Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

A Congenital Malignant Rhabdoid Tumor Revealed By A Blue Berry Muffin Baby Syndrome Misdiagnosed As Bilateral Neuroblastoma: A Case Report.

Nabila Bouterfas

nabila.bouterfas@gmail.com

University of Algiers Benyoucef Benkhedda https://orcid.org/0009-0004-1628-1908

Faiza Oudjida

University of Algiers Benyoucef Benkhedda

Reda Kassa

University of Algiers Benyoucef Benkhedda

Brahim Belaid

University of Algiers Benyoucef Benkhedda

Aida Mohand-Oussaid

University of Algiers Benyoucef Benkhedda

Assia Slimani

University of Algiers Benyoucef Benkhedda

Ayed Belarbi

University of Algiers Benyoucef Benkhedda

Reda Djijik

University of Algiers Benyoucef Benkhedda

Asmahane Ladjouze

University of Algiers Benyoucef Benkhedda

Case Report

Keywords: rhabdoid tumor, aggressive, neonate, subcutaneous nodules, adrenal gland

Posted Date: August 10th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10619087/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: The authors declare no competing interests.

Abstract

Background

Malignant rhabdoid tumor (MRT) is a rare and highly aggressive malignancy of early childhood, most commonly arising in the kidney. Congenital bilateral adrenal involvement has not previously been reported.

Aim

We report a case of congenital bilateral adrenal MRT with extensive metastatic disease, initially misdiagnosed as advanced neuroblastoma, and rapidly complicated by fatal tumor lysis syndrome (TLS).

Methods

We describe the clinical presentation, diagnostic workup, treatment, and outcome of a neonate diagnosed with congenital bilateral adrenal MRT.

Results

A 16-day-old female neonate presented with a left lumbar subcutaneous nodule. At examination she had multiple bluish subcutaneous nodules and progressive abdominal distension. Imaging revealed bilateral adrenal masses, hepatomegaly with nodular lesions, and multiple osteolytic bone lesions. Laboratory investigations showed markedly elevated lactate dehydrogenase (LDH) levels and bone marrow infiltration by undifferentiated round cells, while urinary catecholamines were normal. A diagnosis of stage IV neuroblastoma was initially suspected. The patient rapidly deteriorated, developing brain metastases and severe tumor lysis syndrome, leading to death within a few days. Histopathological examination of a subcutaneous nodule demonstrated malignant rhabdoid tumor, confirmed by loss of INI1 expression on immunohistochemistry.

Conclusion

Congenital adrenal MRT is an exceptionally rare and aggressive malignancy that may closely mimic neuroblastoma in neonates. Early consideration of MRT and prompt histopathological confirmation are essential, although prognosis remains extremely poor in this age group.

Take-Home Message

A particularly aggressive course in a patient with a congenital adrenal tumor comprising small undifferentiated round cells should prompt consideration of MRT diagnosis and the use of immunohistochemical studies.

Introduction

Malignant rhabdoid tumor (MRT) is a rare and highly aggressive malignancy most often diagnosed during infancy. Although it can arise in many anatomical locations, the kidney remains the most commonly reported primary site. According to the World Health Organization (WHO) classification, MRT is defined morphologically by the presence of large rhabdoid cells with abundant cytoplasm, perinuclear eosinophilic inclusions, eccentric vesicular and prominent nuclei[1]. Genetically, MRT is characterized by bi-allelic inactivation of the tumor suppressor gene SMARCB1(previously known as hSNF5, BAF47, and INI-1) located on chromosome 22q11.2. This inactivation is caused by mutations, deletions or duplications resulting in a truncated protein and is demonstrated immunohistochemically by complete loss of nuclear INI-1 expression [1]. Congenital adrenal tumors may be particularly challenging to diagnose, as neuroblastoma represents the most frequent solid tumor in this age group and often presents with similar clinical and radiological features [2]. To the best of our knowledge, no cases of synchronous bilateral adrenal MRT diagnosed at birth have been previously reported. We herein describe the first reported case of a congenital bilateral adrenal MRT in a newborn, revealed by blueberry muffin baby syndrome and initially misdiagnosed as advanced neuroblastoma.

