

CASE REPORTS

A case of annular erythema of infancy accompanied by elevated tryptase

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Email: jennifer.adams@unmc.edu**Abstract**

Annular erythema of infancy (AEI) is characterized by self-limited eruptions of erythematous, annular to polycyclic patches and plaques, the etiology of which is thought to involve a hypersensitivity reaction to an unknown antigen. We present a case of AEI mistaken for systemic mastocytosis due to elevated serum tryptase. We were unable to find prior reports of an association between AEI and elevated tryptase in the literature.

KEYWORDS

annular erythema, infant, mastocytosis, systemic, skin abnormalities, tryptase

1 | INTRODUCTION

Annular erythema of infancy (AEI) is an idiopathic figurate erythema characterized by self-limited eruptions of erythematous, annular to polycyclic patches and plaques. Individual lesions resolve over days without residual scale or hyperpigmentation.¹ This asymptomatic rash predominantly affects the trunk, face, and extremities. Diagnosis of AEI is established by both clinical and histopathologic examination. The condition begins during infancy and the episodic eruptions generally subside after the first year of life without intervention.²

The etiology of AEI is unknown, but it is thought to involve a hypersensitivity reaction to an unknown antigen. Histologic findings are nonspecific with perivascular infiltrates of lymphocytes and either eosinophils or neutrophils.¹ The presence of annular erythema carries a broad differential, and in some cases, aberrant laboratory findings may lead to workup for systemic diseases even in the absence of symptoms. Herein, we report a case of AEI mistaken for systemic mastocytosis.

2 | CASE REPORT

A 5-month-old male born at 34 weeks presented to our dermatology clinic with a 4-month history of a diffuse erythematous rash. He was

referred by pediatric oncology due to concern for systemic mastocytosis. Past medical history included this ongoing rash and a facial infantile hemangioma managed with propranolol. He was seen multiple times by his pediatrician and a local dermatologist prior to this visit with concern for either viral or drug-induced erythema multiforme. However, previous viral testing including herpes simplex virus, Epstein-Barr virus, and cytomegalovirus PCR was negative, and no improvement was seen after discontinuing propranolol for 3 months. At his most recent pediatric visit, further laboratory testing revealed an increased proportion of eosinophils (4.0%, reference range 0–3.0) without eosinophilia (0.4 k/uL, reference range 0–0.8), increased serum IgE (123 kU/L, normal \leq 30), and elevated tryptase (24.8 mcg/L, normal $<$ 11.0). A lesional punch biopsy specimen demonstrated mixed dermal inflammation with numerous eosinophils. Special staining for mast cells (immunoperoxidase CD117) highlighted scattered interstitial cells but no clusters or aggregates of mast cells.

The patient did not scratch at or appear to be bothered by the rash. There were no associated fevers or other systemic symptoms. The rash waxed and waned and resolved briefly after a short course of systemic steroids as well as during a recent bout of otitis media. Physical examination revealed red polycyclic edematous plaques scattered throughout the face, trunk, and extremities (Figure 1). The lesions were without overlying scale and non-tender to palpation. Darier sign was negative.

