

# Infantile Acute Hemorrhagic Edema of the Skin

Mauro Paradisi, MD, Rome, Italy

Giorgio Annessi, MD, PhD, Rome, Italy

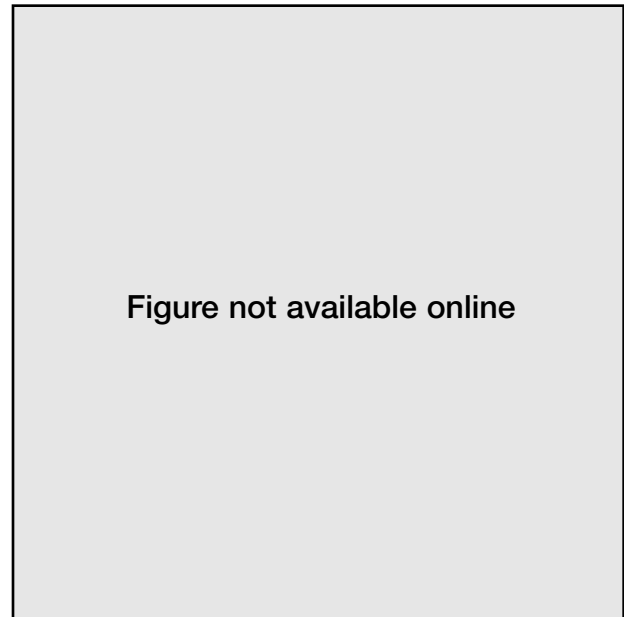
Angelo Corrado, MD, Rome, Italy

*Infantile acute hemorrhagic edema (AHE) of the skin is an uncommon form of cutaneous leukocytoclastic vasculitis that occurs in children younger than 3 years. We describe a 10-month-old boy with AHE, in whom the disease appeared after antibiotic treatment for an acute respiratory illness. AHE presented with fever, acral edema, and rosette-shaped purpuric plaques on the face and limbs. The causes of AHE are unclear, as is its nosologic position. Some authors consider the disease as a purely cutaneous form of Henoch-Schönlein purpura, and others believe that AHE should be regarded as a distinct clinicobiologic entity within the spectrum of leukocytoclastic vasculitis.*

**I**nfantile acute hemorrhagic edema (AHE) of the skin is an unusual form of cutaneous leukocytoclastic vasculitis that primarily affects newborns. AHE is characterized by fever, acral edema, and rosette-shaped purpuric plaques that show leukocytoclastic vasculitis of small dermal vessels on histologic examination.<sup>1-7</sup> The disease is usually confined to the skin, and spontaneous recovery occurs within a few weeks. Since Snow<sup>1</sup> first described the condition in 1913, fewer than 100 cases of AHE have been reported. We describe a child with AHE in whom the cutaneous eruption appeared after antibiotic treatment for an upper airway infection.

## Case Report

A 10-month-old boy presented with a 3-day history of symmetrical, erythematous, and edematous purpuric plaques on the face, buttocks, and distal part of the limbs. The lesions began as edematous papules with central petechiae that rapidly expanded centrifugally to form multiple plaques with a central purpuric component surrounded by a pale palpable



**Figure 1.** Rosette-shaped purpuric plaques on the face and the right upper limb.

ring, which was rimmed by an erythematous halo (Figure 1). Occasionally, these rosette-shaped lesions became confluent to form large purpuric plaques with nummular, arcuate, or polycyclic shapes (Figure 2). The eyelids and the distal part of the limbs were markedly edematous. The skin eruption was accompanied by fever (37.8°C), elevation of the erythrocyte sedimentation rate, and serum  $\alpha$ -2 globulin. Full blood count, measurement of hemoglobin level, urinalysis, creatinine levels, uremia, glycemia, immunoglobulins, fibrinogenemia, coagulation tests, C3 and C4 levels, circulating immune complexes, CD4/CD8 ratio, throat swabs, and examination of stool for ova and parasites all showed normal results. The parents noted that the cutaneous eruption appeared 2 days after treatment with oral clarithromycin for an upper airway infection was discontinued.

