Acute Hemorrhagic Edema of Infancy: A Case Series of Three Cases

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ABSTRACT

Acute hemorrhagic edema of infancy (AHEI) is a poorly known benign vasculitis. With a rapid course, self-limited evolution, and without specific diagnostic tests, it is poorly diagnosed. It has differential diagnosis with Henoch–Schönlein's purpura, multiform erythema, Kawasaki's incomplete disease, or urticaria. We present a case series of three cases of children with a clinical diagnosis of AHEI, and in two of them, a biopsy was performed which confirmed the diagnosis. The three children have a maculopapular purpuric eruption, fever, and edema at the extremities. They were treated with symptomatic medications and showed improvement in a few days. AHEI is a rare vasculitis, sometimes underdiagnosed, due to the similarity with other differential diagnoses, much more prevalent. As it is not frequently described, and due to the exuberance of symptoms, it is a disease susceptible to diagnostic errors and iatrogenic treatments.

Key words: Acute hemorrhagic edema of infancy, Immune mediated, Purpura, Vasculitis

Acute hemorrhagic edema of infancy (AHEI) is an acute, self-limited, benign cutaneous leukocytoclastic small-vessel vasculitis affecting children younger than 2 years of age. The disease is more common in males (2:1) [1]. It is characterized by a triad, composed of fever, large erythematous purpuric skin lesions in a target-like pattern, and marked edema mainly on the face, auricles, and extremities [2]. It was originally described by Snow in 1913 [1]. These cases should be deal in an emergency because families seek the service due to the intensity of the skin condition. Thus, the early recognition of the pathology is important to differentiate it from other potentially lethal purpuric conditions. The rarity and importance of early diagnosis, avoiding unnecessary procedures, motivate this case report.

CASE SERIES

Case 1

A 2-year and 7-month-old male presented with maculopapular, erythematous, purpuric, and pruritic lesions with craniocaudal evolution in the face and lips (Fig. 1a) along with the presence of a febrile peak. Preceding the cutaneous lesions, he presented rhinorrhea and cough. He was taken to the children's emergency room on the 2nd day with lesions progressing to the upper and lower limbs (Fig. 1b), bilateral conjunctival hyperemia, and three more feverish peaks (with a maximum temperature of 38.8°C). On the following day, he presented oropharyngeal hyperemia with hemorrhagic spots on the soft palate, a distal portion of the tongue with a raspberry appearance, and lesions on the face, ears, upper and lower limbs, including palmer, and plantar surfaces. Associated with the cutaneous picture, there was bilateral edema in the feet and ankles and bilateral benign palpable cervical lymph nodes.

The laboratory tests revealed normal blood count, increased C-reactive protein (CRP) (5.9 mg/dL for reference value up to 1.0 mg/dL), transaminases increased by 3 times the reference value at the beginning of condition (however, returning to baseline values with 7 days of history), alkaline phosphatase increased by <1 time the reference value, and gamma-glutamyltransferase (GGT) increased by 4 times the expected value. A biopsy was performed, confirming the diagnosis of AHEI. The patient maintained skin and mucosal lesions for 7 days since the onset of the condition, with spontaneous regression. He was treated with symptomatic medications and antihistamine for itching.

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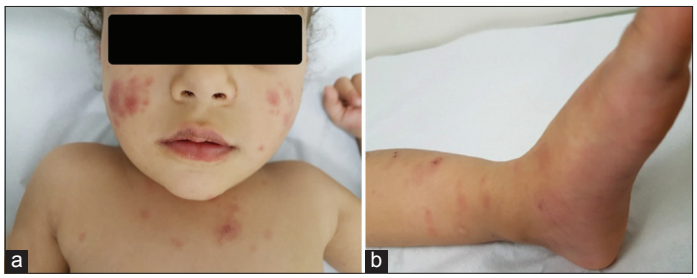

Figure 1: (a) Maculopapular, erythematous, and purpuric lesions, in the face and lips; (b) lesions progressing to the lower limbs (Case 1)

Case 2

A 9-month-old male presented with a history of 4 days of general decline, signs of mild respiratory failure, and appearance of erythematous-purpuric macules and papules on the limbs (Fig. 2a), arms, face, and ears (Fig. 2b) for 1-day onset. The dermatological examination showed erythematous-purple macules and papules almost generalized in the face, auricular pavilions, lower limbs, upper limbs, and few papules on the trunk, back of the feet, and plantar regions. He also had edema of the hands, feet, and ankles bilaterally.

