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Bacterial infections associated with allogenic bone transplantation

Bakterijske infekcije povezane sa transplantacijom koštanog alografta

Željko Lj. Stepanović*†, Branko M. Ristić*†

***Clinic for Orthopaedic and Trauma Surgery, Clinical Center Kragujevac, Kragujevac, Serbia; †Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia**

Abstract

Background/Aim. Bone allografts are frequently used in orthopedic reconstructive procedures carrying a high risk for recipients. To assess the nature and frequency of allograft contamination and associated surgical infection the case records from our institutional bone bank were reviewed. **Methods.** We retrospectively analyzed the microbiology of discarded bone allografts and the surgical site of the recipients. A case series of patients who acquired surgical site infection after allogenic bone transplantation was presented. Swab culturing was conducted on 309 femoral heads from living donors who underwent partial and total hip arthroplasty between January 2007 and December 2013. To prevent potential bone allograft contamination we used saline solution of 2.0 mg/ml of amikacin during thawing. The overall infection rate was analyzed in 197 recipients. **Results.** Of the 309 donated femoral heads, 37 were discarded due to bacterial contamination, giving the overall contamination rate of 11.97%. The postoperative survey of 213 bone allotransplantations among 197 recipients showed the infection rate of 2.03%. The coagulase-negative *Staphylococcus* was the most commonly identified contaminant of bone allografts and recipient surgical sites. **Conclusion.** The allograft contamination rate and the infection rate among recipients in our institution are in accordance with the international standards. The coagulase-negative *Staphylococcus* was the most commonly identified contaminant of bone allografts and recipient surgical sites. There is no strong evidence that surgical site infections were associated with bone allograft utilization. We plan further improvements in allograft handling and decontamination with highly concentrated antibiotic solutions in order to reduce infection risk for recipients.

Key words:
bacterial infections; bone transplantation; postoperative complications; transplantation, homologous.

Apstrakt

Uvod/Cilj. Koštani alograftovi često se koriste u rekonstruktivnim ortopedskim procedurama. U cilju procene prirode i učestalosti kontaminacije koštanih alograftova i pratećih hirurških infekcija, analizirani su podaci koštane banke u našoj instituciji. **Metode.** Retrospektivno je analiziran mikrobiološki nalaz odbačenih koštanih alograftova i hirurškog mesta primalaca. Prikazana je serija bolesnika sa ispoljenom infekcijom operativnog mesta nakon transplantacije koštanog alografta. Zasejavanje briseva 309 glava butnih kostiju živih donora posle preloma vrata butne kosti ili primarne totalne artroplastike kuka obavljeno je od januara 2007. do decembra 2013. godine. U prevenciji kontaminacije koštanih alograftova korišćeno je 2 mg/mL amikacina prilikom njihovog topljenja. Stopa infekcije analizirana je kod 197 primalaca. **Rezultati.** Od 309 doniranih femoralnih glava, zbog bakterijske kontaminacije odbačeno je 37, dajući stopu kontaminacije od 11,97%. Postoperativnim praćenjem 213 koštanih alotransplantacija kod 197 primalaca ustanovljena je stopa infekcije od 2,03%. Koagulaza negativni *Staphylococcus* bio je najčešće identifikovani uzročnik kontaminacije koštanih alograftova i hirurškog mesta primalaca. **Zaključak.** Stope bakterijske kontaminacije koštanih alograftova i infekcije hirurškog mesta primalaca u našoj ustanovi u skladu su sa međunarodnim standardima. Koagulaza negativni *Staphylococcus* bio je najčešće identifikovani uzročnik kontaminacije koštanih alograftova i hirurškog mesta primalaca. Nema čvrstih dokaza da su infekcije operativnog mesta bile u vezi sa upotrebom koštanog alografta. Planiramo dalja unapređenja u rukovanju i dekontaminaciji koštanog alografta visokokoncentrovanim rastvorima antibiotika u cilju sniženja rizika od infekcije kod primalaca.

Ključne reči:
infekcija, bakterijska; transplantacija kosti; postoperativne komplikacije; transplantacija, homologna.

Correspondence to: Željko Stepanović, Clinic for Orthopaedic and Trauma Surgery, Clinical Center Kragujevac, 34 000, Kragujevac, Serbia. Phone.: +381 34 367 169, Fax.: +381 34 370 046. E-mail: zeljko.stepanovic@medf.kg.ac.rs

Introduction

Bone allografts are frequently used in orthopedic reconstructive procedures carrying a high risk for recipients. An allograft-host non-unions and re-fractures may occur and are amenable to surgery, contrary to allograft associated infections which represent the most terrifying complication [1, 2]. Bone allograft-associated infections are largely dependent on its avascularity and porosity leading to biofilm formation by the contaminants [3, 4]. *Staphylococcus aureus* and coagulase-negative *Staphylococci* (mostly *Staphylococcus epidermidis*) are responsible for 36% to 38% of all allograft infections [1, 4]. Reported infection rate after bone allograft transplantation ranges from 1.6% to 12% [5–10]. An infection management after bone allograft transplantation is extremely challenging and may increase the treatment costs and have medico-legal implications.

