

Acute hemorrhagic edema of childhood

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SUMMARY: Suehiro RM, Soares BS, Eisencraft AP, Campos LMMA, Silva CAA. Acute hemorrhagic edema of childhood. *Turk J Pediatr* 2007; 49: 189-192.

Acute hemorrhagic edema (AHE) of childhood, a variant of Henoch-Schönlein purpura (HSP), is a rare vasculitis with benign course, generally no systemic involvement and rare flares. From January 1983 to June 2004, 4,502 patients were followed at the Pediatric Rheumatology Unit, Hospital of Clinics. Diagnosis of HSP was made in 203 cases (4.5%), of which 5 (0.1%) had AHE. All patients with AHE were male and the mean age at onset was 18 months (range: 8 to 21 months). All five cases presented vasculitis with characteristic hemorrhagic and purpuric lesions in malar region of the face, associated with painless edema of the hands and feet. Laboratory exams were normal. Upper respiratory tract infection preceding clinical manifestations occurred in four and mononucleosis in one. Treatment with corticosteroids was necessary only in one patient with necrotic lesions on the face and ears.

Key words: acute hemorrhagic edema, Henoch-Schönlein purpura, mononucleosis, childhood.

Henoch-Schönlein purpura (HSP) is a small vessel vasculitis, the major manifestations of which include arthritis, nonthrombocytopenic purpuric lesions, abdominal pain and renal disease^{1,2}. Some authors consider acute hemorrhagic edema (AHE) as a variant of HSP³⁻¹⁰. AHE was first described by Snow (1913)^{3,4,5,8,9} in a child with purpuric lesions, urticaria and edema of the hands and feet. After 1940, this disease also became known as Finkelstein's disease or Seidlmayer's syndrome^{3,4,5,8,9}. It is a rare disease, with approximately 100 cases described in the literature⁶. AHE predominantly involves infants from 4-24 months of age. There is usually only cutaneous involvement rather than visceral, thus differing from HSP. The course is generally favorable without requiring treatment³⁻¹⁰.

The objective of the present study was to describe the demographic characteristics, clinical manifestations, laboratory exams and treatment of children with AHE followed at the Pediatric Rheumatology Unit, Department of Pediatrics, Hospital of Clinics, Faculty of Medicine, University of São Paulo.

Material and Methods

From January 1983 to June 2004, 4,502 patients were followed at the Pediatric Rheumatology Unit of our University Hospital. The diagnosis of HSP was made in 203 cases (4.5%), and their medical records were analyzed retrospectively.

The diagnosis of AHE was clinical. However, all the patients were submitted to laboratory exams. The following exams were normal in all patients: blood count, erythrocyte sedimentation rate, C-reactive protein, clotting tests, serum urea, serum creatinine and urinalysis.

Results

Of the 203 HSP cases, 5 (0.1%) presented AHE and all were boys. The mean age at onset of AHE was 18 months (range: 8 to 21 months). The demographic characteristics, clinical manifestations, recurrences and treatment of the patients with AHE are shown in Table I.

Upper respiratory tract infection (URTI), preceding the disease by one to two weeks, was present in four cases. One of the patients (Case 3) presented mononucleosis confirmed

Table I. Demographic Characteristics, Clinical Manifestations, Recurrence and Treatment of Five Acute Hemorrhagic Edema Patients

	Case 1	Case 2	Case 3	Case 4	Case 5
Age (months)	8	15	18	18	21
Sex	M	M	M	M	M
Fever	-	-	+	+	+
Purpuric lesions	+	+	+	+	+
Edema of hands and feet	+	+	+	+	+
Diffuse edema	-	-	-	-	+
Arthritis	-	-	-	-	+
Necrotic lesions	-	-	-	-	+
Orchiepididymitis	-	-	-	-	-
GI or renal involvement	-	-	-	-	-
Mononucleosis	-	-	+	-	-
Prior URTI	+	+	-	+	+
Recurrence	-	-	-	-	+
Treatment	-	-	-	-	MP/Pd

+: Present. -: Absent. M: Male. GI: Gastrointestinal. URTI: Upper respiratory tract infection. MP: Methylprednisolone. Pd: Prednisone.

by serology (positive IgM antibodies against viral capsid antigen-VCA of Epstein-Barr virus). Three patients (Cases 3, 4, 5) presented low fever (temperatures below 38°C), with duration of three days at most, and were medicated with antipyretics (dipyron and/or paracetamol).

Four cases presented an initial diagnosis of vasculitis and one of purpura fulminans of the meningococemia, in which cerebrospinal fluid exam was normal. All of the cases presented vasculitis, with purpuric lesions and annular hematomas in the face (particularly in the malar eminence) and limbs, associated with painless edema of hands and feet. Diffuse and painful edema in face, trunk and limbs was observed in only one patient (Case 5), who also had arthritis of elbows and ankles, and

painful purpuric vasculitic lesions in the face and ears (Fig. 1). No gastrointestinal, renal or orchiepididymitis involvement was seen in any of the cases.

