Intramedullary Nailing for Pathological Fractures of the Proximal Humerus Caused by Multiple Myeloma: A Case Report and Literature Review

guoqiang xu
Capital Medical University Affiliated Beijing Friendship Hospital
gang wang
Capital Medical University Affiliated Beijing Friendship Hospital
xiaodong bai
Capital Medical University Affiliated Beijing Friendship Hospital
zhenyu liu
Capital Medical University Affiliated Beijing Friendship Hospital
xinjia wang (docxjwang@163.com)
Capital Medical University Affiliated Beijing Friendship Hospital https://orcid.org/0000-0003-2190-3199
baojun wang
Capital Medical University Affiliated Beijing Friendship Hospital

Case report

Keywords: multiple myeloma bone disease, pathological fractures, intramedullary nailing, case report

Posted Date: March 16th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-308507/v1

Abstract

Background: Multiple myeloma bone disease(MMBD) is indicative of multiple myeloma (MM), and it will reduce patient life quality. In addition to oncological, antineoplastic systemic therapy, surgical therapy in patients with MM represents an essential treatment pillar within the framework of supportive therapy measures and is the task of orthopedic tumor surgery. Nevertheless, there are few reports about applying intramedullary (IM) nailing in treating MM-induced proximal humeral fracture to prevent fixation loss. This paper aims to describe a case of pathological fracture of the proximal humerus caused by multiple myeloma effectively treated with IM nailing without removal of tumors and review the current literature.

Case presentation: This study reported a 64-year-old male patient complaining of serious left shoulder pain and limited movement. X-ray films showed left proximal humeral fracture accompanying with osteoporosis and bone destruction. During the preoperative examinations, tumor markers, whole-body bone imaging and bone marrow biopsy were performed. The patient was finally diagnosed with multiple myeloma (IgAλ, IIIA/II). After the treatment of pathological fracture with IM nailing, the patient's function recovered and the pain was relieved rapidly. The visual analogue scale (VAS) reduced by 7 points to 2 points postoperatively compared with that preoperatively. Histopathological examination results presented plasma cell myeloma. Next, the patient received chemotherapy in the hematology department. Humeral fracture displayed good union in the 40-month follow-up, with complete healing of fracture, and the clinical outcome was still satisfactory.

Conclusion: The pathological fracture of proximal humerus caused by multiple myeloma should be treated by surgery early. IM nail can be used for this kind of fracture without removal of tumors, bone cement augmentation for bone defect or local adjuvant therapy was also employed. Under the combined treatment, the proximal humerus fracture can eventually heal.

Background

Multiple myeloma (MM) represents a kind of plasma cell dyscrasia that is featured by immortalized monoclonal plasma cell proliferation within bone marrow. Different from additional bone metastatic cancers, no new bone is formed in osteolytic bone disease of MM.[1]Complications of osteolysis are fractures of the long bones, which often occur in the proximal humerus and femur - usually after a minor trauma or atraumatic - and vertebral body fractures.[2] The clinical presentations and radiological features are unspecific, making it more difficult for diagnosis. IM nailing accounts for an approach to treat humeral diaphysis fracture with minimal invasion, and it is advantageous in its small lesion, reduced operation time, little soft tissue dissection, as well as early recovery.[3] But, it remains controversial about whether IM nailing should be applied to treat proximal humeral fracture because it may lead to fixation loss.[4] As a result, IM nailing is currently restricted to the treatment of diaphyseal fractures.[3, 5–9]So far, few studies have described the techniques applied in proximal humeral fractures, particularly, the skeletal defect is not augmented by the application of bone cement. This study reported a 64-year-old male

patient suffering from MMBD in proximal humerus. He received combined therapy with IM nailing and chemotherapy. Additionally, related reports of MMBD are reviewed.

Case Presentation

We report a case of a 64-year-old man who came to our emergency department complaining of the left shoulder pain. This cases had mild left shoulder trauma due to accidental falling down from the standing height when he was walking. Besides, his past medical history included atrial fibrillation treated with aspirin enteric-coated tablets (Bayer S.P.A), metoprolol succinate sustained release tablets (AstraZeneca AB) and chronic atrophic gastritis. The patient denied any history of smoking, alcohol consumption or drug medication, or any family history of pathological fracture or osteoporosis. Physical examination demonstrated swelling of the left shoulder, localized tenderness, and percussion pain on the proximal humerus, and limited shoulder motion. The muscular tone of the upper limb was normal, and no hypoesthesia of the upper limb was observed. Physiological reflexes were existent without any pathological ones.

Initially, the X-ray films of the left shoulder were obtained, showing only comminuted fractures and degenerative changes in the upper left humerus (Fig. 1). Then, magnetic resonance imaging (MRI) was performed to show the abnormal signal intensity of proximal humerus associated with comminuted fracture, and there existed multiple soft tissue masses around the broken end, ranging from 4.8cm * 3.9cm, which presented as hypointensity and isointensity, as well as hybrid hyperintensity on T1-weighted (T1-W) together with T2-W images, respectively. The left humerus, glenoid, and clavicle had multiple sheet-like hyperintensity images on T2 weighted (T2-W) images (Fig. 1). It was highly suspected that the patient had a neoplastic lesion with radiological characteristics.

