Rapidly Growing Cutaneous Nodules on the Scalp

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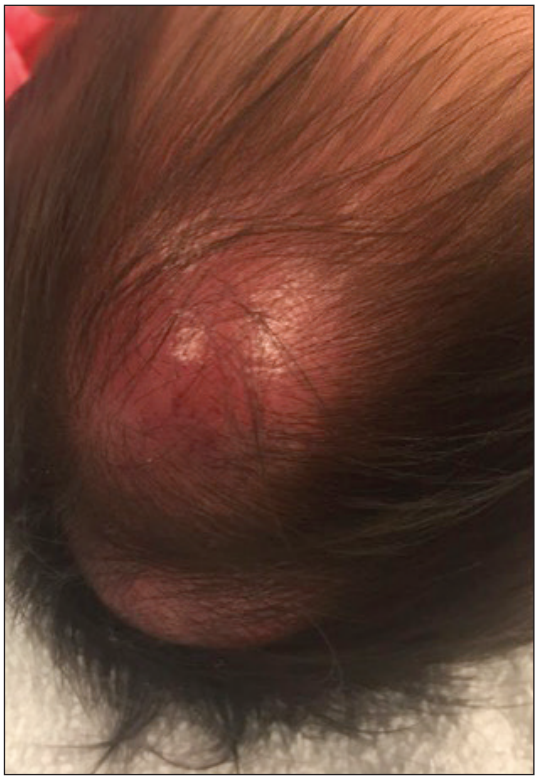

An 8-month-old infant girl presented with rapidly growing cutaneous nodules on the scalp of 1 month's duration. Her parents reported that she disliked lying flat but was otherwise growing and developing normally. Nondiagnostic ultrasonography of the head and brain had been performed as well as a skull radiograph, which found no evidence of lytic lesions. On physical examination, 3 erythematous to violaceous, subcutaneous, firm, fixed nodules were observed on the scalp. Notable cervical lymphadenopathy with several distinct, fixed, firm, subcutaneous nodules in the postauricular lymph chains also were noted. The patient had no pertinent medical history and was born via normal spontaneous vaginal delivery to healthy parents. The remainder of the physical examination and review of systems was negative.

WHAT'S THE **DIAGNOSIS?**

a. B-cell acute lymphoblastic leukemia
b. coccidioidomycosis
c. deep hemangioma
d. infantile myofibromatosis
e. sarcoidosis

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THE **DIAGNOSIS:** B-Cell Acute Lymphoblastic Leukemia

A 4-mm punch biopsy of one of the scalp lesions showed a diffuse infiltrate of intermediately sized cells with variably mature chromatin and irregular nuclear contours, consistent with a neoplastic process. Numerous mitotic figures were present, indicating a high proliferation rate (Figure 1). At that time there was no evidence of systemic involvement. A repeat biopsy with concurrent bone marrow biopsy was scheduled 10 days after the patient's initial presentation for further classification. Laboratory studies at that time revealed leukocytosis with elevated neutrophils and lymphocytes as well as a high absolute blast count.

On immunohistochemical staining, the neoplastic cells were positive for CD45, which indicated the neoplasm was hematopoietic, as well as CD10 and the B-cell antigens PAX-5 and CD79a. The cells were negative for CD20, which also is a B-cell marker, but this marker is only expressed in approximately half of pediatric acute lymphoblastic leukemia (ALL) cases with B-cell precursor origin.[1] Markers that typically are expressed in B-cell acute lymphoblastic leukemia (B-ALL)—CD34 and terminal deoxynucleotidyl transferase—were both negative. These results were somewhat contradictory, and the differential remained open to both B-ALL and mature B-cell lymphoma. A bone marrow biopsy showed approximately 65% blasts or leukemic cells (Figure 2). Flow cytometry showed the cells were positive for CD10, CD19, weak CD79a, and variable lambda surface antigen expression. The cells were negative for expression of CD20, CD34, terminal deoxynucleotidyl transferase, myeloid antigens, and CD3. Ultimately, the morphology and immunophenotype were most consistent with a diagnosis of B-ALL. Fluorescence in situ hybridization revealed mixed lineage leukemia, *MLL*, gene rearrangements.

In general, when considering the differential diagnosis of superficial nodules, 5 elements are helpful to consider: the number of nodules (single vs multiple); the location; and the presence or absence of tenderness, pigmentation or erythema, and firmness.[2] Our patient had multiple nodules on the scalp, which were erythematous to slightly purple and firm. The differential diagnosis can be categorized into malignant; infectious; and benign inflammatory, vascular, and fibrous tumors.

