European Review for Medical and Pharmacological Sciences 2022; 26: 1299-1303

Primary highly differentiated breast angiosarcoma in an adolescent girl

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Abstract. – Primary angiosarcoma of the breast is very rare. Surgery is the principal mode of treatment for primary angiosarcoma of the breast and generally consists of a total mastectomy. To discuss its etiology and treatment principles, we reported a case of primary mammary angiosarcoma in an adolescent girl. The patient had been treated in other hospitals several times due to erythema of the breast as inflammatory treatment was considered, until pathological nature was determined after we performed pathological needle puncture. The case discussed here is unique in its own way, having clinical imaging and pathological features of primary angiosarcoma in an adolescent girl and it is known that primary angiosarcoma is unusual for this age group.

Key Words:
Primary angiosarcoma, Breast cancer, Adolescent girl.

Introduction

Primary angiosarcoma of breast accounts for 0. 05% of all breast malignancies, with rapid progression and poor prognosis[1,2]. Due to its non-specific clinical and imaging manifestations and different histopathological manifestations, it is difficult to accurately diagnose before surgery, often resulting in missed diagnosis and misdiagnosis. We report a case of primary angiosarcoma of the breast in a juvenile female. This is particularly rare. This paper discusses the diagnosis and treatment of primary angiosarcoma of the breast by reviewing the literature, in order to improve the understanding of clinicians to primary angiosarcoma of the breast and reduce misdiagnosis and mistreatment.

Case Report

A 17-year-old adolescent girl presented with a slow-growing painless mass in her right breast that had been present for 7 months. Physical examination revealed a slightly larger right breast than the contralateral breast without pain or nipple discharge. The breast mass spans the whole right breast (13 by 12 cm in size) with an unclear boundary and poor mobility, with two erythematous spots present on the skin. The skin temperature was normal. A cystic lesion of approximately 3 by 4 cm, surrounded by hardened tissue was evident below the larger erythematous spot (on the inner side of the right breast) (Figure 1). The patient's father died of non-Hodgkin's lymphoma of the breast, but she lacked other relevant breast or family histories.

The patient had been admitted to other hospitals in early June of 2020 for breast ultrasound examinations, which indicated right breast cystic solid nodules, inflammation, and BIRADS-3 classification. She was diagnosed as having inflammatory breast disease. Brown fluid (1.6 ml) was aspirated by fine needle puncture of the cystic area below the erythema on the medial side of the right breast at another hospital, and the pathological diagnosis was inflammatory lesions of the right breast. We admitted the patient to our hospital in August 2020 for examinations to rule out malignancy given the inflammatory erythema and painless mass. She underwent a breast enhancement MRI

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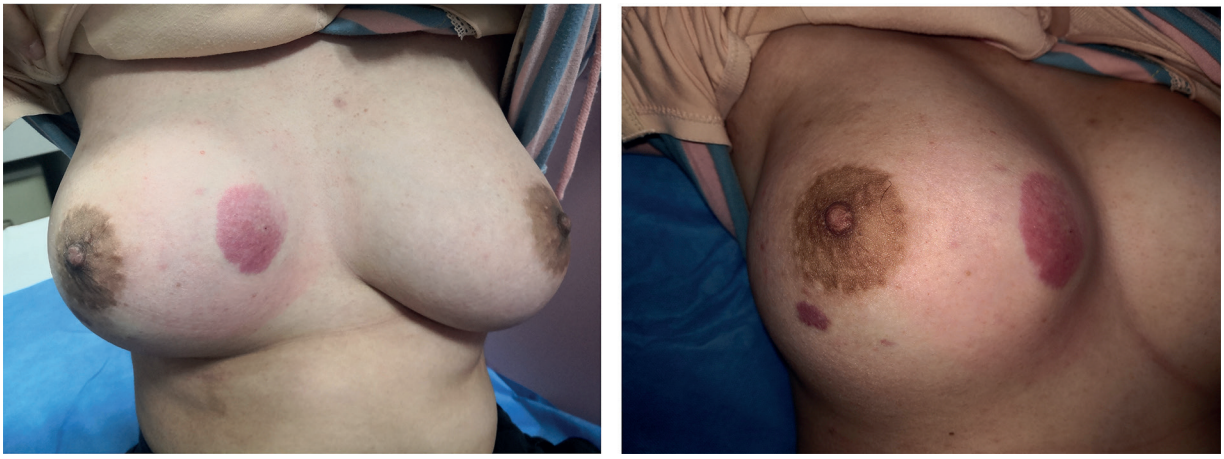

Figure 1. Breast pictures before the hollow needle puncture. Two distinct erythematous spots are present on the inside and below the areola of the right breast.

and breast mass puncture for histopathological and immunohistochemical examinations.