Our case received further laboratory tests and imaging examinations. As revealed by CT scans and X-ray examinations, multiple areas of reduced bone density throughout the body. Besides, high 18-Ffluorodeoxyglucose (18-FDG) metabolism was observed in several ribs on bone scans, the fifth lumbar vertebra (L5), and left proximal humerus (Fig. 2). In contrast, routine laboratory evaluation on admission except anemia remained unremarkable. Finally, plasma cell myeloma was diagnosed by bone marrow aspirate and trephine that microscopically, hematopoiesis accounted for 40%, the ratio of granulocyte to erythrocyte was approximately 2:1, and megakaryocytes were 2–7 / hpf. Additionally, multifocal plasmacytoid cells aggregation was also observed. The immunochemistry showed: CD38 (+), kappa (+), lambda (+); MPO (+), CD61 (+) and CK (-) (Fig. 3).

Following consultation with anesthesiologists and medical oncologists about the perioperative risks as well as life expectancy of the patient, locked IM nailing(Sanatmetal Orthopaedic & Traumatologic Equipment Manufacturer Ltd.)was chosen for strongly fixing the humeral fracture via the trans-deltoid muscle approach. With greater trochanter as the entry point, an IM nailing was directly inserted into the humeral medullary cavity without removal of tumors. Additionally, the bone defect was not augmented with bone cement. No local adjuvant therapy was employed. We inserted the nail with great caution not to

impinge the acromion or rotator cuff tendons by the nail proximal end. In addition, we placed 3 proximal screws as well as 2 distal interlocking screws into this case. On the first day after surgery, the patient was encouraged to move his shoulder gently. At 1 week after surgery, the patient was encouraged to conduct passive stretching as well as gravity-resistance exercises.

After surgery, our case had continuously relieved pain and improved activity in the left upper limb, and no complication was reported. At 24 h postoperatively, the visual analogue score (VAS) declined by 7 points to 2 points. The histopathological examination results of the sample revealed MM (IgAλ, IIIA/II). One week postoperatively, the patient regularly received the dexamethasone and bortezomib regimen chemotherapy at the department of hematology until now. In the 40-month follow-up, the humeral fracture exhibited favorable, complete lesion healing was achieved (Fig. 4), and no pain was reported in our case. In comparison with the contralateral shoulder, forward flexion, and abduction were limited at the terminal 10°, while complete external and internal adduction and rotations were achieved.

Discussion And Conclusion

MM occupies 1% of cancer cases, as well as about 10% of hematologic cancer cases.[10]MM shows a relatively higher morbidity in male than in female, and its morbidity is two-fold in the blacks as high as that in the whites.[11, 12]MM will affect the old population, and 70% cases are diagnosed when they are 60 years old.[13]MM stands for a kind of plasma cell dyscrasia that is featured by immortalized monoclonal plasma cell growth within bone marrow. Nearly each MM case progresses from the asymptomatic monoclonal gammopathy of undetermined significance (MGUS) at the pre-malignant stage.[14, 15] Moreover, MGUS will further develop into MM or associated cancers at an annually growing rate of 1%.[16, 17]

Bone lesions induced by MM are indicative of MM, and they will reduce the patient life quality. About 80% cases develop osteolytic bone disorders when they are diagnosed, besides, they are linked with a higher risk of skeletal-related events (SREs) that will increase the morbidity as well as mortality.[18]About 60% MM cases have fractures in the course of disease.[19]The uncoupled bone-remodeling process lays the pathogenic foundation of bone disorders associated with myeloma. The myeloma cell-bone microenvironment interaction will eventually activate osteoclasts while suppressing osteoblasts, giving rise to bone loss. Multiple intercellular as well as intracellular signal transduction pathways participate in the complicated course of MM. The crosstalk mediated by myeloma across diverse molecular pathways forms a forward feedback to maintain survival of myeloma cells as well as keep the decomposition of bone, even after reaching the disease plateau.[20]

MM is diagnosed when at least one myeloma defining event (MDE) and at least 10% clonal plasma cells are detected through bone marrow examinations or when plasmacytoma is detected in a biopsy. MDEs are constituted by the recognized CRAB (hyperCalcaemia, Renal failure, Anaemia, Bony lesions) characteristics and 3 representative biomarkers, including over one focal lesion detected through MRI, ≥

60% plasma cells in clonal bone marrow, as well as ≥ 100 serum free light chain (FLC).[21] In the case of suspicious MM in clinic, M protein testing is recommended by combining serum immunofixation (SIFE), serum protein electrophoresis (SPEP), as well as serum FLC assay.[22] About 2% MM cases develop the real non-secretory disorder with no M protein tested in the above-mentioned tests.[23] Positron emission tomography/computed tomographic (PET/CT) and low-dose whole body computed tomography (WB-CT) scans are the best ways to assess the bone disorder severity,[22, 24]which can show the changes of bones and the soft tissues more clearly, and display the boundaries of the lesion. Plain radiographs are usually non-specific which even underestimate the extent of the lesion, and they are performed only when no other advanced imaging can be accessed. MRI is a particularly useful imaging technique of choice due to its noninvasive nature and greater anatomic detail, particularly when smoldering multiple myeloma (SMM) is suspected, so as to eliminate the risk of focal lesion in the bone marrow observed prior to the occurrence of the actual osteolytic disorder. MRI also greatly contributes to the assessment of suspicious cord compression and extramedullary disorder, and when it is necessary to visualize a certain symptomatic region.