Potential oncologic processes include leukemia cutis, lymphoblastic leukemia/lymphoma, Langerhans cell histiocytosis, and rhabdomyosarcoma. Initial laboratory test results were reassuring. Infectious processes in the differential include deep fungal infections such as coccidioidomycosis and nontuberculous mycobacterial infections. Coccidioidomycosis was the most likely to cause skin lesions or masses in our patient; however, it was considered less likely because the patient's family had not traveled or been exposed to an endemic area.[3]

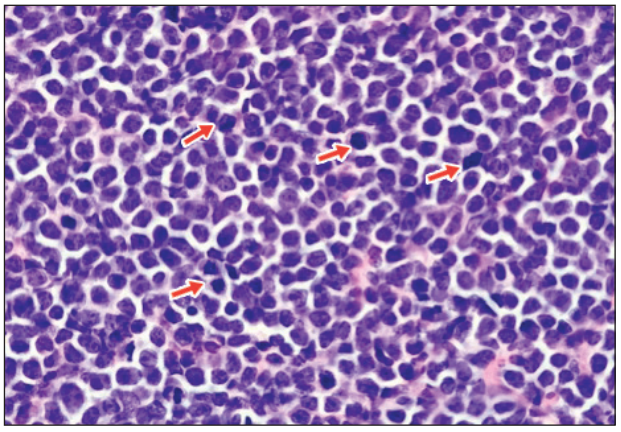

FIGURE 1. Histopathology revealed cells that were intermediate in size with variably mature chromatin and irregular nuclear contours. Numerous mitotic figures were present (red arrows), indicating a high proliferation rate (H&E, original magnification ×40).

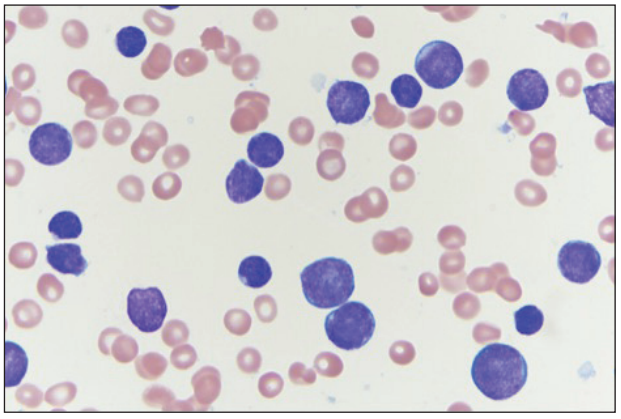

FIGURE 2. A bone marrow biopsy showed 65% blasts or leukemic cells staining (Wright-Giemsa, original magnification ×40).

Benign tumors in the differential include deep hemangioma, which was deemed less likely in our patient because most hemangiomas reach 80% of their maximum size by 5 months of age.[4] Another possible benign tumor is infantile myofibromatosis, which is rare but is the most common fibrous tumor of infancy.[5]

Early-onset childhood sarcoidosis also has been shown to produce multiple nontender firm nodules.[2] This process was considered unlikely in our patient because not only is the disease relatively rare in the pediatric population, but most reported childhood cases have occurred in patients aged 13 to 15 years.[6] Additionally, no uveitis or arthritis was observed in this case.

Ultimately, histopathology and bone marrow biopsy were necessary to determine the diagnosis of B-ALL. Although uncommon, cutaneous involvement can be an early sign of ALL in children.[7] Thus, neoplastic etiologies should be considered in the workup of cutaneous nodules in children, especially when these nodules are hard, rapidly growing, ulcerated, fixed, and/or vascular.[8] Once the diagnosis is established, initial workup of ALL in children should include complete blood cell count with manual differential, prothrombin time, partial thromboplastin time, electrolytes, uric acid, and renal and liver function tests. Often, baseline viral titers such as cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, hepatitis B virus, and varicella-zoster virus also are included. Patients are risk stratified to the appropriate level of treatment based on tumor immunophenotype, cytogenetic findings, patient age, white blood cell count at the time of diagnosis, and response to initial therapy. Treatment typically is comprised of a multidrug regimen divided into several phases—induction, consolidation, and maintenance—as well as therapy directed to the central nervous system. Treatment protocols usually take 2 to 3 years to complete.

Our patient was treated with 1 dose of intrathecal methotrexate before starting the Interfant-06 protocol with a 7-day methylprednisolone prophase. The patient's nodules shrank over time and were no longer present after 14 days of treatment.

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