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Case Report

# Revision Total Hip Arthroplasty Complicated by Metastatic Malignant Gastrointestinal Stromal Tumour
# 病例報告:在全髖關節翻修置換術中出現的胃腸道間質腫瘤轉移

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ABSTRACT

Periprosthetic malignancy causing failure of total hip arthroplasty is a rare entity. Metastasis of malignant tumour to the proximity of orthopaedic implants is even more uncommon. We present a case of a 74-year-old female with an infected Austin Moore prosthesis, requiring a two-stage revision total hip arthroplasty. Within 2 years postoperatively, erosion of the lesser trochanter was noted. Further revision surgery was performed with the insertion of a cement spacer. Despite the expectation of an infected prosthesis, intraoperative frozen section showed sarcoma and the final pathology was metastasis of a recurrent gastrointestinal stromal tumour (GIST). Metastatic GIST to total hip prosthesis had not been reported previously and this case illustrates how intraoperative frozen section can aid diagnosis and management. We also highlighted some diagnostic clues, differentiating this rare diagnosis from septic loosening and osteolysis. Malignant infiltration should be considered as a differential diagnosis in failed total hip arthroplasty, especially in patients with a previous history of malignancy.

中 文 摘 要

惡性腫瘤造成全關節置換失敗的罕見的。惡性腫瘤轉移到骨科義體鄰近的病例更是稀有。我們提出一個病例，關於一名74歲的婦女，在Austin Moore義體受感染的情況下，需要進行兩個階段全髖關節翻修置換術。術後2年以內，小粗隆受到侵蝕，需要進一步進行翻修手術，插入水泥隔板。本來預計義體受感染，但術中冰凍切片顯示肉瘤，最終病理為的一個複發性的胃腸道間質腫瘤（GIST）轉移。GIST轉移到全髖關節義體沒有曾被報導。這病例說明了術中冰凍切片如何可以幫助診斷和治療。我們強調了一些診斷線索，將這種罕見的診斷與假體周圍感染和骨溶解區分。惡性腫瘤侵蝕，尤其是在有惡性腫瘤病史的患者，應被視為在全髖關節置換術失敗的鑑別診斷.

## Introduction

Tumourous condition is an uncommon mode of failure for orthopaedic implants. Multiple reports have already described primary *de novo* malignant tumour arising in the proximity of orthopaedic prosthesis.[1] By contrast, metastatic malignant disease occurring at the site of orthopaedic prosthesis has rarely been documented.[2] We present an unusual case of gastrointestinal stromal tumour (GIST) metastasis to a revision total hip arthroplasty (THA). This case serves to highlight that proper correlation of clinical, biochemical, and radiological findings could make preoperative diagnosis of such a rare entity possible. Intraoperative frozen section is a valuable tool in revision surgery and we hope to heighten the awareness of malignancy as a mode of failure of THA.

## Case report

A 74-year-old female had a history of rectal malignancy with abdominoperineal resection done in 1994, followed by radiotherapy to the pelvis. She later sustained a fracture left hip with Austin Moore hemiarthroplasty performed in another hospital without a traceable record in 1996. In 2004, 8 years after the initial hip operation, she was referred to our clinic for progressive left hip rest pain for a few weeks with rapidly deteriorating walking ability. X-Ray examination showed a radio-opaque line over the medial

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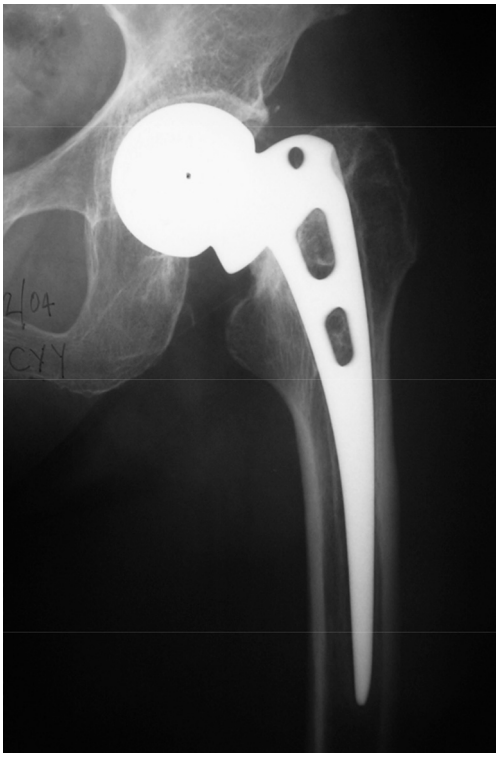

**Figure 1.** X-Ray of the Austin Moore prosthesis 8 years postoperation. A radio-opaque line along the medial side of the stem was noted, signifying probable loosening.

side of the implant (Figure 1). Inflammatory markers were elevated with white blood cell count (WBC) 14.7 $\times$ $10^9$/L, C-reactive protein (CRP) 231 mg/L, and erythrocyte sedimentation rate (ESR) $>$ 120 mm/hour. Hip arthrocentesis yielded 2 mL of pus with culture result of *Streptococcus agalactiae*.