MM accounts for a disorder with progressive relapse. The MM cases may possibly recur with clinical symptoms or with biochemical disorders. Holistic and multidisciplinary treatment is needed for each MM case.[13] Treatment qualification involves multiple factors, which needs the collaboration from radiotherapists, orthopedic surgeons, radiologists, hematologists and anesthesiologists. In this regard, it is necessary to construct a prognostic model to predict disease stage, evaluate patient general conditions, and detect the underlying chronic disorders or the possible adjuvant treatments.[2] For optimizing the outcomes for individuals, elucidating the most suitable maintenance treatment or continuous therapy for specific patient group is important; besides, it is important to consider the clinical safety, effectiveness, tolerability, life quality, convenience, feasibility, together with long-time treatment burden on the patients.[21]

In addition to oncological and antineoplastic systemic therapy, surgical therapy in patients with MM represents an essential treatment pillar within the framework of supportive therapy measures and is the task of orthopedic tumor surgery. For SREs related to myeloma, surgery is mainly performed for the sake of maintaining and restoring the involved skeletal function and recovery, reducing patient sufferings like (pain) and improving patient mobility as well as life quality.[25, 26]There is a need for surgical intervention not only for the care and treatment of stability-threatening bone lesions and manifest pathological fractures, but also for the treatment of tumor-related complications, such as neurological deficits, paraplegic clinical pictures or in the case of conservative therapy-refractory bone pain. The surgical methods and time of treatment should be decided individually depending on the risk and prognostic outcomes for myeloma cases.[25]Osteolyses of non-supporting skeletal sections such as the ribs, skull or scapula usually do not require surgical treatment. The physical status grade established by the American Society of Anesthesiologist (ASA) has been extensively utilized to evaluate the patient general conditions or anesthesia tolerance. Patients with < 2 months survival or ASA = 4 will be treated using conservative methods instead of surgery.[27]

Surgery is usually conducted to treat the MM-induced proximal humeral fracture, so as to relief patient suffering and recover the involved bone function and mobility, as well as patient life quality. However, surgical strategies are complicated and demanding.[28]

Endoprosthetic reconstruction has been extensively used to treat proximal humeral fracture, but it can not achieve satisfactory effect on the impaired function. Prosthesis can be a good way to relieve pain and fix the fracture, but it has poor functional recovery than other treatments.[6, 29–31] Besides, more tendons and muscles are sacrificed during resection, which inevitably impair the function.[30] At the same time, plate fixation is associated with numerous drawbacks, like short protection length, massive soft tissue stripping, and risk of nerve injury.[8, 32, 33] Beside, local relapse may give rise to fixation loss or the need of a second operation.[29, 34]As a result, plates are restricted in treating metastasis.

IM nailing is suggested to be unsuitable to treat proximal humeral fracture because of the bone defect and thin cortex following curettage.[29]Therefore, at present, IM nailing is restricted to treating diaphyseal fractures.[5]Our results reveal that IM nailing can serve as an efficient and robust way to treat proximal humeral fracture. Generally speaking, applying IM nailing to fix proximal humeral fracture is advantageous in its decreased operation time, small lesion, decreased soft tissue dissection, as well as early recovery.

In this case, we applied the technique in treating proximal humeral fracture, particularly when no bone cement is used to augment the lesion. Finally, at our follow-up visits, our case had markedly relieved pain and improved shoulder function. At the 40-month follow-up, the patient had favorably healed humeral fracture, complete lesion healing was observed, and no pain was reported by the patient. In comparison with contralateral shoulder, the forward flexion and abduction were limited at the terminal 10°, meanwhile, complete external and internal adduction and rotations were achieved.

Despite it is generally incurable, the long-time survival of MM is greatly improved because more treatments are developed recently. Besides, the improved survival is also associated with the application of early treatment.[35] As suggested by randomized controlled trials (RCTs) that apply modern treatments, MM has the median survival of about 6 years. The appropriate treatment for metastases is needed to prolong patient survival.[36]

Although this technique has achieved satisfactory effect, there are few reports that describe it for the treatment of pathological fractures of the proximal humerus caused by MM. Therefore, it is necessary to conduct a large sample of studies to further validate the efficacy and to identify the surgical indications and related complications.

The patient was satisfied with the current functional recovery and the treatment of primary disease, and agreed to report his case, hoping to benefit more patients suffering from the same disease.

