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Case Report

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Pathological Humeral Fracture from Bone Metastasis of a Gastrointestinal Stromal Tumour: First Reported Case

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Abstract

Background: Gastrointestinal stromal tumour (GIST) is the most prevalent mesenchymal tumour of the GI tract. Metastases commonly occur in the liver and peritoneum, with very rare reported cases of bone metastases, hence no therapeutic standard has been established for the management of bone metastases. Modern targeted therapy has improved patient survival, and although there are only a small number of reported GIST bone metastases, the incidence will likely continue to increase. Further understanding of GIST bone metastases is required for implementation of an accurate and effective treatment plan.

Case presentation: We report a 56-years-old patient who has a history of bleeding duodenal GIST resected with a Whipple operation. Post-operatively, Imatinib was started, but she developed liver metastasis 6 years later, requiring segmentectomy. She reported pain over the left humerus 2.5 years later and sustained a trivial injury to the left arm, resulting in a distal humerus shaft spiral fracture associated with a radial nerve palsy (Holstein-Lewis injury). Images showed a lytic lesion with cortical erosion and soft tissue extension at the fracture site. Biopsy confirmed GIST bone metastases. She underwent an open reduction and internal fixation with plating and curettage of the lytic lesion, and made a good functional recovery afterwards.

Conclusion: This is the first reported case of a GIST bone metastases pathological Holstein Lewis fracture. It highlights the potential for bone metastasis to present a long time after the diagnosis of a GIST. Although bone metastases are rare, it is now increasing due to the prolonged survival of patients and the introduction of targeted therapy. It is important to conduct long term surveillance in specific patient demographics and future studies should be carried out to facilitate the development of a surveillance protocol in patients with GIST.

Keywords

Bone metastasis, Gastrointestinal stromal tumour, Tyrosine kinase inhibitors, Fracture

Introduction

Gastrointestinal Stromal Tumour (GIST) is the most common mesenchymal neoplasm of the gastrointestinal tract, it consists of a heterogeneous group of nonepithelial neoplasms with spindle or epithelioid cells [1]. GIST originates from interstitial cells of Cajal and incidence is between 10-30 cases per million people [2] and continues to rise. It typically affects the stomach (60-70%), small intestine (20-30%), colorectal (5%), oesophagus (< 5%) and rarely, the omentum and mesentery [3]. Mutations are seen involving the tyrosine kinase protein receptor sex on 9 or 11 of c-Kit gene or exon 18 of platelet derived growth factor receptor alpha gene (PDGFRA) [4]. The immunohistochemical of GIST typically express CD117 (c-Kit protein), CD34 proteins and DOG1 protein.

Surgical resection is the treatment of choice in primary GIST. Targeted therapy is also used and has been shown to improve patient survival. Metastases normally reside within the abdominal cavity, commonly to the liver, and rarely metastases to the bone. There are only a few reported cases of bony metastases from GIST (< 5%), and of those, the majority metastases to the pelvis or spine [5]. There are currently no guidelines on monitoring bone metastases from GIST due to its low reported incidence, however, patient survival rates

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are improving due to advancing medical treatment, hence there is a need to identify those who maybe at higher risk of developing bony metastases and formulate an appropriate treatment plan to prevent complications such as fractures.

We present the first reported case of a GIST bone metastasis with a humeral pathological fracture and radial nerve palsy.

Case Report

A 56-years-old lady presented with left elbow injury following a fall from level ground. She has a background of duodenal GIST, diagnosed with oesphgogastrodudeno scopy as part of investigation for anemia 9 years before the accident and resected in an emergency setting with a Whipples operation due to acute bleeding. Pathology confirmed a GIST measuring at 7.5 cm, c-kit positive with clear resection margins. Postoperatively, she was started on Imatinib 400 milligrams daily to reduce the risk of recurrence. Surveillance imaging reviewed several small liver masses at 1.5 years postoperatively, biopsy confirmed metastatic GIST. Imatinib was increased to 400 milligram twice a day to control disease progression and metastases subsequently reduced in size. Unfortunately, new hypermeta bolic liver metastases at segment IV and VIII were discovered at 5 years postoperatively. An open segment IV and VII resection was performed, pathology confirmed clear resection margins. Imatinib was stopped, Sutentinib 37.5 milligrams daily was started in view of disease progression whilst being on Imatinib.

