# A Case Report of Solitary Bone Metastasis from Primary Angiosarcoma of the Bilateral Breasts – A Rare Diagnosis

Katrina Ysabel R Naraval[1], Daniela Kristina D. Carolino[1], Ma. Lilia Molina P. Jose[1]

## Abstract

**Introduction:** Primary angiosarcoma of the breast is an uncommon subtype of sof-tissue sarcoma known to be aggressive and is associated with distant metastasis and poor prognosis. Solitary bone metastases occurring in these cases are even more rare with the available limited literature based from small retrospective case series.

**Case Report:** We present a case of a 24-year-old Filipino female previously diagnosed with primary angiosarcoma of the bilateral breasts, initially presenting with a 3-month history of the right hip pain and consulted due to a pathologic fracture of the right proximal femur. Diagnostic tests done confimed solitary skeletal metastasis to this area, for which she underwent wide resection and application of a proximal femoral endoprosthesis. Postoperatively, the patient was able to independently ambulate, with follow-up radiographs showing stable implant fxation. Further imaging showed that lesion-free bones, however, noted development of distant recurrence manifesting with pulmonary metastases and hemorrhagic subcutaneous lesions 3 months afer. Adequate tumor resection and radiotherapy are reported to successfully treat isolated skeletal metastasis in the proximal femur. The pesence of the pathologic fracture beforre definite treatment may have contributed to its distant recurrence, in addition to an already aggressive nature of the primary malignancy.

**Conclusion:** In the background of primary breast angiosarcoma, although rare, high suspicion for isolated skeletal metastasis in a symptomatic patient prevents delay in definiti e management, which avoids progression to a poorer prognosis.

**Keywords:** Solitary bone metastasis, angiosarcoma, proximal femur, pathologic fracture.

## Introduction

Angiosarcoma is a subtype of sof-tissue sarcoma, derived from malignant endothelial cell tumors of vascular or lymphatic origin [1]. It accounts for only 2% of all sof-tissue sarcoma cases, commonly affecting those aged 20–50 [2, 3]. Primary angiosarcoma of the breast, which occurs de novo, is, therefore, considered to be an even more rare entity, representing only 0.04% of all breast tumors and about 1% of breast sarcomas [3, 4, 5].

Angiosarcomas are generally known to be aggressive with poor prognosis and overall survival regardless of the treatment. Some reports suggest that metastatic disease at presentation is associated with poorer outcomes [6]. They spead hematogenously with the lung as the most common site for metastases [3, 4, 7]. Other documented sites include the liver, bone, sof-tissue structures, and lymph nodes. Solitary bone metastasis from angiosarcoma in general has been reported to occur at 1.8% [8], while those that originate from breast angiosarcoma alone are extremely rare. Due to the rarity of the diagnosis and the scarcity of data, there are no evidence-based recommendations on the diagnosis and treatment of breast angiosarcoma and their metastases. The current information available of these sarcomas is largely based from case reports and small retrospective case series with limited outcome data [1, 3, 7].

In this study, we present a rare case of a 24-year-old female presenting with a pathologic fracture of the right proximal femur with solitary bone metastasis secondary to bilateral primary breast angiosarcoma. With this report, we hope to provide more information to the limited pool of data that are known of angiosarcoma.

## Case Report

A 24-year-old female first pesented with masses of bilateral breasts and underwent modifid radical mastectommy of the left east last 2016 and of the right breast last 2017 in a different institution. Both breasts showed histopathologic diagnosis of primary breast angiosarcoma for which she subsequently underwent radiotherapy. She was admited because of severe right hip pain and deformity.

Thee months before current admission, the patient first noed sudden onset right hip pain with no history of trauma. She sought consult

