Radiology Case Reports 19 (2024) 1078–1082

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

A case report on pulmonary metastasis of giant cell tumor mimicking arteriovenous malformation ☆,☆☆

Niloofar Ayoobi Yazdi, MD[a], *Sara Parviz, MD*[a], *Sina Delazar, MD*[a], *Sina Azadnajafabad, MD, MPH*[a], *Samira Aleseidi, MD*[b], *Hana Saffar, MD*[c], *Nahid Sadighi, MD*[a,*]

[a] *Department of Radiology, School of Medicine, Advanced Diagnostic and Interventional Radiology Research Center (ADIR), Imam Khomeini Hospital complex (IKHC), Tehran University of Medical Sciences, Tehran, Iran*
[b] *Heumatology and Internal Medicine, Rheumatology Research Center, Tehran University of Medical Sciences, Tehran, Iran*
[c] *Department of Pathology, Anatomical and Clinical Pathology, Cancer Institute, Imam Khomeini Hospital complex (IKHC), Tehran University of Medical Sciences, Tehran, Iran*

ARTICLE INFO

Article history:
Received 8 May 2023
Revised 7 November 2023
Accepted 28 November 2023

Keywords:
Giant cell tumor
Neoplasm metastasis
Lung
Arteriovenous malformation
Case report

ABSTRACT

Giant cell tumor (GCT) is typically a benign tumor of the skeletal system that mainly presents with bone pain. Pulmonary metastasis is one of the distant presentations of GCT in patients who have previously undergone surgical resection of the tumor. Among the various presentations of pulmonary metastasis in GCT, lesions with arteriovenous malformation (AVM) features are rare and have only been reported in a few cases. In this case report, we present the case of a 29-year-old female patient who had previously undergone surgical resection of a GCT in her right lower extremity 4 years ago. The patient was referred to us with progressive dyspnea, and a lesion resembling an AVM was found during radiologic evaluation using chest computed tomography. Pathologic evaluation of the lesion after biopsy revealed that it was a metastasis of GCT presenting with vascular-like features in the lung. This study reports on a very rare occurrence of GCT pulmonary metastasis with an AVM appearance on imaging, highlighting the clinical importance of atypical presentations of pulmonary metastasis in patients with a history of GCT. Appropriate and timely screening and management of such lesions may prevent adverse outcomes such as massive hemorrhage and deterioration of lung function.

☆ Acknowledgements: Authors would like to sincerely thank the studied case in this report.
☆☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
* Corresponding author.
E-mail address: sadighii@yahoo.com (N. Sadighi).
https://doi.org/10.1016/j.radcr.2023.11.075

Introduction

Giant cell tumors (GCTs) are mostly benign tumors of the bone or synovium that have different epidemiology worldwide. They mainly affect young adults [1]. GCTs primarily originate from the osteoclastogenic stroma and consist of mononuclear stromal cells and multinucleated giant cells with osteoclastic activity, similar to their origin [2]. Bone pain and skeletal complications, such as stress fractures, are among the initial clinical manifestations of these tumors [1]. After the presentation of the lesions, diagnosis is made through radiologic evaluation and pathological assessment. Surgical resection, along with various medical strategies, is among the treatment options for affected cases [3]. Despite being categorized as benign lesions, GCTs can be aggressive and have a tendency for local recurrence and distant metastasis, even after complete surgical resection of the primary bone tumor [4].

Pulmonary metastasis of GCTs was initially diagnosed and reported in some studies in the 1990s. Initially presented as case reports, further studies were conducted on patients with this diagnosis [5,6]. Local recurrence of GCTs has been reported to occur in 10% to 25% of cases [2,4,7,8]; however, some studies have reported higher rates of 60% to 75% for local recurrence [2,9,10]. Distant metastasis occurs in approximately 16% of GCTs [1], with rates of distant metastasis to the lungs reported to be less than 5% in several studies [4,11]. It is worth noting that among those with distant pulmonary metastasis either before or at the time of diagnosis, the rates of local recurrence are higher at 80% to 90% [6,12]. The prevalence of pulmonary metastasis in GCTs initially located in bone has been estimated at around 3% of cases and is rarely seen during the initial diagnostic process. Most metastatic lesions appear in recurrent tumors months or years after treatment [11]. Several risk factors have been identified for pulmonary metastasis in GCTs. Among them are tumors located in lower extremities that are generally larger and diagnosed at more advanced stages. Additionally, frequent local recurrence contributes to adverse outcomes such as development of distant lung metastasis [10].

