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CASE REPORT

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Severe bone defects and reduced mineralization caused by massive metallosis after total knee arthroplasty: histopathologic and bone morphometric findings

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Abstract We encountered a patient who developed metallosis after total knee arthroplasty (TKA), resulting in loosening of the implant, bone resorption, reduced bone formation, and fracture. The implant was replaced with a NexGen modular revision TKA system after autologous bone and hydroxyapatite granule grafting. Histopathologic examination showed accumulation of metallic debris and tartrate-resistant acid phosphatase-positive cells around the trabecular and cortical bone. Examination of hard tissue specimens showed a reduced bone volume (determined by bone histomorphometry) and an increase of all osteoid parameters, indicating disturbance of mineralization in addition to increased bone resorption.

Key words Bone histomorphometry · Bone resorption · Metallosis · Mineralization · Total knee arthroplasty

Introduction

It is well known that total knee arthroplasty (TKA) with a metal-backed patellar component can be associated with metallosis when the metal part of the component is exposed by wear of the polyethylene surface and comes in contact with the femoral component.[1,2] Chronic metallosis may cause osteolysis around the implant, leading to loosening of the prosthesis. However, there have been few pathological studies on the effect of metallic debris on bone formation and resorption in vivo. Here we report a patient who developed metallosis caused by titanium (Ti)-based particles after TKA, resulting in loosening of the implant, development of severe bone defects, reduced bone formation and mineralization, and fracture. We discuss the histopathologic and bone morphometric findings of this patient.

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Case report

A 78-year-old female patient presented with right knee joint pain exacerbated by walking. She had undergone right TKA with a Miller–Galante type I prosthesis (MGI; Zimmer, Warsaw, IN, USA) 13 years earlier and dropped from the medical follow-up after 2 years.

Bluish-black pigmentation was observed subcutaneously on the lateral aspect of the right knee. The knee joint was swollen and tender, and there was motion pain at the medial tibial condyle. The range of motion of the right knee was 0° for extension and 105° for flexion. Arthrocentesis was performed and about 40 ml of black fluid was removed. No bacteria were detected by culture.

A plain X-ray film of the right knee joint revealed multiple radiodense masses similar to those seen with heterotopic ossification, which suggested the presence of massive metallosis. There was a fracture at the medial condyle of the tibia and the screw used for initial fixation of the tibial component was broken. A skyline view showed that the metal portion of the patellar component was severely defective due to contact with the femoral component (Fig. 1). Computed tomography scanning showed a bone defect in the tibial medullary cavity and fracture lines running through the anterior and posterior cortex of the medial tibial condyle.

The patient was given oral tetracycline hydrochloride twice for bone labeling before revision surgery. Intraoperative examination showed that the knee joint was full of black metallic debris, that half of the metal back of the patellar component had disappeared, and that the outer part of the groove of the femoral component was abraded. When the failed components were removed, it was found that the medullary cavity of the tibia was occupied by metallic debris intermingled with black granulation tissue. The metallic granulation was removed as completely as possible. The fracture was fixed with absorbable screws. Autologous grafts of cancellous bone from the ilium were implanted around the fracture site and hydroxyapatite granules were used to fill the remaining bone defects. A