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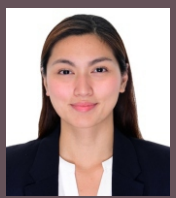
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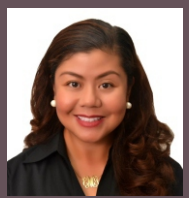
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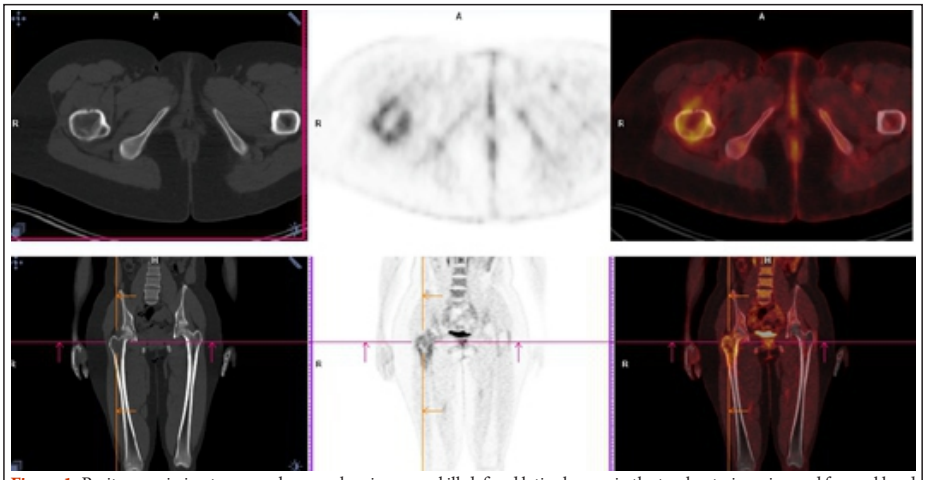

**Figure 1:** Positron emission tomography scan showing several ill-defined l tic changes in the trochanteric region and femoral head of the right femur, associated with cortical thinning and periosteal reaction (top, center).

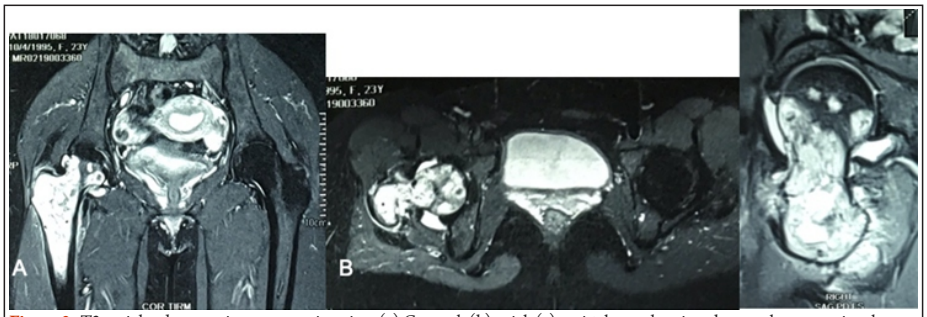

**Figure 2:** T2-weighted magnetic resonance imaging. (a) Coronal, (b) axial, (c) sagittal cuts sh wing abnormal marrow signal involving the right proximal femur with sof-tissue component in the anterior aspect of the femoral neck, measuring 1.9 cm × 2.9 cm × 4.3 cm.

in another institution and underwent positron emission tomography (PET) scan (Fig. 1), which showed several ill-defin d lytic changes in the trochanteric region and femoral head of the right femur, associated with cortical thinning and periosteal reaction, worrisome for metastasis. No other bone lesions seen. Thre was also note of hypermetabolic bilateral inguinal lymph nodes and also subcutaneous nodules in the right arm, which may be metastatic in nature. She then underwent magnetic resonance imaging (MRI) of the pelvis (Fig. 2), which delineated abnormal marrow signals involving the right proximal femur with sof-tissue component in the anterior aspect of the femoral neck, measuring 1.9 cm × 2.9 cm ×4.3 cm. At this point, the patient was referred to an orthopedic oncologist who did an X-ray-guided core needle biopsy. The results showed positive for atypical cells compatible with metastasis and were also noted to be CD34 positive. Two days afer the biopsy, the patient reported a snapping sensation with severe pain along her right hip afer standing up from a chair.

On presentation, the patient was stretcher borne. Thre was swelling of the right hip, with a noted 2 cm shortening of the right lower extremity. Thre were no open wounds and no visible or palpable masses. The atient was unable to tolerate any range of motion of the right hip due to pain. Thre were no palsies or sensory defiits, and pulses were full. The admittg diagnosis of our patient was a pathologic fracture of the proximal femur (intertrochanteric and subcapital), right secondary to metastatic bone disease secondary to angiosarcoma of the bilateral breasts.

