

Radiological Case Report / Caso Clínico

Primary Alveolar Rhabdomyosarcoma of the Breast in Adolescence: A Case Report*Rabdomiossarcoma Alveolar Primário da Mama em Adolescente: Um Caso Clínico***Beatriz Freixo¹, Alexandra Lapa², Joana Abreu¹, Mariana Afonso², Cláudia Carneiro Bilber¹, Susana Dias¹**

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Received: 06/09/2025**Accepted:** 28/06/2026**Published:** 02/09/2026**Abstract**

Primary alveolar rhabdomyosarcoma of the breast is an extremely rare malignancy with aggressive biological behaviour that occurs predominantly in adolescents. We report a case of a 15-year-old girl with progressive enlargement of the left breast. Radiological evaluation revealed an extensive breast lesion associated with ipsilateral nodal involvement, and histopathological and molecular analyses confirmed the diagnosis of FOXO1-positive alveolar rhabdomyosarcoma. This case illustrates the diagnostic challenges involved in distinguishing primary breast rhabdomyosarcoma from secondary breast involvement by metastatic disease and highlights the importance of integrating radiological, histopathological, and molecular findings for diagnosis, staging, and follow-up. Despite a partial response to neoadjuvant therapy and subsequent multimodal treatment, early disease progression was observed. This clinical course reflects the aggressive biological behaviour of FOXO1-positive alveolar rhabdomyosarcoma.

Keywords

Rhabdomyosarcoma, Alveolar; Breast neoplasms; Adolescent; Soft tissue Neoplasms; FOXO1 protein human.

Resumo

O rabdomiossarcoma alveolar primário da mama é uma neoplasia extremamente rara e com um comportamento biológico agressivo, que ocorre sobretudo em adolescentes. Apresentamos o caso de uma jovem de 15 anos com aumento progressivo da mama esquerda. A avaliação radiológica revelou uma extensa lesão mamária, associada a envolvimento ganglionar homolateral, e o estudo histopatológico e molecular confirmou o diagnóstico de rabdomiossarcoma alveolar FOXO1-positivo.

Este caso ilustra os desafios diagnósticos na distinção entre um rabdomiossarcoma primário da mama e o envolvimento mamário secundário e reforça a importância da integração dos achados radiológicos, histopatológicos e moleculares no diagnóstico, estadiamento e seguimento destes doentes.

Apesar da resposta parcial à terapêutica neoadjuvante e do tratamento multimodal subsequente, verificou-se progressão da doença, refletindo a agressividade biológica do rabdomiossarcoma alveolar FOXO1-positivo.

Palavras-chave

Rabdomiossarcoma alveolar; Neoplasias da mama; Adolescente; Neoplasias dos tecidos moles; Proteína FOXO1 humana.

Case Report

A previously healthy 15-year-old female adolescent presented to the emergency department with a one-month history left breast pain, progressive enlargement and abnormal firmness. She also reported nipple inversion, yellowish discharge, and restricted movement of the left upper limb due to discomfort. She denied fever, weight loss, or other constitutional symptoms.

Breast ultrasound performed at the referring hospital revealed a large heterogeneous mass, associated with ipsilateral skin thickening and multiple enlarged axillary lymph nodes. Ultrasound-guided core biopsies of the breast lesion and an axillary lymph node were performed. Histopathological analysis showed a densely cellular and highly proliferative malignant neoplasm, with areas of necrosis. Immunohistochemical studies using a broad panel of markers demonstrated diffuse immunoreactivity of desmin, myogenin and MyoD1. Genetic analysis revealed a rearrangement involving the FOXO1 gene (also known as FKHR, 13q14) (Figure 1). These findings supported the

diagnosis of alveolar rhabdomyosarcoma. Biopsy of the axillary lymph node showed metastatic involvement (Figure 2).

Thoracic computed tomography (CT) (Figure 3A) revealed a large breast-centred mass with preservation of the cleavage plane with the pectoralis major muscle and no evidence of chest wall invasion. No pulmonary metastases were identified. Fluorodeoxyglucose positron emission tomography - computed tomography (FDG PET-CT) (Figure 3B) confirmed intense, heterogeneous fluorodeoxyglucose uptake in the left breast and in ipsilateral axillary, supraclavicular, and internal mammary lymph nodes, with no evidence of distant metastases.

The patient was diagnosed with FOXO1-positive alveolar rhabdomyosarcoma of the left breast with ipsilateral axillary, supraclavicular and internal mammary lymph node metastasis. She began treatment according to the Children's Oncology Group protocol, including dose-compressed cycles of ifosfamide-etoposide and vincristine-doxorubicin-cyclophosphamide.

