Infection is one of the most severe complications of total knee prosthesis implantation. The present study reported the case of a 74-year-old female that developed a *Staphylococcus epidermidis* infection following a cemented total knee arthroplasty. A routine blood test revealed neutropenia and anemia, while *S. epidermidis* was detected in the peripheral blood and bone marrow. In the present case, *S. epidermidis* infection led to acute arrest of hematopoiesis (AAH), also known as aplastic crisis, which is the temporary cessation of red cell production. The development of AAH secondary to *S. epidermidis* infection is rare and, to the best of our knowledge, this is the first case reported in the literature. The present study increased our knowledge of this rare disease and its characteristics, which will enable physicians to be aware of the development of AAH as a rare complication of *S. epidermidis* infection.

**Introduction**

Total knee arthroplasty (TKA) is one of the most common orthopedic procedures and is an effective treatment for patients with severe osteoarthritis of the knees that allows pain relief and improved function and quality of life (1). However, infection is a common complication of the implementation of total knee prosthetics, and the current incidence of prosthetic knee infection is 1-3% (2). The most frequent microorganism involved is *Staphylococcus aureus* (3).

Staphylococcus epidermidis was commonly described as relatively innocuous, but has been recognized as an important opportunistic pathogen, being the most frequent cause of device-associated infections in hospital (4). Overall, 20-36% infections in TKA are caused by methicillin-resistant *Staphylococci*, with methicillin-resistant *Staphylococcus aureus* and methicillin-resistant *S. epidermidis* being increased (5,6). It has been reported that the treatment success rate is only ~18% when the associated bacteria is multi-drug resistant (6,7). The present case study described a case of *S. epidermidis* infection, which developed following cemented TKA. *S. epidermidis* infection led to acute arrest of hematopoiesis (AAH) in the present case. AAH, also known as aplastic crisis, is the temporary cessation of red cell production. A previous study reported that infection may trigger the process of AAH, and exposure to certain drugs may be the possible etiology (8). The patient presented with a high fever, pallor and tiredness. Routine blood test revealed neutropenia and anemia and *S. epidermidis* was detected in the peripheral blood and bone marrow. The aim of the present study was to describe a case of TKA that resulted in infection with *S. epidermidis* infection and subsequent development of AHH. Its objective is to enable physicians to be aware of AAH, a rare complication of patients infected with *S. epidermidis*. To the best of our knowledge, this is the first such case reported in the literature.

**Case report**

A 74-year-old Chinese female patient was referred to the Department of Orthopedics at the China-Japan Union Hospital Affiliated to Jilin University (Changchun, China) on June the 13th, 2014. The patient presented with fever, restricted movement, pain and swelling of the knee, which developed 4 months after left TKA surgery due to gonarthrosis. The patient was receiving regular medical treatment for hypertension for 5 years (oral administration 30 mg nifedipine once/day; Bayer AG, Leverkusen, Germany) and had previously undergone a right TKA due to gonarthrosis 4 years prior to the present admission. Preoperative X-ray scans of the patient’s left knee are shown in Fig. 1A. Following admission, the left knee was aspirated and the fluid was sent for culture.
Prior to the culture results, the patient was administered vancomycin (intravenous administration 1 g/12 h for 18 days; Eli Lilly and Company, Indianapolis, IN, USA) via intravenous and intra-articular injection. Several germicultures of the joint fluid were negative. Routine blood tests and analysis of the renal and liver function were normal upon admission. However, additional testing revealed an elevated C-reactive protein level (129 mg/l; normal range, 0-8 mg/l) and erythrocyte sedimentation rate (64 mm/h). X-ray scans were then performed following implantation of a drainage tube into the articular cavity (Fig. 1B and C). As no improvement was observed following antibiotic therapy and drainage, the components of the prosthetic knee were removed. The temperature of the patient was reduced to <38˚C during the first postoperative
week; however, the patient presented with an increased fever (body temperature, 39.8°C) once again in the second postoperative week. At 3 weeks postoperatively, routine blood tests demonstrated a reduced leucocyte count and anemia: White blood cell (WBC) count, 0.5x10^9/l (granulocytes, 7%; lymphocytes, 88%; and monocytes, 5%; normal range, 4.10x10^9/l); red blood cell count, 2.52x10^12/l (normal range, 3.5-5x10^12/l); hemoglobin concentration, 7.8 g/dl (normal range, 97 g/l); hematocrit, 22.4% (normal range, 0.35-0.47%); mean corpuscular volume, 88.6 fl (normal range, 80-100 fl); and platelet count, 143x10^9/l (normal range, 100-300x10^9/l). The reticulocyte count had decreased to 0% (normal range, 0.5-1.5%). A subsequent bone marrow smear demonstrated marked diminution of hematopoietic cells (Fig. 2). Megakaryocytes were not detected. Predominantly, non-hematopoietic cells, were detected, including stromal cells, plasma cells, macrophages and infiltrate of lymphoid cells, while giant promonoblasts were clearly visible. The results of the peripheral blood and bone marrow cultures were compatible with the diagnosis of AAH (9). The patient was subsequently transferred to the Department of Hematology and Oncology at the China-Japan Union Hospital Affiliated to Jilin University on July the 25th, 2015. Blood and bone marrow cultures detected the growth of S. epidermidis (methicillin-resistant strain), which was subsequently demonstrated to be susceptible to vancomycin and tigecycline (Pfizer Inc., New York, NY, USA). According to the results of the antibiotic sensitivity test, the patient was treated with vancomycin and a supportive treatment, which consisted of nutritional support (intravenous administration of 10 g albumin/day for 5 days; Octapharma AG, Lachen, Switzerland), defervescence (oral administration of 500 mg acetaminophen when fever is >38.5°C; Beijing Shuguang Pharmaceutical Industrial Co., Ltd., Beijing, China), and bone marrow hematopoiesis stimulation (hypodermic injection of 300 µg G-CSF once/day for 12 days; Changchun Jinsai Pharmaceutical Co. Ltd., Jilin, China). However, the symptoms persisted after 1 week of treatment and the WBC count had reduced to 0.1x10^9 cells/l. Furthermore, the patient exhibited left-sided heart failure and brain natriuretic peptide (BNP) levels increased to 35,000 pg/ml; therefore, the patient was administered cardiotonic (three intravenous bolus injections of 200 mg cedilanid; Xudong Haipu Pharmaceutical Co., Ltd., Shanghai, China) and diuretics (eight intravenous bolus injections of 20 mg lasix; Nantong Jinghua Pharmaceutical Co., Ltd., Nantong, China), and the microbiological profile of PJI between two referral centers in Europe and the United States demonstrated that infection or drug exposure may trigger AAH (8). AAH predominantly occurs in patients with hemolytic anemia and, as it is a self-limiting disease, aplasia usually persists for 5-10 days (12,13). Routine blood tests typically demonstrate anemia and a decreased reticulocyte count, and although pancytopenia does not usually occur, mild leukopenia and/or thrombocytopenia are occasionally detected (11). In the present patient, the complete blood count demonstrated neutropenia and moderate anemia. Although the hematopoietic activity was recovered, the patient eventually succumbed to infection with S. epidermidis and the secondary renal and heart failure.