A hip X-ray (Fig. 3) done at the time of admission showed two fracture lines, one involving the right femoral neck and another in the intertrochanteric area with surrounding sof-tissue swelling. An osteolytic lesion with moth-eaten borders of the right proximal femur was noted, measuring 7.9 cm × 6.1 cm.

Consequently, a repeat MRI of the right femur (Fig. 4) was done revealing the previously noted marrow signal abnormality, predominantly hypointense on T1 and heterogeneously hyperintense on T2/STIR involving the right proximal femur, with sof-tissue component that has markedly increased in size. Thre is likewise progression of the hyperintense signals in the adjacent soft tssuess. Theest of the muscles in the anterior, posterior, and lateral compartments, as well as neurovascular bundles are uninvolved.

The atient was then indicated for surgery; a day before which she underwent embolization of the ascending and transverse branches of the lateral circumflex f moral artery and the medial femoral circumflex artery resulting to approximately 90–95% devascularization of the main blood supply to the said mass (Fig. 5).

On the 6th day of admission, the patient underwent wide resection of the right proximal femur with application of proximal femoral endoprosthesis. Intraoperative findi gs include fracture lines on the subcapital and trochanteric regions, and a friable sof-tissue mass on the same areas (Fig. 6). Wide resection of the proximal femur plus the surrounding soft tssue was done followed by osteotomy 13 cm distal to the tip of the greater trochanter, including a 3 cm margin from normal bone. The poximal femur and intramedullary curetti gs from the femoral stump were sent for histopathology. Progressive reaming of the distal femoral shaft unil 13.5 mm was done. Appropriately sized trial implant was applied and checked

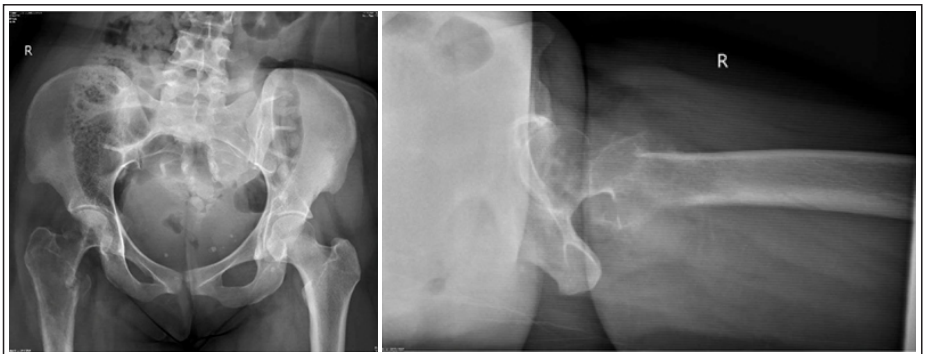

**Figure 3:** Radiographic imaging. (a) AP view, (b) cross table lateral view showing an osteoblastic lesion encompassing the right proximal femur, with noted fractures in the subcapital and trochanteric regions.