Post-chemotherapy breast magnetic resonance imaging (MRI) demonstrated a partial response (Figure 4), with

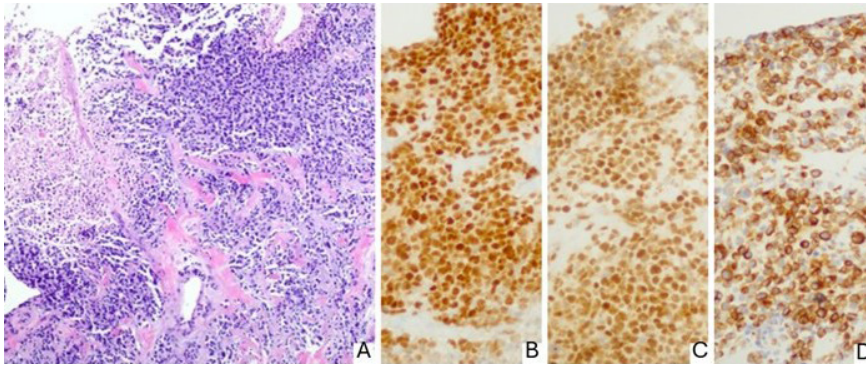


Figure 1 – Histological examination shows fragments of a densely cellular neoplasm, exhibiting multinodular growth. Cells are round, with hyperchromatic nuclei and scant, occasionally eosinophilic cytoplasm, arranged predominantly in solid aggregates within a dense stroma (A). The immunohistochemical study reveals diffuse positivity for myogenin (B), MyoD1 (C) and desmin (D).

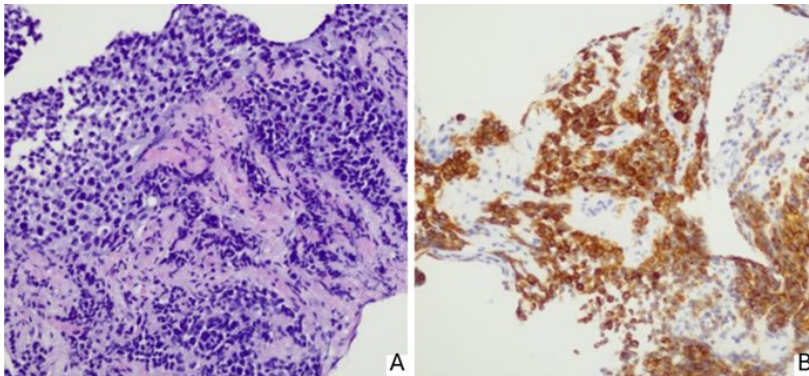


Figure 2 – Histological examination of the axillary lymph node reveals fragments infiltrated by alveolar rhabdomyosarcoma (A). Immunohistochemical study shows diffuse positivity for desmin (B).

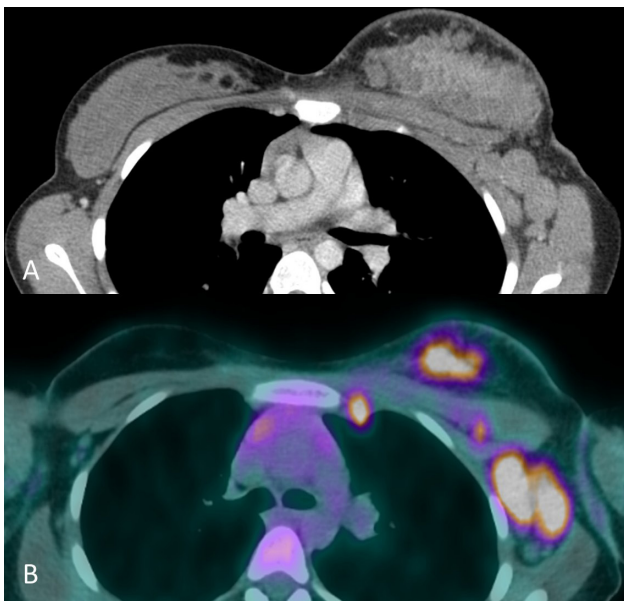


Figure 3 – Staging chest CT and FDG PET-CT. Chest CT (A) showing a large, lobulated, and heterogeneous left breast mass with diffuse skin thickening. The cleavage plane with the pectoralis major muscle is preserved. No pulmonary metastases were identified. FDG PET-CT (B) demonstrates intense and heterogeneous fluorodeoxyglucose uptake in the primary breast lesion and in ipsilateral axillary, supraclavicular, and internal mammary lymph nodes.

residual disease in the left breast and decreased axillary lymphadenopathies.