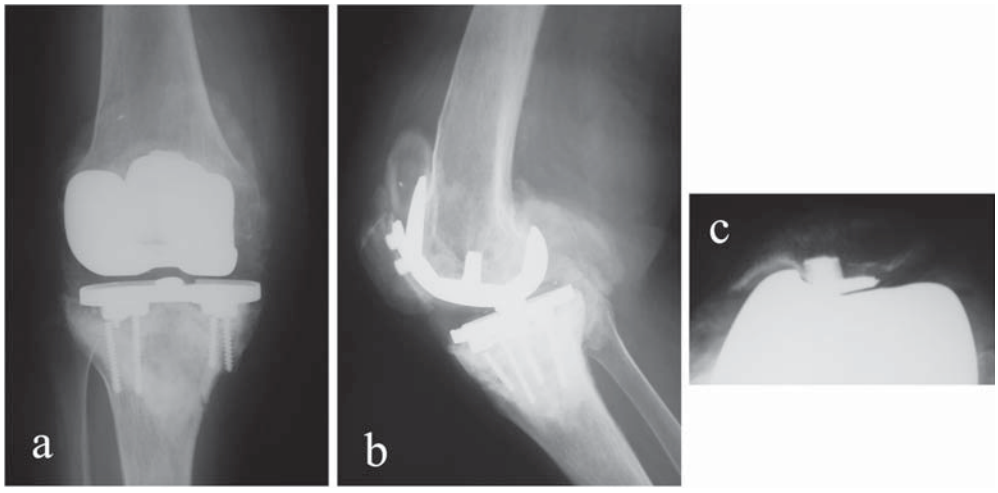

Fig. 1. Preoperative radiographs (**a** anterior–posterior view, **b** lateral view, **c** skyline view) showing multiple radiodense masses in the right knee joint and a fracture of the medial condyle of the tibia. The metal portion of the patellar component had a partial defect

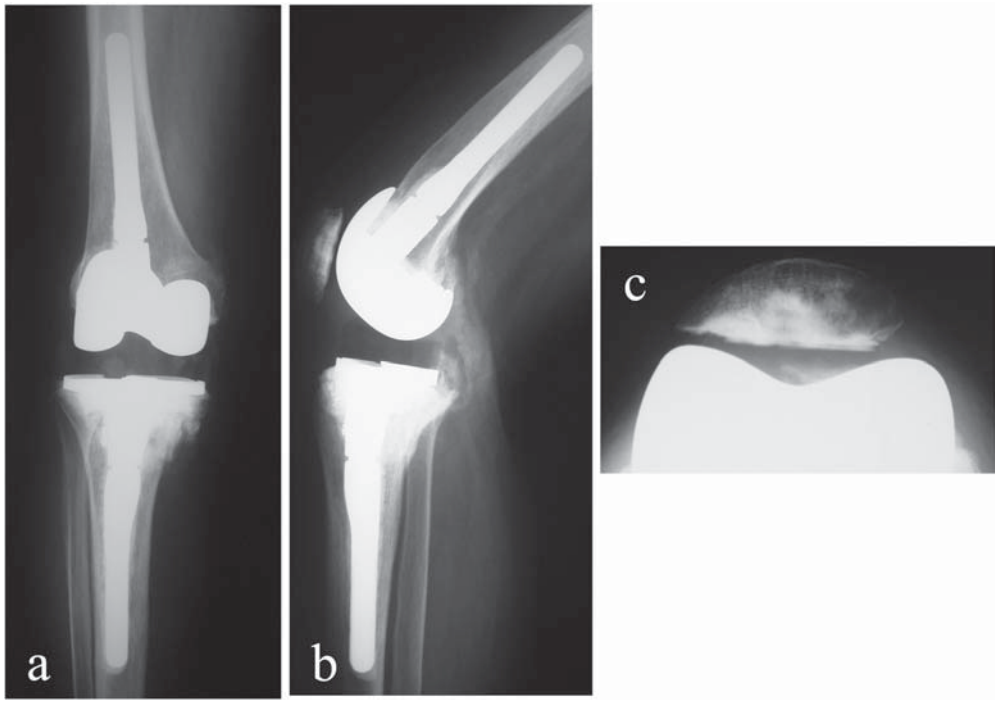

Fig. 2. Follow-up radiographs (**a** anterior–posterior view, **b** lateral view, **c** skyline view) showing bone integration at the medial tibial condyle, and no radiolucent line around the new components or the cement

NexGen modular revision TKA system (Zimmer) was then inserted.

Three years after the revision, her knee achieved a range of motion from 0° to 110° without instability and the Hospital for Special Surgery (HSS) score was 84 points (44 points before surgery). X-ray films showed a femorotibial angle of 176° with fracture healing and good integration of the hydroxyapatite granules. There was no apparent radiolucent line around the new components or the cement (Fig. 2).

