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ORIGINAL PAPER

Minimally invasive treatment of pathological fractures of the humeral shaft

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Abstract Most patients with pathological fractures due to cancer metastasis have a limited life expectancy. Orthopaedic procedures, therefore, should be minimally invasive in order to avoid additional surgical morbidity. The purpose of this study was to analyse the results of minimally invasive approaches, including locked intramedullary nailing, followed by early postoperative radiation for pathological humeral shaft fractures. Twenty-four pathological fractures of the humerus diaphysis in 23 patients were treated with the prospective protocol, including antegrade unreamed intramedullary nailing and postoperative radiotherapy (20 Gy and five fractions). The patients and results of the surgery were evaluated by the Musculoskeletal Tumor Society upper extremity scoring system. All patients had a stable extremity, and the average function of 20 patients was 64% of the normal upper extremity function. Only one patient required revision surgery. The minimally invasive treatment of patients with pathological fractures of the humeral shaft with closed unreamed intramedullary nailing combined with adjuvant radiotherapy is an effective and safe procedure, even in seriously ill patients.

Résumé Un grand nombre de patients avec des fractures pathologiques secondaires à des métastases ont une espérance de vie diminuée. Les traitements orthopédiques avec technique mini-invasive permettent de diminuer la morbidité chirurgicale. Le propos de cette étude est d'analyser les résultats d'une technique avec voie d'abord mini-invasive pour enclouage centro-médullaire verouillé suivi d'une irradiation post-opératoire pour des tumeurs de la diaphyse humérale. 24 fractures pathologiques de la diaphyse humérale sur 23 patients ont été traitées de façon prospective, le protocole incluant un clou centro-médullaire mis sans alésage par voie antérograde et une radiothérapie de 20 Gy en 5 séances. Les patients et les résultats de la chirurgie ont été évalués grâce au score de la Société des tumeurs musculo squelettiques. Tous les patients sont parfaitement stables avec une amélioration globale fonctionnelle chez 20% des patients, une fonction de l'extrémité supérieure normale dans 64%. Un seul patient a nécessité une reprise chirurgicale. La voie d'abord mini-invasive chez ces patients présentant des fractures pathologiques de la diaphyse humérale traités par enclouage centro-médullaire sans alésage combiné à une radiothérapie adjuvante est un traitement qui permet d'avoir des résultats certains avec une bonne sécurité même chez des patients gravement atteints.

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Introduction

The skeleton is the most common site to be affected with metastatic cancer. Postmortem examinations revealed that 70% of patients who died of cancer already had skeletal metastasis [5]. The humerus constitutes the second most frequently involved site in the appendicular skeleton following the femur [24]. The metastatic lesions of the humerus account for 16% to 39% of cases with actual or impending pathological fractures of the long bones [7, 19,

25]. Pathological fractures of the humeral shaft usually occur late in the course of metastatic disease [9]. Most patients present multiple skeletal metastasis. Besides the osseous complications, visceral or cerebral involvement and metabolic problems, either as a result of primary disease or secondary to skeletal metastases, are also frequent [13]. Therefore, the anticipated life expectancy of these patients is short. Orthopaedic procedures should be minimally invasive, if possible, in order to avoid additional surgical morbidity. Rapid functional recovery with pain relief is best achieved by surgical stabilisation. Basically, there are three techniques currently available; plate with adjunctive bone cement, diaphyseal prosthesis and intramedullary locked nailing. The closed interlocking humeral nailing is a simple and quick procedure, and is associated with minimal morbidity and low failure. It also allows the immediate delivery of radiotherapy without the risk of wound compromise [12].

The purpose of this study was to analyse the results of closed intramedullary locking nailing, followed by early postoperative radiation for humeral shaft fractures due to bone metastases, with particular emphasis on the relief of pain, the restoration of function and the failure rate.

Table 1 Patient data

Patient data of the study cohort	
Age	
Median	63
Range	43–81
Gender	
Male	19
Female	5
Primary origin	
Lung	11
Breast	5
Renal cell	3
Myeloma	2
Mesothelioma	1
Unknown	1
Localisation in humeral shaft	
Proximal third	11
Middle third	9
Distal third	3
Segmental	1
Site	
Right humerus	12
Left humerus	10
Bilateral	1

Patients and methods

Between 2002–2006, we treated 24 pathological fractures of the humerus diaphysis in 23 patients according to the prospective protocol, including antegrade unreamed intramedullary nailing and postoperative radiotherapy.