Case Description

A female infant was born at 41 weeks of gestation after an uncomplicated spontaneous pregnancy. There was no family history of malignancy, and third-trimester prenatal ultrasound examinations were unremarkable. At birth, the neonate had normal anthropometric measurements, with a weight of 3400 g and a length of 49 cm. Initial physical examination revealed a single red subcutaneous nodule in the left lumbar region. On day 6 of life, ultrasonography demonstrated a small subcutaneous cystic lesion measuring 9.6 × 6.7 mm, which was initially suspected to be a hemangioma. At 16 days of age, the patient was referred to our institution because of the rapid increase in the number of subcutaneous nodules and progressive abdominal distension. Clinical examination on admission revealed multiple bluish-purple subcutaneous nodules measuring between 35 and 67 mm, distributed over the neck, back, and limbs, associated with marked hepatomegaly (Figure 1). Neurological examination was initially normal. Imaging studies revealed bilateral adrenal masses measuring 56 mm and 32 mm, containing calcifications, along with multiple nodular lesions in the liver and retroperitoneal space. Skeletal radiographs demonstrated multiple osteolytic bone lesions. Initial laboratory work-up showed isolate anemia at 10.9 g/dl (range 15.6+/- 2.6) [3], white blood cells 16,740/mm^3, platelets 342.10^3/mm^3, and normal peripheral smear, but bone marrow examination revealed undifferentiated round cells. Laboratory studies showed hypercalcemia at 11.3 mg/dL (range 9-10.6) [4] and markedly elevated LDH (7 times normal). Other biochemical parameters, including uric acid, renal function, blood urea nitrogen,

electrolytes, bilirubin, and liver enzymes, were normal. Viral serologies (HIV, HCV, HBV) and syphilis testing were negative. Urinary catecholamines were not elevated, nevertheless MIBG scanning could not be performed. Based on these findings, stage 4 congenital bilateral adrenal neuroblastoma(NBL) was suspected at first. Chemotherapy including carboplatin and etoposide was initiated. However, within five days, the patient's condition deteriorated significantly, developing focal seizures and worsening abdominal distension. Brain CT revealed multiple metastases. Laboratory tests showed evidence of tumor lysis syndrome (TLS) with marked abnormalities including hyperuricemia (21.2 mg/dL) (range 1,0 – 7,0), hypocalcemia (6.7 mg/dL), hyperphosphatemia (7.8 mg/dL, normal range 4.3-7.3), hyperkalemia at 6.7 mEq/L(range 3,9 - 5,9), and elevated creatinine levels (1. 8mg/dL, normal range 0,2 - 0,4) [4]. Despite supportive care measures, the patient died rapidly due to progressive and unresponsive disease. Histopathological examination of a biopsy obtained from a subcutaneous nodule showed sheets of malignant cells with abundant eosinophilic cytoplasm containing hyaline globules, vesicular chromatin, and prominent nucleoli. Immunohistochemical analysis demonstrated negativity for myogenin, CD99, and desmin, with complete loss of nuclear INI1 expression, confirming the diagnosis of malignant rhabdoid tumor.

Discussion

Rhabdoid tumor is a rare and highly aggressive embryonal malignant neoplasm affecting mainly infants and young children, with a peak age at diagnosis between 12 and 35 months [5]. This entity was first described by Beckwith as a particular malignant neoplasm of the kidney with a very poor outcome [6]. Incidence remains still unknown with only a few reports of limited series throughout the world, and publications regarding newborns are even rarer highlighting the importance of our observation [5,7, 8]. In addition to kidney involvement, rhabdoid tumors can also occur in soft tissues outside the kidney and in the central nervous system (CNS), those are referred to as atypical teratoid/ rhabdoid tumors (ATRT)[9]. Despite the rarity of soft tissues involvement [10], patients present with a large spectrum of anatomical localizations including subcutaneous tissue, liver, lung, orbit, bladder, ... The first case of MRT involving adrenal gland was reported by Yaris et al, two decades ago, in a 3-year-old boy presenting with a large abdominal mass and a left pleural effusion, suggesting neuroblastoma (NBL) at first [11]. Recently, Nemes et al reported adrenal involvement with a frequency of 1% in infants aged less than 6 months [5]. Interestingly, in addition to the extreme rarity of such tumor at this age, the exceptional adrenal location, herein, we report on a neonate with a congenital MRT, unusual revealing mode and a particular rapid aggressive course mimicking an aggressive congenital NBL. The failure to identify the tumor in this patient prenatally can be attributed to its extremely rapid development during the terminal phase of pregnancy. This is the first case report of a synchronous bilateral adrenal MRT location in a newborn.