Examination of tibial samples showed that metallic debris/particles were present in the granulation tissue within the medullary cavity and on the cortical bone (Fig. 3a). There were various layers of thick osteoid on the border with the metallic debris (Fig. 3b). Many accumulations of multinuclear cells were also observed adjacent to the trabecular and cortical bones (Fig. 3c), and immunohistological staining showed that these cells were positive for tartrate-resistant acid phosphatase (TRAP) (Fig. 3d).

Examination of hard tissue specimens showed a deficit of both trabecular and cortical bone, accumulation of unmineralized osteoid, and absence of tetracycline double labeling (not shown). Bone histomorphometry showed an increase of the eroded surface/bone surface to 37.64% and a decrease of bone volume/tissue volume to 6.11%. The osteoid volume/bone volume, osteoid surface/bone surface, and osteoid thickness were 14.8%, 38.3% and 12.2 μm, respectively. All of the osteoid parameters were increased (Table 1) above the normal range.[3] These results indicated that metallic debris inhibited bone formation and mineralization in addition to increased bone resorption.

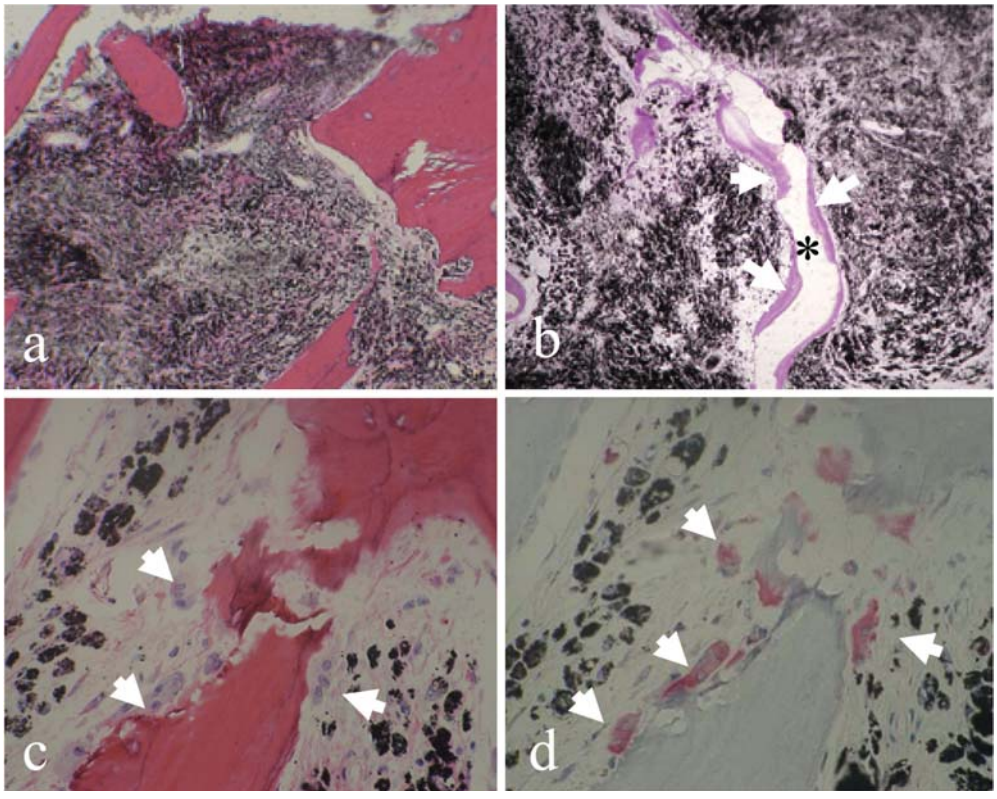

Fig. 3a–d. Photomicrographs. **a** Metallic debris and granulation tissue in the medullary cavity and around the cortical bone (H&E stain, ×40). **b** Hard tissue specimens showed various layers of thick osteoid (*arrowheads*) on the bone (*asterisk*) (Villanueva bone stain, ×40). **c** Higher-magnification photomicrograph, showing collections of multinucleated cells (*arrowheads*) adjacent to the cortical bone (H&E stain, ×200). **d** Immunohistological staining showing the tartrate-resistant acid phosphatase-positive multinucleated cells (*arrowheads*) (×200)

