Pediatric Hematology and Oncology, 25:457–468, 2008
Copyright © Informa Healthcare USA, Inc.
ISSN: 0888-0018 print / 1521-0669 online
DOI: 10.1080/08880010802104494

informa
healthcare

Case Report

SPONTANEOUS RESOLUTION OF A SINGLE LESION OF MYELOID LEUKEMIA CUTIS IN AN INFANT: Case Report and Discussion

John A. D'Orazio, MD, PhD □ *University of Kentucky College of Medicine, Department of Pediatrics, Division of Hematology{Oncology, Lexington, Kentucky, USA*

Joseph F. Pulliam, MD □ *University of Kentucky College of Medicine, Department of Pathology, Lexington, Kentucky, USA*

Jeffrey A. Moscow, MD □ *University of Kentucky College of Medicine, Department of Pediatrics, Division of Hematology{Oncology, Lexington, Kentucky, USA*

□ *Though infantile leukemia has a historically poor prognosis, there may be a subset of patients with cutaneous disease whose disease will resolve without therapy. The authors report a case of infantile leukemia cutis who presented with a single subcutaneous chloroma that spontaneously resolved over the course of several weeks and who remains without evidence of disease nearly two years later. After reviewing the literature of congenital leukemia cutis, the authors conclude that withholding chemotherapy in infants with cutaneous myeloid leukemia in the absence of known negative prognostic factors (*MLL *or* BCR-ABL *translocations) or progressive disease is clinically indicated.*

Keywords AML, chemotherapy, infantile leukemia, leukemia cutis, resolution

Leukemic infiltration of the skin, termed "leukemia cutis," occurs most commonly with AML and is most common among infants newly diagnosed with leukemia [1]. Congenital leukemia historically has had a poor outcome despite aggressive anti-leukemic therapy [2]. However, a subset of very

Received 17 August 2007; accepted 7 February 2008.

This work was supported by the University of Kentucky and the Markey Cancer Center. The authors respectfully thank the family of our patient for allowing us to report clinical events and publish photographs detailing cutaneous findings in this case. We also thank Howard Weinstein (Massachusetts General Hospital) and Franklin Smith (Cincinnati Children's Hospital Medical Center) for useful clinical discussion and management suggestions, Dermatopathology Associates (Pikeville, KY), the University of Louisville Department of Pathology for providing biopsy slides and interpretation of the initial skin biopsy, and Malinda Spry for photographic assistance. This case report and discussion meets with University of Kentucky IRB guidelines.

Address correspondence to John D'Orazio, MD, PhD, Assistant Professor of Pediatrics, University of Kentucky College of Medicine, Markey Cancer Center, Combs Research Building, 800 Rose Street, Lexington, KY, 40536–0096, USA E-mail: jdorazio@uky.edu

young patients may exhibit complete resolution of disease even without treatment [3–6]. Although leukemic skin involvement often heralds more widespread disease [7], it can remit without therapy in certain patients [8–10]. AML treatment regimens have significant morbidity in the very young patient [11, 12], so the decision to administer chemotherapy to an infant with congenital leukemia must be weighed carefully given reports of spontaneously remitting disease. We report a case of spontaneously remitting aleukemic leukemia cutis in an infant who presented with a solitary dermal myeloid chloroma and review the literature relevant to the decision of withholding systemic chemotherapy in infants with leukemia cutis. We suggest that chemotherapy should be withheld in the very young patient with myeloid cutaneous chloroma in the absence of high-risk genetic features, even in the setting of marrow involvement.