We found right breast diffuse non-mass enhancement lesions, multicentral masses and hyperintense and isointense lesions (Figures 2A and B). In addition, we identified a big heterogeneous hyperintense mass reflecting hemorrhage and diffuse non-mass enhancement lesions with multicentral masses in the right breast (BI-RADS 4) (Figures 2 C and D).

A biopsy was performed. The pathological results showed vascular hyperplasia. Most of the lumina were irregular and of different sizes, the focal areas were anastomotic, interspersed, growing within fibrous adipose tissue and interlobular interstitium. Local endothelial cells were heteromorphic. A low-grade angiosarcoma was suspected when considering angiogenic tumors by combining HE morphology and immunohistochemical results. Immunohistochemistry findings were as follows: CD34(+), CD31 (+), D2-40(-), Ki67 (20%+), FLI-1 (1+), ERG(+), AE1/AE3(-), c-MYC (locally weak +). Figure 3A shows vascular tissue proliferation around the duct with irregular lumina of varying sizes. The focal endothelial cells were slightly atypical. Figure 3B shows vascular tissue hyperplasia, irregular lumina, focal anastomosis, slightly abnormal local endothelial cells, and adipose tissue tumor infiltration.

We remitted the patient to another hospital for total breast resection. The final postoperative pathology indicated a primary angiosarcoma of the breast with highly differentiated tissue.

A family history of non-Hodgkin's lymphoma (the father of the patient had died of it the previous year) and the occurrence of breast angiosarcoma have not been reported. Whether an association between the two exists is worth investigating. Primary breast angiosarcoma is rare and difficult to diagnose clinically. Breast ultrasound and fine needle aspiration cytology during the early stages of the patient's disease were diagnostically ineffective and led to initial false-negative results after multiple patient visits. Accurate diseased tissue biopsy or surgery is the key to determining the diagnosis to avoid delaying the treatment. The differential diagnoses of primary breast angiosarcoma include benign hemangioma, metastatic sarcoma, fibrosarcoma, and liposarcoma. The final diagnosis still relies on pathological examination and no treatment standard exists. Total mastectomy remains the most effective treatment at present, but clinical retrospective studies are needed to confirm the effectiveness of the treatment.

Discussion

Primary angiosarcoma of the breast originates from the breast parenchyma, accounting for only 0.05% of breast malignancies. The etiology is not clear, and it tends to occur in young women with an average onset age of 40 years (range: 15-75 years). Most of the cases are unilateral[1,2]. Clinically, rapid enlargement of the painless mass is often the first symptom, with or without pain. When the tumor involves the skin, the skin may be blue purple, which is considered to be the specific clinical manifestation of breast angiosarcoma[3]. Clinically,

very few patients have no evident mass on physical examination, only presenting as subcutaneous persistent bleeding, accompanied by skin thickening and erythema. Due to the hidden clinical manifestations of the disease, diagnosis is difficult, easy to cause missed diagnosis or misdiagnosis. This case presented as a painless, rapidly increasing deep breast mass located in the breast parenchyma with pain and typical erythema changes on the skin. The patient had no history of malignant tumor or chest wall radiation therapy, which was consistent with the clinical manifestations of primary angiosarcoma of the breast.

According to the degree of tissue differentiation, who classifies it into highly differentiated, moderately differentiated and poorly differentiated angiosarcomas. It is divided into primary and secondary hemangiosarcoma according to different sites. Secondary hemangiosarcomas are usually caused by radiation therapy after breast sparing surgery. Primary hemangiosarcomas occur first in the breast parenchyma[4]. Primary angiosarcoma of the breast is rare and has a worse prognosis than invasive ductal carcinoma of the breast. It is also a breast tumor with a high misdiagnosis rate[5].

Conclusions

Hemangiosarcoma is highly malignant and insensitive to radiotherapy and chemotherapy.