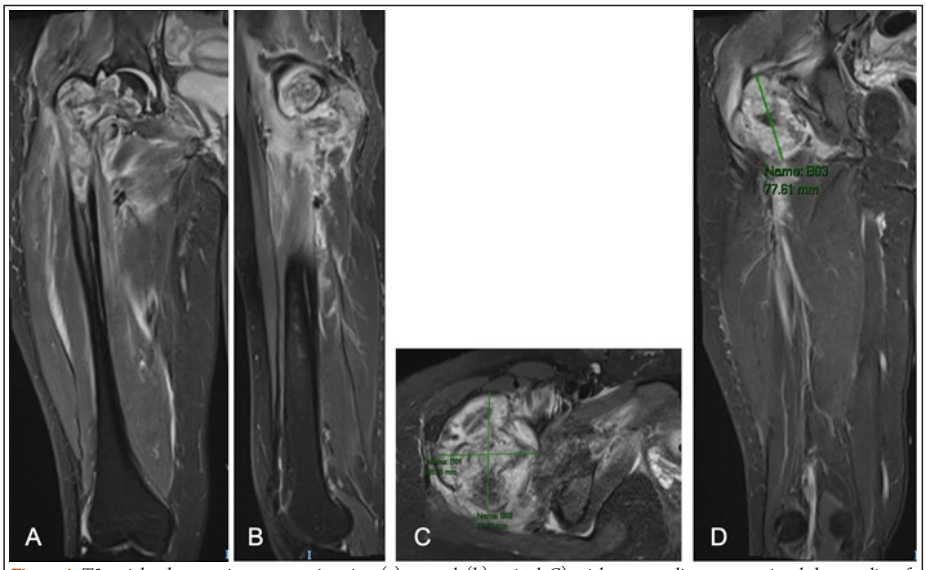


**Figure 4:** T2-weighted magnetic resonance imaging. (a) coronal, (b) sagittal, C) axial cuts revealing marrow signal abnormality of the right proximal femur with a soft tssue (d) measuring 7.8 cm × 6.8 cm × 7.8 cm at the level of the neck.

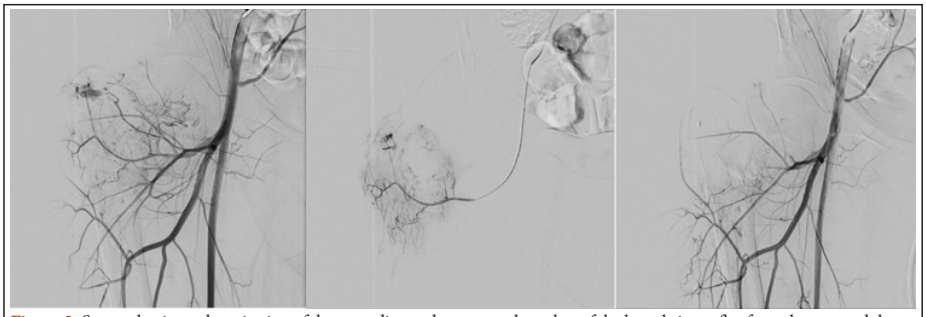

**Figure 5:** Superselective catheterization of the ascending and transverse branches of the lateral circumflex femoal artery and the medial femoral circumflex atery facilitated embolization resulting to approximately 90–95% devascularization of the main blood supplies to the said mass.

for range of motion. Proximal femoral endoprosthesis (USTAR System: S 11 mm × 26 mm × 110 mm, OD43 ID28 N+0 Segment 50 mm) was applied and wrapped with a Prolene mesh, to aid in reattchment of the abductor muscles (Fig. 7). Her estimated blood loss was 1200 mL and underwent two units intraoperative blood transfusion. The patient tolerated the procedure well with no untoward complications.

Histopathology of the specimen showed malignant neoplasm of spindly cells with slightly enlarged hyperchromatic nuclei surrounding atypical vascular spaces, consistent with low-grade angiosarcoma (Fig. 8). Tumor surgical margins (both of bone and soft tssue) were negative for tumor but noted to be only 1 mm (Fig. 9). Histopathology of the intramedullary curetti gs showed no evidence of malignancy distal to the femoral osteotomy.

Postoperatively, another two units of blood transfusion were given. Rehabilitation was done postoperatively and she was able to achieve standing balance tolerance with partial weight-bearing on the 3rd post-operative day. Walker ambulation with full weight-bearing was tolerated on the 6th post-operative day. She was discharged stable and improved on the 6th day postoperatively. Post-operative radiotherapy was done on the right thigh.

At 3 months postoperatively, the patient reported full ambulatory status, however with note of multiple hyperpigmented, non-tender masses along the right costovertebral angle and right trapezial area, worrisome for metastasis. She underwent a repeat PET computed tomography (CT) done at 13 weeks postoperatively, which showed low-grade metabolic activity in multiple subcutaneous nodules in the right mastectomy bed and chest wall, right abdominal wall, and bilateral arms as well as multiple non-calcifid pulmonary nodules in both lungs. No bony lesions were noted. Adjuvant chemotherapy with paclitaxel was started and she received a total of three chemotherapy cycles. On repeat CT of the chest and whole abdomen 30 weeks postoperatively, there was evidence of a left para-aortic lymph node, as well as with interval increase in size of the now hemorrhagic subcutaneous nodules at the right mastectomy bed, right anterior chest wall, and right abdominal wall. No increase in size of the subcutaneous nodules was seen on the bilateral arm. Chemotherapy was stopped when there was bleeding from the superior chest wall mass and the patient was advised to undergo radiotherapy. One year afer her surgery, she is alive with the disease and continuing therapy.