She complained intermittent resting and night pain over her left distal upper arm for 1 month prior to the accident. After the trivial accident, she experienced diffuse pain over left upper arm associated with swelling, reduced wrist and finger extension power, numbness over the radial nerve distribution and good capillary refill. Radiograph showed a displaced spiral fracture at the distal humeral shaft with alytic lesion at the fracture site (Figure 1). Computer tomography showed an expansile, lytic lesion with no matrix, cortical thinning and soft tissue extension (Figure 2). Magnetic Resonance Imaging showed well-defined T1 hypointense, T2 hyperintense enhancing lesion with expansile marrow signals (Figure 3). Position Emission Tomography with Fludeoxyglucose F18 showed increased FDG activity (SUVmax 5.3) in the intramedullary canal involving adjacent soft tissue and progressive liver metastases. The lesion was needle biopsied, it showed a spindle cell neoplasm with high cellularity infiltrating skeletal muscle and adipose tissue. Mitotic count was less than 5 mitoses/5 mm^2 with lympho-vascular permeation but no perineural invasion. Tumour cells were diffusely positive for c-KIT, DOG1, CD34 and smooth muscle actin, whilst negative for Desmin and S1000, the above features were suggestive of metastatic GIST (Figure 4).

Definitive surgery with open reduction and internal fixation was performed with a posterior tricep splitting approach, radial nerve was intact but under tension at the fracture site, intramedullary fleshy tan-coloured tumour was removed (Figure 5), fracture was reduced and fixed with a 3.5 extra-articular distal humerus locking compression plate and locking head screws (Figure 6). The excised tumour showed similar microscopic features to the pre-operative biopsy with extensive haemorrhage and tumour necrosis.

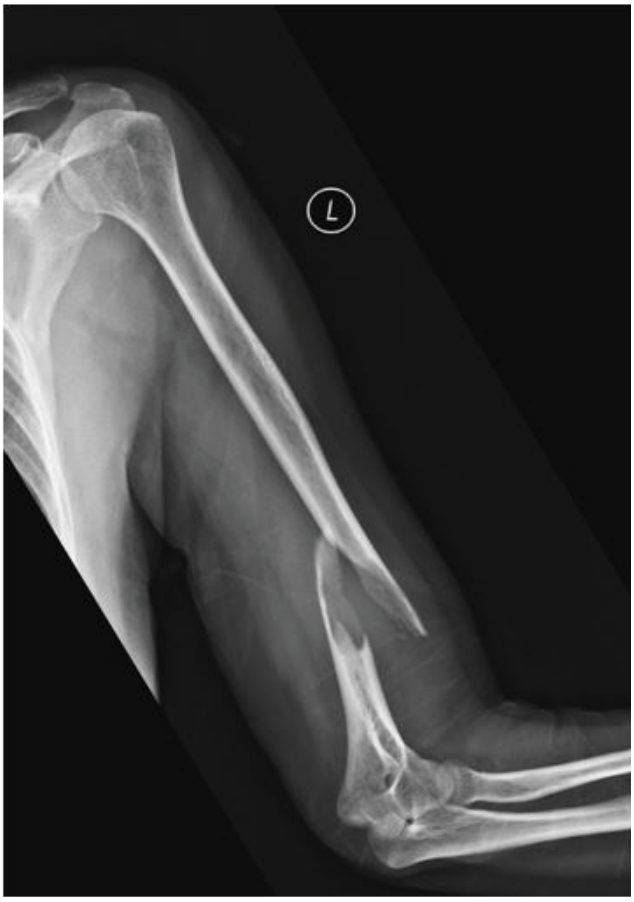

Figure 1: Pre-Op AP Radiograph.

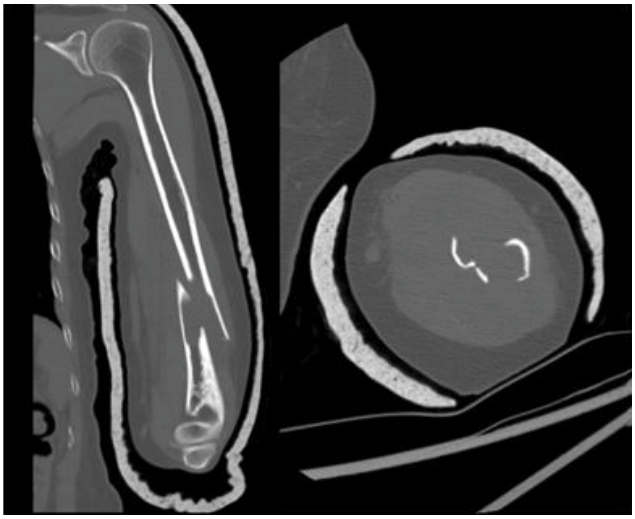

Figure 2: Pre-Op Computer Tomography (Coronal and Axial).