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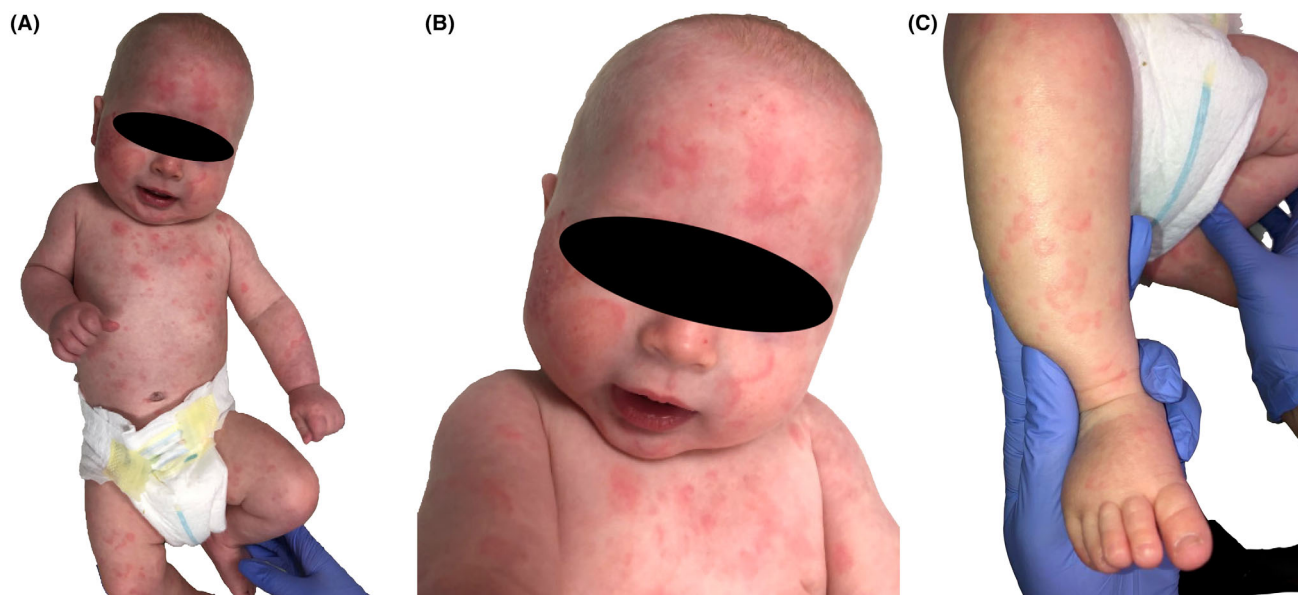


FIGURE 1 Red polycyclic edematous plaques scattered throughout the face, trunk, and extremities

TABLE 1 Differential diagnosis of annular lesions during infancy

Differential	Key features	Important workup
Annular erythema of infancy	Recurrent, self-limited eruptions of annular patches and plaques of erythema. Lesions are asymptomatic and resolve over days. Typically remits by age 1 year ²	Biopsy
Neonatal lupus erythematosus (NLE)*	Photosensitive rash of macular to plaque-like annular erythema, classically affecting the upper eyelids and scalp. Atrioventricular heart block is a distinctive sequelae ⁹	Anti-SSA/Ro, anti-SSB/La, anti-U1RNP, antinuclear antibodies (mother or infant), electrocardiogram, complete blood count (CBC), liver function tests (LFTs). Biopsy if diagnosis is unclear ⁹
Erythema gyratum atrophicans transiens neonatale	Annular patches and plaques with an erythematous raised border and atrophic center. Lesions appear within a few days of birth and resolve by age 1 year ¹⁰	Antibody screen for NLE, biopsy with direct immunofluorescence (DIF) ¹⁰
Erythema marginatum rheumatica	Evanescence eruption of blanchable erythematous macules with sharply demarcated borders. Typically spares the face ¹¹	Throat culture for group A Streptococci, rapid strep antigen test, anti-streptolysin O (ASO) antibody titer
Serum sickness like reaction	Urticaria-like, annular, edematous plaques that may evolve to purplish discoloration. Joint swelling and arthralgias are characteristic ²	Urinalysis; more extensive laboratory testing is indicated when a medication cannot be readily identified as the culprit or in ill-appearing patients
Acute annular urticaria (urticaria multiforme)	Annular to polycyclic erythematous plaques +/- violaceous center. Lesions disappear within 24 hours. Pruritus and dermatographism are characteristic ^{2,10}	None
Erythema annulare centrifugum (EAC)	Erythematous papules that expand centrifugally with central clearing +/- trailing scale ¹²	Age-appropriate cancer screening if paraneoplastic erythema annulare centrifugum eruption (PEACE) is suspected ¹²
Familial annular erythema	Urticarial lesions with raised edges and central clearing that appear within a few days of birth. Like EAC, may expand centrifugally. Look for positive family history ^{10,13}	Biopsy
Tinea corporis	Erythematous patch with a scaly leading edge that expands centrifugally. Eventually develops central hypopigmentation to form an annular plaque	Potassium hydroxide (KOH) preparation