Regarding her rectal tumour status, she had regular follow-up by the surgical team and a colonoscopy 2 years ago did not show any recurrence. Her carcinoembryonic antigen level was also normal.

Two-stage revision THA was performed. During the first stage of revision, pus was noted upon entering the deep muscle plane and the prosthesis was loosened. There was no obvious bone erosion or soft tissue mass. Culture of intraoperative tissue confirmed infection with *S. agalactiae*. An antibiotic-laden cement spacer was inserted and the patient was given a 6-week course of intravenous penicillin.

The second stage revision was performed 4 months later. Intraoperative frozen section was consistent with inflammatory changes and microbacterial culture was negative. A hybrid total hip prosthesis was used, with the femoral component fixed using vancomycin-loaded cement.

At 8 months postoperatively, radiography showed a radiolucent lesion at the lesser trochanter. At 18 months, the erosion progressed and the entire lesser trochanter was eroded away without subperiosteal new bone formation (Figure 2). The patient complained of increasing left hip pain. Blood result showed normal WBC and CRP, but ESR was elevated to 60 mm/hour. Hip arthrocentesis failed to yield any joint fluid.

Revision surgery was performed for suspected residual infection. Upon exploration, the synovium was mildly inflamed and hypertrophied; the joint fluid was blood stained. There was some granulation-like tissue over medial calcar with extensive osteolysis (Figure 3). The femoral stem, however, was not loosened. An extensive trochanteric osteotomy was required for complete removal. The acetabular side was healthy with a well-fixed cup, which was removed. The intraoperative frozen section was reported to be absent of neutrophil and contained spindle cells consistent with sarcoma. Debulking of all suspicious tumourous tissue was carried out and a cement spacer (Spacer G XL, long stem; Zimmer, Warsaw, Poland) was inserted (Figure 4).

The final report, after immunostaining, concluded the pathology to be GIST. Positron emission tomography–computed tomography (PET–CT) was performed, which showed a large mass in the pelvis and over the right groin with increase uptake. There was also bone metastasis to the right seventh rib (Figure 5). There was mild uptake over the left hip prosthesis, consistent with postoperative changes, but no uptake at the left acetabulum was noted.

Careful tracing of all records showed the initial pathology report on the rectal malignancy was leiomyosarcoma. A review of the pathology slides from 1994 and the current pathology showed both specimens to be consistent with GIST. The final pathology was local recurrence of malignant GIST with local invasion to the right groin and metastasis to the left proximal femur and right seventh rib.

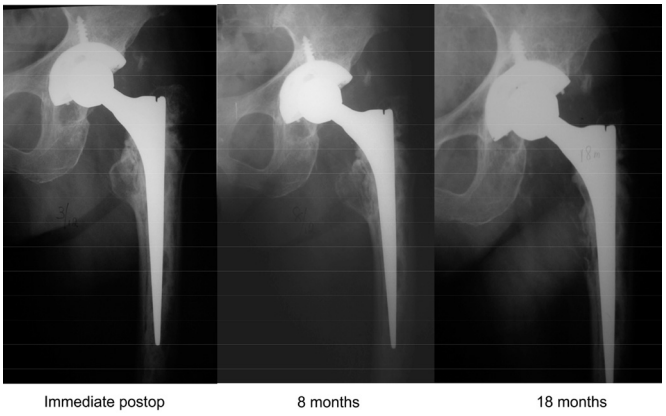


**Figure 2.** Serial radiographs of revision left THA. Progressive lytic lesion over the lesser trochanter was observed as early as 8 months postoperation. Full thickness erosion of the entire lesser trochanter without periosteal reaction was noted at 18 months. THA = total hip arthroplasty.