The laboratory tests revealed a hemogram with slightly reduced red blood cells, hemoglobin, and hematocrit, increased CRP (3.6 mg/dL for reference value up to 1.0 mg/dL), increased erythrocyte sedimentation rate (ESR) with a value of 19 mm/h (mL/hour) (reference value up to 10 mm/h), and other examinations without changes. A biopsy was performed which showed leukocytoclastic vasculitis, confirming the diagnosis of AHEI. The lesions gradually improved over 20 days, only with symptomatic medications such as antihistamines and fever medications.

Case 3

A 1-year and 4-month-old female presented with the appearance of purple spots which was accompanied by pain. Initially, the purple spots were on the back of the feet but slowly progresses to the lower limbs and buttocks. Fifteen days before the onset of the skin condition, she had flu, cough, but without fever, and 4 days before, she had diarrhea lasting for 2 days. On examination, he presented erythematous and purple macules of various sizes on the lower limbs, bilaterally, with more extensive lesions on the left buttock (Fig. 3a). He also had mild foot swelling (Fig. 3b).

The laboratory tests revealed a complete blood count with leukocytes increased by 2 times the reference value, slightly increased CRP (1.9 mg/dL for reference value up to 1.0 mg/dL), ESR increased with a value of 20 mm/h (reference value up to 10 mm/h), and other examinations without changes. As the child had a very good general condition, there was a fast improvement. Furthermore, due to the will of the family, we chose not to perform the biopsy. The patient presented a progressive improvement of the condition, with gradual involution of the lesions in 7 days, being treated only with symptomatic medications.

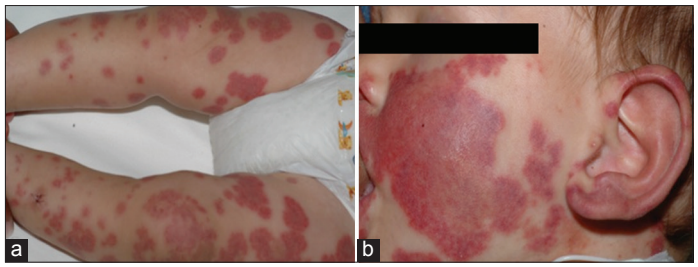

Figure 2: (a) Erythematopurpuric macules and papules on the (a) limbs and (b) on face and ears (Case 2)

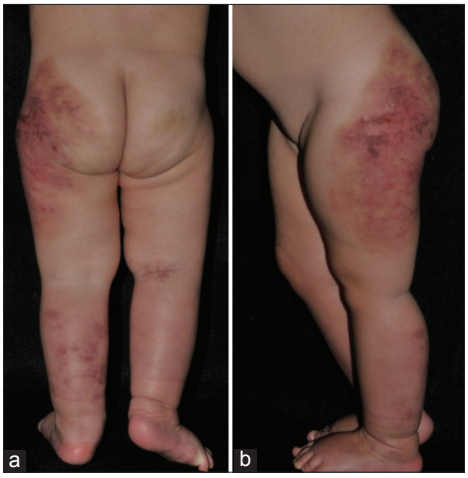

Figure 3: (a) Erythematous and purple macules, of various sizes, on the lower limbs, bilaterally, with more extensive lesions on the left buttock; (b) mild foot swelling (Case 3)

DISCUSSION

Acute hemorrhagic edema of infancy has an unknown etiology, but there is a relationship with infection, drugs, or vaccines in 75% of cases, preceding classical symptoms [3]. There are subsidies to think that AHEI is an immune-mediated reaction to pathological aggression [4]. Most of the cases described are preceded by infectious episodes, predominantly in the respiratory, gastrointestinal, and urinary tract [5,6], which may be viral or bacterial [7]. The peak incidence is during winters when there is a higher incidence of respiratory infections [1]. Fever is typically low grade and is present in approximately 50% of cases [7,8].

