CASE REPORT

A Transient "Blueberry Muffin" Rash in a Neonate with Acute Myeloid Leukemia: A Case Report and Review of the Literature

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J Clin Aesthet Dermatol. 2026;19(2):22–25.

A "blueberry muffin rash," typically attributed to congenital toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus (TORCH) infections, is a rare and underreported cutaneous manifestation of serious underlying pathology, including hematologic malignancies. We report a case of congenital acute myeloid leukemia (AML) in a full-term newborn who presented at day-of-life 0 with multiple blue to purple macules, patches, and indurated papulonodules and plaques on the trunk and extremities consistent with a "blueberry muffin rash". Notably, the rash was transient and spontaneously resolved within 24 hours of life, making it easy to overlook, potentially delaying life-saving treatment. This case reinforces the need for a full diagnostic workup and high clinical suspicion for leukemia in neonates presenting with a "blueberry muffin rash." **KEYWORDS:** Acute myeloid leukemia, blueberry muffin rash, congenital leukemia, leukemia cutis

Congenital leukemia is an exceptionally rare condition that typically presents within the first few weeks of life.[1] Leukemia cutis, a cutaneous infiltration by leukemic cells, is an unusual manifestation of congenital leukemia observed in only 25% to 30% of affected infants.[2] Leukemia cutis may present with a "blueberry muffin rash," characterized by widespread, blue-red or violaceous macules and papulonodules.[3] This eruption is typically associated with congenital TORCH (ie, toxoplasmosis, other, rubella, cytomegalovirus, and herpes simplex virus [HSV]) infections rather than malignancy. Thus, early diagnosis of leukemia may be challenging.[3] Herein, we report the case of a female newborn who initially presented with an extensive, transient violaceous cutaneous eruption suggestive of a blueberry muffin rash that was ultimately diagnosed as congenital leukemia cutis, along with her clinical evaluation, treatment, and clinical course. We also review previously reported cases of blueberry muffin rash exclusively linked to neonatal or congenital leukemia.

CASE REPORT

A newborn girl, born at 38 weeks, 1 day gestation via repeat cesarean delivery, presented at day-of-life 0 with multiple blue to purple macules, patches, and indurated papulonodules and plaques on the trunk and extremities (Figures 1A and 1B), resulting in a "blueberry muffin" appearance. On initial evaluation by dermatology, the patient appeared well with normal vital signs for her age and no other signs of systemic disease. No visible signs of respiratory distress or hemodynamic instability were noted on physical exam. Apgar score, birth weight and height, and head circumference were all within normal limits. Additionally, infectious studies were negative for cytomegalovirus, toxoplasmosis, syphilis, HSV-2, and the patient showed positive HSV-1 and rubella immunoglobulin G (IgG) titers.

A punch biopsy taken from a plaque on the patient's back revealed an extensive dermal mononuclear infiltrate (Figure 1C). The cells were CD33 and CD68 positive, with a subset positive for myeloperoxidase (MPO) suggestive of acute myeloid leukemia (AML) with monocytic differentiation.

Further diagnostic workup, including bone marrow aspirates, revealed hypercellular marrow with maturing trilineage hematopoiesis, myeloid megakaryocytic hyperplasia, and an abnormal immature monocyte population consistent with AML. Interestingly, within 24 hours of the initial clinical presentation, the patient's rash spontaneously resolved. The patient was treated with an intensified fludarabine, high-dose cytarabine, granulocyte colony-stimulating factor, idarubicin chemotherapy regimen with gemtuzumab ozogamicin (FLAG/Ida + GO) regimen and achieved complete remission. She continues to do well and shows no signs of active disease. A multidisciplinary team will provide ongoing monitoring for disease recurrence.