To conclude, when pathological fracture of the proximal humerus caused by multiple myeloma occurs, early surgical treatment is indicated, which could relieve pain effectively and allow early movements. IM nailing can be applied to this kind of fractures, without removal of tumors, bone cement augmentation for bone defect or local adjuvant therapy was employed. Moreover, patients can receive combined therapy and have a good prognosis.

Abbreviations

MMBD: Multiple myeloma bone disease; MM: Multiple myeloma; MMBD: Multiple myeloma bone disease; IM: intramedullary; CT: Computed tomography; MRI: Magnetic resonance imaging; MGUS: monoclonal gammopathy of undetermined significance; CRAB: hyperCalcaemia, Renal failure, Anaemia, Bony lesions; SREs: skeletal-related events; MDE: myeloma defining event; FLC: free light chain.

Declarations

Ethics approval and consent to participate

The case is only involving objective retrospective description, so it is not applicable to ethics approval. The patient has given his consent for the use of physical and imaging information adopted from the patient.

Consent for publication

This case is consented for publication. Written consent for publication was obtained for all potentially identifying data and accompanying images and I state that this is available for review by the editor of the journal

Availability of data and materials

All the data and material are from the patient's assay and examination of Beijing Friendship hospital, Capital Medical University, which are real, credible and for availability

Competing interests

The authors declare that they have no competing interests

Funding

None.

Author Contributions

Guoqiang Xu was responsible for writing and editing the article; Gang Wang was responsible for reviewing the literature; Xiaodong Bai and Zhenyu Liu were responsible for collecting the information of

the current case. Xinjia Wang and Baojun Wang were responsible for the revision of the manuscript for important intellectual content. All authors have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be responsible for all aspects of the study.

Acknowledgements

Not applicable.

References

1. Roodman G D. Pathogenesis of myeloma bone disease[J]. Leukemia, 2009,23(3):435-441.
2. Guzik G. Oncological and functional results of the surgical treatment of vertebral metastases in patients with multiple myeloma"[J]. BMC Surg, 2017,17(1):92.
3. Frassica F J, Frassica D A. Evaluation and treatment of metastases to the humerus[J]. Clin Orthop Relat Res, 2003(415 Suppl):S212-S218.
4. Weiss K R, Bhumbra R, Biau D J, et al. Fixation of pathological humeral fractures by the cemented plate technique[J]. J Bone Joint Surg Br, 2011,93(8):1093-1097.
5. Laitinen M, Nieminen J, Pakarinen T K. Treatment of pathological humerus shaft fractures with intramedullary nails with or without cement fixation[J]. Arch Orthop Trauma Surg, 2011,131(4):503-508.
6. Camnasio F, Scotti C, Peretti G M, et al. Prosthetic joint replacement for long bone metastases: analysis of 154 cases[J]. Arch Orthop Trauma Surg, 2008,128(8):787-793.
7. Capanna R, Campanacci D A. The treatment of metastases in the appendicular skeleton[J]. J Bone Joint Surg Br, 2001,83(4):471-481.
8. Sarahrudi K, Wolf H, Funovics P, et al. Surgical treatment of pathological fractures of the shaft of the humerus[J]. J Trauma, 2009,66(3):789-794.
9. Atesok K, Liebergall M, Sucher E, et al. Treatment of pathological humeral shaft fractures with unreamed humeral nail[J]. Ann Surg Oncol, 2007,14(4):1493-1498.
10. Rajkumar S V, Dimopoulos M A, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma[J]. Lancet Oncol, 2014,15(12):e538-e548.
11. Landgren O, Weiss B M. Patterns of monoclonal gammopathy of undetermined significance and multiple myeloma in various ethnic/racial groups: support for genetic factors in pathogenesis[J]. Leukemia, 2009,23(10):1691-1697.
12. Landgren O, Graubard B I, Katzmann J A, et al. Racial disparities in the prevalence of monoclonal gammopathies: a population-based study of 12,482 persons from the National Health and Nutritional Examination Survey[J]. Leukemia, 2014,28(7):1537-1542.
13. Chavda S J, Yong K. Multiple myeloma[J]. Br J Hosp Med (Lond), 2017,78(2):C21-C27.

