**Annular Erythema of Infancy With Reactive Helper T Lymphocytes**

Patrick Tran, MD; Michael McLemore, MD

**PRACTICE POINTS**
- Annular erythemas of infancy (AEIs) are rare benign skin eruptions characterized by persistent, annular, urticarial, nonpruritic patches and plaques that develop in patients younger than 1 year.
- Although AEIs are benign, lesions with uncommon histologic features such as large mononuclear cells consistent with reactive helper T lymphocytes may pose diagnostic challenges.

Annular erythemas of infancy (AEIs) are rare benign skin eruptions characterized by persistent, annular, urticarial, nonpruritic patches and plaques that develop in patients younger than 1 year. Histologically, a skin biopsy typically demonstrates a perivascular infiltrate in the dermis composed of small lymphocytes, neutrophils, and increased scattered eosinophils. We report a case of an AEI in an 11-month-old girl with uncommon histologic features. Recognition of these benign cells is important to avoid misdiagnosing them as atypical or neoplastic. We also provide a review of the differential diagnosis for AEIs.

Histologically, the biopsy revealed a superficial to mid dermal, tight, coat sleeve–like, perivascular lymphohistocytic infiltrate admixed with rare neutrophils in eosinophils within the dermis (Figure 2A). The infiltrate also contained numerous large mononuclear cells with enlarged nuclei, fine loose chromatin, rare nucleoli, and a thin rim of cytoplasm (Figure 2B). There were associated apoptotic bodies with karyorrhectic debris. Immunohistochemistry exhibited enlarged cells that were strong staining with CD3 and CD4, which was consistent with reactive helper T cells (Figure 3). A myeloperoxidase stain highlighted few neutrophils. Stains for terminal deoxynucleotidyl transferase, CD1a, CD117, and CD34 were negative. These findings along with the clinical presentation yielded a diagnosis of AEI with reactive helper T cells.

**Comment**

**Clinical Presentation of AEIs**—Annular erythemas of infancy are rare benign skin eruptions that develop in the first few months of life. Few cases have been reported (eTable). Clinically, AEIs are characterized by annular or circinate, erythematous patches and plaques. They can occur on the face, trunk, and extremities, and they completely resolve by 1 year of age in most cases. One case was reported to persist in a patient from birth until 15 years of age. It is thought that AEIs may occur as a hypersensitivity reaction to an unrecognized antigen.

**Histopathology**—Histologically, AEIs demonstrate a superficial and deep, perivascular, inflammatory infiltrate in the dermis composed of small lymphocytes, some neutrophils, and eosinophils. Less common variants of AEI include eosinophilic annular erythema, characterized by a diffuse dermal infiltrate of eosinophils and some lymphocytes, and neutrophilic figurate erythema of infancy, characterized by a dermal infiltrate with neutrophils and leukocytoclasis without vasculitis.

Our patient’s skin rash was unusual in that the biopsy demonstrated few neutrophils, rare eosinophils, and larger mononuclear cells consistent with reactive helper

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The eTable is available in the Appendix online at www.mdedge.com/dermatology.

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T lymphocytes. Although these cells may raise concern for an atypical lymphoid infiltrate, recognition of areas with more conventional histopathology of AEIs can facilitate the correct diagnosis.

**Differential Diagnosis**—The main considerations in the differential diagnosis for AEIs include the following: EAC, familial annular erythema, erythema gyratum atrophicans transiens neonatale, erythema chronicum migrans, urticaria, tinea corporis, neonatal lupus erythematosus, viral exanthems, and leukemia cutis.16

Erythema annulare centrifugum typically begins in middle age and follows a course of 2 or more years.2 It occurs in association with an underlying infection or neoplasm, and it can develop on the trunk and proximal extremities. Morphologically, EAC can present with arcuate or polycyclic lesions with trailing scale. Histologically, a skin biopsy shows a tight, coat sleeve–like, perivascular, lymphohistiocytic infiltrate admixed with rare neutrophils in eosinophils within the dermis (H&E, original magnification ×40). B. The infiltrate contained numerous large mononuclear cells with enlarged nuclei, fine loose chromatin, rare nucleoli, and a thin rim of cytoplasm (H&E, original magnification ×400).

Erythema gyratum atrophicans transiens neonatale also can arise in the first few days of life and can affect the trunk, neck, and lips.16 Morphologically, the skin lesions can present as arcuate erythematous patches (3–20 mm) with raised borders and central atrophy. Histologically, there is epidermal atrophy with a dermal perivascular mononuclear cell infiltrate with edema. Our patient’s clinical presentation was not classic for this condition, and the lesions showed no atrophy.

Erythema chronicum migrans can arise in children, often with a history of an arthropod bite.13 Morphologically, lesions can evolve over weeks to months and rarely are multiple.
Erythema chronicum migrans most commonly occurs in the United States in association with Lyme disease from infection with *Borrelia burgdorferi*. Histologically, erythema chronicum migrans shows a superficial and deep, perivascular lymphocytic infiltrate in the dermis with plasma cells and eosinophils. A silver stain can demonstrate dermal spirochetes. Our patient had no history of an arthropod bite. A Warthin-Starry stain performed on the biopsy was negative for spirochetes, and serologies for Lyme disease were negative.

