IJHOSCR

Case Report

International Journal of Hematology-Oncology and Stem Cell Research

Bone Marrow Metastasis of Embryonal Rhabdomyosarcoma in an Adult, Confounding as Acute Leukemia: A Diagnostic Challenge

Shalini Singh[1], Jasmine Porwal[2], Karthik Kumar[2], Neha Singh[1], Uttam Kumar Nath[2]

[1]Department of Pathology and Lab Medicine, All India Institute of Medical Sciences, Rishikesh. Uttarakhand, India
[2]Department of Medical Oncology and Hematology, All India Institute of Medical Sciences, Rishikesh. Uttarakhand, India

Corresponding Author: Karthik Kumar, Department of Medical Oncology and Hematology, All India Institute of Medical Sciences, Rishikesh. Uttarakhand, India
E-mail: drkarthikkumar92@gmail.com

Received: 20, Sep, 2024
Accepted: 21, Dec, 2025

ABSTRACT

Rhabdomyosarcoma (RMS) is a primitive mesenchymal malignancy of childhood and is very rare in adults. In the presence of a soft tissue mass, bone marrow metastasis of RMS is easy to diagnose. However, RMS can rarely present with extensive marrow replacement, without an obvious primary-a very challenging situation for the pathologist as well as the clinician. Owing to the classical round cell morphology, metastatic RMS is morphologically indistinguishable from acute leukemia, especially when the cells are singly scattered, rather than in clusters. We report a rare presentation of bone marrow metastasis of embryonal RMS in an adult, who presented only with pancytopenia and leucoerythroblastic blood picture. Bone marrow aspiration revealed near total replacement of the hematopoietic elements by atypical blast-like cells, which were singly scattered as well as arranged in loose clusters focally. The case was worked up as acute leukemia. Flow cytometric immunophenotyping ruled out acute leukemia. The trephine biopsy was more in favor of a metastatic tumor; hence, a PET-CT was performed. The scan revealed diffuse uptake in the axial and appendicular skeleton, along with enlarged supraclavicular lymph nodes. An excision biopsy of the lymph node clinched the diagnosis of metastatic RMS, which was confirmed by immunohistochemistry for desmin and Myo-D1. This report highlights a rare case of adult embryonal RMS and emphasizes the importance of a multidisciplinary diagnostic approach for metastatic disease in this population.

Keywords: Acute leukemia; Bone marrow aspiration; Embryonal; Metastasis; Rhabdomyosarcoma

INTRODUCTION

Rhabdomyosarcoma is a primitive malignancy of mesenchymal origin that represents 50% of all soft tissue sarcomas in children and adolescents. The most common histological subtypes are embryonal and alveolar RMS[1]. The common sites of presentation of RMS are the head and neck, followed by the genitourinary and extremity regions. Alveolar RMS is characterized by a typical cytogenetic translocation that is t (2:13) (q35; q14) or t (1:13) (p36; q14), which results in PAX3-FOXO1 or PAX7-FOXO1 fusion, respectively. The estimated 5-year overall survival (OS) rate for non-metastatic Rhabdomyosarcoma (RMS) is approximately 65%. Among subtypes, the embryonal variant demonstrates a more favourable prognosis compared to alveolar RMS, with reported 5-year OS rates of 65–90% and 50–65%, respectively. The most common site of metastasis is the lungs. Approximately 20% of RMS can present with

Copyright © 2026 Tehran University of Medical Sciences. This work is licensed under a Creative Commons Attribution-Noncommercial 4.0 International License (http:// creativecommons.org/licenses/by-nc/4.0). Non-commercial uses of the work are permitted, provided the original work is properly cited.

metastasis at presentation[2,3]. However, extensive bone marrow infiltration by metastatic RMS in the absence of an identifiable primary tumor can be diagnostically challenging. We report a case of metastatic embryonal RMS in an adult patient who presented with pancytopenia and leucoerythroblastic blood picture, with bone marrow aspirate smears morphologically mimicking acute leukemia.

Case Presentation

A 31-year-old male presented with epistaxis and easy fatigability for one month. There was no history of fever, breathlessness, jaundice, rash, arthralgia, or weight loss. He had received random donor platelet (RDP) and packed red cell (PRBC) transfusions at a nearby hospital. On examination, he was pale with no organomegaly or lymphadenopathy.