Post-operatively, gentle free mobilisation exercise was started and there was gradual return in radial nerve function. Target therapy was resumed after the wound healed, at the same dose as pre-injury with plan to closely observe diseases status with subsequent imaging.

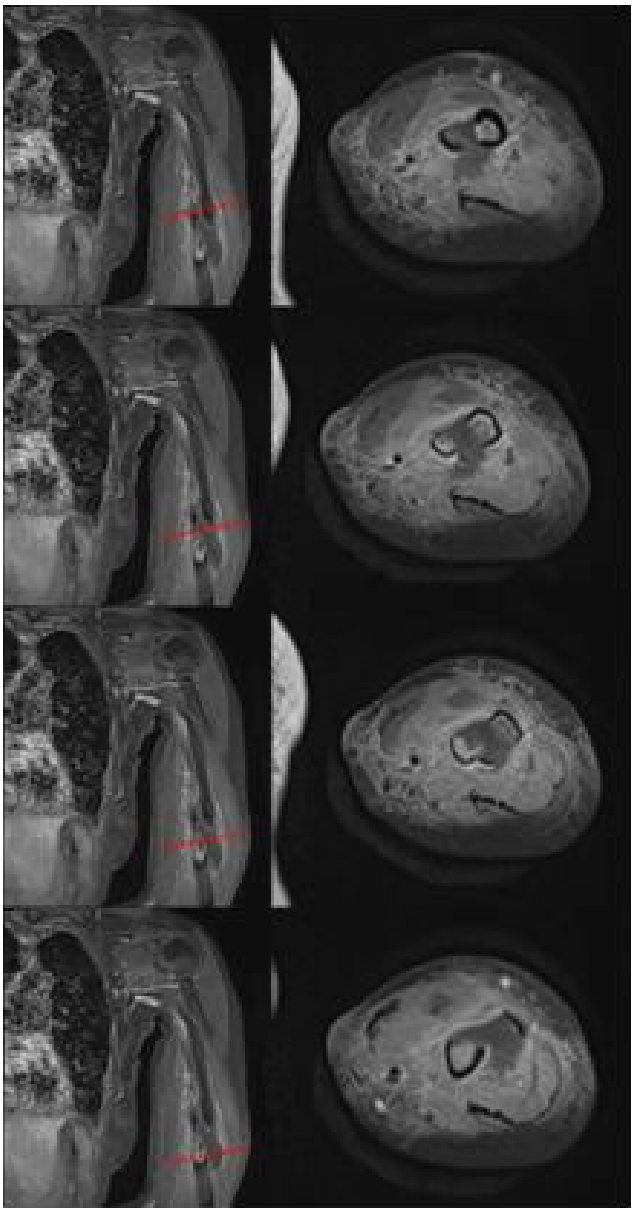

Figure 3: Pre-Op Magnetic Resonance Imaging (T1 weighted with contrast Coronal and Axial).

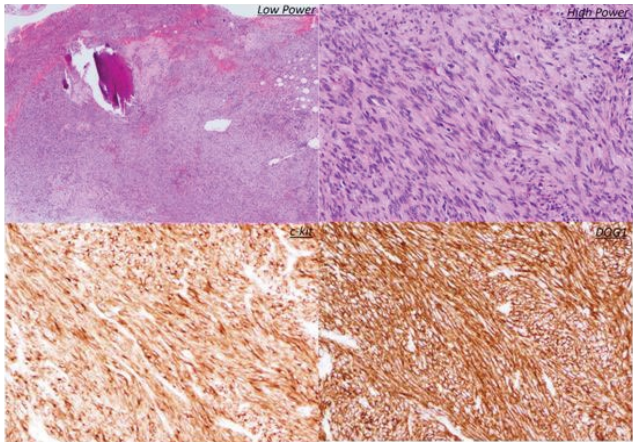

Figure 4: (Low Power) There is a cellular spindle cell tumour permeating the bone and marrow tissue. (High Power). The spindle cells are arranged in fascicles, and they possess elongated nuclei with ill-defined eosinophilic cytoplasm. The spindle cells are positive for c-kit and DOG1.