DISCUSSION

The term "blueberry muffin baby" was first used during the American rubella epidemic in the 1960s to characterize the distinctive

FUNDING: No funding was provided for this article.
DISCLOSURES: The authors have no conflict of interest to declare.
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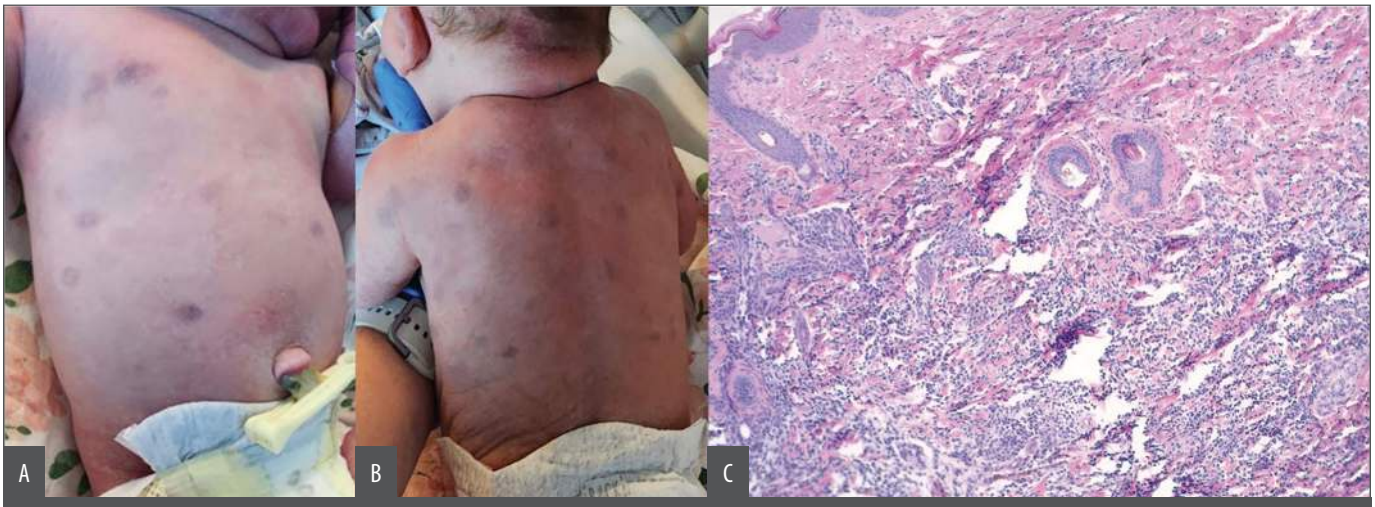

FIGURE 1. Clinical photographs depicting multiple blue to purple macules, patches, and edematous dermal plaques and papulonodules taken on day-of-life 0. **(A)** Images include the anterior trunk, **(B)** posterior trunk, **(C)** and hematoxylin and eosin-stained specimen from skin lesion showing dermal leukemic infiltrations.

TABLE 1. Reported cases of "blueberry muffin rash" in neonatal or congenital leukemia

REFERENCE (YEAR)	AGE	SEX	DIAGNOSIS	PRESENTATION	LOCATION	TRANSIENT (Y/N)	HISTOLOGY	CLINICAL COURSE
Zhang and Lin[10]	Newborn	M	ALL	Midface nodule and multiple firm violaceous papulonodules	Face, trunk, and limbs	N	Dense dermal massive monocytic infiltrate with atypical lymphocytes	Skin lesions presented several days after birth. No information on treatment or disease progression available.
Lo Presti et al[11]	Newborn	F	AML	Multiple firm red-violaceous papulonodular lesions	Face and trunk	N	Dense dermal infiltrate of blast cells; CD15+, CD68+, CD4+, and MPO−; 90% immature cells with monocytic phenotype	Skin lesions present at birth and persisted until chemotherapy was initiated. At postinduction Day 28, all cutaneous lesions had disappeared. Patient achieved complete remission.
Teixeira et al[12]	Newborn	M	AML	Widespread purple nonblanchable nodules	Face, trunk, abdomen, and limbs	N	Dermal infiltrate of blast cells; peripheral blood smear showed immature granulocytes	Skin lesions present at birth. Chemotherapy was started at five months. Patient achieved complete remission.
Kaleta et al[13]	Newborn	M	AML	Widespread purple papules and nodules	Face, scalp, trunk, and limbs	Y	Dense dermal infiltrate of blast cells; CD15+, CD31+, CD34+, CD56+ CD68+, CD71+, and MPO+	Skin lesions present at birth and regressed in the following days. Remission was achieved. Relapsed 6 months later. The disease progressed and the patient died.
Schlegal et al[14]	3 days	M	ALL	Multiple violaceous macules and papules	Face, upper back, and right shoulder	Y	Dermal lymphoblastic infiltrate; PAX5+ and weak nuclear Tdt expression by lymphoblasts	Skin lesions present at birth but spontaneously regressed over the next several days. Lesions reappeared on day 13. Patient achieved full remission.