14. Landgren O, Kyle R A, Pfeiffer R M, et al. Monoclonal gammopathy of undetermined significance (MGUS) consistently precedes multiple myeloma: a prospective study[J]. Blood, 2009,113(22):5412-5417.
15. Weiss B M, Abadie J, Verma P, et al. A monoclonal gammopathy precedes multiple myeloma in most patients[J]. Blood, 2009,113(22):5418-5422.
16. Kyle R A, Therneau T M, Rajkumar S V, et al. A long-term study of prognosis in monoclonal gammopathy of undetermined significance[J]. N Engl J Med, 2002,346(8):564-569.
17. Kyle R A, Larson D R, Therneau T M, et al. Long-Term Follow-up of Monoclonal Gammopathy of Undetermined Significance[J]. N Engl J Med, 2018,378(3):241-249.
18. Terpos E, Morgan G, Dimopoulos M A, et al. International Myeloma Working Group recommendations for the treatment of multiple myeloma-related bone disease[J]. J Clin Oncol, 2013,31(18):2347-2357.
19. Terpos E, Berenson J, Cook R J, et al. Prognostic variables for survival and skeletal complications in patients with multiple myeloma osteolytic bone disease[J]. Leukemia, 2010,24(5):1043-1049.
20. Terpos E, Ntanasis-Stathopoulos I, Gavriatopoulou M, et al. Pathogenesis of bone disease in multiple myeloma: from bench to bedside[J]. Blood Cancer J, 2018,8(1):7.
21. Dimopoulos M A, Jakubowiak A J, McCarthy P L, et al. Developments in continuous therapy and maintenance treatment approaches for patients with newly diagnosed multiple myeloma[J]. Blood Cancer J, 2020,10(2):17.
22. Lakshman A, Paul S, Rajkumar S V, et al. Prognostic significance of interphase FISH in monoclonal gammopathy of undetermined significance[J]. Leukemia, 2018,32(8):1811-1815.
23. Chawla S S, Kumar S K, Dispenzieri A, et al. Clinical course and prognosis of non-secretory multiple myeloma[J]. Eur J Haematol, 2015,95(1):57-64.
24. Hillengass J, Usmani S, Rajkumar S V, et al. International myeloma working group consensus recommendations on imaging in monoclonal plasma cell disorders[J]. Lancet Oncol, 2019,20(6):e302-e312.
25. Takei T, Coles M. Treatment of pathologic fracture and surgical value of prognostic factors in multiple myeloma[J]. Int Surg, 1996,81(4):403-406.
26. Durr H R, Kuhne J H, Hagena F W, et al. Surgical treatment for myeloma of the bone. A retrospective analysis of 22 cases[J]. Arch Orthop Trauma Surg, 1997,116(8):463-469.
27. Choi E, Han I, Cho H S, et al. Intramedullary Nailing for Pathological Fractures of the Proximal Humerus[J]. Clinics in Orthopedic Surgery, 2016,8(4):458.
28. Kehrer M, Koob S, Kehrer A, et al. Multiple Myeloma - Current Standards in Surgical Treatment[J]. Z Orthop Unfall, 2019,157(2):164-172.
29. Siegel H J, Lopez-Ben R, Mann J P, et al. Pathological fractures of the proximal humerus treated with a proximal humeral locking plate and bone cement[J]. J Bone Joint Surg Br, 2010,92(5):707-712.
30. Bickels J, Kollender Y, Wittig J C, et al. Function after resection of humeral metastases: analysis of 59 consecutive patients[J]. Clin Orthop Relat Res, 2005(437):201-208.

31. Piccioli A, Maccauro G, Rossi B, et al. Surgical treatment of pathologic fractures of humerus[J]. Injury, 2010,41(11):1112-1116.
32. Karataglis D, Stavridis S I, Petsatodis G, et al. New trends in fixation of proximal humeral fractures: a review[J]. Injury, 2011,42(4):330-338.
33. Young A A, Hughes J S. Locked intramedullary nailing for treatment of displaced proximal humerus fractures[J]. Orthop Clin North Am, 2008,39(4):417-428.
34. Dijkstra S, Stapert J, Boxma H, et al. Treatment of pathological fractures of the humeral shaft due to bone metastases: a comparison of intramedullary locking nail and plate osteosynthesis with adjunctive bone cement[J]. Eur J Surg Oncol, 1996,22(6):621-626.
35. Vaishya R, Vijay V, Agarwal A K. Healing of pathological fracture in a case of multiple myeloma[J]. BMJ Case Rep, 2017,2017.
36. Thai D M, Kitagawa Y, Choong P F. Outcome of surgical management of bony metastases to the humerus and shoulder girdle: a retrospective analysis of 93 patients[J]. Int Semin Surg Oncol, 2006,3:5.