All patients were staged before surgery with imaging studies, including whole-body bone scanning for skeletal survey and computerised tomography for visceral or cerebral involvement. The magnetic resonance imaging (MRI) study of the involved arm was conducted in patients who had proximal or distal humeral involvement, bulky soft tissue mass or symptoms of nerve involvement. In patients with hypervascular metastasis (renal cell, myeloma), angiography and subsequent selective arterial embolisation was performed just before the surgery. Patients who were admitted with previously unknown primary malignancy underwent percutaneous needle biopsy. All patients had multiple skeletal metastases. Nine of these patients required operative treatment; six of these procedures had been performed in the same surgical session as the humeral nailing and three were delayed for a short while. Nine patients had visceral metastasis and three of them had additional cerebral metastasis (Table 1).

The patients who had life expectancies of less than one month, too poor a medical condition to tolerate the operation, solitary lesions depending on tumour type (renal cell, thyroid cancers and plasmocytoma) and involvement of the humeral head or condyles were excluded from the study. Additionally, the patients who had extensive involvement of major nerves and/or vessels were subjected to other forms of treatment.

Operative technique

All surgical procedures were performed under general or scalene block anaesthesia. The beach-chair position was preferred in all patients. A deltoid-splitting incision was used at the anterior aspect of the acromioclavicular joint and was extended about 2.5 cm. The site of entry for the nail into the humerus was in the sulcus between the greater tuberosity and the articular surface of the humeral head, directly in line with the medullary canal. Then, the supraspinatus tendon was sharply incised parallel to its fibres to expose the entry site. The proximal entry site was perforated with a 3.2-mm drill and guide wire was passed down into the canal. The first 5–6 cm of the proximal canal was prepared by using an 11-mm cannulated drill to allow the rod to pass into the canal. Biopsy was taken by curette or punch. The tumour tissue at the fracture site was curetted out percutaneously. A wide power suction tip was inserted into the fracture site and the contents of the canal were aspirated. The appropriate size nail was driven with small rotary movements over the guide wire without reaming the medullary canal. Proximal interlocking was performed with the assistance of a nail-mounted drill-guide. Three or more multidirectional interlocking nails were used in most

patients, especially those who have proximally localised lesions, in order to enhance the stability of the fixation. The arm was held in neutral rotation and the screws were not placed distally more than 5–6 cm from the acromion in order to minimise the risk of axillary nerve injury. Distal interlocking was performed by the free-hand technique by carrying out a limited dissection through a 5-cm incision to protect the radial nerve. In 16 fractures, MRI-compatible titanium nails (Polarus®; Acumed Hillsboro, OR, USA and PHN®; Synthes, Switzerland) with multiple multidirectional proximal interlocking actions were used. Eight fractures were treated with stainless steel nails (C-75 humeral nail; Hipokrat, Izmir; Turkey) (Figs. 1 and 2).

Adjuvant treatments

Adjuvant radiotherapy was administered two weeks after surgery with a total of 20 Gy and five fractions. Radiation was applied to the whole humerus through the extent of the nail.

Fifteen patients had received palliative chemotherapy before they sustained the humeral fracture. Postoperatively, 12 patients received chemotherapy. Additionally, intravenous bisphosphonate (Zometa®; Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA and Novartis Pharma AG, Basel, Switzerland) was used in patients who had disseminated skeletal metastasis, at monthly intervals.

Patients were evaluated by the American Musculoskeletal Tumor Society score [8] at six weeks after radiotherapy (2 months after surgery). Routine radiographs were taken at monthly intervals in order to assess the bone healing and local recurrence or seeding.

Results

At the end of the study, 13 patients died and ten patients were alive with disease. None of the deaths were related with the humeral nailing procedure. The mean postoperative survival time was 11.4 months (range 1–38 months). There were no deaths in the immediate postoperative period; however, three patients with advanced lung cancer died within one month and four additional patients survived for less than three months after the intramedullary nailing. The mean follow-up in the ten surviving patients was 17 months (range 6–44 months).

The average operation time for the humeral nailing was 40 min (range 25–85 min). Patients treated with closed intramedullary nailing showed minimal operative blood loss, mean 55 ml (range 35–110 ml). The average duration of hospitalisation was 4 days (range 1–13 days). The patients who were treated only for humeral fracture (16

Fig. 2 A 71-year-old man with lung cancer. **a** Preoperative radiograph shows pathological fracture at the middle third of the humerus. **b** Radiological result at 6 months after surgery