In this manuscript, we report a case of an adult female patient initially diagnosed with a GCT in her right lower extremity who developed pulmonary metastasis after 4 years. The lesion mimicked an arteriovenous malformation (AVM), making this case interesting and clinically significant. This reported case adds valuable information to the literature by studying more atypical manifestations of GCT pulmonary metastasis and contributes to earlier and improved management strategies for these patients.

Case presentation

The case presented in this report is about a 29-year-old female patient who had a previous history of GCT in the right lower extremity, specifically in the distal metaphysis of the right femur, with erosion of the medial cortex. This condition was diagnosed and treated 4 years ago (Fig. 1). However, the patient returned with symptoms of progressive dyspnea and cough.

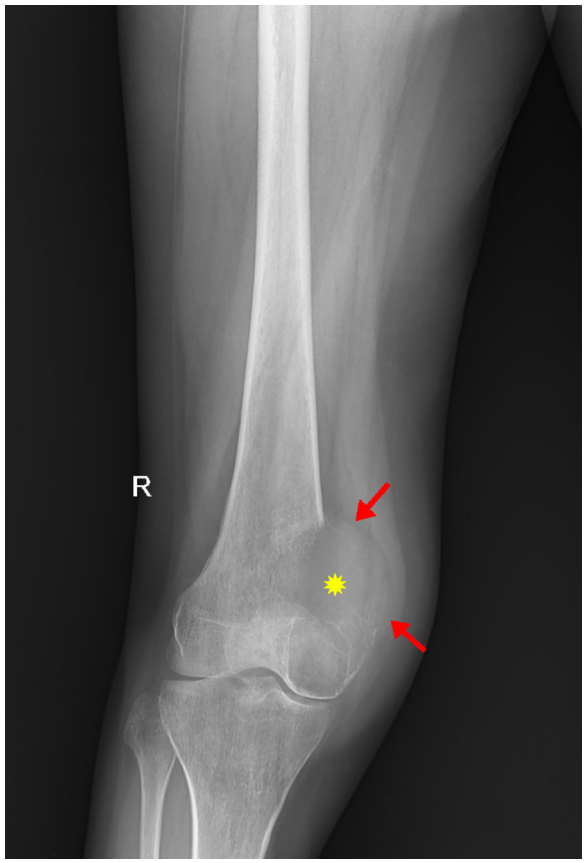

Fig. 1 – The ill-defined lytic lesion (indicated by the yellow asterisk) in the distal metaphysis of the right femur caused erosion in the medial cortex (shown by the red arrows) on the anteroposterior view of the plain radiography. The radiological findings observed in this image were not typical of a long bone giant cell tumor. However, the giant cell tumor was confirmed through pathological examination.

The dyspnea started 1 month prior to presentation and was constant, gradually worsening in severity. It was not related to physical activity. The patient had no significant medical history or family history of major diseases, except for her previous GCT diagnosis. At the time of presentation, she was not taking any specific medications and had no history of smoking or alcohol consumption.

On physical examination, apart from the scar from the previous surgery on her right lower extremity, no other notable findings were observed. Chest auscultation revealed the absence of normal lung sounds on the right side, while heart auscultation was normal. Vital signs were within the normal range, except for an oxygen saturation of 90% on pulse oximetry examination and a respiratory rate of 26 breaths per minute.

A contrast-enhanced chest computed tomography (CT) scan revealed a large heterogeneous mass in the right lung measuring 139*100*94 millimeters. The mass showed avid enhancement of tortuous vessels in both arterial and venous phases. It occupied almost the entire right lung, while the tho-