There have been dramatic improvements in the understanding of MRT. Recent results suggest that patients with germline mutations or deletions affecting SMARCB1 are predisposed to develop MRTs. SMARCB1 is identified as a member of the SWI/SNF chromatin-remodeling complex and functions as a tumor suppressor in the majority of patients with such tumors [12]. Clinically, genetically predisposed patients are more likely to present with multifocal primary tumors and CNS involvement, especially

within the first year of life [12]. The clinical features in our case including age at diagnosis, bilateral adrenal disease, and multiple distant metastases especially to the CNS are consistent with these findings. Compared to other pediatric malignancies, it is well known that MRT is a fast-growing neoplasm with a high potential to metastasize early[7]. Metastases mainly involve the lymph nodes, lungs, peritoneal area, liver and the central nervous system [13, 14], while subcutaneous metastases those were the presenting signs in our case are exceptional and are described in neonatal forms especially [15, 16]. Clinically, designed as «Blue Berry Muffin Baby Syndrome», this syndrome, manifesting as bluish, red, brown, or purple subcutaneous nodules in newborns, can be associated with various underlying conditions including infections, benign tumors, malignancies, and acute leukemia especially nammed Leukemia cutis [17, 18]. Diagnosis can be difficult when the patient presents with an isolated skin lesion suggestive of an hemangioma[19], as described in our case. Only a few cases of congenital MRT with cutaneous involvement as first presentation are previously reported in neonates [15, 16, 20]. This revealing location raises questions regarding its primary versus metastatic status in this observation. However, with the rapid progression and subsequent appearance of hepatomegaly associated with imaging data revealing bilateral adrenal tumor and osteomedullary involvement, based on the relative incidence of neuroblastoma at this age as well as the clinical presentation, diagnosis of stage 4 neuroblastoma seemed the most likely. Later, histological examination of transcutaneous needle biopsy specimen revealed definitive diagnosis of MRT. A similar situation has also been reported by Yaris et al[11]. In addition to particular clinical revealing symptoms, our patient demonstrated hypercalcemia at admission a well-recognized feature occurring in 4 to 18% of the cases[14].The occurrence of tumor lysis syndrome, however, was exceptional, as this complication is predominantly associated with hematological malignancies rather than solid tumors[21]. Due to their rarity and aggressive nature, MRT management remains challenging, and no standard therapy has been defined except in cases with renal involvement. Treatment of such tumors consists on multimodality therapy including chemotherapy, surgery, radiation, in addition to myeloablative therapy with stem cells rescue. Currently, the most common chemotherapy regimens include platinum agents, epipodophyllotoxins, vinca alkaloids, alkylants, methotrexate, and anthracyclines [7]. Despite receiving a combination chemotherapy with platinum agents, etoposide and supportive care, our patient died rapidly due to progressive disease and complications of tumor lysis syndrome. Prognosis remains very poor in patients with 5-year survival rate of 20% despite intensive therapeutic [10]. Prognostic factors defining outcome in children with MRT are not clearly identified, and remain strictly clinical, including age at diagnosis, primitive tumor site and the presence of metastases. MRT originating from kidney and those arising in older children are associated with a better outcome while advanced stages (Stage III and IV) had a significantly poorer prognosis[7, 22]. However, the presence of germline mutations has recently been identified as a significant prognostic factor [5]. This case illustrates the difficulties in distinguishing MRT from other adrenal tumors in neonates in the absence of immunohistochemical study. These tumors continue to have an extremely poor prognosis being one of the most challenging malignant neoplasms for the pediatric oncologist.

Conclusion

This is a complex clinical case, typical of an aggressive neonatal malignant rhabdoid tumor.

A particularly aggressive course in a patient with a congenital adrenal tumor comprising small undifferentiated round cells should prompt consideration of MRT diagnosis and the use of immunohistochemical studies. Despite remarkable advances in treatment options, behaviour remains very poor especially in neonates. Collaborative studies will undoubtedly allow a better understanding of underlying molecular mechanisms to develop more effective treatment strategies and to improve survival rates in children with these tumors.

Abbreviations

ATRT: Atypical teratoid/ rhabdoid tumors; CNS: Central nervous system; LDH: Lactate dehydrogenase; MIBG : Metaiodobenzylguanidine; MRT: Malignant rhabdoid tumor; NBL: Neuroblastoma ; TLS: Tumor lysis syndrome; WHO: World Health Organization.

Declarations

Ethical Approval: As a retrospective study, Ethics Approval is not required in our institution.

Patient consent. Hereby, it is confirmed that informed consent was obtained from the guardians of this patient for the use of diagnostic images and related clinical information for publication purposes. The patient's identity has been kept confidential in this manuscript and will not be disclosed at any time during or after publication.