To assess the allogenic bone related infection rate, the case records of 309 living donors and 197 recipients were reviewed. We report a case series of four surgical site infections following bone allograft transplantation in tertiary care academic medical center.

Methods

We retrospectively analyzed the microbiology of discarded bone allografts and the surgical site of the recipients. A case series of patients who acquired a surgical site infection after allogenic bone transplantation was presented. Swab culturing was conducted on 309 femoral heads from patients who underwent primary total hip arthroplasty (THA) or sustained a fresh femoral neck fracture between January 2007 and December 2013. Informed consent was obtained, and a detailed history was taken to exclude malignancy, systemic and infectious diseases before retrieval. Potential donors with severe degenerative changes or osteoporosis of the femoral head were excluded from bone harvesting. Patients that failed the selection criteria were excluded as potential donors. A prophylactic antibiotic (cefuroxime, 1.5 g or cefazolin 1.0 g) was given 30 minutes before surgery. We took swab samples from the surgical site and from the femoral head. The container was sealed tightly, immediately isolated with three sterile separate bags, labeled and stored in a freezer at -70°C within 30 minutes. Swab samples were sent to hospital laboratory for microbiological evaluation. Two cultures of aerobic and anaerobic microorganisms in blood agar, MacConkey agar, and chocolate blood agar were analyzed. The donors were tested for hepatitis B and C, HIV and syphilis at donation and at six months after surgery, according to the hospital bone bank protocol. All the blood test results at retrieval were documented in the donor's bone bank records. All donors and recipients were followed up periodically to detect any clinical surgical site infection (SSI). Postoperative SSI was defined as persistent wound discharge and erythema with positive isolation of organisms from wound swabs. According to the Center for disease control and prevention (CDC), a superficial incisional SSI occurs within 30 days after operation when only skin and subcutaneous tissue of the incision were involved. Deep incisional SSI occurs within 30 days after the operation if no implant is left in place, or within one year if implant is in place and infection appears to be related to operation, where infection involves deep soft tissues, such as fascia and muscles [11]. Acceptable bone allografts are stored for a maximum of 5 years. Before application, 213 allografts were thawed 30 minutes in 500 mL of 0.9% sterile saline at 37°C with 1g of amikacin (2 mg/mL). A prophylactic antibiotic (cefuroxime, 1.5 g, cefazolin 1.0 g or vancomycin 1.0 g) was given 30 minutes before surgery to all recipients. Intraoperative allograft culturing was not performed because there is no clinically relevant association between such positive cultures and postoperative wound infections [6, 9].

Results

Of the retrieved 309 femoral heads, 228 (73.78%) were harvested after primary total hip arthroplasty and 81 (26.21%) after fresh femoral neck fracture. Swab cultures were positive for at least one microorganism in 37 allografts giving an overall contamination rate of 11.97%. The coagulase-negative *Staphylococcus* was the most commonly identified contaminant of the bone allografts and the recipient surgical site (Table 1). Swab cultures of the surgical site were negative in all 37 donors. Surgical site infection was not recorded in those patients during the follow-up period of at least 12 months, according to the CDC [11]. A total of 213 (68.93.%) allografts were implanted to 197 recipients. Deep incisional SSI was identified in 4 out of 197 (2.03%) recipients (Table 2).

Table 1
Organisms cultured from allograft bone retrieved and surgical site of the recipient

Microorganism	Number of cultures	
	Bone allograft n (%)	Surgical site n (%)
Coagulase-negative Staphylococcus	9 (24.32)	2 (33.33)
Staphylococcus aureus	5 (13.51)	1 (16.67)
Staphylococcus epidermidis	6 (16.22)	
Streptococcus viridans	2 (5.40)	
Enterococcus faecalis	3 (8.11)	1 (16.67)
Gram-positive anaerobic cocci (GPAC)	5 (13.51)	
Proteus mirabilis	2 (5.40)	2 (33.33)
Acinetobacter species	2 (5.40)	
Bacillus subtilis	1 (2.70)	
Pseudomonas aeruginosa	1 (2.70)	
Providencia species	1 (2.70)	
Total	37 (100)	6 (100)

Discussion

We performed a retrospective case series study reporting the main causes of bone allograft contamination and associated surgical infection in tertiary care academic medical center. Deep wound infection after bone allograft transplantation may ha-