CLINICAL HISTORY

A female infant presented at 6 weeks of life for evaluation of an enlarging subcutaneous mass on her forehead. Gestation and neonatal course were unremarkable, and she was otherwise normal and without fever, pallor, petechiae/purpurae, irritability, feeding intolerance, or respiratory distress. The skin nodule was first noticed at 2 weeks of life and grew over the next two weeks. A biopsy obtained at 6 weeks of age was interpreted as leukemic infiltrate by an outlying institution. The child was referred to our service for further evaluation and management. Our initial physical examination revealed a 9-week-old baby in no distress with a nodular, rubbery, nontender 1.5 × 0.5-cm cutaneous, flesh-colored, slightly blue-tinged mass on her forehead (Figure 1). No other cutaneous lesions or organomegaly, lymphadenopathy, or gingival hyperplasia were appreciated. Initial blood work (including a CBC, LDH, electrolytes, phosphorus, uric acid) and a chest roentogram were entirely unremarkable. Coagulation studies were entirely normal, and the patient manifested no clinical evidence of coagulopathy. A repeat biopsy of the forehead lesion revealed myelogenous leukemic infiltration (Figure 2). Specifically, there was replacement of dermis and subcutaneous tissues by a sheet of uniform intermediate-sized primitive lymphoreticular cells that stained uniformly positive for CD15, CD45, lysozyme, and CD43, weakly and focally positive for myeloperoxidase and negative for CD68, CD1A, CD3, CD117, CD30, CD79 (an early pan B lineage marker), cytokeratin AE1/AE3, factor VIII, and CD34. Together, the biopsies confirmed the diagnosis of acute myeloid leukemia cutis with prominent monocytic differentiation. Cytogenetic evaluation of biopsy tissue was unsuccessful because the sample yielded no metaphase cells, but FISH studies were negative for the *MLL* gene rearrangement on chromosome 11q23 (using the Vysis LSI *MLL* Dual Color, Break Apart Rearrangement Probe). A bone marrow aspirate and biopsy showed no evidence of increase in blasts or of

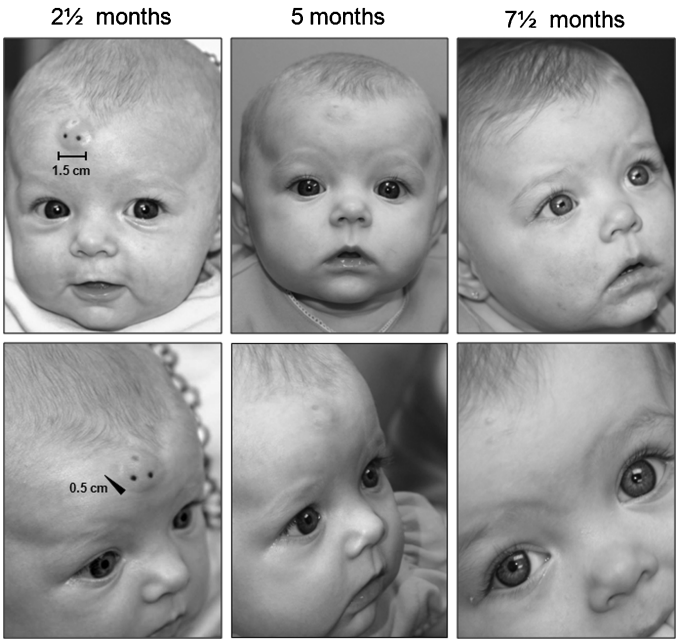

FIGURE 1 Photographs of the cutaneous forehead lesion soon after presentation (left) and at subsequent clinic visits (middle and right). Shown are the dimensions of the lesion in width (upper left) and depth (lower left). The age of the patient at the time of documentation is indicated. Note that the patient is now 25 months old and remains free of disease.

myelodysplastic changes at 9 weeks of age. We considered the possibility that this might represent transient myeloproliferative disease (TMD) associated with trisomy 21, but the patient exhibited no phenotypic features of Down syndrome, and multiple cytogenetic analyses of the bone marrow resulted in a 46,XX karyotype. Furthermore, FISH for the *ETO/AML1* gene fusion characteristic of the t(8;21) translocation gave two normal signals for *AML1,* providing further evidence against trisomy 21. Multiple marrow specimens were negative for *MLL*, *CBF-beta,* or *ETO/AML1* rearrangements by metaphase FISH testing.