Figures

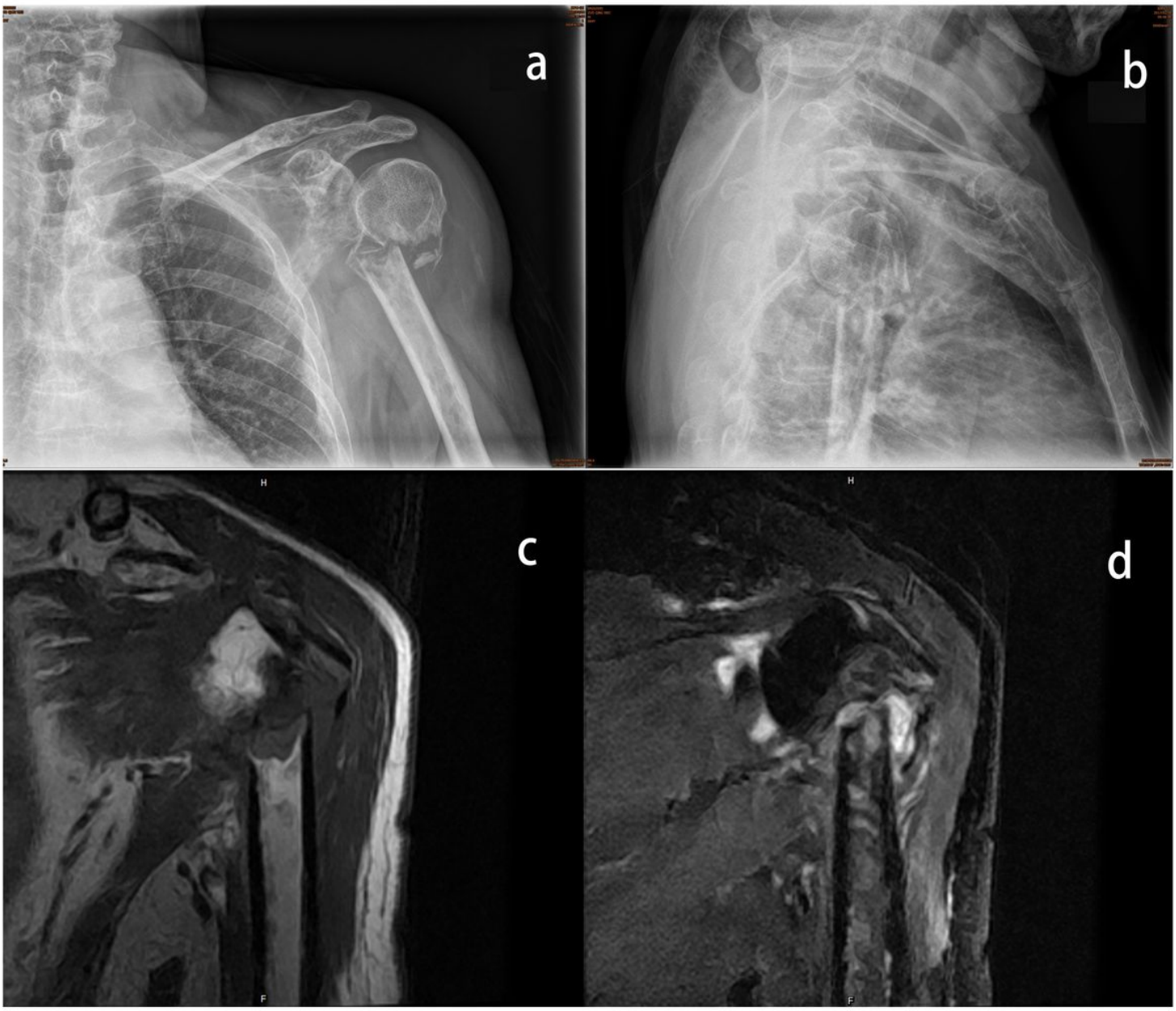

Figure 1

Preoperative X-ray films (a, b) of the left shoulder revealed only comminuted fractures and degenerative changes in the upper left humerus. Multiple soft tissue masses around the broken end presented as hypointensity and isointensity on T1-W images (c) and hybrid hyperintensity on T2-W images (d).