The most common cause of severe aplastic crises for patients with chronic hemolytic anemia is infection with parvovirus B19 (11,14). However, rare cases of severe aplastic anemia due to acute parvovirus B19 infection have been reported in previously healthy individuals (15,16). In addition to parvovirus B19, there are various viral infections that contribute to AAH, including the Epstein Barr virus, cytomegalovirus, HIV and rubella (17,18). Additional triggering agents in transient aplastic crises include pharmacological agents (such as methotrexate) and irradiation (18,19). Patients typically present with increased fatigue, pallor, activity intolerance or shortness of breath. For the vast majority of patients with acute aplastic anemia, only supportive and symptomatic treatment can be offered. Transfusion of red blood cells (RBC) is required to relieve the symptoms of anemia for certain patients.

The present study described a case of AAH caused by S. epidermidis infection which appeared following the application of cemented TKA. Periprosthetic joint infection (PJI) is one of the most severe complications following TKA. This is a difficult issue for orthopaedic surgeons, as well as for patients and their families, due to its challenging management and the impact on the patients' quality of life (3,20).

Epidemiologic studies investigating various trends in the microbiological profile of PJI between two referral centers in Europe and the United States demonstrated that PJI caused by methicillin-resistant S. aureus is becoming
increasingly prevalent (21,22). In the present case, growth of methicillin-resistant Staphylococcus epidermidis was detected in blood and bone marrow cultures; however, a germ culture of joint fluid remained negative following various repeats. Biofilm formation may explain the phenomenon of culture-negative PJI. Novel methods, including DL-dithiothreitol and polymerase chain reaction using various probes, are being developed in order to improve the ability of microbiological culture in detecting the pathogenic causes of PJI (23,24).

Wu et al (25) conducted a case-control study in order to investigate the effects of patient factors on the risk of PJI in a Chinese population. The results demonstrated that an increased risk of PJI in this Chinese population was associated with: Diabetes; age of 65-75 years; body-mass index of ≥28 kg/m²; a history of alcohol abuse; and residence in rural areas. For the present patient, old age and obesity may have been influential risk factors.

The present patient was not receiving any medication that could trigger transient aplastic crises, and had no history of irradiation therapy. Therefore, it is hypothesized that the cause of AAH was infection with Staphylococcus epidermidis. The pathogenesis of acute aplastic anemia induced by Staphylococcus epidermidis infection is yet to be elucidated.

In conclusion, the present study described a case of AAH induced by Staphylococcus epidermidis infection, which developed following cemented TKA. AAH induced by methicillin-resistant Staphylococcus epidermidis infection is a rare and life-threatening complication. The present study increased our knowledge of this rare disease and its characteristics, which will enable physicians to be aware of the development of AAH as a rare complication of Staphylococcus epidermidis infection. Further studies are required in order to elucidate the exact pathogenesis of AAH.

References