(Continues)

TABLE 1 (Continued)

Differential	Key features	Important workup
Cryopyrin-associated periodic syndromes (CAPS) ^a	Includes familial cold autoinflammatory syndrome (FACS), Muckle–Wells syndrome (MWS), and neonatal onset multisystemic inflammatory disease (NOMID). Characteristic dermatologic manifestation is a recurrent, nonpruritic urticarial eruption. May be cold-induced (FACS) or tender to touch (MWS) ¹⁴	CAPS is a multi-system inflammatory disease requiring extensive workup based on level of suspicion, including CBC, inflammatory markers, skin biopsy, and genetic testing (NLRP3 gene), among others ¹⁴

^aNeonatal autoimmune/autoinflammatory diseases are important to consider in the differential diagnosis. NLE and CAPS classically present with annular lesions. Given the appropriate clinical picture, other neonatal autoimmune diseases with cutaneous involvement to consider include Behcet's disease, neonatal dermatomyositis, neonatal anti-phospholipid syndrome, and neonatal scleroderma.¹⁵

Anti-SSA/Ro antibodies, anti-SSB/La antibodies, and an electrocardiogram were obtained to rule out neonatal lupus, all of which were within normal limits. Due to the polycyclic nature of his rash, negative Darier sign, and no mast cell aggregates on biopsy, further workup for systemic mastocytosis was not pursued. Given the asymptomatic, waxing and waning nature of his rash, the clinical features and histopathologic findings fit the diagnosis of AEI. The parents opted for watchful waiting and complete resolution of the rash was observed by age 15 months.

3 | DISCUSSION

AEI is a benign condition with a self-limited course. Most cases remit by 1 year of age, though chronic courses persisting beyond infancy have been reported.^{3,4} Two variants exist, which are classified by a predominance of either eosinophils (eosinophilic annular erythema) or neutrophils (neutrophilic figurate erythema of infancy) on histopathology. The present case was most consistent with the eosinophilic variant. There is no standard treatment, but several options may be considered for the eosinophilic variant including topical and systemic steroids, antimalarials, dapsone, and monoclonal antibodies such as dupilumab.^{5,6} In practice, AEI is really a diagnosis of exclusion given its relatively nonspecific clinical presentation and histopathology. Although benign, AEI must be differentiated from other conditions that may present with annular lesions during infancy, especially neonatal lupus erythematosus (Table 1).

Prior to evaluation in our dermatology clinic, the patient was being worked up for systemic mastocytosis based on an elevated tryptase level. Persistent elevation of serum tryptase above 20 ng/mL is one of the minor criteria for systemic mastocytosis and is present in the vast majority of patients.⁷ It should be noted that tryptase was measured only once in this case and whether its elevation persisted is unknown. An elevated tryptase level should also be interpreted in the context of the entire clinical picture, as elevations can be seen in various hypersensitivity reactions such as anaphylaxis, urticaria, angioedema, familial hypertryptasemia, and drug eruptions.⁸ We were unable to find prior reports of elevated tryptase in association with AEI, although it is not routinely measured in this setting. Given that AEI is thought to be a hypersensitivity reaction to an unknown antigen, hypertryptasemia may be more common than we realize.

Our case report highlights the importance of interpreting laboratory findings in the context of the entire clinical picture. Recognizing when an annular pattern is present is key to establishing an accurate differential diagnosis (Table 1). In the present case, this approach prevented the patient further unnecessary testing (e.g., bone marrow biopsy) and potential morbidity. The asymptomatic, polycyclic and waxing and waning nature of his rash, negative Darier sign and absence of mast cell aggregates on biopsy were evidence against mastocytosis in spite of the elevated serum tryptase. In theory, hypertryptasemia could be seen in other cases of AEI. However, further research is necessary to assess the incidence and clinical value of this association.

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CONFLICTS OF INTEREST

No conflict of interest.

CONSENT STATEMENT

Informed consent and releases from the parent(s)/guardian(s) to publish photographs were obtained and submitted with the manuscript.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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