+: positive; −: negative; AL: aleukemic leukemia; ALL: acute lymphoblastic leukemia; AMKL: acute megakaryoblastic leukemia; AML: acute myeloid leukemia; CD: clusters of differentiation; F: female; LCA: leukocyte common antigen; M: male; MPO: myeloperoxidase; PAX: paired box; Tdt: terminal deoxynucleotidyl transferase

TABLE 1, CONTINUED. Reported cases of "blueberry muffin rash" in neonatal or congenital leukemia

REFERENCE (YEAR)	AGE	SEX	DIAGNOSIS	PRESENTATION	LOCATION	TRANSIENT (Y/N)	HISTOLOGY	CLINICAL COURSE
Debord et al[15]	Newborn	M	AML	Multiple nodular purple cutaneous lesions	Face, back, and legs	N	Bone marrow aspiration revealed 6% myeloid blasts, 17% promonocytes, and 36% monocytes; MPO+, CD4+, CD14+, CD15+, CD33+, CD36+, CD65+, CD34–, and CD117–	Skin lesions present at birth. Treated with chemotherapy. Patient achieved full remission.
Darby et al[16]	3 weeks	M	AML	Scattered, ecchymotic, purpuric, dark purple macules and papules	Scalp, forehead, trunk, abdomen, and inguinal region	N	Dermal infiltrate of blast cells; MPO+, CD43+, CD68+; Tdt–, CD1a–, CD3–, CD5–, CD99–, and PAX 5–	Skin lesions appeared at 2 weeks of life and continued to spread over the next week. Treated with chemotherapy. Patient achieved complete remission.
Tsujimoto et al[17]	1 day	M	AMKL	Widespread dusky red papules and nodules with ecchymoses	Scalp and distal extremities	Y	Diffuse infiltration of mononuclear cells with large oval nuclei; CD43+, CD42b+, CD30+, CD1a–, CD68–, CD34–, CD56–, CD99–, and S100–	Skin lesions appeared at birth and gradually disappeared within a month before chemotherapy treatment. Chemotherapy was initiated and patient achieved full remission.
Eberst et al[18]	Newborn	M	AL	Multiple diffuse purplish skin nodules	Face and legs	N	Dense dermal infiltrate of mononuclear cells; MPO+, CD4+, CD15+, CD68+; CD117– and CD1a–	Skin lesions appeared at birth and persisted. Clinical course was spontaneously favorable despite no specific therapy. Patient was asymptomatic after one year of follow-up.
Hsiao et al[19]	2.5 months	F	AML	Multiple diffuse bluish-purpuric macules and subcutaneous nodules	Chest, abdomen, and back	Y	Diffuse infiltrates in dermis and superficial subcutis; MPO+, CD43+, and KP1+; CD117–, Tdt–, tryptase–, neuron-specific enolase–, and synaptophysin–	Patient presented with a 7-day course of skin lesions. The skin nodules regressed spontaneously without chemotherapy. A diagnosis of AML was made; however, the patient went under spontaneous remission. Two months later, relapse occurred with no cutaneous nodules present. Four courses of chemotherapy were administered. Patient died at 16 months.
Dongen et al[20]	Newborn	F	AML	"Blueberry-muffin spots"	Unspecified	N	Peripheral blood smear showed leukoerythroblastosis with monoclonal expression of CD71a and CD235a	Skin lesions present at birth. Treated with chemotherapy. Patient achieved complete remission.
Choi et al[2]	Newborn	M	AML	Diffuse dusky red papules and nodules and purpuric macules and ecchymoses	Face, scalp, neck, upper chest, and arms	N	Dense, diffuse, and atypical dermal infiltration of leukemic cells; LCA+, CD3-, CD20–, CD34–, CD45–, and CD68–	Skin lesions present at birth. Patient was treated conservatively without chemotherapy due to parental refusal and died 28 days after birth.
Torello et al[21]	40 days	F	AL	Multiple violaceous macules and papules	Face, trunk, thighs, and limbs	N	Dense dermal infiltrate of monomorphous cells; MPO+ and CD45+; S100–, CD1a–, and CD34–	Skin lesions appeared during the second week of life and persisted. Patient died at 7 months.