Knowing that there were reports in the literature of spontaneously resolving aleukemic leukemia cutis, we elected to withhold AML therapy. Over the next 2 months, the lesion persisted and grew slightly, but the remainder of the physical exam (along with CBCs, LDH, and serum uric acid) remained normal. A surveillance marrow (3 months of age) showed an increased blast population of 9% by morphology. Flow cytometric interpretation of the marrow was confounded by the indistinct immunohistochemical profile of the patient's cutaneous blasts: strong lysozyme, weak myeloperoxidase, strong CD15, strong CD45, negative CD34 (clearly monocytic but not otherwise aberrant). Nonetheless, flow cytometric analysis of the marrow demonstrated a population of monocytic cells comprising 8%

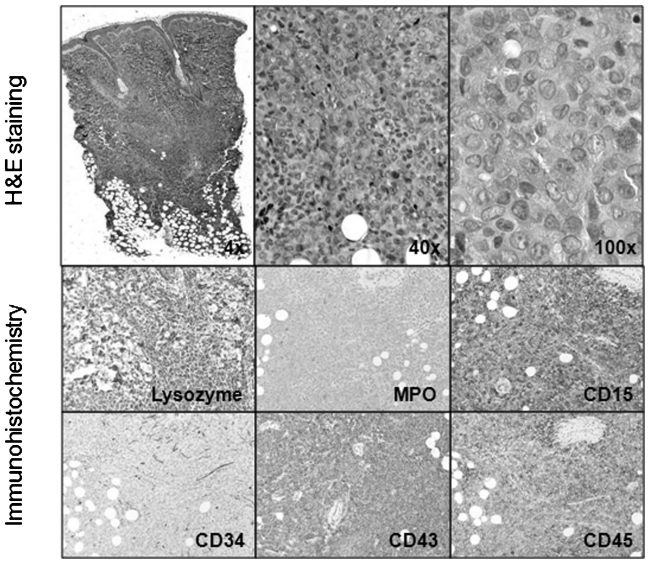

FIGURE 2 Images of sections of the cutaneous nodule: hematoxylin & eosin-stained tissue (top) and immunohistochemistry (bottom). Note replacement of dermis and subcutaneous tissue by blasts that stained strongly for CD15, CD45, lysozyme, and CD43, weakly for myeloperoxidase, and negative for CD34. Blasts stained negatively for CD3, CD30, CD68, CD79, cytokeratin, factor VIII, and CD117 (not shown). Together, the biopsies confirmed myeloid leukemia cutis with prominent monocytic differentiation.

of total CD45-positive cells that expressed strong CD15, strong CD45, and negative CD34, with the addition of other relatively mature monocytic markers, including strong homogenous CD33, CD13, CD14, HLA-DR, and Fc-receptor. Therefore, there was an increased number of blasts/promonocytes of monocytic lineage in the marrow. Because the marrow findings suggested that progression of disease and the cutaneous lesion had increased in size, we decided to begin anti-leukemic chemotherapy. Thus, a central line was placed and a repeat bone marrow was done. Concurrently, a lumbar puncture with administration of intrathecal cytarabine (20 mg) was performed with the intention of initiating systemic chemotherapy. To our surprise, however, the marrow showed 5% blasts by histology, which represented a spontaneous decrease in the blast percentage from 2 weeks prior. In addition, the forehead lesion seemed smaller than it had been 2 weeks previously, prompting us to withhold systemic chemotherapy. The cutaneous lesion then continued to diminish in size over the next several weeks until it was no longer distinctly palpable 6 weeks later. A subsequent marrow at 4 months of age was normal. The lesion has since regressed and blood indices have since remained normal to date. Therefore, in our patient's case, the cutaneous lesion was first noted by the family at 2 weeks of life, evaluated by biopsy at 6 and 9 weeks of life, grew and darkened in color over the next 4–6 weeks (until the age of 3.5 months) then began

regressing until it was no longer identifiable by 7.5 months of life (Figure 1). The patient is now 25 months old and is growing and developing normally without clinical evidence of disease.

DISCUSSION

Congenital leukemia, presenting either with symptoms of marrow failure or as more focal disease, has historically been associated with a very poor prognosis [1, 5, 13, 14]. Leukemia cutis occurs in about a quarter of infants with leukemia and typically consists of generalized bluish or purplish dermal nodules [15, 16], and is most often myeloid of the FAB M4 or M5 variety [9]. As opposed to the infant with "blueberry muffin syndrome" with widespread bluish skin lesions, our patient presented with an isolated nodule. The differential of such dermal processes in an infant includes infectious (congenital TORCH infections such as rubella), malignant (leukemia, neuroblastoma), and other causes (e.g., histiocytosis). Our patient presented with a single cutaneous lesion of leukemia cutis without evidence of marrow involvement and was therefore diagnosed with aleukemic leukemia cutis at 9 weeks of age.