Table 1: Laboratory Investigations

Parameters	Value
Hb (g/dl)	6.4
White cell counts (10^9/L)	3.7
Platelets (cu.mm)	26000
Serum LDH (<248) (U/L)	3829
Fibrinogen (mg/dl) (150-400)	50

The peripheral blood smear showed a leucoerythroblastic blood picture with 25–30 nucleated RBCs/100 WBCs, occasional macrocytes, polychromasia, basophilic stippling, lymphocytic predominance, and 2–3% blasts (Figure 1A). These findings prompted an evaluation for acute leukemia. Bone marrow aspiration and trephine biopsy revealed near-total replacement of hematopoietic elements by atypical blast-like cells, accounting for ~90% of the cellularity (Figure 1B, 1C). The abnormal cells were large, with round to convoluted nuclei, open chromatin, 2–3 prominent nucleoli, and moderate vacuolated basophilic cytoplasm, mimicking acute leukemia morphologically.

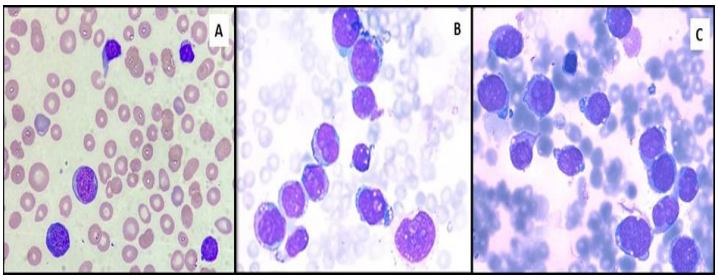

Figure 1. A) Peripheral smear (Leishman stain, ×400) showing leucoerythroblastic picture B) Bone marrow aspirate (Giemsa, ×1000) showing singly scattered blast-like cells C) Loose clusters of atypical cells.

Flow cytometry (BD FACS Canto II) using the stain-lyse-wash protocol revealed a CD45-dim/negative, low side-scatter population (~40%). These cells were positive for CD117, CD56, and negative for CD34, CD19, CD20, cytoplasmic CD3, CD5, CD7, CD13, CD33, MPO, and CD38—not consistent with acute leukemia.

Bone marrow biopsy showed fibrosis with diffuse infiltration by round-to-ovoid atypical cells, forming loose clusters and cords (Figure 2A, 2B). On IHC, the tumor cells were focally positive for CD163 and CD68, and negative for CD45 (Figure 2C), pancytokeratin (CK), MPO, CD3, CD19, CD34, TdT, INSM1, chromogranin, synaptophysin, and NSE. Findings raised suspicion for a metastatic malignancy; histiocytic tumors were considered in the differential.

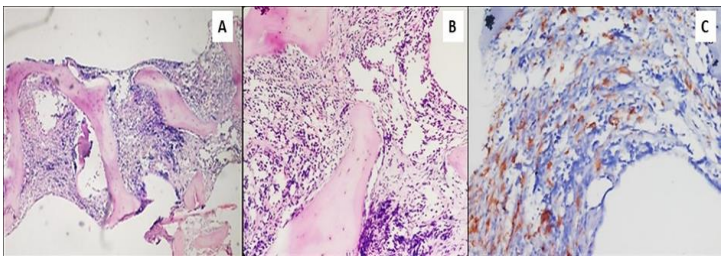

Figure 2. A) Bone marrow biopsy showing cells in fibrotic background (H&E, ×40); B) Low power showing atypical cells in cords/clusters (H&E, ×400); C) Negative CD45 staining on IHC (×400)

The above picture was more consistent with a metastatic malignancy. However, the possibility of a histiocytic tumor was kept as a close differential diagnosis.

PET-CT demonstrated diffuse skeletal uptake (axial and appendicular skeleton), including humerus, femur, pelvic bones, and a left supraclavicular lymph node (1.8 × 1.5 cm) along with a left testicular swelling.

Excision biopsy of the supraclavicular lymph node showed diffuse architectural effacement by tumor cells in sheets and lobules (Figure 3A, 3B). The tumor cells had irregular hyperchromatic nuclei, coarse chromatin, and scant cytoplasm. On IHC, the tumor cells were positive for desmin (Figure 3C) and MyoD1, and negative for CK (Figure 3D), CD45, CD20, CD3, TdT, S100, SALL4, NKX2.2, WT1, CD23, CD4, and synaptophysin, with a Ki-67 index of 90%. These findings were diagnostic of metastatic embryonal rhabdomyosarcoma (RMS).