She underwent a left modified radical mastectomy with axillary lymph node dissection, followed by adjuvant chemotherapy and radiotherapy. Microscopically, the neoplasm involved all quadrants of the breast without skin or skeletal muscle involvement. A partial pathological response was observed, and surgical margins were uninvolved. Together with the absence of an alternative primary site on staging examinations, these findings further supported a primary mammary origin.

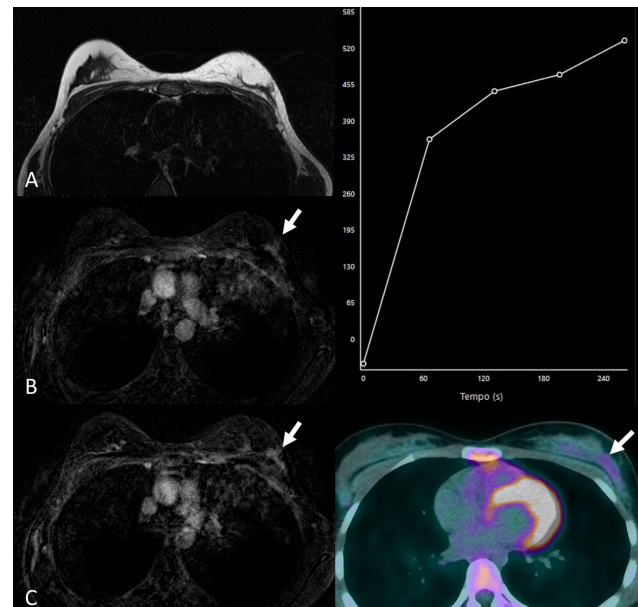


Figure 4 – Breast MRI and FDG PET-CT after neoadjuvant chemotherapy. Axial T2-weighted images (A) and dynamic contrast-enhanced subtraction images (B, C) demonstrate regional non-mass enhancement involving the upper quadrants of the left breast (arrows), with heterogeneous enhancement and a persistent (type I) kinetic curve (D). Correlation with FDG PET-CT findings (E) supports a partial tumour response (arrow).

Six months after surgery, follow-up MRI revealed a new lesion in the contralateral breast (Figures 5A and 5B). Targeted ultrasound (Figure 5C) and subsequent biopsy confirmed metastatic alveolar rhabdomyosarcoma.

Two months later, FDG PET-CT (Figure 6) demonstrated multiple areas of intense fluorodeoxyglucose uptake involving not only the right breast, but also the left mastectomy bed, and bilateral axillary lymph nodes, consistent with local recurrence and metastatic disease.

The patient declined further intravenous chemotherapy and was referred to palliative care.

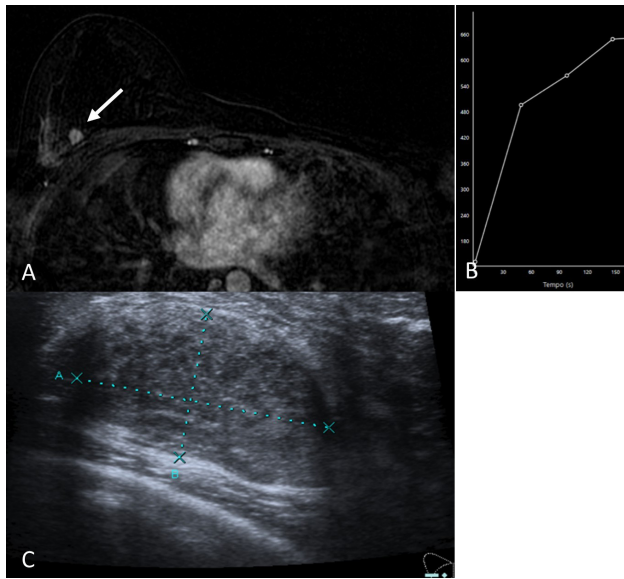


Figure 5 – Follow-up MRI and targeted ultrasound. Axial dynamic contrast-enhanced subtraction image (A) on follow-up revealed a new mass in the upper outer quadrant of the right breast (arrow), exhibiting a type I kinetic curve (B). Targeted ultrasound (C) was performed, and subsequent biopsy confirmed metastatic involvement of the contralateral breast.