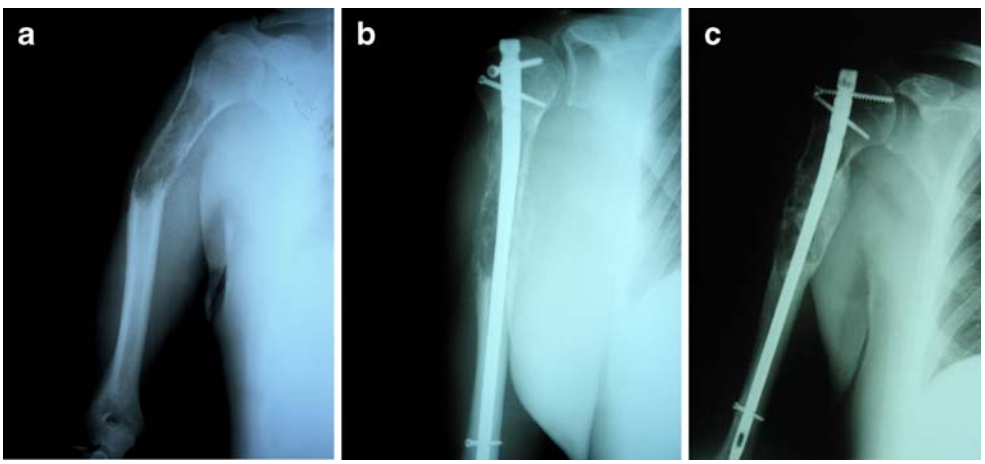

Fig. 1 A 62-year-old man with multiple myeloma. **a** Antero-posterior radiograph of the right arm demonstrates pathological fracture at the proximal third of the humeral shaft. **b** Immediate postoperative radiograph. **c** Four months later, the fracture had healed completely

patients) were discharged from the hospital after an average of 3 days (range 1–7 days), when they were able to use their arms during daily activities. The remaining seven patients progressed more slowly and stayed for longer, due to their general medical condition.

The relief of pain was successful in all but two patients at an early postoperative period. At four weeks after surgery, 18 of 20 living patients reported minimal or no pain. Twelve fractures healed completely. However, there was no or incomplete healing in the other eight fractures. The range of motion (ROM) of the adjacent joints was documented. There was no limitation at the elbow joint in any patient; however, except for three patients, none of them had full ROM at the shoulder joint. Two patients developed shoulder stiffness. The mean abduction of the shoulder was 60° (range 0 to 160°) and forward flexion was 80° (range 30 to 140°). An inappropriate length of nail left outside of the bone at the proximal entry site was responsible for limited abduction in four patients. Sixteen of 20 patients began to use their limb for daily activities at the end of the fourth week postoperatively. The overall Musculoskeletal Tumor Society score for the 20 patients was 64% of the normal upper extremity function.

There was no perioperative complication. None of the patients developed clinical signs of respiratory distress syndrome or fat embolism intra- or postoperatively. There were no neurological or vascular injuries from this procedure and no deep infections. The fixation failed in one patient, resulting in the loosening of proximal locking screws and subsequent upward migration of the nail. This case was the only patient who underwent revision in this series. In one patient, the loosening of one of the proximal locking screws led to local tenderness, which required removal of the screw. The lesion progressed in another patient with lung cancer; however, the revision surgery could not be performed due to the patient's poor medical condition. The patient died two months after the surgery. One renal cell cancer patient developed tumour seeding 14 months after surgery, localised at the distal end of the nail. The lesion was asymptomatic and did not progress and, hence, no surgical treatment was given at the time of the diagnosis. The patient died because of widespread lung metastasis three months later.

Discussion

Skeletal metastasis occurs at an advanced stage of many cancers, including lung, breast, renal, thyroid and others. Most patients with pathological fractures secondary to metastatic carcinoma have a limited life expectancy. The pathological fracture itself is negative criteria for prognosis [2]. Katagiri et al. [15] also showed that the primary tumours with rapid growth (lung, hepatocellular, gastric), poor general performance and the presence of visceral or cerebral metastases or multiple skeletal metastases indicate poor prognosis. All patients in our series had at least one of these negative criteria. Therefore, the goals of operative intervention were focussed on achieving immediate pain relief, increasing mobility and easing nursing care with minimal additional morbidity on patients' already compromised general conditions.

The alternatives to reconstruction of the pathological shaft fracture of the humerus are plates combined with bone cement, intramedullary nails and diaphyseal spacers. Open surgery has advantages, which include less intramedullary spread, a greater rigidity of the construction after cementing, reduction of the local tumour mass and slower progression of the tumour [17]. However, the complications rate resulting from open surgical intervention are considerably higher, and complications can include bleeding, wound problems and nerve injury [6, 12, 25]. Open surgical procedures are also associated with a delay in delivering postoperative radiotherapy.

Rigid intramedullary nailing of pathological fractures of the humerus is a convenient and effective means of stabilisation. The advantages of intramedullary nailing are reduced blood loss and lower local complication rate [1, 12]. Furthermore, intramedullary fixation offers an advantage compared with plate fixation in that the implant is load-sharing rather than load-bearing and it can achieve stabilisation of the whole bone [23]. The newer interlocking systems have larger diameter intramedullary nail alternatives and multiple, multidirectional proximal locking screws, which allow good rotational and axial control, especially for metaphyseal lesions. By using advanced intramedullary systems, the use of supplemental polymethylmethacrylate (PMMA) is frequently unnecessary [12].