## Discussion

The xial skeleton is more commonly affected in metastatic disease (40%) while the involvement of long bones is rare (15%) and typically involves the diaphysis [9]. Isolated proximal femur metastasis occurs at 10% of all skeletal metastases – 50% found along the femoral neck, 30% in the subtrochanteric area, and 20% along the intertrochanteric site [10]. The most common primary malignancy that metastasizes to the proximal femur is breast

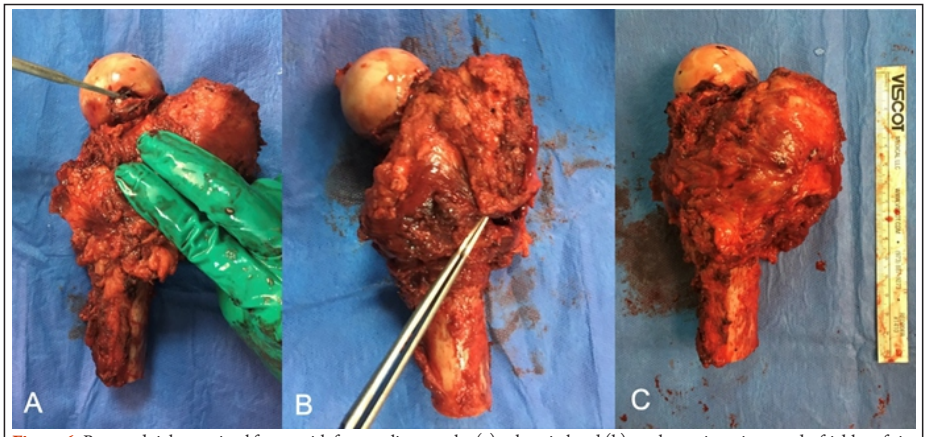


**Figure 6:** Resected right proximal femur with fracture lines on the (a) subcapital and (b) trochanteric regions, and a friable sof-tissue mass on the same areas with hemorrhagic areas ©.

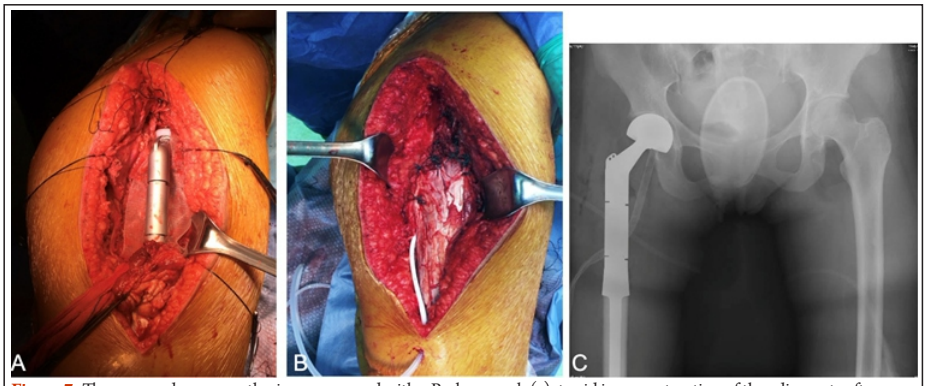


**Figure 7:** The cemened megaprosthesis was wrapped with a Prolene mesh (a), to aid in reconstruction of the adjaacent soft ssues (b); AP radiograph of the pelvis shows good placement of the implant (c).

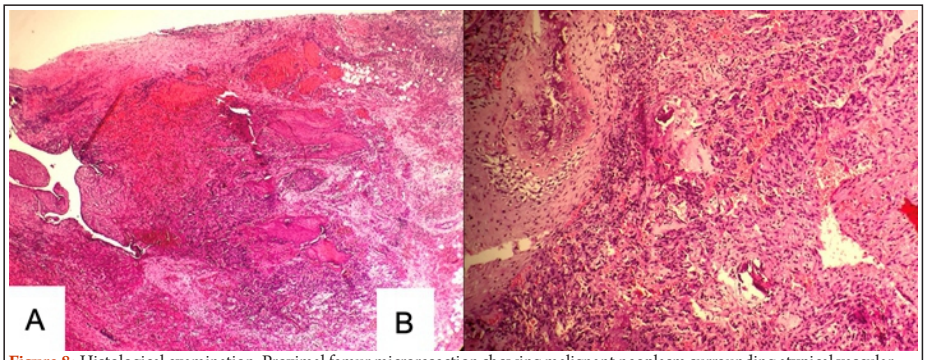


**Figure 8:** Histological examination. Proximal femur microresection showing malignant neoplasm surrounding atypical vascular spaces (a) and is composed of infltrating and complex anastomosing vascular channels lines by spindled cells. NNo significant motic count was noted (b).