ve dreadful outcome. Literature confirmed that allograft- associated infection was not the same as allograft-transmitted infection. The most of the recipients who received contaminated allografts were clinically with no signs of infection [6, 8]. Three-quarters of these allograft-associated infections occured within 4 months of allogenic bone transplantation and led to osteomyelitis and osteolysis, which posed a huge challenge to both physicians and patients, as well [1, 4]. Sommerville et al. [12] performed a 4-specimen-culture study of 232 femoral heads, and found an overall 22% contamination rate. The majority of organisms cultured were *Staphylococcus epidermidis*. The overall infection rate was 2.4%. In our institution, the surgical site infection rate among recipients compared favorably with other reports as well as the allograft contamination rate. All 4 allograft related infections occurred within four months after transplantation. Three of 4 cases were high energy trauma patients with severe soft tissue injuries. The coagulase-negative *Staphylococcus* was the most commonly identified contaminant of the bone allografts and the recipient surgical site. Two or more pathogens were isolated in 2 of 4 patients with SSI. Thorough analysis of the patients' records revealed that none of these infections were obviously connected with bone allograft utilization. In case of distal femoral non-union, an infection occurred following revision surgery. In case 2, a 30-year-old patient suffered a comminuted Sandres IV left calcaneal fracture and right Schatzker II tibial plateau fracture after fall from height of 6 meters [13, 14]. He suffered an urinary tract infection immediately after surgery and positive urin cultures were found. No signs of surgical site infections were recorded postoperatively. The same bone allograft was used for two surgical sites. Three weeks after surgery, *Enterococcus faecalis* was isolated after debridement of necrotic skin on the medial side of the foot. A tibial plateau fracture healed uneventfully 12 weeks after surgery, with no signs of infection. Our assumptions are directed toward urinary tract infection following surgery as the primary source for hematogenous dissemination of bacteria into the severely injured hindfoot. In 3 of 4 cases, SSI successfully healed with full allograft incorporation. Two low virulent coagulase-negative *Staphylococcus* species and one highly virulent *Staphylococcus* aureus indicate the importance of strict monitoring system, aseptic handling technique and clean environment in the operating theatre. It is likely that graft surface is ideal for bacterial adherence and leads to selection of contaminants that exhibit marked adhesive properties, biofilm as well as increased resistance towards antibiotics. It seems that allograft associated infection may be prevented the same way as the implant associated infection. There are attempts to bond antibiotics to amine groups of allograft bone collagens and provide long-term bactericidal concentrations to prevent allograft associated infections [4]. The swab cultures had been proven insufficient to detect bacterial contamination of musculoskeletal allografts due to low sensitivity. Recent reports indicate that swab cultures after thawing were different from the wound cultures in most of the infected patients [15]. Our previous results based on

Table 2

Characteristics of infection cases after allogenic bone transplantation

No.	Gender/ Age (years)	Surgery	Bacteria	Clinical findings	Antimicrobial therapy
1	Woman/ 76	Fracture non-union Revision surgery	Methicilin-resistant *Staphylococcus aureus*.	Severe osteoporosis; Early low grade infection 3 months after revision surgery, wound debridement, implant removal	Vancomycin (1g/12 h) Rifampicin (600 mg/24 h) Trimethoprim/sulfamethoxazole (960 mg/12 h)
2	Male/ 30	Sanders IV calcaneal fracture, Schatzker II tibial plateau fracture	*Enterococcus faecalis, Proteus mirabilis Pseudomonas aeruginosa*	Positive urin cultures after surgery. Early high grade infection one month after surgery, multiple soft tissue revisions, implant removal, lower leg amputation	Ciprofloxacin (100 mg/12 h) Ofloxacin (200 mg/12 h) Amikacin (1.0/24 h) Amoxicillin/clavulanic acid (1.2g/8 h) Ceftazidime (2 g/8 h) Metronidazole (400/8 h)
3	Woman/ 39	Sanders III-calcaneal fracture	Coagulase-negative *Staphylococcus*	Early deep wound infection one month after surgery, multiple soft tissue revisions, implant removal	Vancomycin (1 g/12 h)
4	Male/ 55	Schatzker V tibial plateau fracture	Coagulase-negative *Staphylococcus, Proteus mirabilis*	Early deep wound infection two months after surgery, wound debridement, implant removal	Ceftazidime (2 g/8 h) Ceftriaxone (2 g/24 h) Gentamicin (240 mg/24 h)

the overall audit of bone bank performance, indicate that the highest risk of bone allograft contamination exists during its harvesting and thawing. We concluded that microbial contamination and allograft associated infection rate were predominantly influenced by the surgical team and its immediate environment [16]. Antibiotic rinsing of the allograft has been proposed by some authors, but it does not affect the risk of contamination in large studies with postmortem donors [17–21]. Bone allograft immersion in saline solution with high concentration of bactericidal antibiotics such as aminoglycosides may promote infection control and act as simple as effective secondary sterilization [16]. An antibiotic selection for such prophylactic decontamination should be variable and may be determined by the specific susceptibility of strains (if any) isolated in the operating theatre, or by the strains mostly isolated from the surgical site and coordinated with epidemiology department.

Conclusion

The allograft contamination rate and the infection rate among recipients in our institution are in accordance with the international standards. The organism most commonly identified as contaminant of bone allografts and surgical sites was coagulase-negative *Staphylococcus*. There is no strong evidence that surgical site infections are associated with bone allograft utilization. We plan further improvements in allograft handling and decontamination with highly concentrated antibiotic solutions in order to reduce infection risk for recipients.

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