Table 1. Histomorphometric results

Parameters	Value	Normal range
Metallic volume/Tissue volume	71.7%	
Eroded surface/Bone surface	37.64%	1.75–7.00
Bone volume/Tissue volume	6.11%	14.00–30.00
Osteoid volume/Bone volume	14.8%	0.30–3.10
Osteoid surface/Bone surface	38.3%	7.00–25.00
Osteoid thickness	12.2 μm	5.50–12.00

Discussion

The patellar component of the MGI prosthesis frequently causes metallosis because it has a domed shape that tends to focus stress at one point and because it has a metal back with a thin polyethylene surface.[1,2] Since the metal components are made of Ti-6Al-4V, an alloy composed of 90% titanium, 6% aluminum and 4% vanadium, contact between the metal part of the patellar component and the femoral component produces many Ti-based particles.[4]

Previous in vitro studies have reported that Ti particles can elicit bone resorption primarily by inducing osteoclast differentiation[5] and this process may be partly mediated by stimulated cytokine release and increased expression of receptor activator of nuclear factor κB ligand (RANKL) by osteoblastic cells.[6–8] Tissue responses to Ti particles in vivo have also been reported. Agins et al.[9] and Witt and Swann[10] reported that metallosis due to Ti particles was associated with the invasion of numerous histiocytes containing metallic debris into the synovial membrane and periarticular soft tissues. Takai et al.[11] reported that multinuclear giant cells, having a large quantity of dark particles, appeared in the synovium. These reports, however, did not refer to the histopathologic changes of the bony tissue. There have been few pathological studies with regard to the effect of metallic debris on bony tissue in vivo.

In the present case, there was enhanced bone resorption associated with metallic debris and TRAP-positive multinuclear cells aggregated on and around the cortical bone as well as the cancellous bone, supporting the hypothesis that prolonged metallosis and Ti-based particles stimulate bone resorption in vivo.

In addition to the enhanced bone resorption, we observed a marked reduction in local bone formation and inhibition of mineralization. The reduction in bone formation could be explained by the adverse effects of Ti-based particles which could potentially suppress osteoblast proliferation and function in vitro and in vivo.[6,8,12] Therefore, Ti-based particles and prolonged metallosis are likely to affect both bone resorption and formation, and aggravation of this equilibrium failure could have caused loosening and fracture in the present case. Ti-based particles also inhibited mineralization as demonstrated by increased osteoid surface and thickness. However, the effect of Ti itself on mineralization is unclear.

It has been reported that the chemical composition of the Ti-6Al-4V particles in the soft tissues around the loosened implant may differ from that of the implanted alloy and Al could persist in the Ti-based particles in the soft tissues and also in the serum after dissolution and ionization.[11,13] It is already well documented that Al shows various

effects on bone metabolism in chronic renal disease and causes undermineralization of the bone and osteomalacia. Aluminum administration seems to decrease the rate of osteoid maturation and initial mineralization,[14] and such an inhibitory effect of Al on bone mineralization is dose dependent.[15] Although the in vivo effect of locally deposited Al on bone mineralization is still obscure, it is plausible that the Ti-based particles containing Al could have played a topical role in the inhibition of mineralization observed in the present case.

In conclusion, prolonged metallosis induces bone resorption and has adverse affects on bone formation. It is very important to make the early diagnosis of metallosis. Therefore, periodic physical examination and radiologic monitoring is necessary before apparent metallosis occurs. When a possibility of metallosis exists, it is also useful to evaluate a joint fluid and a serum level of metal ion.[16,17] And once it happens, a complete removal of the metallic debris is preferable during revision surgery.