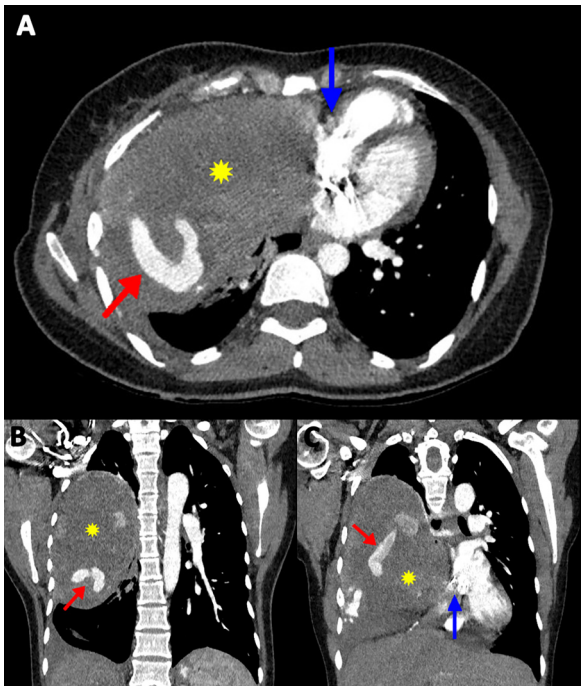

Fig. 2 – The mediastinal view of the spiral lung computed tomography scan showed a large, heterogeneous mass in the right lung measuring 139*100*94 millimeter (indicated by yellow asterisks). This mass exhibited tortuous vessels that were intensely enhanced, resembling an arteriovenous malformation (highlighted by red arrows). As a result of the lung mass, the heart and mediastinum were displaced towards the left side (indicated by blue arrows). The different perspectives of the scan are presented as follows: (A) axial view, (B and C) coronal views.

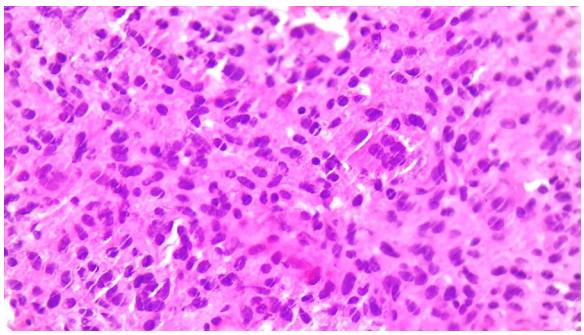

Fig. 3 – The histopathology examination revealed a presence of mononuclear oval cells mixed with multinucleated giant cells (stained with Hematoxylin and Eosin at a magnification of x400).

racic bony structures appeared normal without any evidence of destructive lesions (Fig. 2).

Microscopic examination of a needle biopsy taken from the lung mass revealed infiltration of a neoplasm consisting of relatively uniform mononuclear oval cells mixed with multinucleated giant cells. Based on these findings, the pathologist confirmed a diagnosis of GCT metastasis (Fig. 3).

During the clinical and radiological evaluation of the lower limb, no evidence of tumor recurrence was found at the surgical site. However, due to the significant size of the lung mass and the patient's preference, systemic chemotherapy was determined to be the most appropriate treatment.

Discussion

In this report, we described the case of a 29-year-old woman who had previously been diagnosed with GCT in her right lower extremity. Four years later, she returned with symptoms of dyspnea and cough. Upon examination, a large mass was discovered in her right lung, resembling an AVM. This type of pulmonary metastasis with AVM-like characteristics is rare and has only been reported in a few cases [13,14], which we will discuss further in this section.

Haseli et al. presented a case of a 19-year-old female patient who was diagnosed with GCT of the patella after experiencing severe right knee pain. She underwent surgical resection 2 years prior to her presentation to the clinic with progressive dyspnea. The initial chest X-ray showed multiple opacities of different sizes in both lungs, as well as pleural effusion in the right lung. Contrast-enhanced CT scan imaging revealed engorged varicose vessels. Biopsy of the lesion confirmed metastatic GCT, while there was no local recurrence observed in the knee MRI evaluation. The patient underwent thoracotomy with pneumolysis and metastatectomy on both sides of the lungs for management [13].

Yeo et al. reported a case of a 22-year-old woman with a history of right distal femur GCT, which had been treated with intraregional curettage followed by bone cementing 5 years earlier. She experienced tumor recurrence and severe pain at the site of the previous excision, which was also treated by curettage and cementing. She presented to the emergency department with severe dyspnea, chest pain, and right pleural effusion on chest X-ray. Further helical CT revealed a well-defined oval hypervascular mass with feeding arteries in the right lower lobe, suggestive of AVM. The patient underwent thoracotomy and wedge resection of the mass, and histological evaluation confirmed classic GCT metastasis with benign features [14].

