CASE REPORT

Rare progression of cholangiocarcinoma: distal femoral metastasis

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SUMMARY

Cholangiocarcinoma (CCA) is a rare cancer of the bile duct epithelial cells, with metastases to long bones rarely reported. We present the case of a woman aged 61 years, diagnosed with CCA 6 years previously. She presented with right thigh discomfort, rapidly progressing to immobility with severe pain. Radiological investigations revealed a lytic lesion in her right distal femur, most likely a metastatic deposit, at high risk of pathological fracture. This was managed with an en bloc resection and implantation of a distal femoral replacement. Pathology specimens from theatre confirmed metastatic CCA. Despite sustaining a subsequent fractured neck of femur on the operative side, she recovered well from surgery, with minimal pain and improved mobility on discharge. She restarted palliative chemotherapy. This case illustrates the option of definitive major surgery for the management of metastatic bone disease. As in this case, this can lead to improved symptom control and quality of remaining life.

BACKGROUND

Cholangiocarcinoma (CCA) is a rare cancer arising from the bile duct epithelial cells. It has an annual incidence of 1–2 per 100 000 in Western Countries.¹ CCA is increasing in incidence in the UK and has an extremely poor prognosis, almost always resulting in death, with a median survival of <2 years.² CCA typically advances locally and has a low tendency to metastasise, but metastases to lungs, brain, adrenal glands and the axial skeleton have been frequently reported.^{3–4} Appendicular skeletal disease, in particular long bone metastases from CCA, is exceedingly rare. To the best of our knowledge, few cases have been reported in the literature. Three cases of humeral metastases from CCA have been reported by other authors.^{5–7} Two of these cases involved surgical fixation, the other being managed with palliative radiotherapy and bisphosphonates alone. Another case reports a distal fibula metastasis revealing a diagnosis of CCA.⁸

To the best of our knowledge, this is the first case reported on femoral metastasis from CCA. We believe this case is important because it highlights the rare occurrence of long bone metastasis from CCA. Furthermore, despite the poor prognosis, major surgery can be of benefit to a patient in this position to improve their pain, mobility and quality of remaining life.

CASE PRESENTATION

We present the case of a Caucasian woman aged 61 years who presented with a 10-day history of

rapidly worsening right thigh pain, becoming progressively unable to weight-bear. There was no history of preceding trauma. She was initially diagnosed with CCA 6 years prior to this presentation, which was treated with an extended right hepatectomy, portal vein excision and adjuvant chemotherapy. Resection margins were positive for disease and pathology confirmed CCA with local lymph node metastasis. Unfortunately, 4 years later, there was evidence of disease recurrence on follow-up CT scans and further curative surgery was not possible. She was managed with palliative chemotherapy (cisplatin and gemcitabine combination).

Four months prior to her presentation, she was also diagnosed with a localised grade 1 endometrial cancer, which was treated with palliative radiotherapy. CT and MRI scans at this time also revealed a lytic lesion within her right inferior pubic ramus and her right proximal femur, for which she also received radiotherapy.

She did not have any other significant medical history, and on admission, the only medications she was taking were laxatives, omeprazole and analgesics (morphine sulfate modified release, paracetamol, gabapentin).

She was previously employed as a teacher, but had taken medical retirement soon after her original diagnosis of CCA. She had no smoking history, and no history of alcohol excess. Prior to her admission, she had a good level of mobility and was independent with all activities of daily living. Of note, in her family history, her grandmother died of endometrial cancer.

The patient was very active in raising awareness of CCA and promoting research in CCA. She was knowledgeable about the disease, and was aware of its prognosis. She was involved in CCA support groups, which had been of great help to her throughout her diagnosis. She had also received support from Clinical Psychology, and was of strong Christian faith.

INVESTIGATIONS

A nuclear medicine whole-body scan 1 month prior to her presentation showed multiple pelvic metastases and a large area of increased uptake within the right distal femur (figure 1). Radiographs of her thigh at this time showed a lytic lesion with anterior cortical destruction in the distal third of the right femur (figure 2).