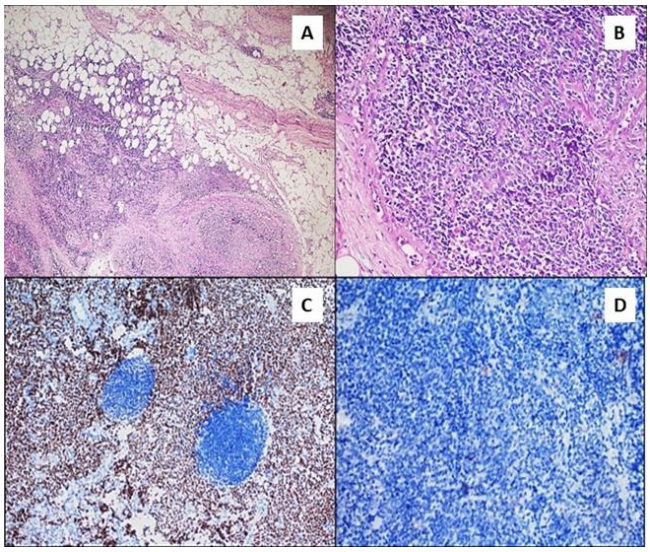

Figure 3. A) Lymph node biopsy with diffuse infiltration (H&E, ×40); B) High power shows hyperchromatic tumor cells (H&E, ×400); C) Positive IHC for MyoD1 (×400); D) Negative CK staining (×400)

Bone marrow karyotyping revealed a complex hyperdiploid karyotype with 60 chromosomes, including: Gains of Y, 2, 5, 7, 8, 11, 12, 17, 19, and 21, Three copies of t(2;11)(q37;q13), Derivative chromosome 9 due to t(1;9)(q21;q34) with 1q gain, Loss of one copy of chromosome 13.

The patient was initiated on VAC chemotherapy (Vincristine, Adriamycin, and Cyclophosphamide) every three weeks. He showed complete resolution of testicular and lymph node swellings after two cycles. However, after the fourth cycle, he developed severe neutropenia and succumbed to sepsis-related complications.

DISCUSSION

Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma in children and adolescents; however, it is exceedingly rare in adults. It arises from primitive mesenchymal cells with skeletal-muscle differentiation. The majority of cases occur in children under six years of age; they commonly involve the head and neck region and typically exhibit the embryonal subtype. In adolescents, RMS most often affects the extremities, where the alveolar subtype is more frequent; approximately 25% of patients present with distant metastasis at diagnosis. RMS generally spreads via the hematogenous route—most commonly to the lungs—but can also involve the bone marrow, lymph nodes, bones, liver, and brain [4,5].

Infrequently, RMS may present with features of disseminated intravascular coagulation (DIC) and can mimic acute leukemia—both clinically and morphologically—without an identifiable primary tumor or soft-tissue mass[5–9]. Similarly, our patient initially presented with pancytopenia and hypofibrinogenemia, without any detectable soft-tissue lesion.

Differentiating bone marrow metastasis from acute leukemia can be challenging based on morphology alone, especially when no primary tumor is evident. The blastoid morphology of RMS is characterized by primitive, round cells similar to leukemic blasts. Furthermore, when bone marrow aspirates are highly cellular and poorly spread, tumor cells may artifactually appear in loose clusters, which can be misinterpreted or overlooked by the pathologist. In our case, such clusters were initially not emphasized, reinforcing the impression of a leukemic process due to predominantly singly scattered atypical cells.

Flow cytometric immunophenotyping revealed malignant cells positive for CD56 and CD117, and negative for all lymphoid (B- and T-cell) and myeloid

markers—effectively ruling out acute leukemia. This immunophenotyping pattern may also be seen in neuroblastoma, small-cell carcinoma, neuroendocrine tumors, and rhabdomyosarcoma[10]. Nearly 99% of embryonal RMS cases express desmin and other reliable markers, including muscle-specific actin, myogenin, and myoglobin.