carcinoma, which is the most common malignancy diagnosed in the breast. In cases of breast sarcomas, metastasis to the proximal femur occurs in <1% of cases [11].

Angiosarcoma is a subtype of sof-tissue sarcoma and is a malignant endothelial cell tumor. They re further subdivided into (1) cutaneous, (2) lymphedema-associated, (3) radiation-induced, (4) primary breast, and (5) sof-tissue angiosarcomas. Primary breast angiosarcoma is a rare and aggressive tumor that is known to recur locally and metastasize. Ths is evident in its histopathologic features in which it is described as a pleomorphic, malignant neoplasm with surrounding atypical vascular spaces composed of infltrating and complex anastomosing vascular channels lined by spindled cells. The histologically distinguishable low-grade variant, such as that seen in our patient, does not metastasize frequently, and has a 5-year disease-free survival rate of 76% [5]. The high-grade lesions, on the other hand, have poor prognosis with a 5-year survival rate as low as 10–15% [2, 12].

Patients with angiosarcoma of the breast present with localized disease (50–80%) and has a propensity for local recurrence [6]. Metastatic spread to distant sites may occur. It spreads hematogenously and nodal involvement is uncommon. Given its vascular origin, it has the tendency to spread rapidly especially to the lungs, with other organs involved including bone, soft tssues, and solid organs such as the liver. It has a rather poor prognosis particularly when the patient is diagnosed with metastases.

Distant metastases of angiosarcoma of the breast are diagnosed in 27–42% of patients and are ofen associated with a 75–89% mortality rate [6]. In the study of Wang et al., [7] among the 33 primary breast angiosarcomas, there was only one documented case of bone metastasis (3%), however, it has not been mentioned if this was a solitary bone affectation. Aside from this case series, to our knowledge, there are no other documented bone metastases from primary breast angiosarcoma.

Thre are no evidence-based guidelines to when it comes to treatment of primary breast angiosarcoma but according to the available literature, surgery consisting of modifid radical mastectomy with or without axillary lymph node dissection is still gold standard [1, 3, 13]. In the available literature regarding the management of proximal femur bone lesions with or without pathologic fracture, recommendation involves operative intervention through curettge or wide resection with stabilization options including intramedullary nailing, open reduction and internal fxation, or replacement [10, 14]. In lesions that are large, performing wide resection of solitary bone metastasis is advocated as treatment due to the decrease of local recurrence thereafeer [8]. The involvement of the proximal femur with the presence of pathologic fracture, extensive bony destruction such as our patient, and those lesions resistant to radiation therapy are good candidates for replacement [14]. Functional status and overall life expectancy are also considered; hence in younger patients, the option for use of a prosthesis is also offered as this provvides beer stabilization leading to immediate weight-bearing and early-onset rehabilitation. Pre-operative embolization of the feeding vessel is done as closely as possible – within 24 h – to the definiive surgery to avoid excessive bleeding intraoperatively given the vascular nature of the tumor [14].

Given the aggressive nature of this tumor and high propensity for both local recurrence and distant metastasis, a multimodal approach to treatment is advocated to improve the clinical outcomes of patients. Those tat undergo

