Case report

Chondrogenesis in the synovial tissue is associated with the onset of pseudogout after total knee arthroplasty

Ryosuke Sato, MD a, *, Shunji Nakano, MD, PhD a, Tomoya Takasago, MD a, Masaru Nakamura, MD a, Masahiro Kashima, MD a, Takashi Chikawa, MD, PhD a, Daisuke Hamada, MD, PhD b, Tomohiro Goto, MD, PhD b, Koichi Sairyo, MD, PhD b

a Department of Orthopedics, Tokushima Municipal Hospital, Tokushima, Japan
b Department of Orthopedics, Institute of Biomedical sciences, Tokushima University Graduate School, Tokushima, Japan

ARTICLE INFO

Article history:
Received 25 July 2015
Received in revised form 12 October 2015
Accepted 19 October 2015
Available online 11 November 2015

Keywords:
Pseudogout
Total knee arthroplasty
Chondrogenesis
Histologic finding

ABSTRACT

Postoperative pseudogout after total knee arthroplasty (TKA) is very rare, and its physical findings are very similar to infectious symptoms. In pseudogout, the mechanism underlying the deposition of calcium pyrophosphate dehydrate crystals remains unclear. Here, we report the histologic findings in a pseudogout attack in the late postoperative period after TKA. She had acute onset of arthritis of the knee 2 years after TKA. Histologic examination showed significant neutrophil infiltration. Interestingly, chondrogenesis was noted in the synovial tissue, and calcium pyrophosphate dehydrate crystals were synthesized mainly at the site of chondrogenesis, suggesting a potential mechanism underlying the occurrence of pseudogout after TKA.

© 2015 The Authors. Published by Elsevier Inc. on behalf of The American Association of Hip and Knee Surgeons. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Pseudogout is defined as a disease that involves the deposition of calcium pyrophosphate dehydrate (CPPD) crystals in the affected joint. An attack is characterized by acute onset of inflammatory arthritis with pain, swelling, local warmth, and joint dysfunction. Pseudogout after total knee arthroplasty (TKA) is rare; to the best of our knowledge, there are few detailed reports concerning pseudogout after TKA [1-3]. Moreover, the mechanism underlying CPPD deposits remains unknown.

The aim of this study was to clarify the histologic findings of pseudogout after TKA and help the elucidation of the mechanism underlying the occurrence of pseudogout after TKA.

Case history

The patient was a 79-year-old woman with a long history of pain in the right knee. She had a history of hypertension. She had no diabetes mellitus nor had she received steroid therapy that could affect her immune status. Preoperative radiographs showed signs of osteoarthritis of the right knee and no calcification in the joint space (Fig. 1A). Therefore, she underwent right posterior-stabilized TKA (Fig. 1B) for osteoarthritis of the knee via a medial parapatellar approach. The patella was resurfaced using polyethylene. There were no complications during the intraoperative and immediate postoperative periods. After surgery, the pain in the right knee was ameliorated. The patient could move her right knee from 0° to 110° and had good mobility in her daily life. Two years postoperatively, she experienced acute onset of right knee pain associated with local warmth and swelling. No other joint showed any symptoms of acute inflammation. At the time of presentation, her temperature was 38.5°C and she could neither actively flex nor extend the right knee because of severe knee pain. There were no other symptoms...
in the respiratory or digestive system indicative of the cause of pyrexia. The patient had not received any dental treatment around the onset of the symptoms. Plain radiographs of the knee joint revealed no obvious abnormalities; neither radiolucent lesion around the implant at the femur and tibia nor joint space calcification (Fig. 1C) was observed. Blood analyses demonstrated that an elevated white blood cell count of 12,400 cells/μL (normal range: 4200-8000 cells/μL) and an elevated C-reactive protein level of 2.8 mg/dL (normal range: 0.00-0.50 mg/dL). Preoperative synovial fluid aspiration (20 mL) on the affected side revealed yellow and turbid fluid. Microscopic examination of this aspirate demonstrated an elevated white blood cell count of 24,000 cells/μL with 77% neutrophils. Pyogenic arthritis was suspected, and surgery involving debridement and synovectomy was performed. Perioperatively, we noted that the implant was well fixed and that synovial hyperplasia was minimal and there was no sphacelus intra-articular tissue (Fig. 2). The polyethylene liner was not exchanged since no damage was noted. The synovial tissue samples obtained perioperatively were examined by microbiological and histologic analyses. No organisms were identified in the synovial tissue. However, histologic examination showed significant neutrophil infiltration along with fibrin deposition (Fig. 3A and B). Interestingly, chondrogenesis was observed in the synovial tissue (Fig. 3C and D). Furthermore, the presence of CPPD crystals was noted, which were mainly deposited in the area of chondrogenesis and synthesized by chondrocytes (Fig. 3E and F). Postoperatively, the patient’s pain and pyrexia improved, and she could walk independently 3 days after the surgery. Synovial fluid culture was performed on the preoperative and perioperative fluid samples, but no organisms were identified. Microscopy of the synovial fluid demonstrated the presence of CPPD crystals but no microorganisms. Intravenous antibiotic therapy was administered for 4 days while waiting for the microbiological report. Postoperative changes in the C-reactive protein level and white blood cell count are presented in Fig. 4. At 8 days after the onset of symptoms, the patient was able to walk without any further medication and was therefore discharged. Five years after the occurrence of acute pain in the right knee, the patient has remained free of inflammatory symptoms, such as pain, swelling, and local warmth and no loosening of the implant.

