A 70-year-old man with an uncemented metal-on-polyethylene total hip prosthesis underwent revision arthroplasty 33 months later because of pain, swelling and recurrent dislocation. There appeared to be corrosion and metal release from the prosthetic head, resulting in pseudotumour formation and severe local soft-tissue destruction. The corrosion occurred at the junction between the titanium-molybdenum-zirconium-iron taper and the cobalt-chrome-molybdenum head, but the mechanism was unproven.

Case report

A 70-year-old retired entrepreneur with a previous history of coronary heart disease underwent an uncemented left total hip replacement for osteoarthritis. The components (Accolade and Trident; Stryker Inc., Mahwah, New Jersey) were implanted through a direct anterior approach. This prosthetic stem is manufactured from a titanium-molybdenum-zirconium-iron (TiMoZrFe) alloy and covered proximally with a plasma-sprayed porous Ti and hydroxyapatite (HA) coating. The 28 mm prosthetic head used created a +4 mm neck length and was manufactured from Vitallium cobalt-chromium-molybdenum (CoCrMo) alloy. The acetabular component was a shell of titanium-aluminium-vanadium (TiAlV) alloy with a porous coating of Ti and HA; a highly cross-linked polyethylene insert was used. The patient was discharged after five days and at a follow-up visit two months later he had no pain, a normal range of movement with no abductor weakness, and was able to walk unaided.

At one year post-operatively he attended for routine follow-up, but reported he had experienced a short period of pain in the buttock and groin. Nevertheless he walked without a limp and his hip movements and abductor strength were normal. The pain had not completely resolved and there was some swelling of the left leg. Standard radiographs were unremarkable (Fig. 1) and a venogram was normal, but CT showed increased volume of the iliopsoas, which was displacing and compressing the external iliac vein (Fig. 2). An abscess was suspected and 11 ml of yellowish fluid were aspirated by interventional radiologists 15 months post-operatively. Cultures were negative and cytology revealed scanty mature lymphocytes and cell debris indicative of a benign reactive process. The ESR was 22 mm, CRP 18 mg/l and haemoglobin 12.8 g/dl. As the symptoms were manageable no treatment was instituted but observation was continued.

Two years post-operatively the hip dislocated during moderate forward bending. Reduction under general anaesthesia was relatively easy, but the hip redislocated twice during the following six months and the swelling of the left leg persisted. An MR contrast
arthrogram showed dye around the greater trochanter extending proximally in front of the joint, and a cystic lesion anteromedially in the iliopsoas muscle was again noted.

As a result of the recurrent dislocations and discomfort, revision surgery was undertaken at two years and nine months after the original operation. At that time routine blood chemistry was normal. The CRP was 7 mg/l and serum creatinine was within normal limits. Analysis of serum cytokines (Luminex LABscan 100 with Milliplex human cytokine/chemokine 14-plex kit; Millipore, St Charles, Missouri) showed no abnormality for eotaxin, granulocyte-macrophage colony-stimulating factor (GM-CSF), interferon (IFN)-α 2, IFN-γ, interleukin (IL)-10, IL-12(p40), IL-12(p70), IL-17, IL-β, IL-4, IL-5, IL-6, IL-7 and tumour necrosis factor (TNF)-α. In particular, serum interleukins and TNF-α and -β levels were normal. These have not been previously analysed in a case of adverse reaction.

The hip was approached through a lateral incision. The joint was filled with a greyish, relatively viscous fluid and the abductor insertion at the tip of the greater trochanter was disrupted. A large amount of necrotic tissue was removed, revealing the head-neck junction of the prosthesis, where there was a black deposit (Fig. 3). The prosthetic head was firmly fixed to the taper and a disassembly instrument was necessary for its removal. Inside the head, the surface appeared uneven and was covered with the black deposit (Fig. 4). An extended trochanteric osteotomy was performed to remove the femoral component. After preparation of the femur and insertion of a constrained acetabular insert in the Trident shell, a stainless steel Exeter stem with a 22 mm head was cemented in place. Stainless steel was chosen to eliminate exposure to cobalt. Following reduction and copious irrigation, the wound was closed in layers using absorbable sutures. The post-operative course was uneventful and he was discharged after five days. Prophylactic oral cephalosporin was to be continued until the wound was dry. There was no sign of infection but a small serous drainage; no cultures were sent.

Biopsies showed necrosis and lymphocytic infiltration (Fig. 5), but no metal particles were detected by light microscopy. After sputter-cleaning of organic material, the black deposit on the prosthetic neck was analysed using time-of-flight secondary mass spectrometry (ToF-SIMS; Trift III; Physical Electronics Inc., Chanhassen, Minnesota). It contained organic material and mainly Co and Cr ions; the levels of Ti and Mo were negligible. The exudate was analysed for cytokines and showed high levels of IL-10, IL-12(p40) and (p70), IL-1β, IL-5 and TNF-α compared with normal serum. The levels of Co, Cr, Mo and Ti were measured using high resolution internally coupled mass spectrometry (HR ICPMS; I Rodushkin; ALS Scandinavia AB, Lulea, Sweden), which revealed remarkably high levels of
Co and Cr compared with the findings under normal conditions by Hallab and Jacobs (Table I).