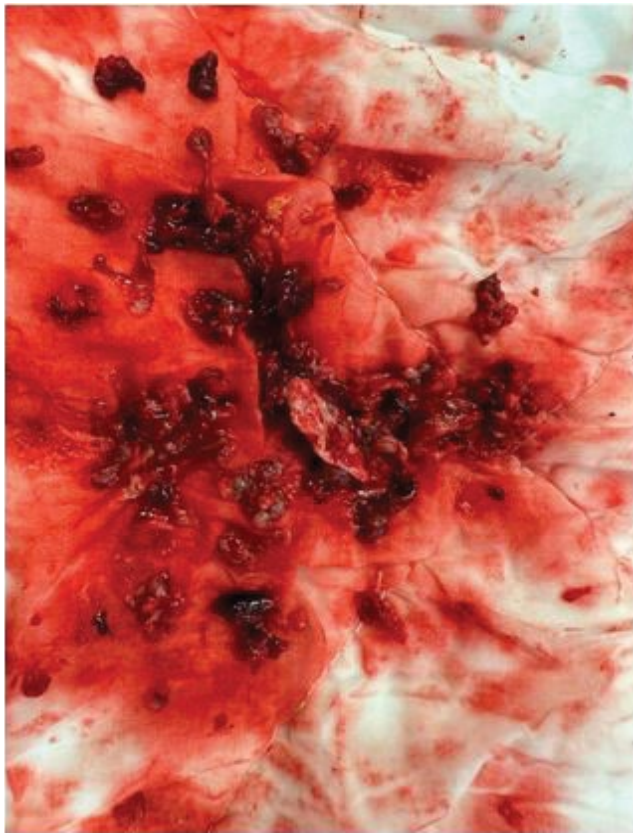

Figure 5: Tumour material removed intraoperatively with curettage.

Discussion

The treatment of primary GIST involves surgical resection of the tumour and to avoid tumour rupture. Systemic therapy may be offered in the neoadjuvant setting to decrease tumour burden prior to surgical resection or in the adjuvant setting to decrease recurrence risk. The five year survival rate for GIST patients is 50% and the introduction of molecular-targeted therapy has improved survival rate and increased progression-free period [6]. Risks stratification tools such as the American Force Institute of Pathology, Miettinen classification [7] and National Health Institute classification are used to calculate recurrence and metastatic risks based on tumour size, mitotic count and location of the GIST. Metastases typically appear around 4 years after the diagnosis [8] of primary GIST, but has been reported to appear as late as 20 years post initial diagnosis, hence there is a need for long term follow up and surveillance.

Around 50 cases of bony metastases from GIST had been reported in the literature, of which the majority are axial skeletal metastases with fewer than 5 cases of metastases to extra-axial skeleton reported. GIST bone metastases may present incidentally during radiological surveillance or with

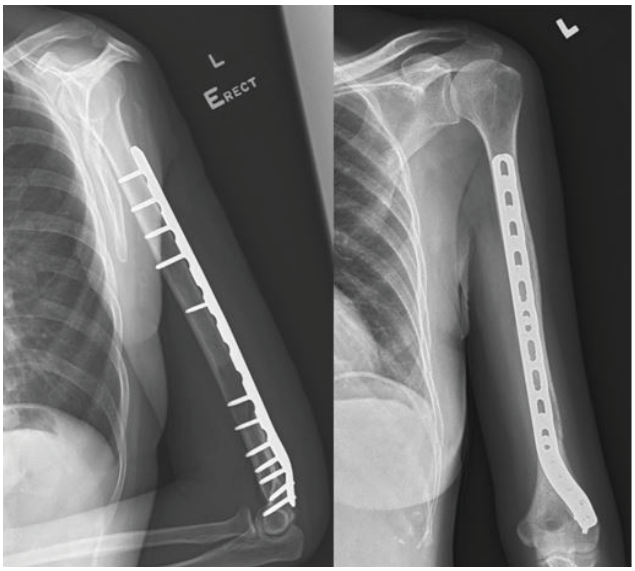

Figure 6: Post-operative AP and Lateral Radiograph.

pain, hypercalcaemia, pathological fracture and spinal cord compression. When patients develop pathological fracture of long bones or spinal cord compression, this can cause a detrimental effect on patient's mobility, limit their social contact and impact their quality of life [9]. Early detection of bony metastases is desirable to minimise morbidity and control disease progression.