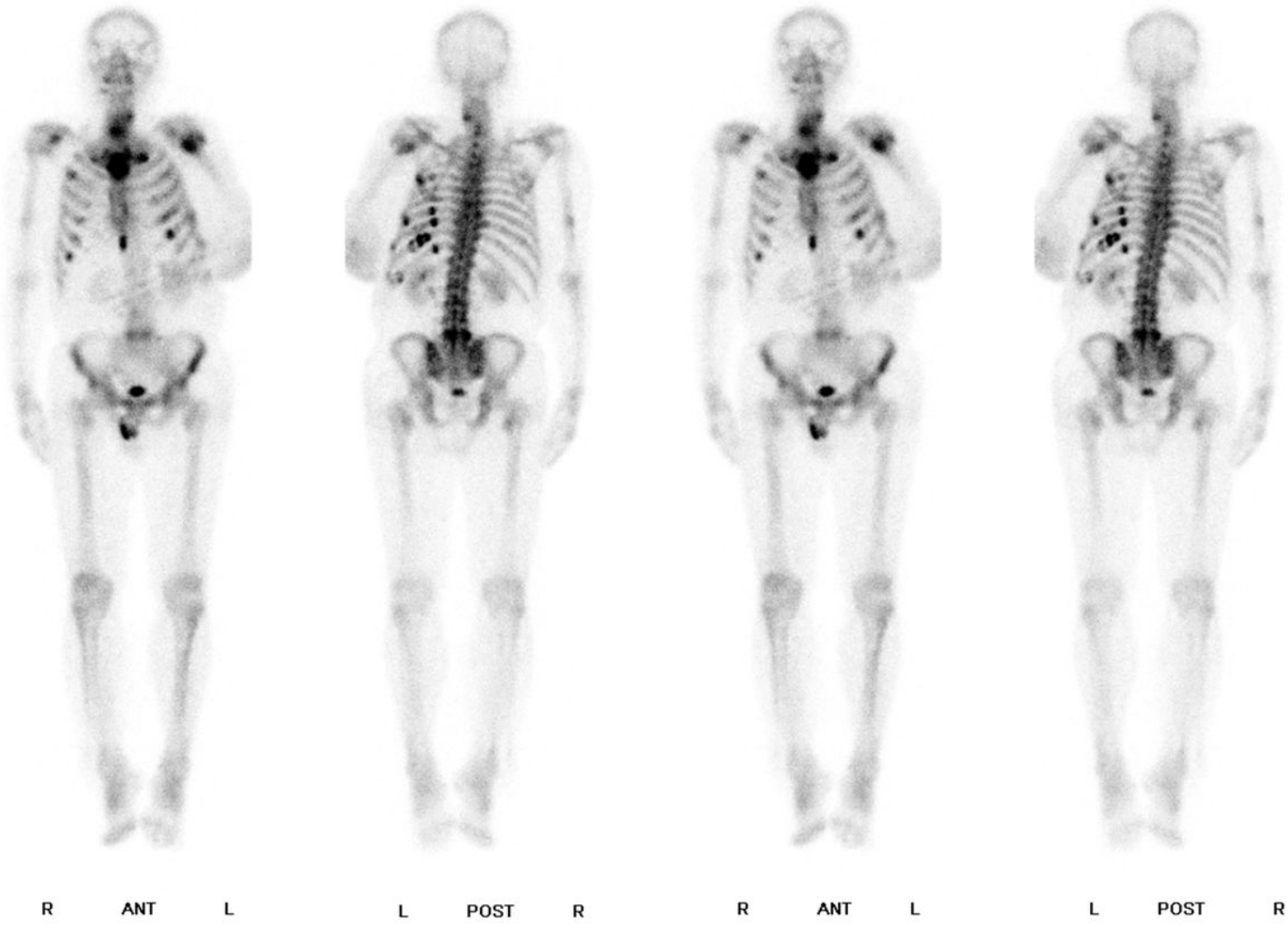

Figure 2

Bone scan showed high metabolism of 18-Ffluorodeoxyglucose (18-FDG) in multiple ribs, the fifth lumbar vertebra (L5), and left proximal humerus.