A subsequent MRI scan of her right thigh, to investigate the extent of this likely metastatic deposit, confirmed extensive anterior cortical destruction in the distal third of the femur,

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Figure 1 Nuclear medicine isotope bone scan (^{99m}Tc) demonstrating increased uptake in the right distal femur.

Figure 2 Plain radiograph (lateral view) of the right distal femur demonstrating anterior cortical destruction.

Figure 3 MRI of the metastatic deposit preoperatively.

suggesting that there was a high risk of impending pathological fracture ([figure 3](#)).

Admission blood tests showed a haemoglobin of 112 g/L, normal white cell count of $4.2 \times 10^9/\text{L}$, a normal creatinine of 58 $\mu\text{mol/L}$, a moderately elevated C reactive protein of 32 mg/L, normal liver function tests and normal coagulation studies. She had a mildly raised adjusted calcium of 2.67 mmol/L (2.2–2.6 mmol/L reference range), and a low phosphate 0.56 mmol/L (0.8–1.4 mmol/L). She was initially given intravenous fluids to treat her hypercalcaemia and intravenous phosphate replacement.

DIFFERENTIAL DIAGNOSIS

On the basis of the clinical assessment and radiological investigations, the top differential diagnoses were:

1. Metastatic bone disease either from CCA or endometrial cancer
2. Osteomyelitis
3. Primary solitary bone tumour, for example, osteosarcoma due to the location of the lytic lesion

TREATMENT

The patient's treatment involved a large multidisciplinary team (MDT) approach, including but not limited to oncologists, radiologists, anaesthetists, surgeons, medical staff, physiotherapists, clinical psychologists and the hospital chaplain service.

The risks and benefits of surgery were discussed with the patient, including the options for fixation and replacement. Non-operative management was also discussed. Given her high level of activity prior to admission, the patient elected for en bloc excision and distal femoral replacement. Given her overall fitness and reasonable life expectancy, the MDT also felt that this was an appropriate treatment option.

The distal femoral replacement was performed under a general anaesthetic with epidural supplementation. The tumour was exposed via a longitudinal incision centred over the knee joint. Careful dissection of the surrounding structures, with meticulous haemostasis, was performed until the extent of the tumour was identified. All the feeding blood vessels to the tumour were ligated prior to tumour excision with a 5 cm proximal margin. The proximal tibia was excised and a standard distal femoral replacement was cemented in situ. The whole specimen was sent to the pathology laboratory for analysis. There were no complications in the immediate postoperative period, with a recorded total blood loss of 500 mL. Check radiographs showed satisfactory positioning of the femoral and tibial components ([figure 4](#)).

Figure 4 Postoperative radiographs (anteroposterior and lateral views) showing the position of the distal femoral replacement.

Day 1 postoperative bloods showed a haemoglobin of 88 g/L, with no other abnormalities. She recovered well in the coming days and started to mobilise with the physiotherapists. She required further phosphate replacement in the coming days and had two episodes of hypercalcaemia requiring treatment with intravenous bisphosphonates. Her wound healed well and surgical clips were removed 14 days postoperatively.

On the planned day of discharge, while mobilising, she sustained a twisting injury with immediate pain in the right hip. X-ray showed a right-sided intertrochanteric proximal femoral fracture, but no displacement of the distal femoral replacement. This fracture was surgically repaired with a dynamic hip screw. She recovered well from this operation, with no other complications. Once mobile and deemed safe for discharge 1 week later, she went home to spend the rest of her recovery with family.

OUTCOME AND FOLLOW-UP

The patient was reviewed by the oncology team during her admission, with a plan for a repeat CT scan of her abdomen, as an outpatient, to examine disease progression, with a view to restarting her palliative chemotherapy.

Pathology results from theatre confirmed metastatic CCA and that it was higher grade than previous pathology.

