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Case Report

Case Report Primary Alveolar Rhabdomyosarcoma of the Breast in an Adult: An Extremely Rare Case

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Abstract

Background: Primary breast sarcoma (PBS) is rare, comprising approximately 1% of breast malignancies. Rhabdomyosarcoma (RMS) accounts for an extremely small proportion of PBSs, often leading to delayed histologic confirmation. RMS is common in children and adolescents and rare in adults. Primary RMS arising from the breast is exceedingly rare in adults. We report a case of a primary RMS of the breast in a 18 year-old woman, who presented in an advanced stage.

Key Words: alveolar rhabdomyosarcoma; Primary sarcoma of the breast

Introduction

Rhabdomyosarcoma (RMS), the most common pediatric soft tissue tumor, rarely occurs in the adult population. It represents less than 3% of all adult primary soft tissue sarcomas. The breast is an exceedingly rare primary site of occurrence and occurs mainly in children. We present here a case of alveolar, which was treated in our Cancer Institute according to the IRS III (Intergroup Rhabdomyosarcoma Study) protocol. To better understand the clinicopathological characteristics of these rare conditions, we searched and reviewed the literature related to this disease.

Case Presentation/Methods

Our Patient was a 18-year-old girl, who had a 10-cm mass in her left breast. Imaging examination at an outside hospital revealed a breast mass and multiple metastatic lesions in the lumbar spine and left axillary lymph nodes. She underwent core needle biopsy of the breast mass; the tumor was diagnosed as aRMS. After receiving the first neoadjuvant chemotherapy cycle, she was referred to our center and continued to receive the treatment for 8 cycles. However, MRI showed no change in the status of the left breast and metastatic masses. The patient underwent palliative mastectomy. The surgical specimen consisted of a lump of breast tissue that measured 9.5× 8.5×4 cm and weighed 114 g. A well-demarcated lobulating soft mass measuring 4×2.5×2 cm was identified in the breast parenchyma; the resection margins were clear. The mass was composed of nests and sheets of primitive round cells separated by fibrous septa. These nests exhibited a

central loss of cellular cohesion. IHC staining of the tumor cells yielded positive results for desmin , CD56, and myogenin and negative results for CK AE/AE3 and SMA. PAX3-FKHR (FOXO1) fusion transcripts [t(2;13)(q35;q14)] were identified using nested RT-PCR, supporting the diagnosis of aRMS. Post-surgery, she received eight chemotherapy cycles (carboplatin, VP-16, and ifosphamide), which was interrupted by fungal infection and low platelet counts. Followup imaging examination revealed recurrence of the chest wall mass and exacerbation of the multifocal bone metastasis with bone marrow involvement. The patient died due to respiratory suppression 22-month post-diagnosis.

Discussions

PBSs are a group of mesenchymal-derived de novo malignancies, accounting for less than 1% of breast cancer.4,10 Due to their rarity, large scale analyses have been limited, and PBS has no known etiology.4,11 Some breast sarcomas are related with previous treatment (radiation therapy, therapy-associated chronic lymphedema and variable chemicals), and they are categorized as secondary breast sarcoma.4,11,12 Thus far, angiosarcoma is the most commonly reported PBS; virtually any type of sarcoma can occur in the breast as a PBS.13 Based on our 18-year institutional experience, angiosarcoma is the most common type of PBS, followed by extra-skeletal osteosarcoma and liposarcoma. However, the distribution of PBS subtypes is not consistent across age groups; angiosarcomas were mostly found in middle-aged women (age, 40 to 60 years). Among young females (age, 10 to 30 years), angiosarcoma was rare. RMS was the most common subtype of PBS in this age group. Only 26 cases of RMS of breast origin have been reported in English literature, almost exclusively in the young females.7. Among the 29 cases, aRMS was the most common type (n= 17, 59%), followed by eRMS (n=6, 21%), ssRMS (n=2, 7%), and pleomorphic RMS (n=1, 3%). Subtype-related information was not available for three cases (n=3, 10%). All cases involved female patients; median age was 16.4 years (range, 11 to 60 years). Majority of the cases involved adolescents and young adults (range, 10 to 30 years; 24 cases, 83%); five cases (19.2%) involved middle-aged patients. All but one aRMS cases involved teenage girls; contrastingly, eRMS cases were almost equally distributed between adolescents and middle-aged women; the other RMS types mostly involved middle-aged patients. Interestingly, aRMS cases frequently presented with axillary lymphadenopathy, mimicking mammary carcinomas. To the best of our knowledge, the ssRMS case in this series is the second to be reported in the literature. ssRMS is a newly classified subtype that accounts for 5%–10% of all RMS cases; it mostly involves paratesticular lesions in pediatric populations and head and neck and genitourinary lesions in adults.8 As ssRMS was defined as a variant of eRMS, we reviewed all reports of eRMS for reclassification; however, none of the eRMS cases had