The patient and her family were informed that data from the case would be submitted for publication and provided their consent.

**Discussion**

TKA is a highly effective technique for recovering knee joint function in osteoarthritis of the knee. Prosthetic joint infection is a potential complication of surgery that often results in poor outcomes, and so orthopedic surgeons are highly vigilant for signs of infection. Infection is typically suspected in a patient with acute onset of inflammatory arthritis after TKA. The clinical features of an acute attack of pseudogout are very similar to those of pyogenic arthritis. In addition, pseudogout after TKA is rare, rendering it difficult to diagnose accurately. The identification of calcium pyrophosphate crystals is necessary for the diagnosis of pseudogout. A plain radiograph can reveal calcification in the joint space, but in the present case, radiograph
The pathomechanism of CPPD crystal deposition remains unknown. Several in vitro studies suggest that the accumulation of inorganic pyrophosphate in the articular cartilage, not synovial tissue, plays an important part in the development of pseudogout [4-6]. Harato and Yoshida [1] and Hirose and Wright [2] reported pseudogout after TKA in the early postoperative period and described its clinical features, including the results of blood tests and physical findings before and after the surgery [1,2]. In their case, the synovial fluid sample collected intraoperatively contained CPPD crystals and the patella was not resurfaced, suggesting the development of pseudogout. In our patient, all articular cartilage of the affected knee joint was removed for placement of the implant and the onset of pseudogout occurred in the late postoperative period, indicating the existence of another mechanism of CPPD crystal deposition. Our report is the first to describe histologic findings that indicate the association of chondrogenesis in the synovial tissue with CPPD crystal deposition in a human being. An experimental in vitro study has shown that synovial mesenchymal stem cells in synovial tissue have chondrocyte differentiation potential [7]. However, the factors that induced chondrogenesis in the replaced knee in our patient remain unclear and require further study.

Figure 3. Findings of the histologic examination of synovial tissue after the onset of pseudogout. (a, c) Hematoxylin-eosin (H&E)–stained section at low magnification. (b, e, f) H&E-stained section at higher magnification. (d) Alcian blue–stained section with the lesion shown in panel c at low magnification. (e) The black-boxed area from panel c, wherein the black arrowhead indicates CPPD deposits in the chondrogenic lesion. (f) The white-boxed area from panel c, wherein the white arrowhead indicates CPPD synthesis in the chondrocytes.
We have reported here the histologic findings of pseudogout after TKA. The mechanism of pseudogout in our patient, which occurred after the complete loss of articular cartilage in TKA, did not conform to the generally accepted theory that inorganic pyrophosphate is solely produced in the articular cartilage. The histologic findings in our case suggested that chondrogenesis in the synovial tissue was associated with CPPD crystal deposits in the replaced knee joint, causing postoperative pseudogout.

**Summary**

We reported the histologic findings of pseudogout after TKA wherein the articular cartilage tissue in the knee was completely removed. Chondrogenesis in the fibrous tissue and CPPD crystal deposition in the cartilaginous area was associated with the onset of pseudogout in our patient.

**References**


![Figure 4. Changes in the C-reactive protein (CRP) level and white blood cell (WBC) count after the onset of pseudogout after TKA.](image)