Conflict of interest. The authors declare no conflicts of interest regarding the publication of this paper.

Aknowledgement. During the preparation of this manuscript, the author used Claude (Anthropic, version Claude Sonnet 4.6, 2025) to assist with English language reformulation and editing of certain sections. After using this tool, the author thoroughly reviewed and edited the content as necessary. The author takes full responsibility for the accuracy, integrity, and originality of the published work."

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

References

1. WHO Classification of Tumours Editorial Board. Soft tissue and bone tumours. 5th ed. Lyon: International Agency for Research on Cancer; 2020. Available from: https://publications.iarc.fr/Book-And-Report-Series/B/WHO-Classification-Of-Tumours/Soft-Tissue-And-Bone-Tumours-2020.
2. Isaacs H Jr. Congenital and neonatal malignant tumors. A 28-year experience at Children's Hospital of Los Angeles. Am J Pediatr Hematol Oncol. 1987;9(2):121-9.

3. Maheshwari A, Carlo WA. Blood disorders. In: Kliegman RM, St Geme JW, Blum NJ, Shah SS, Tasker RC, Wilson KM, editors. Nelson textbook of pediatrics. 20th ed. Philadelphia: Elsevier; 2016. p. 880-7.
4. Pagana KD, Pagana TJ, Pagana TN. Mosby's diagnostic and laboratory test reference. 17th ed. St. Louis: Elsevier; 2024.
5. Nemes K, Bens S, Kachanov D, Teleshova M, Hauser P, Simon T, et al. Infants and newborns with atypical teratoid rhabdoid tumors (ATRT) and extracranial malignant rhabdoid tumors (eMRT) in the EU-RHAB registry: a unique and challenging population. Cancers (Basel). 2022;14(9):2185.
6. Beckwith JB, Palmer NF. Histopathology and prognosis of Wilms tumors: results from the First National Wilms' Tumor Study. Cancer. 1978;41(5):1937-48.
7. Reinhard H, Reinert J, Beier R, Furtwängler R, Alkasser M, Rutkowski S, et al. Rhabdoid tumors in children: prognostic factors in 70 patients diagnosed in Germany. Oncol Rep. 2008;19(3):819-23.
8. Heck JE, Lombardi CA, Cockburn M, Meyers TJ, Wilhelm M, Ritz B. Epidemiology of rhabdoid tumors of early childhood. Pediatr Blood Cancer. 2013;60(1):77-8.
9. Palmer NF, Sutow W. Clinical aspects of the rhabdoid tumor of the kidney: a report of the National Wilms' Tumor Study Group. Med Pediatr Oncol. 1983;11(4):242-5.
10. Oda Y, Tsuneyoshi M. Extrarenal rhabdoid tumors of soft tissue: clinicopathological and molecular genetic review and distinction from other soft-tissue sarcomas with rhabdoid features. Pathol Int. 2006;56(6):287-95.
11. Yaris N, Dilber E, Ahmetoglu A, Saruhan H, Okten A. Malignant rhabdoid tumor of adrenal gland. Med Pediatr Oncol. 2002;39(2):128-31.
12. Geller JI, Roth JJ, Biegel JA. Biology and treatment of rhabdoid tumor. Crit Rev Oncog. 2015;20(3-4):199-216.
13. Fernandez C, Bouvier C, Sevenet N, Liprandi A, Coze C, Lena G, et al. Congenital disseminated malignant rhabdoid tumor and cerebellar tumor mimicking medulloblastoma in monozygotic twins: pathologic and molecular diagnosis. Am J Surg Pathol. 2002;26(2):266-70.
14. Weeks DA, Beckwith JB, Mierau GW, Luckey DW. Rhabdoid tumor of kidney. A report of 111 cases from the National Wilms' Tumor Study Pathology Center. Am J Surg Pathol. 1989;13(6):439-58.
15. Isaacs H Jr. Fetal and neonatal rhabdoid tumor. J Pediatr Surg. 2010;45(3):619-26.
16. Dominey A, Paller AS, Gonzalez-Crussi F. Congenital rhabdoid sarcoma with cutaneous metastases. J Am Acad Dermatol. 1990;22(5 Pt 2):969-74.
17. Fraitag S, Bodemer C. Nodules multiples chez un nouveau-né. Ann Dermatol Venereol. 2009;136(2):211-3.
18. Mehta V, Balachandran C, Lonikar V. Blueberry muffin baby: a pictorial differential diagnosis. Dermatol Online J. 2008;14(2):8.
19. Albregts AE, Hebert AA, Aboul-Nasr RA. Malignant rhabdoid tumor presenting as a hemangioma. Pediatr Dermatol. 1996;13(6):468-71.