+: positive; –: negative; AL: aleukemic leukemia; ALL: acute lymphoblastic leukemia; AMKL: acute megakaryoblastic leukemia; AML: acute myeloid leukemia; CD: clusters of differentiation; F: female; LCA: leukocyte common antigen; M: male; MPO: myeloperoxidase; PAX: paired box; Tdt: terminal deoxynucleotidyl transferase

cutaneous manifestations of congenital rubella infections.[3] The skin lesions result from extramedullary hematopoiesis, a process in which blood cells are produced outside of the bone marrow, and are typically triggered by congenital TORCH infections, hematologic dyscrasias (eg, hereditary spherocytosis, hemolytic disease of the newborn, twin-to-twin transfusion syndrome), or neoplasms (mastocytosis, histiocytosis, neuroblastoma, rhabdomyosarcoma, leukemia).[3] Rarely, blueberry muffin rash has been associated with Langerhans cell histiocytosis and juvenile xanthogranuloma.[4,5]

We present a case of AML presenting as a transient blueberry muffin rash in a female newborn. Leukemia is the most commonly diagnosed malignancy in childhood and is most commonly reported in infants with Down syndrome.[6,7] However, congenital leukemia is extremely rare, accounting for less than 1% of all reported cases of pediatric leukemia.[8] The typical clinical presentation of AML in neonates includes anemia, bleeding, febrile neutropenia, lethargy, leukocytosis, central nervous system involvement, and hepatosplenomegaly.[9] Additionally, leukemia cutis is a rare manifestation of congenital leukemia that can often mimic other conditions such as congenital TORCH infections.[9] A blueberry muffin rash is an exceptionally unusual presentation of AML in neonates and can be easily mistaken for other pathologies.

A literature search identified only 13 previously published cases of blueberry muffin rash exclusively linked to congenital leukemia in the past 20 years, a summary of which is included in Table 1. Lesion characteristics were similar across all cases, with widespread violaceous macules, papules, and nodules present at birth being the most common presentation. Additionally, most cases reported similar locations of the rash with facial, truncal, and abdominal involvement being the most prevalent, similar to our patient. On histology, the most common finding was a dense dermal infiltrate of leukemic cells, similar to our patient.

In four of the 13 previously reported cases, the skin lesions appeared at birth and persisted until the patient was treated. In these cases, all patients achieved full remission and are doing well with no residual skin lesions. Four other cases reported a transient cutaneous eruption with varying presentations.[13,14,17,19] Interestingly, the eruption in one infant appeared paroxysmal, spontaneously regressing and reappearing before treatment was initiated.[17] Of these four transient cases, only two patients achieved full remission and remain in good health; the other two experienced relapse and ultimately succumbed to their disease. Our patient presented with a transient rash similar to these cases and was treated accordingly with a FLAG/Ida + GO chemotherapy regimen. Although our patient achieved full remission, close follow-up with a multidisciplinary team is critical to monitor for any signs of relapse to ensure she remains disease-free.

To our knowledge, this is only the fifth documented report of a transient blueberry muffin rash in a newborn diagnosed with AML. Given its rarity, it is critical for providers to recognize that while a blueberry muffin rash is most commonly associated with congenital infections, it may be an early manifestation of serious hematologic malignancies. The transient nature of the rash, as shown in this case, presents an additional diagnostic challenge. Its spontaneous resolution may lead to a false sense of reassurance or a missed diagnosis, potentially delaying workup and treatment. Increased awareness among providers about the potentially deceptive course of leukemia cutis is crucial to avoid missing or underestimating the significance of a blueberry muffin rash in neonates.

