important nosocomial pathogens [19]. Even 2 days of cefazolin prophylaxis before surgery was associated with a significantly higher rate of *Enterobacter* colonization than that seen in patients who did not receive antibiotic prophylaxis (p 0.001) [17].

Most isolates of *E. cloacae* are susceptible to trimethoprim/sulfamethoxazole, fluoroquinolones, chloramphenicol, tetracyclines, aminoglycosides, piperacillin-tazobactam and carbapenems. If they produce extended-spectrum β-lactamase, they become resistant to fourth-generation cephalosporins; there are thus concerns about spread of carbapenemase-producing *E. cloacae* [20]. Although ciprofloxacin treatment was one of the best alternatives for his pathogen, nasal septum perforation was unavoidable. There are also some reports explaining low resistance to fluoroquinolones by the mechanisms consisting of target mutations for DNA gyrase and topoisomerase IV, decreasing permeability or augmenting expression of efflux pumps [20,21].

What was the mechanism of necrosis in the present case? *E. cloacae* strains produce enterotoxins, α-hemolysin and thiol-activated pore-forming cytotoxins similar to Shiga-like toxin II; thus, it involves curli fimbriae in the formation of biofilms. Genes of type III secretion system, which delivers toxins into the host cells, were found in E. *cloacae* strains and contribute to its pathogenesis [20].

Conclusion

Necrosis resulting in nasal septum perforation after septoplasty is infrequent. It is surprising that unusual pathogens such as *Enterobacter cloacae*, which probably has low colonization in nasal mucosa, can cause this bothersome situation. Antibiotic prophylaxis with first- or second-generation cephalosporins was not adapted in this case because *E. cloacae* is known to be naturally resistant to these agents. All rhinology surgeons must be aware of different infectious pathogens in the aetiology of necrosis after septoplasty to prevent further complications such as nasal septal perforation. In case of postoperative infection, nasal swab cultures must be taken, and oral wide-spectrum antibiotics should be administrated until the specific pathogen is identified by microbiologic analysis.

Conflict of Interest

None declared.

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