Leukemia cutis may also be a feature of transient myeloproliferative disorder (TMD) seen occasionally in infants with Down syndrome [17] and, like the peripheral blasts in TMD, will usually clear without treatment. Though some phenotypically normal babies mosaic for trisomy 21 have been reported with TMD-associated leukemia cutis [18], our patient demonstrated neither physical nor laboratory evidence of Down syndrome, exhibiting a normal karyotype in multiple bone marrow specimens. Importantly, a variety of other conditions of infancy can cause cutaneous nodules and must be considered in the differential diagnosis, most notably certain TORCH infections and neuroblastoma. In older children and adults, leukemia cutis usually signifies an ominous clinical course and few clinicians would argue against immediately proceeding with systemic chemotherapy in such patients. However, the prognosis is much more variable in the very young infant. Certainly, there have been cases of infantile leukemia cutis that coincide with or progress to more widespread disease and are associated with a poor prognosis [19]. In a summary of the BFM experience of congenital leukemias, Reinhardt and colleagues noted that skin infiltration often preceded bone marrow involvement and systemic disease and the authors concluded that delays in starting chemotherapy in such infants coincided with higher rates of relapse [7]. However, several reports of infants with spontaneously remitting leukemia have been published, including many cases with isolated skin involvement [10, 18] or in combination with more widespread disease [4, 6, 9], [20]]. Thus, the clinician is challenged by determining the appropriate criteria for beginning systemic chemotherapy in such patients.

We reviewed published cases of congenital leukemia cutis and have compiled pertinent findings in a comprehensive table describing 26 independent cases, including our own (Table 1). Of the 6 patients reported to have died from their disease, 3 were treated at least 25 years ago, 1 had CNS involvement, and 2 had *MLL* (11q23) translocations. In all, we found 16 case reports published after 1980 of infants with myeloid leukemic cutis whose disease went into remission spontaneously without treatment (Table 1). In each case, the patient presented with leukemia cutis at birth or before 2 weeks of life. The mean age of resolution ± SEM of myeloid leukemia cutis among these 16 cases was 2.2 ± 0.5 months of life, and none of these infants received systemic chemotherapy to induce remission. We found only 1 case report of a patient with generalized myeloid leukemia cutis who did not achieve remission and went on to succumb to generalized leukemia at 22 days of life; importantly, this patient had myeloid leukemia cutis associated with an MLL gene rearrangement. Notably, we have also observed poor outcomes (relapse and/or death) in two infants who presented to our service over the last 3 years with generalized leukemia cutis and *MLL* gene-rearranged AML. It is generally accepted that certain high-risk cytogenetic features such as the *MLL* (11q23) rearrangement or the *BCR-ABL* (t(9;22)) translocation portend aggressive clinical course and bad outcomes [21, 22] and warrant prompt administration of anti-leukemic therapy [10]. Because of their importance with respect to prognosis and treatment decisions, these genetic features should be tested by various molecular tests (FISH, PCR, Southern blot) if possible, particularly those leukemias or myeloid sarcomas with evidence of complete or even partial monocytic differentiation. Conversely, there are favorable chromosomal rearrangements (e.g., *MOZ-CBP* fusion), which, when identified, probably merit a more cautious therapeutic approach [20]. Unfortunately, many cases do not exhibit clear-cut genetic mutations associated with prognostic significance that would help guide treatment decisions.

The remaining patients described in the literature with infantile leukemia cutis had evidence of either a normal karyotype or the favorable *MOZ-CBP* fusion (t(8;16) translocation), and fared better with most cases resolving spontaneously without treatment (Table 1). Those patients who relapsed typically did so after 1 year of age, affording significant time for growth and development while delaying chemotherapy. Of the 16 patients who achieved spontaneous clinical remission of their disease, only 5 suffered clinical relapses (at the mean age of 13.2 ± 3.5 months). These patients were then treated with chemotherapy and/or stem cell transplantation and 3 of 5 patients were reported to have extended remissions (6–16 years disease-free). Involvement of the marrow at the time of diagnosis of leukemia cutis was present in 8 of 14 case reports and seemed to