Dijkstra et al. [7] compared plate osteosynthesis with adjunctive bone cement and intramedullary locking nail in the treatment of pathological fractures of the humeral shaft. No significant difference between the two techniques was noted with regard to survival rate, pain relief, the restoration of function and complications. The authors concluded that both the interlocking intramedullary nailing with postoperative irradiation and plate osteosynthesis with bone cement were equally safe ways to restore arm function and improve quality of life for patients with pathological humeral fractures.

In the retrospective series of Redmond et al. [22], 13 patients with 16 pathological fractures of the humerus were treated with closed interlocking nailing. Eleven patients, 14 humeri, received radiation therapy in the early postoperative period. A good or excellent pain relief associated with early functional use of the extremity was achieved in the majority of the patients. The authors also reported brief

operative time, short duration of hospitalisation and minimum surgical morbidity [22].

Regardless of whether the ultimate course of treatment of metastatic bone lesions is nonoperative or operative, radiation therapy is mandatory for local tumour control and effective pain relief. Disease progression with the loss of fixation occurs in approximately 15% to 20% of patients treated with only surgery [11]. No concrete evidence exists on the best dose fractionation schedule to use. Doses of 8 to 40.5 Gy administered in varying fractionation schedules offer at least partial pain relief in 90% of patients and complete pain relief in approximately 50% of patients [20]. Lower doses delivered over a shorter course may be more suitable for the debilitated patient with a short life expectancy. Higher doses over a more protracted course are appropriate for patients with a limited number of skeletal metastases and no visceral metastases who may have longer life expectancies, in an effort to provide improved local disease control and to minimise late toxicity [10]. We preferred to give a dose of 20 Gy in five fractions because most of our patients were not able to attend longer sessions. Radiation was delivered including over the full extent of the nail. Postoperative radiation was successful in achieving local tumour control in all but two patients (one local recurrence and one distal seeding).

We think that the selection of the nail is important to avoid fixation failure. For diaphyseal lesions with good bone stock and contact at the fracture site, one proximal nail and one distal interlocking nail provide enough rotational stability. However, for proximal fractures, diaphyseal fractures with extensive bony defect and fractures occurring in osteoporotic bone, advanced nail systems which allow multiple and multidirectional proximal interlocking is preferred.

The major disadvantages of antegrade nailing are rotator cuff irritation and shoulder stiffness [11]. With sharp and careful dissection and repair of the cuff, this problem can be minimised. It is also important to countersink the tip of the nail into the humeral head to avoid impingement. In four patients, we observed nail tip irritation in higher degrees of abduction, although none of them required revision.

The nerve lesions may be observed during intramedullary nailing of the humerus [16, 21]. There is a potential risk of nerve injury during proximal interlocking due to the proximity of the axillary nerve. It is recommended that lateromedial proximal interlocking screws placed within 4–5 cm distal from the lateral edge of the acromion will not injure the nerve if the arm is held in neutral rotation [16, 18]. In a cadaveric study, Noger et al. [18] showed that neurovascular structures, including the radial and ulnar nerves and also the brachial artery, are at risk during closed Lateromedial distal interlocking. We always performed open distal interlocking under direct vision and to protect the radial nerve at risk of injury. No nerve lesion occurred in this series.

An important complication of the intramedullary nailing of pathological fractures of the long bones is the development of pulmonary embolism [3]. The decreased pulmonary reserve due to pre-existing lung disease, such as primary or metastatic lung cancer, carries a further risk [4]. It is shown that the reaming procedure results in a significant rise in the intramedullary pressure and the liberation of bone marrow fat [14]. The cementation may induce an additional force in the intramedullary pressure during pressurisation and nail insertion. We think that unreamed nailing without intramedullary cementation was also helpful in avoiding embolic phenomena. In spite of the fact that the majority of our patients had primary or metastatic lung cancer, no clinical symptoms of pulmonary embolism were observed in any of the patients.

In conclusion, minimally invasive treatment of patients with pathological fractures of the humeral shaft with closed unreamed antegrade humeral nailing combined with adjuvant radiotherapy is an effective and safe procedure, even in seriously ill patients. The surgical method is associated with a low rate of systemic and local complications and hardware failure. According to current knowledge, the patients who have solitary metastasis of the renal cell, thyroid cancer or plasmocytoma should be treated with a wide resection. Additionally, patients with extensive bone destruction, massive soft-tissue involvement or the invasion of major neurovascular structures must be advised other forms of treatment.

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