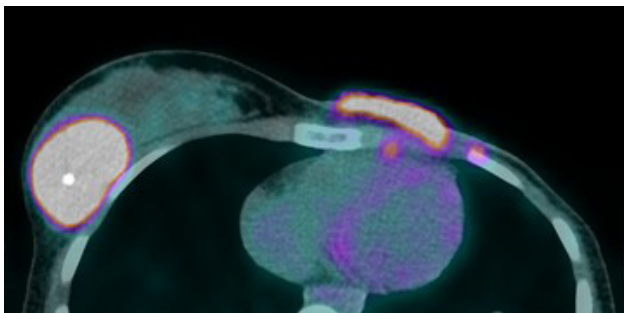


Figure 6 – Follow-up FDG PET-CT. Axial FDG PET-CT demonstrates intense fluorodeoxyglucose uptake within the left mastectomy bed, consistent with local recurrence, and in a nodular lesion of the contralateral breast, consistent with metastatic involvement.

Discussion

Primary breast rhabdomyosarcoma is extremely rare, representing less than 1% of all rhabdomyosarcoma cases,¹ with only 25 cases reported in the literature.² It occurs predominantly in adolescent females and is most commonly associated with the alveolar subtype, which is characterized by a greater propensity for metastatic dissemination and poorer outcomes than embryonal rhabdomyosarcoma.¹ Determining whether the breast represents the primary site of disease or a site of metastatic involvement is an important diagnostic consideration, as breast involvement may occur as a manifestation of metastatic alveolar rhabdomyosarcoma. In our patient, the absence of an alternative primary tumour on staging examinations, preservation of the cleavage plane with the pectoralis major muscle on CT, and pathological confirmation of extensive intramammary disease without skeletal muscle involvement supported a primary mammary origin.

From a breast imaging perspective, despite its location, alveolar rhabdomyosarcoma should not be approached according to conventional breast carcinoma paradigms.

Unlike epithelial breast malignancies, management is not driven by breast cancer molecular subtype or traditional breast cancer staging systems. Instead, diagnosis and treatment rely on sarcoma-specific histology, molecular characteristics, nodal involvement, and metastatic burden.³

Consequently, comprehensive locoregional and systemic staging are essential components of the diagnostic workup. Current recommendations consider MRI the preferred modality for locoregional assessment because of its superior soft-tissue contrast and ability to evaluate chest wall invasion, skin involvement, multifocal disease and contralateral lesions, while FDG PET-CT is recommended for the assessment of nodal, skeletal and distant metastatic disease.^{3,4} However, MRI was not performed at baseline in our patient, representing a limitation when assessing subsequent treatment response.

Recent advances in molecular classification have further refined prognostic stratification, with FOXO1 fusion status emerging as one of the most important biological predictors of outcome. Most alveolar rhabdomyosarcomas harbour PAX3-FOXO1 or PAX7-FOXO1 fusion genes, molecular alterations associated with increased metastatic potential, treatment failure and reduced survival.^{5,6} In contrast, fusion-negative alveolar rhabdomyosarcomas demonstrate biological behaviour and outcomes more closely resembling embryonal rhabdomyosarcoma.⁵ The prognostic significance of FOXO1 status is reflected in contemporary risk stratification systems, which integrate molecular, clinical and staging factors.^{5,6}

Our patient presented with multiple adverse prognostic features, including FOXO1-positive disease, age greater than 10 years, a large primary tumour, regional nodal involvement and an unfavourable primary site, consistent with a high-risk disease profile and likely contributing to the aggressive clinical course observed.⁷

Despite a locoregional partial response to neoadjuvant chemotherapy, complete surgical resection with negative margins and subsequent adjuvant treatment, our patient developed early contralateral breast metastasis followed by recurrence within the mastectomy bed. This clinical course is consistent with the adverse biological behaviour associated with FOXO1-positive disease and illustrates how tumour biology may outweigh conventional radiological and pathological indicators of treatment response.

Conclusion

Primary alveolar rhabdomyosarcoma of the breast is an exceptionally rare malignancy that poses important diagnostic and therapeutic challenges. Although arising within the breast, it should not be approached according to conventional breast carcinoma paradigms, requiring sarcoma-oriented histological, molecular and imaging assessment. In our patient, multimodality imaging, pathological evaluation and molecular characterization were essential to establish a primary mammary origin and guide staging and treatment planning. Despite multimodal therapy, the presence of FOXO1-positive disease and multiple adverse prognostic factors was associated with early disease progression, including contralateral breast metastasis and local recurrence within the mastectomy bed, highlighting the aggressive biological behaviour of this entity and the limitations of current therapeutic strategies.

Ethical Disclosures / Divulgações Éticas

Conflicts of interest: The authors have no conflicts of interest to declare.

Conflitos de interesse: Os autores declaram não possuir conflitos de interesse.

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Confidentiality of data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Confidencialidade dos dados: Os autores declaram ter seguido os protocolos do seu centro de trabalho acerca da publicação dos dados de doentes.

Protection of human and animal subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Proteção de pessoas e animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial.

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