Since the first series of cases reporting pulmonary metastasis in patients with GCT, several studies have been conducted in this field. Pulmonary metastasis is now recognized as one of the differential diagnoses in patients with a history of GCT who present with dyspnea and other pulmonary signs and symptoms [4,11]. It is suggested that pulmonary metastasis in bone GCTs may be associated not only with tumor location and histological grade but also with factors such as age, sex, and general health status [11]. Patients who experience local recurrence of bone GCTs and exhibit high expression levels of specific genes, cytokines, and chemokines may have an increased chance of developing pulmonary metastasis based on existing literature [11].

In an institutional experience involving 291 patients diagnosed with benign GCT over a 30-year period, it was found that there is an increased risk of pulmonary metastasis in patients who are younger in age, present with Enneking stage-

3 tumors, experience local recurrence, or have axial location primary GCTs. Multivariate analysis revealed that local recurrence is an independent risk factor for pulmonary metastasis. Additionally, this study showed that the mode of treatment for the primary tumor does not influence the occurrence of pulmonary metastasis [15]. The earlier mentioned Enneking Classification system is used to classify benign and malignant neoplasms of the musculoskeletal system. Malignant tumors are categorized into 3 stages (I-III) based on surgical grade, local extent, and presence or absence of regional or distant metastasis [16,17]. Another large-scale study involving 310 patients with GCT over more than a decade demonstrated that patients presenting with soft tissue masses and overall recurrence are susceptible to developing pulmonary metastasis. The study recommended including chest CT examination as part of follow-up protocols to facilitate early detection and management of such complications [12].

Although pulmonary metastasis in cases of GCT has been well studied, lesions mimicking AVM are rare and have only been observed in a few cases, as mentioned in our literature review [13,14]. Vascular-like lesions have also been observed in some cases of diagnosed GCT with aneurysmal bone cyst as a secondary complication, highlighting the unique features of this benign tumor and its potential association with vascular components [18,19]. This concept suggests the need for further studies on the biological and histological characteristics of GCT metastasis and its tendency to develop vascular-like lesions. In vivo and in vitro studies could be designed to explore the possible pathophysiological pathways and biological connections between GCT and these complications.

The development of acquired pulmonary AVMs within pulmonary metastases from extrathoracic tumors is rare, but aside from GCT, it has also been observed in other malignancies. A previous report described 2 cases where pulmonary metastasis mimicking AVMs developed after chemotherapy in these patients [20]. One case involved a 73-year-old female patient with a history of renal cell carcinoma who had undergone radical nephrectomy 12 years prior and presented with progressive dyspnea over the past 3 months. The other case involved a 47-year-old woman with metastatic uterine leiomyosarcoma who had undergone tumor resection and was receiving adjuvant chemotherapy. The authors suggest that chemotherapy regimens may contribute to the formation of pulmonary AVM-like metastases. The study also highlights the usefulness of CT angiography for detecting and evaluating AVM lesions in these patients [20].

Since reported cases of GCT and similar cases are very rare among patients, there are no concrete guidelines for diagnosing and managing patients with suspected pulmonary AVM-like metastasis. However, considering the vascular nature of these lesions, it is highly recommended to evaluate patients with a history of GCT and pulmonary symptoms using modalities such as contrast-enhanced chest CT scans to examine the details of the lesions. Additionally, in cases where there is suspicion of pulmonary AVM in patients with a history of GCT, it is suggested to conduct more sophisticated imaging evaluations and confirm the diagnosis through a biopsy of the lesion for histopathologic assessment. Further studies on these patients are necessary to provide clinicians and radiologists with sufficient information for appropriate and timely management.

Conclusion

This manuscript highlights the importance of detailed follow-up and pulmonary evaluation using imaging measures like chest CT in cases where GCT metastasizes to the lungs and mimics AVM. Although GCT is typically benign, the formation of AVM-like lesions in the lungs and associated complications can lead to adverse outcomes if neglected. Therefore, timely and appropriate management is necessary in the follow-up routines for these cases.

Patient consent

Written informed consent in native language was obtained from the patient for publication of this case report and any accompanying images.

Ethical approval

The ethical committee of the Tehran University of Medical Sciences approved this case report; however, the institution does not provide ethical codes for case reports. The discussed case in this manuscript provided the informed consent about the participation in this study.

Author contributions

NAY, SP, and NS conceptualized study and chose the case to report. SA and SD prepared the first draft. All authors reviewed the manuscript majorly and revised it for publication. NS was the corresponding author and supervised all steps of this case report preparation and publication.

