HUMERAL PATHOLOGICAL FRACTURE AND EXTENSIVE OSTEOLYTIC LESIONS IN CHRONIC LYMPHOCYTIC LEUKAEMIA

a case report

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INTRODUCTION

Chronic Lymphocytic Leukaemia (CLL) is a fairly common and frequently indolent proliferative disorder of B lymphocytes. Prognosis depends on stage, but in uncomplicated stage A disease survival does not differ from that of the general population. In most patients, however, median survival from diagnosis is six to eight years. The tumour cells appear mature but are monoclonal and long lived. Typically there is a lymphocytosis in the peripheral blood and widespread infiltration of bone marrow, lymph nodes and other tissues.

It is, however, a rare cause of lytic bone lesions, hypercalcemia and pathological fracture. In the few case reports, a paraprotein – often Ig A – has been a feature⁽¹⁾.

We report a case of CLL in which widespread lytic bone lesions with pathological fractures were prominent features and discuss the management.

CASE REPORT

A 77-year-old lady was referred to the Medical Assessment Unit (MAU) of the Royal Lancaster Infirmary by her general practitioner with malaise and left shoulder pain.

She was diagnosed with B-Cell CLL two weeks prior to her admission. On admission she was afebrile with stable vital signs. Pallor and right-sided supraclavicular lymph nodes were noted on physical examination. The initial investigations revealed that haemoglobin was 7.4 g/dl, white cells $305 \times 10^9/L$ (neutrophils 4.9, lymphocytes 300.7, platelets $62 \times 10^9/L$). Plasma calcium level was raised at 3.03 mmol/L (2.18 to 2.6). X-rays showed extensive osteolytic lesions in the proximal ends of both humerus and a pathological fracture in the surgical neck of the left humerus (Figure 1). Isotope bone scan showed increased uptake throughout the femurs, vertebra and ribs. Retroperitoneal lymphadenopathy and splenomegaly were noted on abdominal ultrasound. A search for a paraprotein revealed only immune paresis (IgG 3.43, IgA 0.98, IgM 0.59). There was no band on electrophoresis.

Hypercalcemia was treated by intravenous normal saline and zoledronic acid infusion. The patient was given a blood transfusion as the haemoglobin dropped to 5.7g/dl. She underwent an interlocking intramedullary nailing of the left

Figure 1 Left shoulder

humerus and as a prophylactic measure the same procedure was performed on the right humerus (due to significant bone loss associated with almost certain future fracture and significant pain) within one week (Figure 2). She was transferred back to the MAU where chemotherapy was commenced (five days of fludarabine). A recurrence of hypercalcemia was treated with intravenous fluid and bisphosphonate (zoledronic acid).

There was a moderate response to the chemotherapy in that her white cell count fell but she remained thrombocytopenic and required blood transfusion to maintain her haemoglobin. Pain was a major problem and this plus the dependency induced by the temporary loss of function of both arms led to a profound lowering of her mood. She became withdrawn, refusing food and being disinclined to mobilise.

A urinary tract infection led to a proven septicaemia (with coli). This was treated successfully and by the 20th postoperative day she was brighter and doing more for herself. Radiation therapy was considered but not offered for fear of inducing further pathological fracture and pain control became the main problem. A combination of Cox II inhibitors and opioids was only partly successful. A week later she deteriorated suddenly with increasing back pain and signs of bronchospasm and died the same day. No post mortem was carried out.

Figure 2 Intra-operative image intensifier picture, proximal end of right humerus

DISCUSSION

Although haemopoietic malignancies such as leukaemia arise from medullary tissue, destructive bone lesions with pain and pathological fracture are uncommon features⁽²⁾. The exception is myeloma in which lytic lesions are usual and some non-Hodgkin lymphomas which can produce similar problems. Acute leukaemias may occasionally produce bone pain but the occurrence of these lesions in CLL is very rare and reported cases emphasise the extensive disease and poor prognosis of these patients⁽³⁾. The skeleton is the third most common site for cancer to spread after the liver and lungs⁽³⁾. Although bony metastases usually involve the axial skeleton, approximately 25% of all metastases are located in the shoulder girdle⁽⁵⁾.