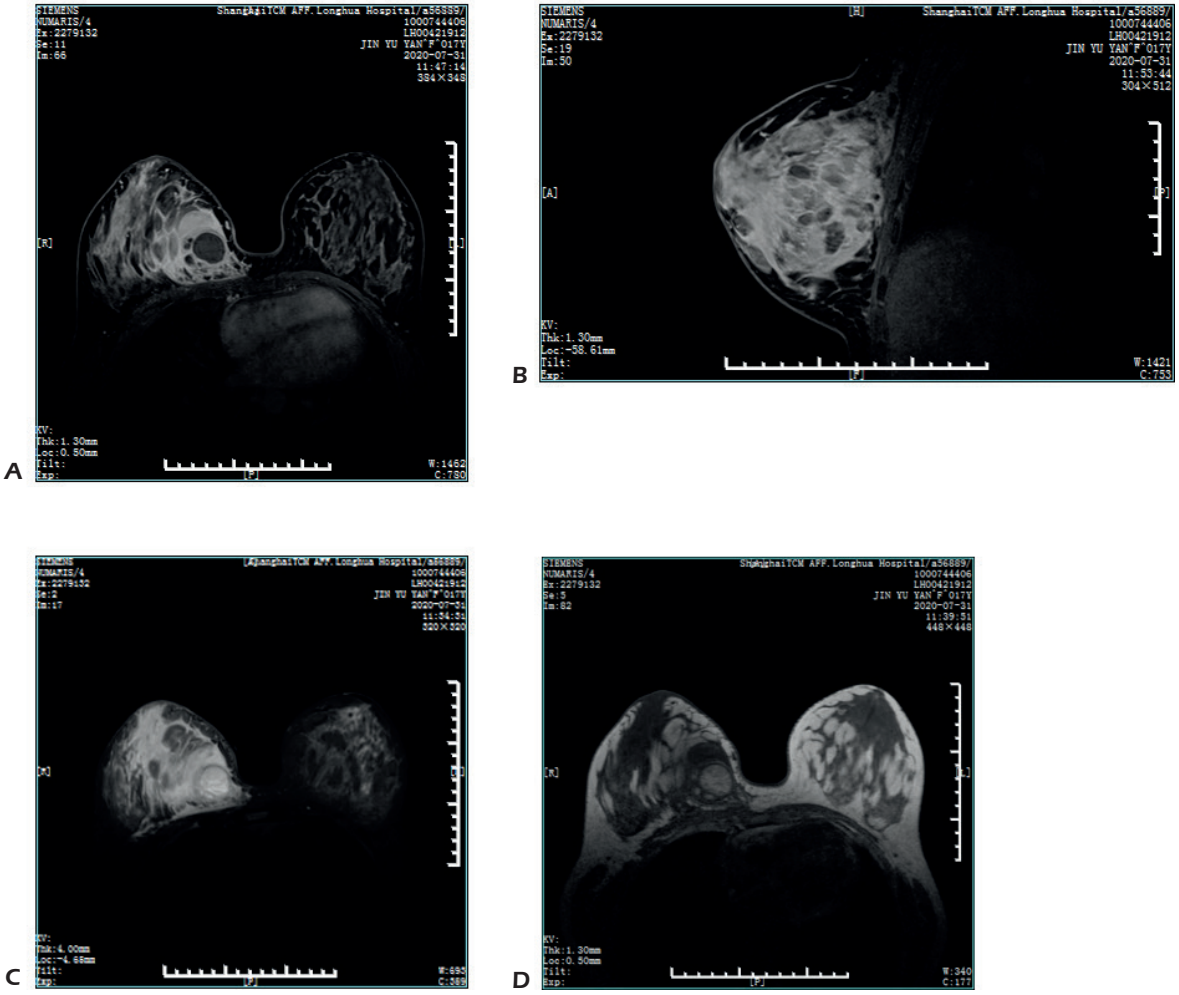

Figure 2. **A**, and **B**, Axial and sagittal T1-weighted images with fat saturation after gadolinium administration show diffuse non-mass enhancement lesions with mult icentral masses and a big adjacent rim enhanced mass with multiple small rim enhanced satellites in the upper inner quadrant (arrow). **C**, and **D**, Axial T2-weighted fat saturation and T1-weighted images show hyperintense and isointense lesions, respectively. A big heterogenous hyperintense mass with fluid-fluid levels and adjacent hyperintense small masses (arrow) in the upper inner quadrant reflects hemorrhage.