TABLE 1 Published Cases and Abbreviated Outcomes of Congenital Leukemia Cutis (1955–Present)

Year Reference	Sex	Age at diagnosis	Subtype	Skin findings	Initial WBC ($\times 10^9$/L)	Marrow at presentation	Genetics	Chemotherapy given?	Age at Remission	Clinical Outcome
This report	F	2 wks	AML- M5	Single flesh-colored 1.5 cm nodule	9.3	Normal (2% blasts)	46 XX FISH analysis revealed no evidence of *MLL* (11q23) or CBFB (16q22) rearrangements or ETO/AML1 translocation	Only 1 intrathecal dose of cytarabine (20 mg)	7.5 mo	No relapse; well at 25 months
2005 [20]	F	Birth	AML	Multiple blue nodules on forehead, trunk and extremities, up to 2 cm	Normal		Cytogenetics of cutaneous blasts: t(8;16)(p11;13)	None given	3 mo (skin) 1 yr (epidural)	No relapse; well at 5 yrs.
2005 [6]	M	Birth	AML- M4	Generalized 0.5–2 cm nodules blue-purplish	8.5	23% blasts	FISH *MLL*-negative	None given	3 mo	No relapse; well at 8 mo.
2004 [18]	F	Birth	AML- M2	Pink-purple subcutaneous nodules, 3–10 mm, generalized	6.7	Normal	Marrow: 46 XX	None given	3.5 mo	No relapse; well at 3.5 yrs
2002 [5]	F	Birth	ALL- pro B	Blueberry muffin appearance	140	66% lymphoblasts	46, XX with *MLL* gene rearrangement t(11;19)(q23;p13)	Yes	Remission not obtained	Refractory disease; died at 5 mo (leukemia)
2002 [5]	M	Birth	AML- M4	Multiple generalized purple skin nodules	187	Not performed	46 XY with *MLL* gene rearrangement t(4;11)(q21;q23)	Yes	Unstable condition at diagnosis	Died at 22 d (leukemia)
2000 [10]	M	Birth	AML- M4/5	Red-magenta subcutaneous nodules, initially only one on face, then widespread, 4–30 mm	10.0	Normal	Marrow: 46 XY	None given	10 wk	No relapse; well at 10 mo
2000 [26]	M		AML- M4				46 XX, t(8,16)	None given	5 mo	No relapse; well at 15 mo

(*Continued on next page*).

TABLE 1 Published Cases and Abbreviated Outcomes of Congenital Leukemia Cutis (1955–Present) (Continued)

Year reference	Sex	Age at diagnosis	Subtype	Skin findings	Initial WBC ($\times 10^9$/L)	Marrow at presentation	Genetics	Chemotherapy given?	Age at Remission	Clinical Outcome
2000 [9]	F twins	Birth	AML- M5	Blueberry muffin appearance	20 (A), 106 (B)	Not performed (A) Replacement with blasts (B)	46 XX	None given	4 wk	No relapse; both well at 2 yrs
1998 [27]	M	Birth	ALL- T Cell		Normal	Normal	Abnormalities at 21 (q12,q13)	None given	1.5 mo	No relapse; well at 8 mo
1998 [28]	F		AML- M5	Blue papules and macules	Involved	Involved			14 d	
1997 [4]	M	Birth	AML- M5	Red/purple macules and nodules	9	Normal	Marrow: 46 XY, inv (9)	None given	3 d	No relapse; well at 4 yrs
1997 [4]	F	1 wk	AML- M4	Red/purple macules, papules and nodules	16	30% blasts	Marrow: 46 XX	Only after relapse	3 mo	Relapses at2 yr and 3.7 yrs; alive at 3.8 yrs
1997 [4]	M	Birth	AML- M5	Red-brown to purple papules and nodules	13.6	Not performed	Marrow: 46 XY at relapse	Only after relapse	3 wk	Relapse at 16 mo; alive at 6 yrs after BMT
1996 [24]	M	Birth	AML- M5	Brownish skin nodules 1–10 mm in diameter distributed over body	9.8	Involved—62% blasts	Marrow: 46 XY t(8,16) (p11,p13)		3 mo	No relapse; alive at 2 yrs
1996 [29]		Birth		Leukemia cutis	67	Dry tap		None given	1 mo	Relapse at 3 mo; died after CNS relapse
1995 [23]	F	Birth	AML- M5	Multiple blue-gray thick 1–1.5 cm nodules on face, scalp, trunk, extremeties	79	90% blasts	Marrow:46 XX t(5,6) (q31,q21)	None given	1 mo	No relapse; alive at 10 mo
1989 [8]	M	Birth	AML- M5	Red-brown to purple nodules	64	Involved	Marrow: 46 XY	Only after relapse	3 mo	Relapse at 1 yr; alive at 10 yrs after BMT
1989 [16]	M	Birth	AML- M5	Dusty red to purple papuls and nudules 3–5 mm in diameter	14.8	25% blasts	-	None given	1 mo	No relapse; alive at 2 yrs