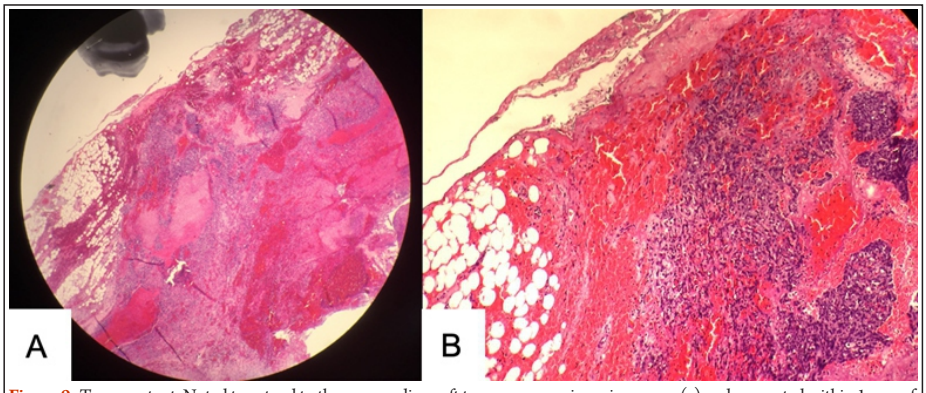


**Figure 9:** Tumor extent. Noted to extend to the surrounding soft tssues on scanning microscopy (a) and was noted within 1 mm of nearest sof-tissue margin in high-power view (b).

surgery or chemotherapy alone have unsatisfactory results [9]. An adequate surgery combined with the use of neoadjuvant and adjuvant chemoradiotherapy seems to improve the survival rate [15]. Although standard chemotherapeutic regimens and its effectiveness are not yet established, patients with high-grade tumor or those with high risk of recurrence may benefit rom adjuvant chemotherapy, with 48% response rate if given at the time of recurrence [15, 16]. Metastatic angiosarcoma may benefit rom different chemotherapeutic options including paclitaxel, similar to what was given to our patient. In a prospective study by Apice et al. [16] involving 32 patients diagnosed with advanced angiosarcoma treated with paclitaxel, the overall response rate was 62% with a median progression-free survival of 7.6 months. In our patient, however, despite adjuvant paclitaxel administration, there was note of an increase in size and extent distant metastases. Adjuvant radiotherapy has been reported to prevent local disease recurrence or distant metastasis in patients that are refractory to chemotherapeutic agents [12]. It has also been established to provide palliative treatment in controlling pain and bleeding, especially those presenting with cutaneous lesions [15], such as that in our case.

Local or distant recurrence from time of primary surgery averages to 27.5 months [3]. The atient presented with solitary proximal femur metastasis 31 months from the second modifid radical mastectomyy. Ts is similarly reported by Hosaka et al. [8], where the median disease-free interval from completion of treatment of primary breast cancer in general to detection of solitary bone metastasis was 35 months. They aso reported that the median metastatic free interval from completion of treatment of the solitary bone metastasis was 23 months. In contrast, our patient manifested with metastatic cutaneous lesions presented 3 months afer wide resection and replacement surgery.

Overall prognosis is poor at 10% 5-year survival rate [12]. The numbr of bone metastasis has no significnce in the overall survival, however, the presence of pathologic fracture and other skeletal related events (i.e., hypercalcemia and refractory pain) are associated with decreased overall survival [9]. In a retrospective study by Yu et al., patients with proximal femur metastasis manifesting with pathologic fracture treated with wide resection and endoprosthetic replacement have survival rates of 19.0, 11.4, and 3.8% at 1, 2, and 3 years, respectively [17]. Ths is more compared to a study by Sarahrudi et al. where survival rates are 16.2, 7, and 4% at 1, 2, and 3 years, respectively [18]. Despite these, however, tumor recurrence and metastasis were found to be an independent predictor of disease-free survival and an indicator of prognosis [7]. Primary breast angiosarcoma, although limited in data, is known to have poor prognosis, especially those presenting with metastasis.

## Conclusion

To date, there has been limited availability of literature regarding solitary metastasis to bone of primary breast angiosarcoma proving it is truly rare. It is vital to become familiar with both clinical and histological features of this disease entity to avoid a delay of definiti e treatment, considering the primary tumor in itself has high propensity for local recurrence and wide spread. Wide resection and prosthesis replacement of the proximal femur ofen controls local recurrence as stated in a small number of case reports, however, the patient in our case presented otherwise. The pesence of the pathologic fracture before definiti e treatment may have contributed to its distant recurrence, in addition to the aggressive nature of the primary malignancy. On the basis of this case report, control of both local recurrence and distant metastasis from primary angiosarcoma requires a multidisciplinary but ultimately individualized approach to prolong the survival and maintain the quality of life of such patients.