the histological characteristics that indicated ssRMS. Differential diagnoses vary according to RMS subtype, however, differentiation of malignant phyllodes tumor (MPT) with sarcomatous overgrowth is always important regardless of subtypes.2 Age can be used to differentiate these malignancies; most MPTs occur in the fifth or sixth decade of life, whereas primary RMS of the breast mainly affects young patients.3,14,15 Extensive tissue sampling is necessary, especially in middle-aged patients, as the epithelial component of the MPT can be very small.2 IHC results are critical after excluding MPT with sarcomatous overgrowth; single staining or a combination of desmin, MyoD1, and myogenin staining have been used to diagnose RMS. However, Parham et al.16 suggested that desmin should always be used as part of a panel and never as a sole diagnostic marker, as it can non-specifically stain other small round cells and smooth muscle cells. However, despite positive IHC results, the possibility of other myogenic neoplasms cannot be excluded in some cases; therefore, genetic analysis is useful for both histological typing and diagnosis.8 Two characteristic cytogenetic changes— t(2;13)(q35;q14) resulting in PAX3-FHKR (FOXO1) fusion and t(1;13)(p13;q14) resulting in PAX7-FKHR (FOXO1) fusion— are identified in about 80% of aRMS cases, which allow aRMS to be distinguished from other types of round cell neoplasms and RMS.8 These fusions are known to be associated with the activation of transcription from PAX3/PAX7-binding sites and to contribute to tumorigenesis.17 In the D9803 COG study, failurefree survival of fusion-positive aRMS patients was lower than that of fusion-negative patients, and PAX3-FKHR (FOXO1) fusion-positive patients showed higher overall survival than PAX7- FKHR (FOXO1) fusion–positive patients.17 Due to its rarity, definite treatment has not been established for RMS of the breast. Generally, axillary dissection of PBS is not recommended as sarcoma usually does not metastasize to lymph nodes; axillary dissection is only required in cases involving palpable lymphadenopathy. However, more than 50% of breast aRMS cases (12/17 cases, 71%) showed axillary node metastasis; moreover, 58% of these cases had no disseminated metastases (7/12 cases). These findings might suggest that axillary node metastasis of aRMS is not only incidental findings of disseminated metastasis, but also early event of disease spreading. Therefore, axillary node dissection or sentinel node sampling of aRMS needs to be considered in cases that require surgery.

Conclusion

RMS of the breast is an aggressive malignancy. Although very rare, it has to be thought of, as one of differential diagnoses, particularly in adolescent females. Small round cell malignancy in the breasts of young females should be suspected for the possibility of primary or secondary RMS. Although cytology is efficient in diagnosing small round cell tumors, a high index of suspicion, good knowledge of the cytological criteria

in conjunction with clinical and radiological fndings and immunochemical stains are prerequisites for the correct diagnosis. Histopathology remains the means for the defnitive diagnosis and formulation of treatment plan.

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