20. Hsueh C, Kuo TT. Congenital malignant rhabdoid tumor presenting as a cutaneous nodule: report of 2 cases with review of the literature. Arch Pathol Lab Med. 1998;122(12):1099-102.
21. Howard SC, Jones DP, Pui CH. The tumor lysis syndrome. N Engl J Med. 2011;364(19):1844-54.
22. Tomlinson GE, Breslow NE, Dome J, Guthrie KA, Norkool P, Li S, et al. Rhabdoid tumor of the kidney in the National Wilms' Tumor Study: age at diagnosis as a prognostic factor. J Clin Oncol. 2005;23(30):7641-5.

Tables

Table 1

Clinical profile of neonatal-onset rhabdoid tumor in our patient

Parameters	Characteristics
Initial manifestation at birth	Isolated red subcutaneous nodule
Involved sites (Staging)	Bilateral adrenal glands, liver, retroperitoneum, osteo-medullar, CNS, and subcutaneous tissues
Biological findings	Anemia; Bone marrow infiltration by undifferentiated cells, Hypercalcemia, Elevated LDH (7 N)
Metabolic complications	Tumor Lysis Syndrome (TLS): Hyperuricemia, hyperphosphatemia, hypocalcemia, hyperkalemia, and acute kidney injury (elevated creatinine)
Chemotherapy regimen	Carboplatin and Etoposide
Clinical outcome	Rapid disease progression leading to a fatal outcome

Figures

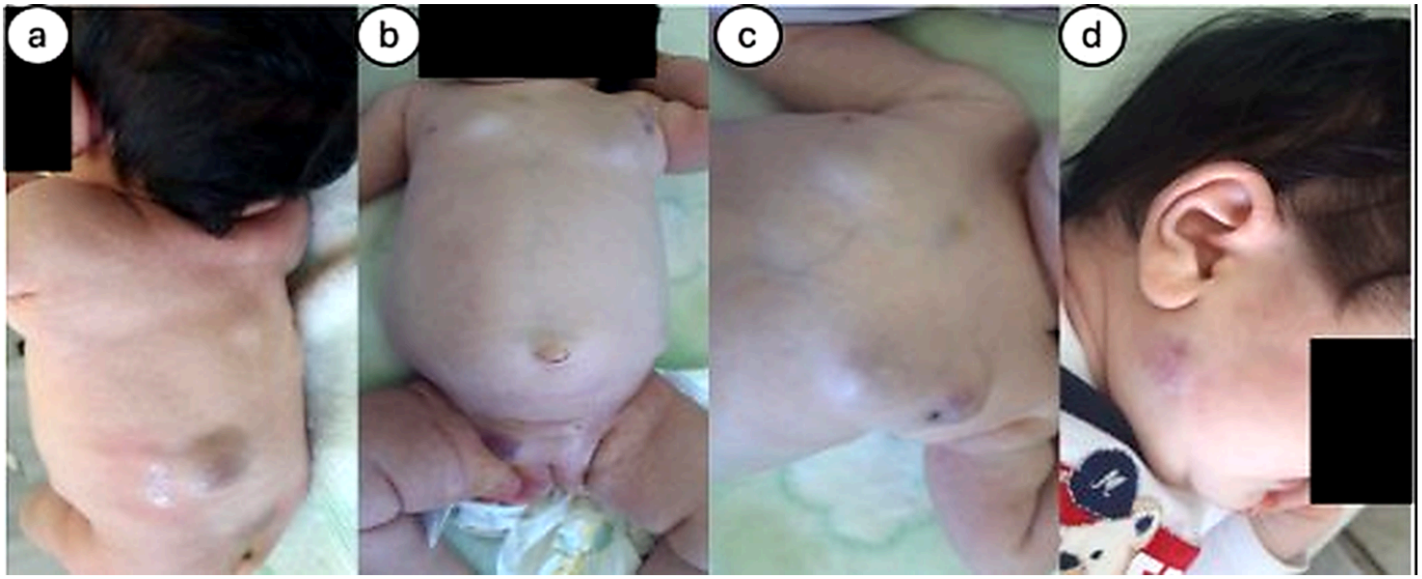


Figure 1

Multiple blue nodules with abdominal distension at admission

a. Initial left lumbar region progressing nodule **b**. Abdominal distension with inguinal nodule **c**. multiple nodules on the chest wall **d**. Submandibular nodule