Postoperative deep infection in tumor endoprosthesis reconstruction around the knee

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Abstract

Background. Although deep infection remains one of the most difficult complications to manage in the treatment of musculoskeletal tumor reconstructed with an endoprosthesis, limited information with respect to its incidence and risk factors has been reported.

Methods. This multicenter, retrospective, uncontrolled study reviewed the medical records of 82 patients who underwent reconstruction with an endoprosthesis or temporary spacer for bone-immature patients after resection of malignant bone tumor around the knee. Risk factors for deep infection and the impact of deep infection on prosthesis survival and oncological outcomes were analyzed. Deep infection was defined according to the Centers for Disease Control and Prevention (CDC) guidelines with minor modification.

Results. Deep infection occurred in 14 cases (17%), identified at a mean of 10.9 months (range <1 to 48 months) after initial surgery. Univariate analysis identified surface infection ($P < 0.001$) and skin necrosis ($P < 0.001$) as risk factors associated with deep infection. Conversely, tumor origin, chemotherapy, number of postoperative antibiotics, and length of bone resection were not associated with infection. Subclass analysis in femur cases identified a correlation between infection and the extent of partial resection of the quadriceps muscle ($P = 0.04$). In the multivariate analysis, surface infection represented an independent risk factor for deep infection ($P = 0.03$). Deep infection was a risk for endoprosthesis survival ($P = 0.003$) but did not affect the oncological outcome.

Conclusions. A strong correlation between the condition of soft tissue and establishment of deep infection is suggested in this study. Although practical options for preventing deep infection seem limited, the present data allow a form of perioperative evaluation for patients with a higher risk of deep infection.

Introduction

Deep infection is one of the most severe complications in endoprosthesis reconstruction, resulting in long-term hospitalization, multistep operations for recovery, reduced quality of life, and sometimes failure of limb salvage.1–4 Despite an urgent need for high-quality evidence, little knowledge or evidence has been reported regarding current tumor endoprostheses today. Difficulty defining a standardized definition for deep infection, the limited number of patients, and the heterogeneity of patient characteristics all complicate the design of studies regarding tumor endoprostheses. As a result, controversial aspects still exist regarding the diagnosis, pre- and perioperative management, mechanisms of establishment, risk factors, and treatment options for deep infection. The wide variation in infection rate, 2.2%–28.6%,3,5–9 is a fine example of the confusion in this field.

We report herein the clinical results of endoprosthesis reconstruction in five hospitals specializing in orthopedic oncology due to the scarcity of reports on deep infection with tumor endoprostheses. This study focused on endoprostheses around the knee because of the frequency of infection in those sites and the need to rule out heterogeneity of the site.4,7 Our aims in this study were to: (1) create an overview of the situation regarding tumor endoprosthesis infection; (2) extract perioperative risks for endoprosthesis infection; and (3) identify the impact of infection on prosthesis survival and oncological outcome.

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Methods

A retrospective, multicenter, uncontrolled study based on medical records and images was designed. Inclusion criteria for this study were (1) musculoskeletal tumor around the knee treated at a registered musculoskeletal specialist hospital; (2) application of an endoprosthesis for reconstruction; (3) treatment after 2000; (4) a standard oncological resection; and (5) at least 12 months of follow-up, except in the case of death before that time. Tumors with intact or unaflected physeal plate, were also included in the study. These cases were not included because local conditions such as lack of soft tissue resembled conditions in cases reconstructed using a conventional tumor endoprosthesis.

Definitions of infection were based on the Centers for Disease Control (CDC) guideline with the following exceptions. First, organ-specific infection and deep incisional infection were managed together as “deep infection.” Second, the detection period for deep infection was not limited to within 12 months from the operation as mentioned in the CDC guideline. Study endpoints were (1) deep infection; (2) oncological outcome (local recurrence, metastasis, or tumor-specific death); and (3) survival of the prosthesis.

Independent variables in the present study were age; sex; tumor site; tumor origin; administration of systemic chemotherapy; intraarterial chemotherapy; bone resection length; operating time; blood loss; use of a clean air operating room; extracapsular resection; prosthesis type; skin necrosis; surface infection; number of antibiotics administered postoperatively; application of a posterior muscle flap for coverage of the prosthesis (for proximal tibia cases); and extent of partial resection of the quadriceps muscle (for distal femur cases). In terms of bone resection length, operating time, and blood loss, patients were divided into two groups about the mean value for each independent variable. Patients with co-morbidities associated with an increased infection risk (e.g., diabetes mellitus, atopic dermatitis) were marked. However in the present study, this subclass was not subject to statistical analysis because of the scarcity of the cases.

For statistical analysis, Kaplan-Meier methods, logrank tests, Cox proportional hazards modeling, the Spearman rank correlation coefficient, and Mann-Whitney's U-test were used. Differences were considered significant for values of \( P < 0.05 \). The study design and publication of this study were approved by the institutional review board of the first author's institution.

Results

Subjects comprised 82 patients who met these criteria. Their mean age at first operation was 31.1 years (range 5–86 years). The site was the distal femur in 52 patients and the proximal tibia in 30 patients. Histological diagnosis was osteosarcoma in 51 patients, chondrosarcoma in 9 patients, malignant fibrous histiocytoma of bone in 3 patients, other primary malignant bone or soft tissue tumor in 10 patients, bone metastasis of cancer in 6 patients, and giant cell tumor of bone in 3 patients.

Preoperative systemic chemotherapy was performed for 58 cases. In 54 cases, the chemotherapy regimen comprised a combination of methotrexate, cis-platinum, and adriamycin, with or without ifosfamide. Intraarterial chemotherapy based on cis-platinum and caffeine was performed in 12 cases. For the remaining 4 cases, a regimen combining adriamycin and ifosfamide was used. Radiotherapy was performed in only one case preoperatively.

Co-morbidities as risks for infection were detected in three cases: vesicoureteric reflux, Crohn’s disease, and diabetes mellitus. Preoperative antibiotics were given within 2 h preoperatively. For all cases, postoperative antibiotics were administered for >72 h.

For reconstruction, an Howmedica Modular Resection System (Stryker Japan, Tokyo, Japan), Kyocera limb salvage system (Kyocera), and others were used for 44, 18, and 3 cases, respectively. For the remaining 17 bone-immature patients, a temporary custom-made spacer was applied. For these cases, limb-length discrepancy was corrected by replacement with a growing prosthesis following confirmation of bone maturation.

The mean duration of follow-up was 52.3 months (range 9–105 months). Local recurrence and distant metastasis occurred in 7 and 31 cases, respectively. Status of the primary lesion at final follow-up was continuously disease-free in 46 cases, alive with disease in 5 cases, no evidence of disease in 9 cases, and dead of disease in 13 cases. Status of metastatic lesions was alive in five cases and dead in one case.

Deep infection was detected in 14 cases (17%), identified at a mean of 10.9 months (range <1 to 48 months) after initial surgery (Fig. 1). In 10 of the 14 cases (70%), infection was detected within 12 months after the initial surgery. In all cases, blood, joint fluid, exudative fluid, and/or scar tissue was cultured. No pathogens were isolated in four cases, and in these cases, diagnosis of infection was based on clinical findings. In the remaining 10 cases, pathogenic bacteria were isolated from the patients. Culture analysis revealed Staphylococcus aureus in five cases, coagulase-negative staphylococci in three cases (including one case of methicillin-resistant S. epidermidis), and Pseudomonas aeruginosa in one case. A combined infection with methicillin-resistant S.