Image findings are similar to bony metastases from other primary malignancy. Of the reported GIST bone metastases, they are well-defined lytic lesions and cortical erosion with occasional extraosseous extension. PET CT typically shows high FDG activity. Metastases to the axial skeleton are more common due to the close proximity with abdominal organs and valve less vascular routes [10]. Axial skeletal metastases often involve neurovascular structures and most reported cases were not resected. On the contrary, reported extra-axial skeletal metastases were treated with combination of resection, medical therapy and radiotherapy. In a review of 45 GIST bone metastases cases, the use of surgical resection in addition to medical therapy prolonged patient survival to 78 months compared to 43 months, this illustrated the benefits of resecting the bone metastases when possible. Spinal metastases were associated with a reduced in survival (42 months) compared with extra-axial metastases (83 months), likely due to the morbidities associated with spinal metastases, such as progressive neurological deficit leading to reduced motor function, impaired sensation and sphincter disturbance.

Imatinib and Suntimib are first and second line targeted therapy respectively, these are tyrosine kinase inhibitors (TKI) and bind to the tyrosinase receptor on the surface of tumour cells to block signal transmission and restrict tumour growth. There is no guideline on the duration of target therapy for treating bony metastases, the common practices derived from published case reports include continuing Imatinib until the patient develops disease progression, drug resistance or side effects, at which point, Suntimib is used. Two thirds of GIST bony metastases shows resistance to the medical therapy hence there is a need to better understand the molecular pathways of GIST bone metastases in inducing resistance to TKI therapy.

Due to the low number of reported GIST bony metastases, there are currently no established consensus or surveillance recommendations. Multidisciplinary approach has been shown to significantly increase the overall survival. Patient with bony metastases often have concurrent liver metastases and the primary location of GIST is more likely the small intestine. A longer surveillance and a prolonged course of TKI post index resection of GIST is recommended to reduce risks of distant metastases. Clinicians should be aware of the increased incidence of bony metastases in these demographics.

Conclusion

Bone metastases from GIST are becoming more prevalent due to the increased patient survival. There are currently no established surveillance criteria for GIST bone metastases. Patients with small bowel GIST and concomitant liver metastases are more likely to develop bony metastases. A multi-disciplinary team approach should be adopted to improve quality of life and facilitate management plan. Further studies into the risk factors, management, prognosis of GIST bone metastases are required.

References

1. Mazur MT, Clark HB (1983) Gastric stromal tumors reappraisal of histogenesis. Am J Surg Pathol 7: 507-519.
2. Søreide K, Sandvik OM, Søreide JA, et al. (2016) Global epidemiology of gastrointestinal stromal tumours (GIST): A systematic review of population-based cohort studies. Cancer Epidemiol 40: 39-46.
3. Nowain A, Bhakta H, Pais S, et al. (2005) Gastrointestinal stromal tumors: Clinical profile, pathogenesis, treatment strategies and prognosis. J Gastroenterol Hepatol 20: 818-824.
4. Corless CL, Fletcher JA, Heinrich MC (2004) Biology of gastrointestinal stromal tumors. J Clin Oncol 22: 3813-3825.
5. Jati A, Tatli S, Morgan JA, et al. (2012) Imaging features of bone metastases in patients with gastrointestinal stromal tumors. Diagn Interv Radiol 18: 391-396.
6. DeMatteo RP, Ballman KV, Antonescu CR, et al. (2009) Placebo-controlled randomized trial of adjuvant imatinib mesylate following the resection of localized, primary gastrointestinal stromal tumor (GIST). Lancet 373: 1097-1104.
7. Miettinen M, Lasota J (2006) Gastrointestinal stromal tumors: Pathology and prognosis at different sites. Semin Diagn Pathol 23: 70-83.
8. Yang J, Yan J, Zeng M, et al. (2020) Bone metastases of gastrointestinal stromal tumor: A review of published literature. Cancer Manag Res 12: 1411-1417.
9. Coleman RE (2006) Clinical features of metastatic bone disease and risk of skeletal morbidity. Clin Cancer Res 12: 6243s-6249s.
10. Waterman BR, Kusnezov N, Dunn JC, et al. (2015) Aggressive gastrointestinal stromal tumor with spinal metastases: A case report. Mil Med 180: e618-e621.