Although it was known that the increased number and activity in osteoclasts play a central role in osteolysis or bone resorption in leukaemia, the exact mechanism for osteolysis has been unclear until recently. Recent studies have implicated a number of factors, including the ligand for receptor activation of NF κ B(RANKL) and macrophage inflammatory protein-1 α . Both of these are expressed by lymphocytes and are osteoclastogenic⁽⁶⁾.

Figure 3 Isotope bone scan was reported as showing 'extensive patchy increased uptake throughout the femur in both sides. A little irregularity of uptake in dorsal spines and in the ribs particularly in the left anterior ribs and possibly clavicle'

Radiographic evidence of leukaemic bone involvement has been described as a 'moth-eaten' pattern, but most lesions are not visible radiographically by conventional radiography⁽⁷⁾.

Management of malignancies of the bone involves a multimodal approach. Therapies include analgesia, hormone

therapy (such as calcitonin or glucocorticoids), chemotherapy, surgery, radiation therapy and the use of bisphosphonate⁽⁴⁾.

Interlocking intramedullary nailing of the humerus for pathological fractures provides immediate stability and can be accomplished with a closed technique, brief operative time and minimum morbidity, with a resultant early return of function to the extremity⁽⁸⁾. There are certain indications for prophylactic intramedullary nailing, including continued pain after irradiation, presence of destructive lesions >2.5cm, loss of 50% or more of the cortex of any long bone and life expectancy of more than one month⁽⁹⁾.

Bisphosphonates are potent inhibitors of both normal and pathologic osteolysis, localising preferentially to sites of active bone formation and resorption. Clinical studies have shown that long-term bisphosphonate treatment in patients with breast cancer and multiple myeloma decreases skeletal morbidity, skeletal-related events and pain, and improves quality of life. Currently, there is insufficient data to recommend their routine use for other types of tumours. Bisphosphonate treatment should be started as soon as bone metastases have been identified and be continued for as long as there is a significant clinical problem⁽¹⁰⁾.

Figure 4 Isotope bone scan was reported as showing 'extensive patchy increased uptake throughout the femur in both sides. A little irregularity of uptake in dorsal spines and in the ribs particularly in the left anterior ribs and possibly clavicle'

CONCLUSION

This unusual case illustrates the difficulties in treatment of patients suffering from widespread bone disease, whether this is due to a primary haematological malignancy or extensive metastatic involvement. This case also emphasises the importance of a multidisciplinary approach with the problems of this nature. Although it is not unexpected to experience pain following an orthopaedic operation it usually responds to routine analgesic treatments and we believe the patient's ongoing bilateral shoulder pain was mostly related to her underlying disease and depression status she went through. Integrated orthopaedic/haematological approach is necessary for the patient's management.

Orthopaedic surgeons have routinely been stabilising pathological fractures in femur and tibia for a number of years. The development of locked intramedullary humeral nail has allowed effective stabilisation of painful humeral lesions with marked improvement in local symptoms⁽⁸⁾.

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NEWS & NOTES

Letter to the Editor

Sir:

One of my colleagues has sent me a copy of the journal (September 2004), because of the small paragraph on page 233 regarding tongue tie, in the paper by Drs Ireland and Placzek on common GP queries in infancy and childhood.

In the paragraph it is written that tongue tie does not cause feeding or speech problems, so referral is not indicated.

In view of the fact that we have our tongue tie protocol currently in place and working well, I wondered what your views were about the comments made in the article.

Yours sincerely

Alison Jones
Speech and Language Therapist

The protocol is set out in a letter from Dr JJ O'Donovan, Chairman of the Barrow Local Health Group, circulated on 18 April 2001 to all GPs within Morecambe Bay, all health visitor managers, Speech and Language department, and the Maxillofacial Unit.

Re: Tongue Tie in Paediatric Patients Service Development

Through the work of the Children's Long Term Service Agreement Development Group a protocol has been agreed with the relevant providers for the management of children with suspected "tongue tie".

If a clinician suspects tongue tie, referral should be made to the local Speech and Language Therapist. The therapist will conduct a specialist assessment and, if needed, refer direct to the Maxillofacial Unit at the appropriate hospital, naturally informing the referring clinician.

QUID EST HOC

This object is made of vulcanite. It is hollow with perforations at the bulbous end and there is a screw in the rectangular base. What is its name? What is it used for?

Please send any information to the Editor, Morecambe Bay Medical Journal, Education Centre, RLI.

A £20 book token will be awarded for the first correct answer to be drawn at random.