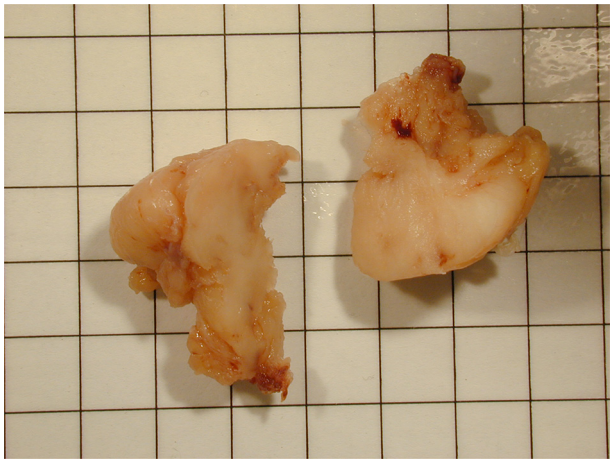

**Figure 3.** Gross appearance of the granulation-like mass eroding onto the lesser trochanter. The final pathology result was GIST. GIST = gastrointestinal stromal tumour.

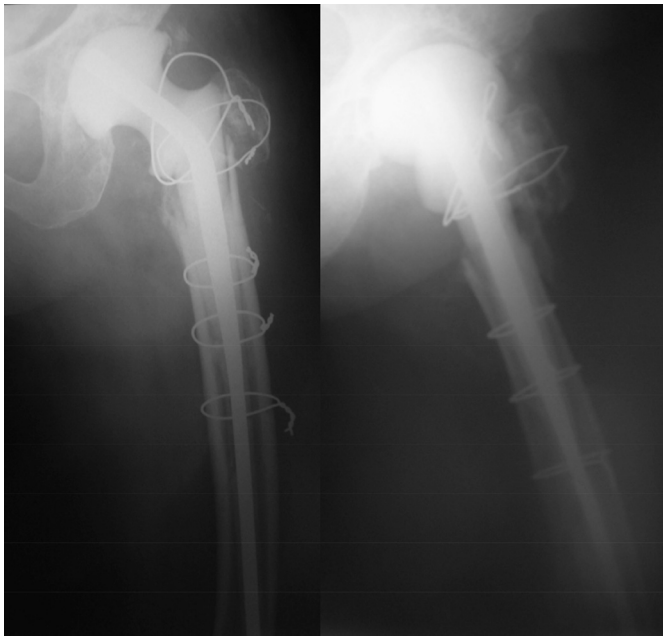

**Figure 4.** Cement spacer was inserted after complete removal of all prosthesis.

In view of metastasis, she was referred to oncology for further management. She was given imatinib (Glivec), a selective inhibitor against the mutated KIT protein. The pain over the left hip had decreased, but the patient never regained full ambulatory ability. Her response to treatment was poor and she died 1 year after the last orthopaedic operation.

## Discussion

Three possibilities exist for periprosthetic tumour: (1) *de novo* malignancy, and for patients which previous radiotherapy to the surrounding area, postradiation sarcoma can be considered; (2) metastasis; and (3) direct invasion from nearby regions. We believe our case is one of metastasis. The final pathology of GIST is consistent with local recurrence in the pelvis. Moreover, intraoperatively, the tumour erosion was isolated to the proximal femur and no debulking was performed on the acetabulum. Postoperative PET–CT also confirmed no uptake at the left acetabulum. The patient had also another metastasis to the right seventh rib. The intense activity over the pelvic and right groin region was the recurrence of the tumour, which did not invade into the left hip.

Reviewing the English literature from 1974 to 2003, Visuri et al[1] found 46 reported cases of primary malignant tumour at the site of total hip prosthesis. The majority of the cases were malignant fibrous histiocytoma or osteosarcoma, whereas other common pathologies were fibrosarcoma, leiomyosarcoma, and spindle cell sarcoma.

Compared with a primary malignant tumour at the proximity of prosthesis, periprosthetic metastasis has much fewer occurrences. Bali et al,[3] in a recent paper, found only 14 cases of metastasis at the site of THA in the English literature since 1986. The primary tumours include lung, renal, lymphoma, gastric, squamous cell carcinoma, heptatocellular carcinoma, or unknown primary. The proximal femur was the usual site of involvement. Periacetabular involvement was relatively less common in metastasis. In most of the reported cases, periprosthetic metastases were discovered intraoperatively during revision THA, which were performed on the assumption of septic or aseptic loosening of the hip prosthesis.[2–4]

In this reported case, the previously established periprosthetic infection misdirected our attention when a painful lytic bone lesion was noted upon follow-up. With residual infection as the main diagnosis, the intraoperative frozen section report of sarcoma was unexpected. Debulking the tumour and the insertion of the cement spacer had relieved pain, and it is the mainstay of management for malignancy in the proximal femur.[5] In retrospect however, there were atypical features regarding the clinical presentation and radiographic features that warrant further investigations prior to the revision operation. Had the diagnosis of metastatic GIST been made preoperatively, the patient could be treated with chemotherapy (imatinib) and radiotherapy instead of major revision surgery.