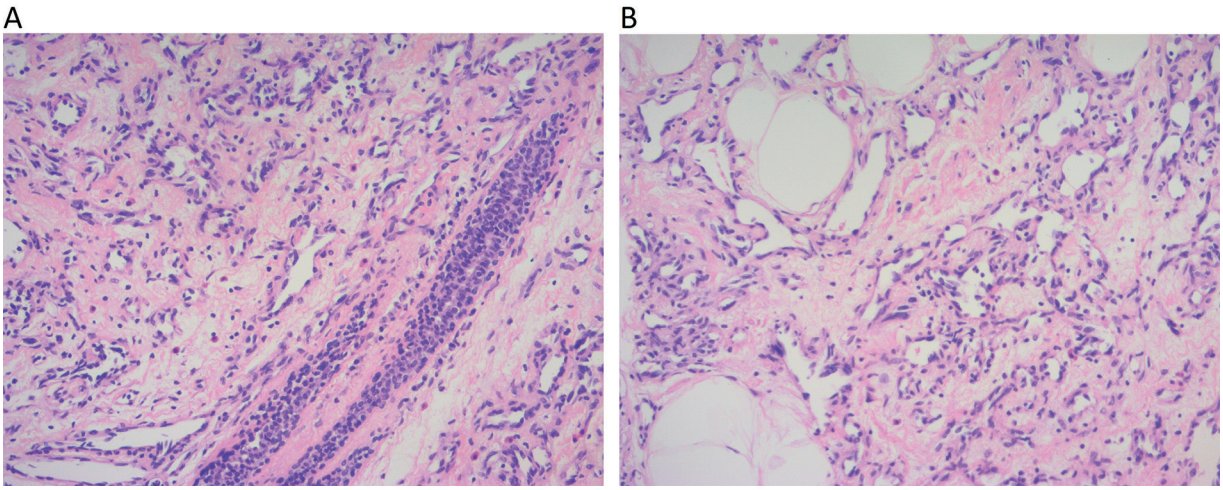

Figure 3. A, Vascular tissue proliferation around the duct. Irregular lumina of varying sizes. Slightly atypical focal endothelial cells (HE*200). **B,** Vascular tissue hyperplasia, irregular lumina, focal anastomosis, slightly abnormal local endothelial cells, and adipose tissue tumor infiltration (HE*200).

Complete surgical resection is the key to the treatment of local mammary hemangiosarcoma, which is also the most effective treatment currently recognized. About the choice of surgical method, Benevento et al[6] showed that patients' disease-free survival and overall survival were improved with resection to 5 cm of tumor margin. For larger tumors, this may seem impractical. Clinical breast angiosarcoma local staging generally relatively late, and the tumor has the characteristics of multicenter, lump expanded resection. It is difficult to achieve local control and postoperative local recurrence rate is extremely high. In addition, angiosarcoma is derived from the interstitial tissue, rare lymph node involvement, the axillary lymph node was so unusual, single mastectomy breast angiosarcoma is the first choice[7-9]. Axillary lymphadenectomy is not necessary because hemangiosarcomas tend to metastasize by vascular diffusion[10]. Clinically, angiosarcomas should be considered in young women with rapidly increasing tumors with abundant blood supply.

Authors' Contributions

Tian Meng was the patient's attending doctor and wrote the article. Yue Zhou was the patient's resident doctor. Jing-jing, Wei and Xiao-yun Zhang provided the pathological results. Qiu-feng Zhao analyzed the preoperative MRI results and radiological imaging data. Mei-na Ye was the patient's consultant and is the corresponding author of the article. She guided the writing of the article. All authors have read and approved the final manuscript.

Conflicts of interest

Authors Tian Meng, Mei-na Ye, Yue Zhou, and Qiu-feng Zhao declare having no conflicts of interest. Authors Jing-jing Wei and Xiao-yun Zhang declare having no conflicts of interest.

Ethical Approval

Not needed.

Informed Consent

We obtained informed consents from all individuals mentioned in the study. The patient and her mother reviewed and approved all of the contents of this manuscript.

Data Availability Statement

The data used to support the findings of this study are available from the corresponding author upon request.

Funding Information

This study was supported by the Construction project of Shanghai Association of Chinese Medicine Specialists (Special disease), grant/award number: ZY(2018-2020)-FWTX.

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