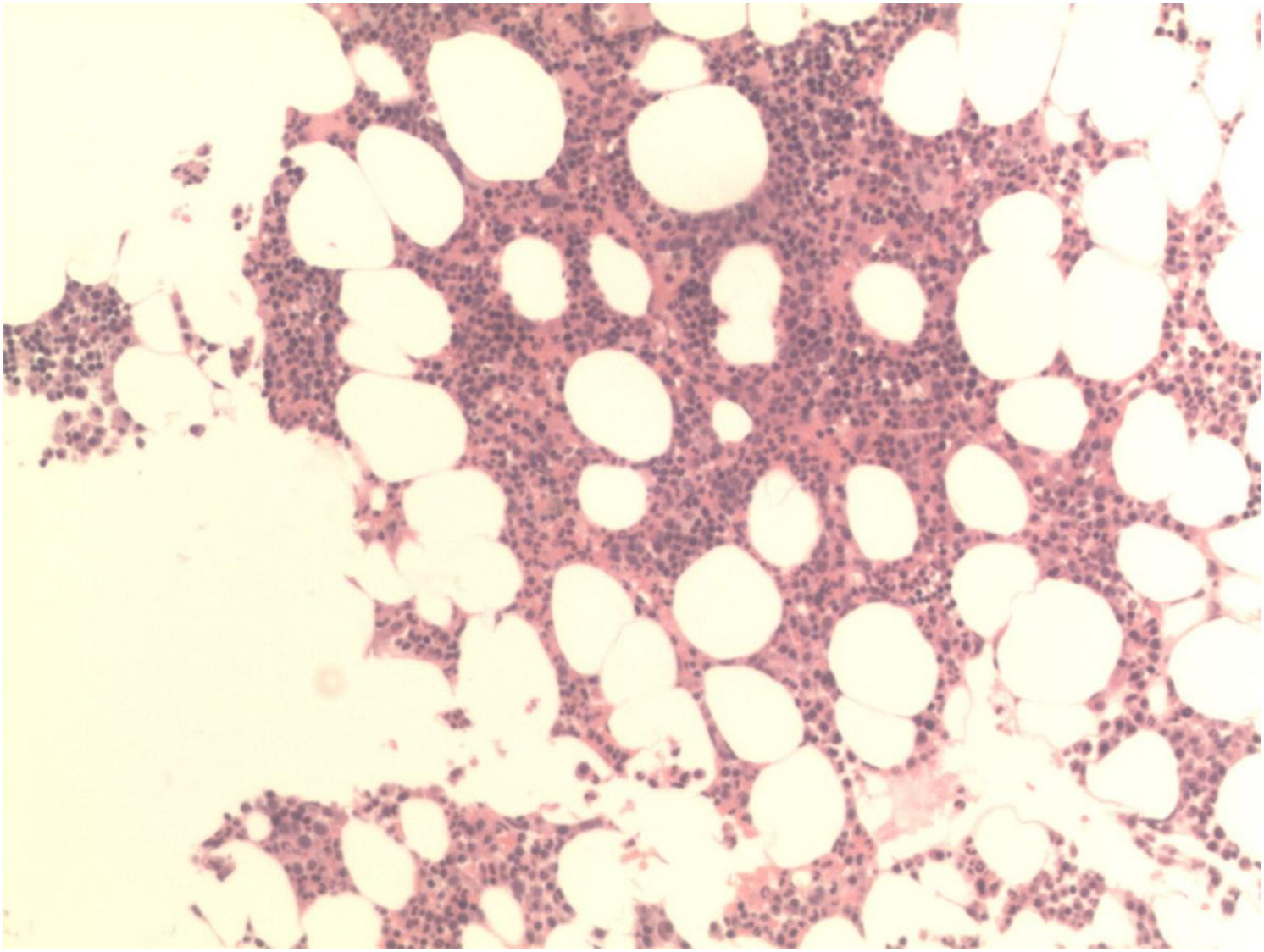

Figure 3

Finally, plasma cell myeloma was diagnosed by bone marrow aspirate and trephine.

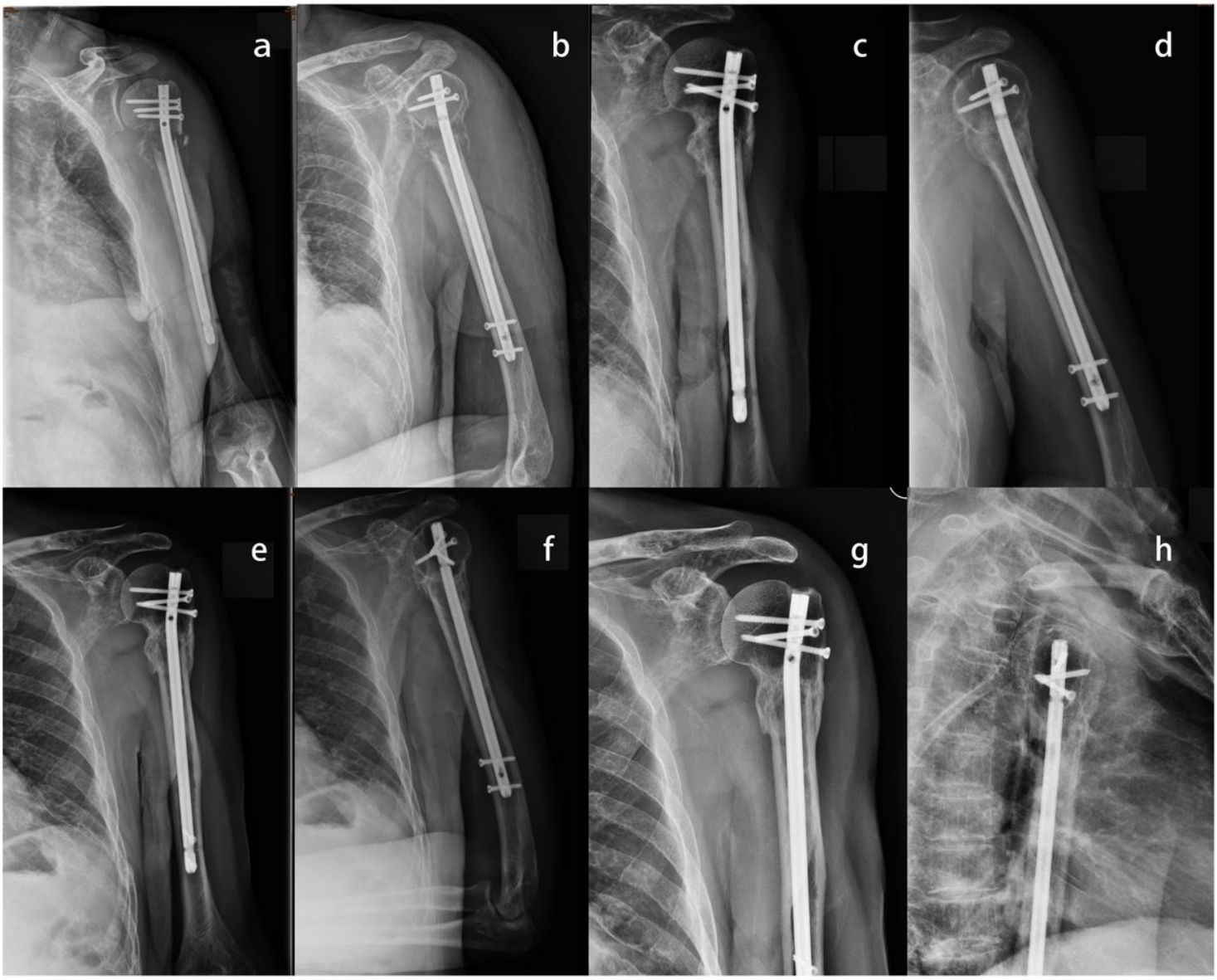

Figure 4

Postoperative X-ray films of left shoulder (a, b). Follow-up after 6 months (c, d), 15 months (e, f) and 40 months (h, i) of surgery of the patient. Eventually, proximal humerus fracture healed.