## Clinical relevance

Ths study provides additional information on the existing scarce data of primary angiosarcoma of the breast and its metastasis, which in itself is rare. A clear history, clinical course, and treatment done to a patient presenting with isolated skeletal metastasis from the aforementioned primary malignancy are discussed in detail. The dta presented can provide orthopedic oncology surgeons an option on how patients presenting with such can be evaluated and managed.

## References


1. Bordoni D, Bolletta E, Falco G, Cadenelli P, Rocco N, Tessone A, et al. Primary angiosarcoma of the breast. Int J Surg Case Rep 2016;20:12-5.

2. An I, Harman M, Ibiloglu I. Topical ciclopirox olamine 1%: Revisiting a unique antifungal. Indian Dermatol Online J 2017;10:481-5.

3. Kunkiel M, Maczkiewicz M, Jagiełło-Gruszfeld A, Nowecki Z. Primary angiosarcoma of the breast-series of 11 consecutive cases-a single-centre experience. Curr Oncol 2018;25:e50-3.

4. Bhosale SJ, Kshirsagar AY, Patil MV, Wader JV, Nangare N, Patil PP. Primary angiosarcoma of breast: A case report. Int J Surg Case Rep 2013;4:362-4.

5. Zahir ST, Sefidrokh Sharahjin N, Rahmani K. Primary breast angiosarcoma: Pathological and radiological diagnosis. Malays J Med Sci 2014;21:66-70.

6. Gaballah AH, Jensen CT, Palmquist S, Pickhardt PJ, Duran A, Broering G, et al. Angiosarcoma: Clinical and imaging features from head to toe. Br J Radiol 2017;90:20170039.

7. Wang L, Lao IW, Yu L, Wang J. Clinicopathological features and prognostic factors in angiosarcoma: A retrospective analysis of 200 patients from a single Chinese medical institute. Oncol Lett 2017;14:5370-8.

8. Hosaka S, Katagiri H, Honda Y, Wasa J, Murata H, Takahashi M. Clinical outcome for patients of solitary bone only metastasis. J Orthop Sci 2016;21:226-9.

9. Vincenzi B, Santini D, Schiavon G, Frezza AM, Dileo P, Silletta M, et al. Bone metastases in soft tissue sarcoma patients: A survey of natural, prognostic value, and treatment. J Clin Oncol 2012;30 Suppl 15:10063.

10. Guzik G. Oncological and functional results after surgical treatment of bone metastases at the proximal femur. BMC Surg 2018;18:2-9.

11. Li N, Cusidó MT, Navarro B, Tresserra F, Baulies S, Ara C, et al. Breast sarcoma. A case report and review of literature. Int J Surg Case Rep 2016;24:203-5.

12. Saimura M, Mitsuyama S, Anan K, Koga K, Ono M, Toyoshima S. A rare case of rapidly progressing angiosarcoma of the breast with multiple metastases to the bone, liver, ovary, and gingiva. Int Cancer Conf J 2012;1:159-63.

13. Soeharno H, Povegliano L, Choong PF. Multimodal treatment of bone metastasis-a surgical perspective. Front Endocrinol (Lausanne) 2018;9:518.

*14. Khattak MJ, Ashraf U, Nawaz Z, Noordin S, Umer M. Surgical management of metastatic lesions of proximal femur and the hip. Ann Med Surg (Lond) 2018;36:90-5.*

*15. Pramanik R, Gogia A, Malik PS, Gogi R. Metastatic primary angiosarcoma of the breast: Can we tame it the metronomic way. Indian J Med Paediatr Oncol 2017;38:228-31.*

*16. Apice G, Pizzolorusso A, di Maio M, Grignani G, Gebbia V, Buonadonna A, et al. Confirmed activity and tolerability of weekly paclitaxel in the treatment of advanced angiosarcoma. Sarcoma 2016;2016:6862090.*

*17. Yu Z, Xiong Y, Shi R, Min L, Zhang W, Liu H, et al. Surgical management of metastatic lesions of the proximal femur with pathological fractures using intramedullary nailing or endoprosthetic replacement. Mol Clin Oncol 2017;8:107-14.*

*18. Sarahrudi K, Hora K, Heinz T, Millington S, Vécsei V. Treatment results of pathological fractures of the long bones: A retrospective analysis of 88 patients. Int Orthop 2006;30:519-24.*

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