The patient was reviewed in the orthopaedic outpatient clinic 8 weeks following surgery. She was mobilising independently and with significantly less pain than before surgery. Despite this, she developed a severe pneumonia and sadly died 4 weeks after her last review in the comfort of her own home and in the company of family.

DISCUSSION

CCA is a rare malignancy often resulting in early mortality. The 5-year survival rate is <5% in patients who undergo surgical resection.⁹ The patient in this case, still having a high level of function and quality of life 6 years postdiagnosis, is unfortunately in the minority of patients with CCA.

To the best of our knowledge, there are only four published cases of long bone metastases from CCA. Carlisle and Roberts⁵ describe a female patient, of similar age to this case, who presented with shoulder pain 4 months after a right hepatectomy for CCA. Serial radiographs revealed a displaced pathological fracture through a metastatic lesion. This was treated with an intramedullary nail with subsequent palliative radiotherapy offered, but the patient declined. Federico *et al*⁷ reported the case of a man aged 75 years with a humeral metastasis from

CCA. The patient was managed with a combination of bisphosphonates, radiotherapy and chemotherapy. The case of a man aged 58 years with a low-energy proximal humerus fracture was reported by Lahrach *et al*.⁶ Pathology from theatre revealed metastatic CCA, confirmed via a CT scan, with the patient dying 3 months later. A woman aged 75 years was presented by Karanjia *et al*.⁸ She was found to have a lesion in her distal fibula. Biopsy and further investigation revealed a diagnosis of CCA with a metastasis in her distal fibula. She was managed with palliative radiotherapy.

This is the only case, to the best of our knowledge, reporting a femoral metastasis from CCA.

The goal of treatment in cases such as this is to control unpleasant symptoms (usually pain), allowing theoretical immediate weight bearing and mobility. This ensures the highest possible quality of remaining life. We believe this to be the only case reported where an endoprosthetic replacement has been used for the surgical management of metastatic CCA, instead of internal fixation or palliative radiotherapy.

Large endoprostheses, such as distal femoral replacement, have been shown to allow patients with metastatic bone disease to return to a good level of function.¹⁰ It was proposed in a systematic literature review that patients who have metastatic bone disease with a life expectancy >1 year should be considered for en bloc resection and prosthetic reconstruction. This was more favourable than less invasive surgical techniques, including intramedullary nailing, which have a much greater mechanical failure rate over time compared with endoprosthetic replacements.¹¹ Stabilisation of an impending pathological fracture has been shown to permit early resumption of ambulation and improved patient quality of life.¹²

In contrast to this patient, many with CCA will not be suitable for definitive major surgery such as distal femoral replacement. This is a complex decision; therefore, a multidisciplinary approach is required to evaluate all possible treatment options and assess fitness for surgery. Following discussion, the patient is required to make an informed decision regarding the management of their condition. Close input is essential from the oncology team regarding further radiotherapy and chemotherapy, which depend heavily on the results from the postoperative pathology analysis.

In patients with CCA who present with bone pain, long bone metastases should be considered as a possible rare progression of their disease. This report highlights femoral metastases from CCA as possible disease sequelae and, importantly, illustrates the principle of endoprosthetic reconstruction as a successful treatment. This can provide superior symptom control and improved quality of remaining life, even in patients with advanced metastatic disease.

Learning points

- ▶ Long bone metastases from cholangiocarcinoma are very rare but can occur.
- ▶ In long bone metastases, endoprosthetic replacement is often a better treatment option than fixation, allowing improved pain control, quicker mobilisation and enhanced quality of remaining life.
- ▶ Despite the poor prognosis, patients may be suitable for major definitive surgical management of their metastatic disease.
- ▶ Each patient should be assessed individually, employing a multidisciplinary approach.

Contributors SAM and TC were involved in the treatment of the patient and the planning of the case report. JSOG and CR contributed with the literature search and final drafting. All authors read and approved the final version of the manuscript.

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