1987 [30]	M	Birth	AML	Leukemia cutis	117	Involved	Marrow: 46 XY		?	No relapse; alive at 6 yrs
1985 [3]	F	Birth	AML- M5	Blueberry muffin appearance	394	52% blasts	Marrow: 46 XX	None given	16 d	No relapse; alive at 3 yrs
1983 [31]	F	9.5 wks	Undifferentiated	Small blue papules on scalp, back and chest	148	Involved	Blood: 46 XX	None given	7 d	Relapse at 22 mo; alive at 16 yrs.
1980 [32]	M	Birth	AML- M5	Pink-purple nodules	12.7	Involved	Marrow: 46 XY		Few days	Relapsed; died at 7 mo (leukemia)
1969 [33]	F	Birth	AML	Blue-red nodules	8	40% blasts	Marrow: 46 XX	Only after relapse	5.5 mo	Relapsed; died at 9 mo (leukemia)
1955 [34]		Infant	AML	Leukemia cutis	6.9	Not performed			6 wks	Relapsed at 13 wks; died at 14 wks (leukemia)

portend increase risk of relapse, with the majority of relapses occurring in this subset of patients. However, it is important to recognize that there have been multiple reports of cases of spontaneously remitting myeloid infantile leukemia cutis even in the face of widespread disease (multiple skin nodules, hepatosplenomegaly, marrow involvement (>5% blasts) or in the presence of circulating blasts) [3, 4, 6, 9, 20, 23, 24]. Although marrow involvement may be predictive of disease progression in some cases (Table 1), a conservative approach even in the face of widespread disease in the infant with leukemia cutis may be warranted. Significantly, infants with spontaneously resolving congenital leukemia who subsequently relapsed and then received anti-leukemic therapy demonstrated similar outcomes as age-matched similarly treated peers presenting with leukemia without a history of antecedent congenital disease [4, 18]. There is at least one report, however, in which a relapse 12 months after spontaneously resolving