A few days after leaving hospital the patient was draining serous fluid from the wound. Oral antibiotics were continued, but two weeks later increasing CRP, persistent drainage and cultures positive for coagulase-negative staphylococci required his readmission for irrigation and debridement. Unfortunately, the infection could not be controlled, and three months after the revision an intrapelvic abscess was removed through an ilio-inguinal incision, and the hip again approached through a lateral incision for debridement and removal of all prosthetic material. Analysis of serum and peri-prosthetic fluid showed metal levels considerably lower than at the first revision (Table I). Six months after this operation the patient was not considered free of infection and a new prosthesis has not been implanted.

**Discussion**

Severe tissue reactions related to metal implants include lymphocytosis, vasculitis, necrosis, excessive production of exudates, and sinus and pseudotumour formation. Cobalt-based alloys are involved in virtually all reported cases of serious adverse reactions and an *in vitro* study has shown that cobalt is more toxic to macrophages than other metals commonly used in implants. These idiosyncratic tissue reactions have been called aseptic lymphocyte-dominated vasculitis-associated lesion (ALVAL), or adverse reaction to metal debris (ARMD). Our findings suggest both a Type 1 (Th1) and a Type 2 helper cell (Th2) inflammatory response: Type 1 and Type 2 helper cells are lymphocytes that produce different cytokines and promote cellular and humoral immune reactions. Although there seems to be a tendency for type IV allergy to implanted metals to be more common in cases with adverse reactions to metal implants than in controls, skin tests and lymphocyte migration and proliferation tests are of little diagnostic help.

The Aclocade prosthesis is manufactured from a TiMo-ZrFe alloy, which has not previously been used as a prosthetic alloy. It is considered to be biocompatible and is reported to have higher strength and lower elastic modulus than earlier Ti alloys. It has also been shown to have lower friction against polyethylene than other commonly used Ti alloys, suggesting that the surface oxide differs in some respect. Micromovement at the head-neck junction means there is a risk of fretting corrosion. The Aclocade prosthesis is prominent among those hips using ceramic-

**Table I** Metal concentrations (parts per billion (ppb) × 10) of cobalt (Co), chromium (Cr), Molybdenum (Mo) and titanium (Ti) in body fluids compared with the reference values of Hallab and Jacobs (N, normal; TJR, total joint replacement).

<table>
<thead>
<tr>
<th></th>
<th>Co</th>
<th>Cr</th>
<th>Mo</th>
<th>Ti</th>
<th></th>
<th>Co</th>
<th>Cr</th>
<th>Mo</th>
<th>Ti</th>
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<tr>
<td>Serum N</td>
<td>0.003</td>
<td>0.001</td>
<td>-</td>
<td>0.06</td>
<td>TJR 0.007</td>
<td>0.006</td>
<td>-</td>
<td>0.09</td>
<td>0.5/0.09</td>
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<tr>
<td>Peri-articular fluid N</td>
<td>0.085</td>
<td>0.058</td>
<td>0.219</td>
<td>0.27</td>
<td>TJR 10.0</td>
<td>7.4</td>
<td>0.6</td>
<td>11.5</td>
<td>220.0/9.0</td>
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**Fig. 4** Photograph of the inside of the head of the prosthesis showing signs of corrosion.

**Fig. 5** Histological section from the neocapsule showing infiltrate with CD3 T-lymphocytes (brown) and CD20 B-lymphocytes (red) (stained with CD3-diaminobenzine/CD20-alkaline phosphatase, magnification × 40).
on-ceramic bearings, which can generate a squeaking sound during walking.\textsuperscript{15,20} Whether this is related to the alloy or the taper is uncertain, but hard impaction of ceramic heads is often avoided because of concerns regarding fracture. A V40 taper used in the manufacture of the Accolade prosthesis has less contact area than a C taper. In addition, the Accolade prosthesis has a slender neck and accordingly a relatively short V40 taper.\textsuperscript{20} When, as in our patient, a +4 mm modular femoral head is used, the junctional stresses are likely to be higher than with a standard head. Finally, low flexural rigidity of the prosthetic neck has been noted as a predictor of interface corrosion.\textsuperscript{21}

Our findings are consistent with a corrosive process affecting the prosthetic head at its junction with the taper. We have no proof that fretting occurred, as the release of metal came mainly from the CoCrMo surface, which is harder than that of the Ti alloy. Also, we found no metal particles in the surrounding tissues and the prosthetic head appeared well fixed to the taper. We suspect that the release of metal was probably caused by crevice corrosion. Galvanic corrosion appears less likely because the electrochemical gradient between CoCrMo and Ti alloys is reported to be small, although we have found no published data on this particular Ti alloy.\textsuperscript{22}

In some cases where the levels of Co and Cr are high, activation of T lymphocytes and B-helper cells may occur in the tissue surrounding the prosthetic joint, especially in the peri-vascular region.\textsuperscript{5,6} Vasculitis has also been reported although this was not seen in our patient.\textsuperscript{5,6} Macrophages are widespread and apoptosis is common.\textsuperscript{5,6} Analysis of the peri-prosthetic fluid indicated inflammatory Th1 and Th2 reactions, with a slight predominance of the latter.

Even though this is an isolated case, the serious consequences illustrate the need for further investigation. The decisive event is the release of metal ions, especially cobalt, and from this perspective the nature of couplings in modular prostheses needs more attention. Although the determination of metal levels in the peri-prosthetic and body fluids is necessary, the reaction to metal may be triggered by immunological mechanisms which are largely unknown. Unexplained pain after a joint replacement, perhaps accompanied by swelling or instability, should raise the suspicion of a metal-related adverse reaction that requires investigation.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References