One suspicion was the periprosthetic radiolucency. Differential diagnosis includes osteolysis, infection, and tumour. Osteolysis induced by wear particles should occur no earlier than 12 months postoperation.[6] Moreover, the typical feature of osteolysis is endosteal scalloping that may be extensive in size but rarely involves the full thickness of the cortex. Maloney et al[7] also found that the most common sites for osteolysis were Gruen zones 2 and 3 on the anteroposterior view and zones 5 and 6 on the lateral view. A solitary, rapidly progressive lesion in Gruen zone 7 that occurs within 1 year postoperation indicates a sinister diagnosis.

Differentiating a tumour from infection is more challenging. Classical symptoms and signs of infection such as severe joint pain, fever, and chills can occur in the case of malignancy. However, biochemical inflammatory markers can provide a clue to the unusual nature of the disease. The use of CRP and ESR levels in detecting infection has reported sensitivity and specificity of over 80%, with CRP being the more sensitive test.[8] The ESR level is more nonspecific and can remain elevated as long as 1 year after surgery or in cases of chronic illness. Elevation of ESR with a normal CRP level could be a clue to noninfectious origin of pathology.

Radiological appearances of periprosthetic infection can be nonspecific. These include periosteal reaction and generalised

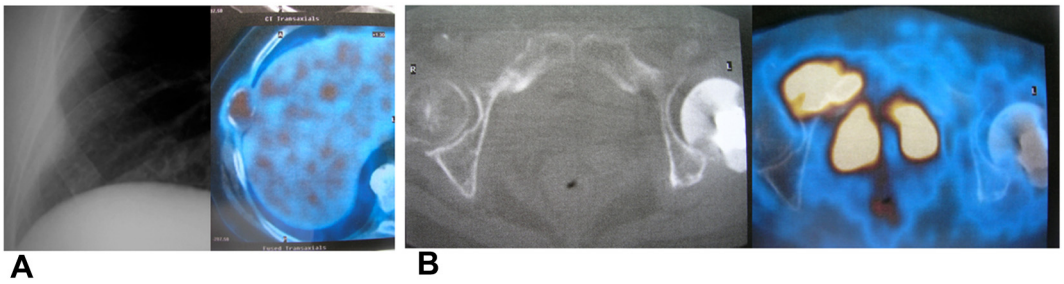


**Figure 5.** Positron emission tomography–computed tomography showed (A) metastasis to the right seventh rib and (B) recurrence of gastrointestinal stromal tumour in the pelvis with local invasion into the right groin. No significant uptake over the left acetabulum was noted.

bone resorption without evidence of implant wear.[9] Absence of periosteal reaction can be seen in acute, uncontrolled infection. In such an instance, the blood parameters would have been markedly abnormal. Correlating the radiographic features and the blood result, the diagnosis of periprosthetic infection should be questioned. Further preoperative investigations should be systemic such as PET–CT and bone scan. Local investigation such as magnetic resonance imaging and tru-cut biopsy should also be considered.

Intraoperatively, extensive trochanteric osteotomy was carried out prior to waiting for the frozen section report. In the past, surgeons have relied on the frozen section result mainly to decide whether to reimplant a new prosthesis or insert a cement spacer. It may now be worthwhile to wait for the frozen section result prior to contemplating on the removal of prosthesis, especially when the intraoperative finding does not correlate with the expectation.

In conclusion, this is the first reported case of periprosthetic metastasis of GIST to a revision THA. Periprosthetic metastasis is a rare phenomenon and a rare cause of failure for THA. Nonetheless, it is an important differential diagnosis, especially in patients with a previous history of malignancy. A rapidly progressing lytic lesion, without periosteal reaction, involving the full thickness cortices of the lesser trochanter in the early postoperative period, combined with relatively normal blood parameters were definite clues. Further investigations should be performed, not only to target the site of prosthesis but also to look for any recurrence of malignancy. Intraoperative frozen section is valuable in aiding diagnosis. If doubt arises about the exact pathology, waiting for the frozen section result will be beneficial.

## Conflicts of interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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