Urticaria is rare in neonates and can occur on any part of the body. Morphologically, the skin lesions can present as annular, erythematous, and polycyclic plaques that wax and wane. Histologically, there is dermal edema with a mild, perivascular and interstitial, mixed inflammatory infiltrate. Our patient’s biopsy did not reveal notable edema, and the perivascular infiltrate was coat sleeve–like with few neutrophils and eosinophils. The patient did not respond to initial treatment with antihistamines, making urticaria less likely.

Tinea corporis is rare in neonates and can occur on any part of the body. Morphologically, it can present as annular lesions that are fixed and more persistent. Histologically, there are fungal hyphae and/or yeast in the stratum corneum with spongiform dermatitis and parakeratosis. Our patient’s lesions were not scaly, and the biopsy demonstrated minimal spongiosis. A periodic acid–Schiff special stain was negative for fungal microorganisms.

Neonatal lupus erythematosus can arise at birth or during the first few weeks of life. Morphologically, the skin lesions occur on the scalp, forehead, or neck in a periorbital or malar distribution. They can present as erythematous, annular, scaly patches and plaques. Transplacental transmission of material autoantibodies has been implicated in the etiology, and a complication is infantile heart block. Histologically, a skin biopsy typically shows interface/lichenoid dermatitis. However, our patient’s biopsy did not demonstrate interface changes, and serologically she was negative for autoantibodies.

Viral exanthems are skin eruptions that accompany underlying viral infections. Morphologically, patients can present with an erythematous maculopapular rash, sometimes with vesicular or petechial, and urticarial lesions. Laboratory confirmation is made by virus-specific serologies. Histologically, viral exanthems can show a superficial, perivascular, lymphocytic infiltrate in the dermis, with reactive T cells and epidermal spongiosis. Our patient was afebrile and had no known sick contacts. A cytomegalovirus immunohistochemical study on the biopsy was negative, and an Epstein-Barr encoding region in situ hybridization study was negative.

Leukemia cutis is the infiltration of the skin by leukemic cells, most often in conjunction with systemic leukemia. In infants and children, the most common leukemia is B-cell acute lymphoblastic leukemia. Morphologically, the skin lesions are characterized by single or multiple violaceous papules, nodules, and plaques. Histologically, there is a perivascular to interstitial infiltrate of atypical mononuclear cells in the dermis and sometimes subcutis. The leukemic cells demonstrate enlarged nuclei with coarse chromatin and prominent nucleoli. Increased mitotic activity may be seen with karyorrhectic debris. Immunohistochemically, the tumor cells can be positive for myeloperoxidase, CD43, CD68, CD34, and CD117. Although our patient’s biopsy demonstrated mononuclear cells with karyorrhexis, the cells did not have striking atypia and were negative for blast markers. A recent complete blood cell count on the patient was normal.

**Conclusion**

We report an unusual case of AEI with mononuclear cells consistent with helper T cells. One must keep these cells in mind when evaluating a biopsy of AEI, as they are benign and not suggestive of an atypical lymphoid infiltrate or leukemia cutis. This will prevent misdiagnosis and ensure that the patient receives appropriate management.