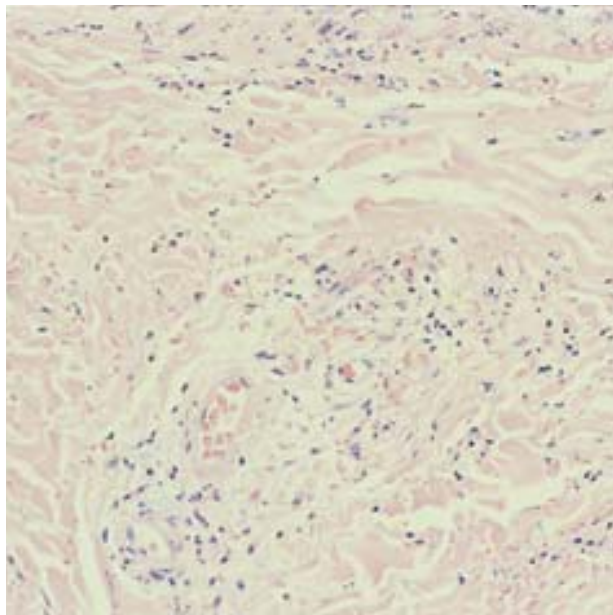
Results of a histologic examination of a plaque showed a superficial and deep perivascular and

Drs. Paradisi, Annessi, and Corrado are from the Istituto Dermatologico dell'Immacolata, Rome, Italy.

Reprints: Giorgio Annessi, MD, Servizio di Istopatologia, Istituto Dermatologico dell'Immacolata, IRCCS, Via Monti di Creta 104, 00167 Rome, Italy. (e-mail G.Annessi@idi.it).



**Figure 2.** Hemorrhagic macules, papules, and plaques are present on the lower limbs. Some of the lesions have an arciform configuration and others are arranged in concentric rings.



**Figure 3.** Deposits of fibrin are seen in the walls of dermal vessels. An infiltrate of neutrophils, nuclear dust, and extravasated erythrocytes is present around the vessels and in the interstitium (H&E, original magnification  $\times 200$ ).

interstitial infiltrate composed mostly of neutrophils and abundant nuclear dust. Deposits of fibrin were present in the walls of small dermal vessels in association with many extravasated erythrocytes and edema of the papillary dermis (Figure 3). Direct immunofluorescence study results were negative.

The patient was treated with betamethasone (1mg/kg per day), which resulted in rapid fading of the lesions and complete recovery within 6 days. No recurrence was observed over a 1-year follow-up period.

### Comment

The clinical, histologic, and biologic features of our case fit the classic description of AHE. Typically, the lesions occur in crops and may be seen at different stages of evolution. Laboratory studies usually show an elevated erythrocyte sedimentation rate, leukocytosis, an increase in  $\alpha$ -2 globulin and, occasionally, serum IgG and IgM levels.<sup>4</sup> On histologic examination, AHE shows typical changes of leukocytoclastic vasculitis. Results of direct immunofluorescence study are typically negative.<sup>1-3,5-7</sup>

A characteristic feature of AHE is the sharp contrast between the impressive clinical picture and the usually benign course of the disease. Despite the extent of skin lesions, children affected by them are otherwise healthy.<sup>1-7</sup> In rare cases, the cutaneous eruption is accompanied by diarrhea, melena, arthralgia, transient microscopic hematuria, and mild proteinuria. However, persistent visceral

changes have not been reported.<sup>2,8,9</sup> Skin lesions usually resolve spontaneously within 2 or 3 weeks, leaving residual postinflammatory hyperpigmentation. To our knowledge, no recurrences have been reported. There is no specific treatment for AHE. In our patient, systemic corticosteroid treatment produced complete recovery in 6 days, shortening the natural course of the disease.

The causes of AHE are unknown. The usual appearance of the disease during winter months and its frequent association with vaccination, upper airway infections, otitis, or conjunctivitis indicate that, in most cases, AHE may be the consequence of an immunologic response to infectious agents.<sup>4</sup> The report by Cunningham et al<sup>7</sup> of a case of congenital AHE associated with maternal gastroenteritis 6 weeks before delivery suggests that the disease also could be mediated by maternal-fetal transfer of either infectious agents or immune complexes. However, many of these patients had been treated with various antibiotics or anti-inflammatory drugs before the onset of the cutaneous eruption.<sup>4,10</sup> Thus, the hypothesis that AHE may be a peculiar reaction to drug intake cannot be excluded.

In our patient, both an upper airway infection and an antibiotic treatment with clarithromycin preceded the appearance of AHE by a few days. Unfortunately, we were not able to discern whether the infection, the drug, or their combined effect was the primary cause that triggered the cutaneous eruption.

Although the nosologic position of AHE is still debated, we believe its clinicobiologic features are specific enough to consider it a distinctive variant of cutaneous childhood leukocytoclastic vasculitis. Its clinical recognition allows a good prognosis to be made for infants, because the disease runs an invariably self-limiting and benign course.

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