Unlike pediatric RMS, overall survival for adult RMS remains significantly poor, with an estimated 5-year overall survival rate of 20–40%. Factors such as advanced age, unfavorable histology, delayed presentation, treatment-related toxicity, and frequent metastatic spread are associated with poor survival. Most adult RMS patients are treated with pediatric-inspired protocols as per the Intergroup Rhabdomyosarcoma Study Group (IRSG). Current treatment involves a multidisciplinary approach, including surgery, radiotherapy (RT), and chemotherapy. Chemotherapy regimens based on cyclophosphamide/Ifosfamide and anthracyclines are associated with improved survival and a lower risk of disease progression. Response to chemotherapy is an important independent predictor of survival. Various groups have demonstrated that overall survival in adult RMS is around 40–50% [11-13].

Interestingly, most published cases of RMS presenting with leukemia-like features involve the alveolar subtype, which is associated with characteristic chromosomal translocations t(2;13)(q35;q14) and t(1;13)(p36;q14). In contrast, the embryonal subtype lacks specific chromosomal rearrangements [14]. Our case demonstrated complex cytogenetic abnormalities with chromosomal gains and structural rearrangements. Traditionally, bone marrow involvement in RMS is seen as part of widespread metastatic disease; however, an exclusive marrow presentation without a clinically detectable primary tumor remains a rarity.

CONCLUSION

This case underscores the importance of recognizing atypical presentations of RMS, particularly in adults, where it may mimic acute leukemia due to extensive bone marrow infiltration. It also emphasizes the need for a multidisciplinary diagnostic approach integrating morphology, immunophenotyping, histopathology, cytogenetics, and imaging for accurate diagnosis and appropriate management. Awareness of such rare presentations can prevent misdiagnosis and guide timely intervention.

REFERENCES

1. Chen J, Liu X, Lan J, et al. Rhabdomyosarcoma in adults: case series and literature review. Int J Womens Health. 2022, 28:405-14.

2. Bailey KA, Wexler LH. Pediatric rhabdomyosarcoma with bone marrow metastasis. Pediatr Blood Cancer. 2020;67(5):e28219.

3. Shinkoda Y, Nagatoshi Y, Fukano R, et al. Rhabdomyosarcoma masquerading as acute leukemia. Pediatr Blood Cancer. 2009, 52(2):286-7.

4. SEER cancer statistics review (CSR). Available: https://seer.cancer.gov/statistics/reports.html

5. Huang D, Watal P, Drehner D, et al. Rhabdomyosarcoma with diffuse done marrow metastases. Cureus. 2022;14(2):e21863.

6. Aida Y, Ueki T, Kirihara T, et al. Bone marrow metastasis of rhabdomyosarcoma mimicking acute leukemia: a case report and review of the literature. Intern Med. 2015;54(6):643-50.

7. Pasvolsky O, Heiman L, Popovtzer A, et al. Genomic analysis of metastatic rhabdomyosarcoma masquerading as acute leukemia. Pathol Res Pract. 2020 Jan;216(1):152779.

8. Sandberg AA, Stone JF, Czarnecki L, et al. Hematologic masquerade of rhabdomyosarcoma. Am J Hematol. 2001;68(1):51-7.

9. Ambrosiani L, Bellone S, Betto FS, et al: Rhabdomyosarcoma presenting as acute hematologic malignancy: case report and review of the literature. Tumori. 1996, 82(4):408-12.

10. Mechtersheimer G, Staudter M, Möller P. Expression of the natural killer cell-associated antigens CD56 and CD57 in human neural and striated muscle cells and in their tumors. Cancer Res. 1991;51(4):1300-7.

11. Elsebaie MA, Amgad M, Elkashash A, et al. Management of low and intermediate risk adult rhabdomyosarcoma: A pooled survival analysis of 553 patients. Sci Rep. 2018; 8(1):9337.

12. Dumont SN, Araujo DM, Munsell MF, et al. Management and outcome of 239 adolescent and adult rhabdomyosarcoma patients. Cancer Med. 2013;2(4):553-63.

13. Bisogno G, Compostella A, Ferrari A, et al. Rhabdomyosarcoma in adolescents: a report from the AIEOP Soft Tissue Sarcoma Committee. Cancer. 2012;118(3):821-7.

14. Lee DH, Park CJ, Jang S, et al. Clinical and cytogenetic profiles of Rhabdomyosarcoma with bone marrow involvement in Korean children: a 15-year single-institution experience. Ann Lab Med. 2018;38(2):132-138.