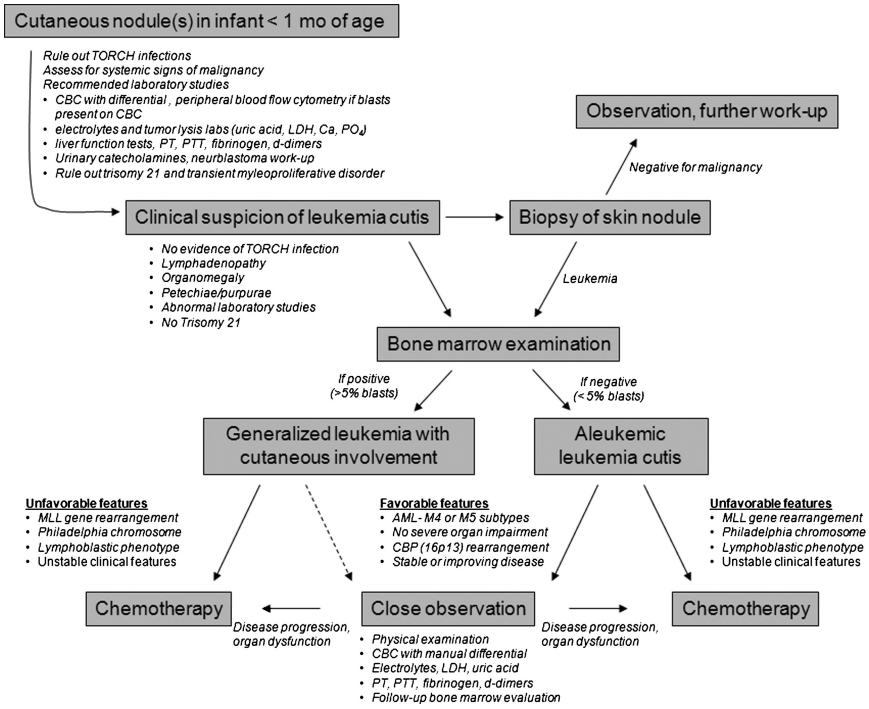

FIGURE 3 Suggested management algorhythm for congenital leukemia cutis. Close observation and withholding of systemic chemotherapy may be warranted in cases of congenital leukemia cutis without high-risk genetic features. If disease high-risk features are apparent (as outlined in the figure), then systemic therapy should be considered. Leukemia cutis in an older child warrants prompt administration of systemic chemotherapy. It should be noted that only a limited number of case reports have been published showing spontaneous resolution of disease in the setting of leukemia cutis with bone marrow involvement; therefore, we recommend a cautious approach to withholding chemotherapy in this setting (as indicated by the dashed arrow in the figure).

neonatal leukemia cutis had a poor outcome despite aggressive therapy instituted after the relapse [8].

Taken together, the case reports published over the last several decades suggest a rationale for the approach of watchful waiting in select cases of infantile leukemia cutis. We recognize peril in drawing conclusions based only on scant anecdotal experiences, but we feel that a cautious observational approach for infantile myeloid leukemia cutis in infancy may be warranted in infants with myeloid leukemia cutis in the absence of high-risk cytogenetics, even if the marrow is involved at presentation (Figure 3). Additionally, our case raises the possibility that a single cutaneous nodule (rather than the more typical widespread "blueberry muffin" rash of leukemia cutis) may be a favorable prognostic indicator and may support a conservative approach to treatment. Leukemic cutis in very young infants in the absence of unfavorable tumor genetic abnormalities may represent a subset of AML patients wherein spontaneous remission of disease, akin to that of stage IV-S neuroblastoma [25], is expected. If therapy is initially withheld in this context, we recommend close surveillance over several months to monitor for progression or relapse (Figure 3). Lastly, development of a national or international database within the leukemia field to prospectively study and define criteria for withholding therapy in the context of congenital leukemia would clearly be of benefit to the greater pediatric oncology community and to future affected patients.

REFERENCES

[1] Resnik KS, Brod BB. Leukemia cutis in congenital leukemia: analysis and review of the world literature with report of an additional case. *Arch Dermatol.* 1993; 129: 1301–1306.

[2] Ozdemir MA, et al. Two fatal cases of infants with congenital leukemia presenting with skin lesions. *J Emerg Med.* 2002;23: 422–423.

[3] Lampkin BC, et al. Spontaneous remission of presumed congenital acute nonlymphoblastic leukemia (ANLL) in a karyotypically normal neonate. *Am J Pediatr Hematol Oncol.* 1985; 7: 346–351.

[4] Dinulos JG, et al. Spontaneous remission of congenital leukemia. *J Pediatr.* 1997; 131: 300–303.

[5] Bresters, D et al . Congenital leukaemia: the Dutch experience and review of the literature. *Br J Haematol.* 2002; 117: 513–524.

[6] Landers MC, et al. Spontaneous regression of aleukemia congenital leukemia cutis. *Pediatr Dermatol.* 2005; 22: 26–30.

[7] Reinhardt D, Creutzig U. Isolated myelosarcoma in children—update and review. *Leuk Lymphoma* 2002; 43: 565–574.

[8] Francis JS. Sybert VP, Benjamin DR. Congenital monocytic leukemia: report of a case with cutaneous involvement, and review of the literature. *Pediatr Dermatol.* 1989; 6: 306–111.

[9] Mora J, et al. Spontaneous remission of congenital acute nonlymphoblastic leukemia with normal karyotype in twins. *Med Pediatr Oncol.* 2000; 35: 110–113.

[10] Grundy RG, et al. Spontaneous remission of congenital leukemia: a case for conservative treatment. *J Pediatr Hematol Oncol.* 2000; 22: 252–255.