REFERENCES

[1] Beebe-Dimmer JL, Cetin K, Fryzek JP, Schuetze SM, Schwartz K. The epidemiology of malignant giant cell tumors of bone: an analysis of data from the Surveillance, Epidemiology and End Results Program (1975-2004). Rare Tumors 2009;1(2):e52.
[2] Amelio JM, Rockberg J, Hernandez RK, Sobocki P, Stryker S, Bach BA, et al. Population-based study of giant cell tumor of bone in Sweden (1983-2011). Cancer Epidemiol 2016;42:82–9.
[3] Montgomery C, Couch C, Emory CL, Nicholas R. Giant cell tumor of bone: review of current literature, evaluation, and treatment options. J Knee Surg 2019;32(4):331–6.
[4] Chakarun CJ, Forrester DM, Gottsegen CJ, Patel DB, White EA, Matcuk GR Jr. Giant cell tumor of bone: review, mimics, and new developments in treatment. Radiographics 2013;33(1):197–211.
[5] Kay RM, Eckardt JJ, Seeger LL, Mirra JM, Hak DJ. Pulmonary metastasis of benign giant cell tumor of bone. Six histologically confirmed cases, including one of spontaneous regression. Clin Orthop Relat Res 1994(302):219–30.

[6] Siebenrock KA, Unni KK, Rock MG. Giant-cell tumour of bone metastasising to the lungs. A long-term follow-up. J Bone Joint Surg Br 1998;80(1):43–7.
[7] Jamshidi K, Karimi A, Mirzaei A. Epidemiologic characteristics, clinical behavior, and outcome of the giant cell tumor of the bone: a retrospective single-center study. Arch Bone Jt Surg 2019;7(6):538–44.
[8] Errani C, Ruggieri P, Asenzio MA, Toscano A, Colangeli S, Rimondi E, et al. Giant cell tumor of the extremity: a review of 349 cases from a single institution. Cancer Treat Rev 2010;36(1):1–7.
[9] Rosario M, Kim HS, Yun JY, Han I. Surveillance for lung metastasis from giant cell tumor of bone. J Surg Oncol 2017;116(7):907–13.
[10] Yayan J. Increased risk of lung metastases in patients with giant cell bone tumors: a systematic review. Adv Exp Med Biol 2019;1176:1–17.
[11] Muheremu A, Niu X. Pulmonary metastasis of giant cell tumor of bones. World J Surg Oncol 2014;12:261.
[12] Wang J, Liu X, Yang Y, Yang R, Tang X, Yan T, et al. Pulmonary metastasis of giant cell tumour: a retrospective study of three hundred and ten cases. Int Orthop 2021;45(3):769–78.
[13] Haseli S, Malekpour S, Jafari SH. Varicose vessels within pulmonary metastasis of giant cell tumor: unusual radiological manifestation. 2018;15(4):e64221.
[14] Yeo CD, Roh SY, Shin OR, Bahk WJ, Kim KH, Kim JW. A case of pulmonary metastasis of giant cell tumor of bone presenting as pulmonary arteriovenous malformation. J Formos Med Assoc 2015;114(4):369–72.
[15] Chan CM, Adler Z, Reith JD, Gibbs CP Jr. Risk factors for pulmonary metastases from giant cell tumor of bone. J Bone Jt Surg Am Vol 2015;97(5):420–8.
[16] Jawad MU, Scully SP. In brief: classifications in brief: enneking classification: benign and malignant tumors of the musculoskeletal system. Clin Orthop Relat Res 2010;468(7):2000–2.
[17] Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma. Clin Orthop Relat Res 1980(153):106–20.
[18] Li M, Gan Y, Shi D, Zhao J. Huge aneurysmal bone cyst secondary to giant cell tumor of the hand phalanx: a case report and related literature. BMC Cancer 2020;20(1):233.
[19] Wu Z, Yang X, Xiao J, Feng D, Huang Q, Zheng W, et al. Aneurysmal bone cyst secondary to giant cell tumor of the mobile spine: a report of 11 cases. Spine 2011;36(21):E1385–90.
[20] Bruzzi JF, Truong MT, Gladish GW, Wallace MJ, Moran CA, Munden RF. Development of pulmonary arteriovenous communications within pulmonary metastases after chemotherapy. J Thorac Oncol 2007;2(3):243–6.