There seems to be a relationship with Group A hemolytic *Streptococcus* beta infections, as well as with the Coxsackie A and B viruses. There is also a relationship with vaccination, especially diphtheria, tetanus, pertussis (DTP), and *Haemophilus* type B vaccines, as well as cases preceded by medication use, such as amoxicillin, cephalosporins, sulfamethoxazole-trimethoprim, and paracetamol. Finkelstein gave a detailed description in Europe in 1938 and since then it has been recognized in the literature under various terms: Finkelstein disease, Seidlmayer syndrome, and infantile post-infectious iris-like purpura, and edema [1,3].

The diagnosis is usually clinical. Krause *et al*. in 1996 suggested the following criteria for diagnosing AHEI: Age <2 years, purpuric or ecchymotic target-like skin lesions with edema on the head, face, and extremities, with an abrupt appearance

occurring primarily on the dorsum of the hands and feet, with or without mucosa involvement, and lack of systemic disease, or visceral involvement. Spontaneous recovery occurs within a few days or weeks. Despite the extent of the cutaneous findings, the child looks well and non-toxic with normal vital parameters and normal blood tests that allowed to exclude more serious diseases [3,7,8].

A typical feature of AHEI is the discrepancy between dramatic cutaneous involvement and good clinical conditions of the affected children [3,9]. Despite the suggested criteria, 20% of cases are described outside this age group, in addition to visceral involvement being described in 10% of cases, which disappear with skin lesions.

Diagnostic confirmation is possible through biopsy of the lesion, having as histopathological findings polymorphonuclear and perivascular lymphocyte infiltrate with nuclear debris, and fibrinoid necrosis, as well as other leukocytoclastic vasculitis [3,10]. In immunohistochemistry, C1q (Complement C1q), fibrinogen, IgM (immunoglobulin M), IgG (immunoglobulin G), and IgE (immunoglobulin E) are deposited on the wall and around the small vessels. IgA (immunoglobulin A) can be found only in 10–35% of cases.

The main differential diagnosis of AHEI is Henoch–Schönlein purpura (HSP) [11]. Other differential diagnoses include meningococcemia, Kawasaki disease, urticaria, urticarial vasculitis, idiopathic thrombocytopenia, erythema multiforme, Sweet syndrome, Gianotti-Crosti disease, drug-induced vasculitis, child abuse, and trauma-induced purpura [1,3-5,12,13]. In American literature, some authors consider AHEI to be a variant of HSP, due to purpuric lesions and feverish conditions. There is also the similarity of the previous existence of infections. However, several differences were observed between the two comorbidities. While AHEI predominates between 2 and 24 months and leads to lesions on the face and extremities, without systemic involvement, HSP predominates in patients aged 3–8 years, with lesions in the lower limbs and commonly affects joints, kidneys, and gastrointestinal tract. Systemic findings, such as abdominal pain, renal disease, and arthritis, are common and can negatively influence the final prognosis of the disease. HSP can be distinguished clinically by the presence of palpable purpura on the extensor surface of legs and buttock, whereas, in AHEI, the face and extremities are prominently involved and are accompanied by edema.

Histopathological findings are very similar [1,12]. Both AHEI and HSP show leukocytoclastic vasculitis on histopathology [4]. In addition, IgA deposits are rare in AHEI, while in HSP, IgA, fibrin, and C3 (complement C3) deposits predominate in the periphery of the vessels [14]. In this way, the two vasculitides are shown as two different entities.

Clinically, despite the exuberant presentation, with high fever and lesions that can progress quickly to bruises, spontaneous resolution is the expected prognosis, and skin manifestations progressively diminished and disappeared spontaneously within approximately 1–3 weeks in the majority of cases [7-9,12,15]. There is no indication of drug treatment since the disease is self-limiting and benign. The use of corticosteroids and antihistamines is also not indicated, as there is no scientific evidence of improvement in the duration of the disease.

CONCLUSION

AHEI is a rare vasculitis, sometimes underdiagnosed, due to the similarity of the other differential diagnoses, much more prevalent. As these patients arrive at the service through emergency units, they need to be prepared to make the differential diagnosis, avoiding unnecessary diagnostic procedures. Attention should be paid to clarifications regarding the evolution and benignity of the condition for the families, avoiding incorrect and unnecessary use of medications.

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