References

1. Bayley JC, Scott RD, Ewald FC, Holmes GB. Failure of the metal-backed patellar component after total knee replacement. J Bone Joint Surg Am 1988;70:668–74.
2. Bayley JC, Scott RD. Further observations on metal-backed patellar component failure. Clin Orthop Relat Res 1988;236:82–7.
3. Recker RR, Kimmel DB, Parfitt AM, Davies KM, Keshawarz N, Hinders S. Static and tetracycline-based bone histomorphometric data from 34 normal postmenopausal females. J Bone Miner Res 1988;3:133–44.
4. Jacobs JJ, Silverton C, Hallab NJ, Skipor AK, Patterson L, Black J, et al. Metal release and excretion from cementless titanium alloy total knee replacements. Clin Orthop Relat Res 1999;358:173–80.
5. Bi Y, Motter RR, Ragab AA, Goldberg VM, Anderson JM, Greenfield EM. Titanium particles stimulate bone resorption by inducing differentiation of murine osteoclasts. J Bone Joint Surg Am 2001;83:501–8.
6. Vermes C, Chandrasekaran R, Jacobs JJ, Galante JO, Roebuck KA, Glant TT. The effects of particulate wear debris, cytokines, and growth factors on the functions of MG-63 osteoblasts. J Bone Joint Surg Am 2001;83:201–11.
7. Shida J, Trindade MCD, Goodman SB, Schurman DJ, Smith RL. Induction of interleukin-6 release in human osteoblast-like cells exposed to titanium particles in vitro. Calcif Tissue Int 2000; 67:151–5.
8. Choi MG, Koh HS, Kluess D, O'Connor D, Mathur A, Truskey GA, et al. Effects of titanium particle size on osteoblast functions in vitro and in vivo. Proc Natl Acad Sci USA 2005;102:4578–83.
9. Agins HJ, Alcock NW, Bansal M, Salvati EA, Wilson PD, Pellicci PM, et al. Metallic wear in failed titanium-alloy total hip replacements. A histological and quantitative analysis. J Bone Joint Surg Am 1988;70:347–56.
10. Witt JD, Swann M. Metal wear and tissue response in failed titanium alloy total hip replacements. J Bone Joint Surg Br 1991; 73:559–63.
11. Takai S, Nobuyuki Y, Kusaka Y, Watanabe Y, Hirasawa Y. Dissemination of metals from a failed patellar component made of titanium-base alloy. J Arthroplasty 2003;18:931–5.
12. Yao J, Cs-szabo G, Jacobs JJ, Kuettner KE, Glant TT, Illinois C. Suppression of osteoblast function by titanium particles. J Bone Joint Surg Am 1997;79:107–12.
13. Shahgaldi BF, Heatley FW, Dewar A, Corrin B. In vivo corrosion of cobalt-chromium and titanium wear particles. J Bone Joint Surg Br 1995;77:962–6.
14. Goodman WG, Gilligan J, Horst R. Short-term aluminum administration in the rat. Effects on bone formation and relationship to renal osteomalacia. J Clin Invest 1984;73:171–81.
15. Bellows CG, Aubin JE, Heersche JN. Aluminum inhibits both initiation and progression of mineralization of osteoid nodules formed in differentiating rat calvaria cell cultures. J Bone Miner Res 1995;10:2011–6.
16. von Schroeder HP, Smith DC, Gross AE, Pilliar RM, Kandel RA, Chernecky R, et al. Titanemia from total knee arthroplasty. A case resulting from a failed patellar component. J Arthroplasty 1996; 11:620–5.
17. Leopold SS, Berger RA, Patterson L, Skipor AK, Urban RM, Jacobs JJ. Serum titanium level for diagnosis of a failed, metal-backed patellar component. J Arthroplasty 2000;15:938–43.