[11] von der Weid N. Late effects in long-term survivors of ALL in childhood: experiences from the SPOG late effects study. *Swiss Med Wkly.* 2001; 131: 180–187.

[12] Arndt C, et al. Age is a risk factor for chemotherapy-induced hepatopathy with vincristine, dactinomycin, and cyclophosphamide. *J Clin Oncol.* 2004; 22: 1894–1901.

[13] Darbyshire PJ, et al, Monocytic leukemia in infancy: a review of eight children. *Cancer*. 1985; 56: 1584–1589.
[14] Biondi A, et al, Biological and therapeutic aspects of infant leukemia. *Blood*. 2000; 96: 24–33.
[15] Koga M, Furukawa S. Leukemia cutis in three children: clinical and immunohistochemical studies. *Pediatr Dermatol*. 1996; 13: 200–206.
[16] Gottesfeld E, et al. Transient blueberry muffin appearance of a newborn with congenital monoblastic leukemia. *J Am Acad Dermatol*. 1989; 21(2 Pt 2): 347–351.
[17] Weinstein HJ. Congenital leukaemia and the neonatal myeloproliferative disorders associated with Down's syndrome. *Clin Haematol*. 1978; 7: 147–154.
[18] Van Den Berg H, et al. Spontaneous remission in congenital leukemia is not related to (mosaic) trisomy 21: case presentation and literature review. *Pediatr Hematol Oncol*. 2004; 21: 135–144.
[19] Torrelo A, et al. Aleukemic congenital leukemia cutis. *Pediatr Dermatol*. 2004; 21: 458–461.
[20] Classen CF, et al. Spontaneous complete and sustained remission of a rearrangement CBP (16p13)-positive disseminated congenital myelosarcoma. *Ann Hematol*. 2005; 84: 274–275.
[21] Douet-Guilbert N, et al. Rearrangement of MLL in a patient with congenital acute monoblastic leukemia and granulocytic sarcoma associated with a t(1;11)(p36;q23) translocation. *Leuk Lymphoma*. 2005; 46: 143–146.
[22] Zhang IH, et al. Congenital leukemia cutis with subsequent development of leukemia. *J Am Acad Dermatol*. 2006; 54(2 Suppl): S22–S27.
[23] Mayer JL, Seashore MR, Hajjar FM. Translocation (5;6) associated with spontaneously remitting congenital leukemia. *Cancer Genet Cytogenet*. 1995; 81: 38–41.
[24] Sainati L, et al. Transient acute monoblastic leukemia with reciprocal (8;16)(p11;p13) translocation. *Pediatr Hematol Oncol*. 1996; 13: 151–157.
[25] Miale TD, Kirpekar K. Neuroblastoma stage IV-S. *Med Oncol*. 1994; 11: 89–100.
[26] Weintraub M, et al. Spontaneous regression of congenital leukaemia with an 8;16 translocation. *Br J Haematol*. 2000; 111: 641–643.
[27] Zenon C, Bouffioux B, Louis J. ["Blueberry muffin baby"]. *Ann Dermatol Venereol*. 1998; 125: 199–201.
[28] Marsh E, et al. Blue papules and macules in a newborn. *J Cutan Med Surg*. 1998; 2: 229–232.
[29] Monpoux F, et al. Congenital leukemia cutis preceding monoblastic leukemia by 3 months. *Pediatr Dermatol*. 1996; 13: 472–476.
[30] 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: 121–129.
[31] Chu JY, et al. Congenital leukemia: two transient regressions without treatment in one patient. *Pediatrics*. 1983; 71: 277–279.
[32] Lilleyman JS. *Congenital monocytic leukaemia. Clin Lab Haematol*. 1980; 2: 243–245.
[33] Van Eys J, Flexner JM. Transient spontaneous remission in a case of untreated congenital leukemia. *Am J Dis Child*. 1969; 118: 507–514.
[34] Reimann DL, Clemmens RL Pillsbury WA. Congenital acute leukemia; skin nodules, a first sign. *J Pediatr*. 1955; 46: 415–418.

Copyright of Pediatric Hematology & Oncology is the property of Taylor & Francis Ltd and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.