REFERENCES

1. Bayhan T, Çiki K, Tavil B, Gümrük F, Çetin M, Ünal Ş. An infant with congenital leukemia cutis and AML-M5 with MLL gene rearrangement. *J Pediatr Hematol Oncol.* 2015;37(7):566-567.
2. Choi JH, Lee HB, Park CW, Lee CH. A case of congenital leukemia cutis. *Ann Dermatol.* 2009;21(1):66-70.
3. Mehta V, Balachandran C, Lonikar V. Blueberry muffin baby: a pictoral differential diagnosis. *Dermatol Online J.* 2008;14(2):8.
4. Clark EE, Walton M, Chow LML, Boyd JT, Yohannan MD, Arya S. Disseminated juvenline xanthogranuloma with a novel MYH9-FLT3 fusion presenting as a blueberry muffing rash in a neonate. *AJP Rep.* 2023;13(1):e5-e10.
5. Shaffer MP, Walling HW, Stone MS. Langerhans cell histiocytosis presenting as blueberry muffin baby. *J Am Acad Dermatol.* 2005;53(2 Suppl 1):S143-S146.
6. Metayer C, Dahl G, Wiemels J, Miller M. Childhood leukemia: a preventable disease. *Pediatrics.* 2016;138(Suppl 1):S45-S55.
7. Baruchel A, Bourquin JP, Crispino J, et al. Down syndrome and leukemia: from basic mechanisms to clinical advances. *Haematologica.* 2023;108(10):2570-2581.
8. Yang CX, Yang Y, Zhang FL, et al. Congenital leukemia: a case report and review of literature. *World J Clin Cases.* 2023;11(29):7227-7233.
9. Calvo C, Fenneteau O, Leverger G, Petit A, Baruchel A, Méchinaud F. Infant acute myeloid leukemia: a unique clinical and biological entity. *Cancers (Basel).* 2021;13(4):777.
10. Zhang Z, Lin Z. Blueberry muffin rash in neonatal leukemia. *Br J Dermatol.* 2025;193(4):806.
11. Lo Presti C, Szymanski G, Lefebvre C, Jacob MC, Mossuz P, Gil H. Aleukemic congenital leukemia cutis preceding monocytic leukemia with favorable outcome: a case report. *EJHaem.* 2024;5(1):162-165.
12. Teixeira B, Losa A, Meireles A, et al. Blueberry muffin syndrome and hyperleukocytosis in a newborn: a diagnostic challenge. *Cureus.* 2024;16(1):e52869.
13. Kaleta K, Kłosowicz A, Juśko N, Kapińska-Mrowiecka M. Blueberry muffin baby syndrome. A critical primary sign of systemic disease. *Postepy Dermatol Alergol.* 2022;39(2):418-420.
14. Schlegel S, Hamm H, Reichel A, et al. Neonatal acute lymphoblastic leukemia with t(9;11) translocation presenting as blueberry muffin baby: successful treatment by all-BFM induction therapy, allogeneic stem cell transplantation from an unrelated donor, and PCR-MRD-guided post-transplant follow-up. *Am J Case Rep.* 2020;21:e927153.
15. Debord C, Grain A, Theisen O, Boutault R, Rialland F, Eveillard M. A blueberry muffin rash at birth. *Br J Haematol.* 2018;182(2):168.
16. Darby JB, Valentine G, Hillier K, et al. A 3-week-old with an isolated "blueberry muffin" rash. *Pediatrics.* 2017;140(1):e20162598.
17. Tsujimoto H, Kounami S, Mitani Y, Watanabe T, Takifuji K. Neonatal acute megakaryoblastic leukemia presenting with leukemia cutis and multiple intracranial lesions successfully treated with unrelated cord blood transplantation. *Case Rep Hematol.* 2015;2015:610581.
18. Eberst E, Michel B, Stoebner P, Dandurand M, Meunier L. Lésions cutanées à type de leucémie congénitale "aleucémique" de rémission spontanée. Spontaneous remission of congenital leukemia cutis. *Ann Dermatol Venereol.* 2011;138(8-9):586-590.
19. Hsiao YW, Tseng FW, Shih JL, Kuo TT, Jaing TH, Hui RCY. Blueberry Muffin Baby with acute myeloid leukemia and spontaneous remission. *Dermatol Sin.* 2011;29(2):47-49.
20. van Dongen JCA, Dalinghaus M, Kroon AA, de Vries ACH, van den Heuvel-Eibrink MM. Successful treatment of congenital acute myeloid leukemia (AML-M6) in a premature infant. *J Pediatr Hematol Oncol.* 2009;31(11):853-854.
21. Torrelo A, Madero L, Mediero IG, Baño A, Zambrano A. Aleukemic congenital leukemia cutis. *Pediatr Dermatol.* 2004;21(4):458-461. JCAD