**REFERENCES**


### eTABLE. Summary of Annular Erythema of Infancy Cases

<table>
<thead>
<tr>
<th>Reference (year)</th>
<th>Sex/age</th>
<th>Clinical description of rash</th>
<th>Anatomic location of rash</th>
<th>Duration of rash</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peterson and Jarratt² (1981)</td>
<td>M/6 mo</td>
<td>Intermittent urticarial eruption; some papules appeared to have enlarged centrifugally into 2–3-cm rings with urticarial borders</td>
<td>Generalized, sparing the palms and soles</td>
<td>8 mo</td>
<td>Moderate perivascular infiltrate of lymphocytes and eosinophils</td>
</tr>
<tr>
<td>Toonstra and de Wit³ (1984)</td>
<td>F/8 mo</td>
<td>Large, irregularly shaped, annular lesions with red, raised, urticarial borders</td>
<td>Face, back, distal extremities</td>
<td>11 mo</td>
<td>Moderately dense perivascular infiltrates of lymphocytes, histiocytes, and numerous eosinophils present in the mid and lower dermis</td>
</tr>
<tr>
<td>Hebert and Esterly⁴ (1986)</td>
<td>F/7 mo</td>
<td>Recurrent asymptomatic arcuate and annular skin lesions beginning as &quot;little red dots&quot; that enlarged rapidly into a palpable erythematous arc or ring</td>
<td>Shoulder, back, buttocks</td>
<td>14 mo</td>
<td>Mid acanthosis and a dense dermal perivascular infiltrate composed of lymphocytes, histiocytes, eosinophils, and a few plasma cells</td>
</tr>
<tr>
<td>Cox et al⁵ (1987)</td>
<td>F/2 y</td>
<td>Asymptomatic annular plaques with wide, raised, firm, erythematous borders without vesiculation or formation of bullae</td>
<td>Generalized, face, upper trunk, feet</td>
<td>4 wk</td>
<td>Edematous dermis with an inflammatory infiltrate of lymphocytes, polymorphonuclear leukocytes, and histiocytes around blood vessels and to a lesser extent around nerves and sweat glands with no excess of eosinophils in the inflammatory infiltrate</td>
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<tr>
<td>Helm et al⁶ (1993)</td>
<td>M/22 mo</td>
<td>Widespread erythematous eruption with no appreciable scale; lesions were annular and arciform with no vesicles, pustules, ulcers, or papules</td>
<td>Lower extremities</td>
<td>14 mo</td>
<td>Perivascular infiltrate with eosinophils</td>
</tr>
<tr>
<td>Kunz et al⁷ (1998)</td>
<td>M/4 y</td>
<td>Nonitching erythematous papules on the trunk that evolved into annular and gyrate erythemas within weeks</td>
<td>Trunk</td>
<td>Several months</td>
<td>Striking eosinophilic inflammatory infiltrate predominantly in perivascular areas, without peripheral blood eosinophilia</td>
</tr>
<tr>
<td>Stachowitz et al⁸ (2000)</td>
<td>M/4.5 mo</td>
<td>Well-demarcated, slightly itching, biocular erythema with a raised border</td>
<td>Periorbital regions</td>
<td>2.5 mo</td>
<td>NA</td>
</tr>
<tr>
<td>Wong et al⁹ (2002)</td>
<td>F/15 y</td>
<td>Persisting extensive annular erythematous eruption since birth</td>
<td>Trunk</td>
<td>NA</td>
<td>Heavy mixed inflammatory infiltrate of lymphocytes, neutrophils, histiocytes, and eosinophils, both perivascularly and extending diffusely throughout the dermis</td>
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<tr>
<td>Patrizi et al(^8) (2008)</td>
<td>M/21 mo</td>
<td>Annular erythematous lesions with elevated borders and central resolution without scaling, vesicles, or crusts</td>
<td>Face, lower and upper extremities</td>
<td>NA</td>
<td>Diffuse interstitial and perivascular infiltrate of neutrophils and lymphocytes with nuclear dust</td>
</tr>
<tr>
<td>Saha et al(^9) (2014)</td>
<td>M/5 d</td>
<td>Multiple brightly erythematous, annular plaques with palpable expanding borders and no detectable scaling or atrophy</td>
<td>Chest, back, arms, thighs, and face</td>
<td>NA</td>
<td>Superficial and deep perivascular lymphohistiocytic inflammatory infiltrate</td>
</tr>
<tr>
<td>Pfingstler et al(^10) (2014)</td>
<td>F/5 d</td>
<td>Discrete, annular, erythematous plaques with raised borders and central clearing</td>
<td>Chest, arms, and neck</td>
<td>3–6 wk</td>
<td>Diffuse inflammatory infiltrate with a predominance of eosinophils</td>
</tr>
<tr>
<td>Del Puerto Troncoso et al(^11) (2015)</td>
<td>F/2 y</td>
<td>Multiple annular and polycyclic, erythematous plaques with indurated borders and petechiae on the rims</td>
<td>Upper chest, abdomen, and upper back</td>
<td>NA</td>
<td>Superficial and deep perivascular and interstitial mixed-cell dermatitis, composed predominantly of neutrophils with abundant nuclear dust</td>
</tr>
<tr>
<td>Hamidi et al(^12) (2018)</td>
<td>F/9 mo</td>
<td>Annular erythematous lesions with raised borders and central clearing</td>
<td>Face, arms, and legs</td>
<td>6 mo</td>
<td>Superficial and deep perivascular and interstitial infiltrate composed of numerous neutrophils and scattered eosinophils with nuclear dust</td>
</tr>
<tr>
<td>Patel et al(^13) (2018)</td>
<td>Young child</td>
<td>Faint, nonscaling, annular, serpiginous, erythematous plaques with central clearing and barely elevated borders</td>
<td>Lower legs, abdomen, and buttocks</td>
<td>6 mo</td>
<td>Superficial and deep, perivascular, and interstitial inflammatory infiltrate consisting of lymphocytes, histiocytes, neutrophils, and eosinophils</td>
</tr>
<tr>
<td>Current case</td>
<td>F/11 mo</td>
<td>Annular erythematous patches and plaques</td>
<td>Back, arms, and legs</td>
<td>6 mo</td>
<td>Superficial to mid dermal, tight, coat sleeve–like, perivascular, lymphohistiocytic infiltrate admixed with rare neutrophils in eosinophils within the dermis</td>
</tr>
</tbody>
</table>

Abbreviations: M, male; F, female; NA, not available.