Only Case 5 needed treatment: initially with non-hormonal anti-inflammatory (naproxen 15 mg/kg/day) to control the arthritis, which improved. However, after one day there was worsening of the vasculitis with necrotic and painful lesions in the face and ears, and corticosteroid therapy was initiated (methylprednisolone 1 mg/kg/day for 3 days and later prednisone 1 mg/kg/day for 1 week). After a week, he returned and the lesions had regressed, consequently prednisone was suspended. The other patients' coursed with complete remission of the picture after one to three weeks (Fig. 2).



Fig. 1. Patient with painful and necrotic purpuric lesions on the face and ears.



Fig. 2. Patient with cutaneous vasculitis, after one week of disease course.

Discussion

Acute hemorrhagic edema is a rare and underdiagnosed vasculitis of childhood, particularly in our population, as it is rarely recognized by the pediatrician³⁻¹⁰. The present Pediatric Rheumatology reference service has 21 years of experience, during which time 0.1% of the patients presented AHE.

Since it is a leukocytoclastic vasculitis, there are authors that consider AHE to be a variant of HSP^{1,2,13}. On the other hand, given the early age of onset, benign clinical course that generally does not require treatment and immunohistological differences, other authors consider AHE to be a different entity from the classic HSP³⁻⁶.

The presence or absence of perivascular IgA deposition is an important immunohistological finding that can differentiate HSP from AHE⁷. However, the maturation of B lymphocytes into IgA-producing plasmocytes occurs mainly after five years of age. At birth, the serum IgA levels only correspond to 1% of an adult's levels, while at 12 and 24 months of life, the IgA levels correspond to 19% and 25%, respectively, of those of an adult¹³. In other words, there is a functional immaturity of the IgA immune system during childhood, which explains the presence of perivascular IgA deposition in only one-third of the patients with AHE^{3,9}, while in HSP this occurs in almost 100% of the cases¹³. Consequently, IgA may have an important role in the pathogenesis of visceral involvement among these patients¹³.

The etiopathogenesis of AHE is still unknown. However, URTI, urinary tract infection, acute gastroenterocolitis, conjunctivitis, vaccination and drugs can precede the picture of EHA by one to two weeks³⁻¹⁰. Many reports have proposed infection due to adenovirus, streptococci, staphylococci, *E. coli*, *Campylobacter* and tuberculosis^{3,7,8,12}. One of our patients presented AHE associated with mononucleosis. This association has not been described previously in the medical literature.

Saraclar et al³. studied 12 patients with AHE and observed that there was no difference between sexes and that all patients were under 24 months of age. Poyrazoglu et al¹¹. described seven AHE patients aged 7-27 months, of which six were male. In the present study, all were male infants with a mean age of 18 months.

The most important characteristic of AHE is cutaneous involvement located predominantly in the face, ears and upper limbs, usually without affecting the trunk. The presence of purpuric and hemorrhagic lesions mainly in the face differentiates AHE from HSP. Patients with AHE initially present urticarial plaques or maculopapular rash, coursing to palpable purpuric lesions that are annular or resemble a shooting target, from 1 to 5 cm in diameter that can converge and assume an ecchymotic aspect⁷. Urticaria, petechiae and necrosis of the ear lobes are rare cutaneous manifestations of AHE^{3,5}. Systemic involvement is extremely rare, but there have been descriptions of diarrhea, abdominal pain, gastrointestinal hemorrhage, mild proteinuria and transitory microscopic hematuria^{6,9}. Painful edema of the extremities and face can resemble the edema of nephrotic syndrome³. Only one of our cases developed necrosis of the ear lobes and also presented arthritis and painful diffuse edema. None of the other patients presented systemic involvement.

The laboratory exams are usually normal¹¹, except for erythrocyte sedimentation rate, which can be slightly elevated⁶. Eosinophilia can also occur³ associated with necrosis of the tissue, and in some cases, circulating immunocomplexes may be determined. In our patients, all of the laboratory exams were normal.

The differential diagnosis for AHE includes urticaria, other vasculitis (such as Sweet syndrome, Kawasaki disease and juvenile systemic lupus erythematosus), purpura fulminans in meningococemia, streptococci, multiform erythema and Caffey disease^{8,11,12}.

The course is benign and there is no need for treatment, with complete remission of the picture between one and three weeks, as observed in our cases. Recurrences are rare^{11,12}. Corticosteroids should only be used if necrotic lesions are present. Antibiotic therapy is indicated when there is secondary infection of the cutaneous lesions^{11,12}. Only one of our patients needed corticosteroid therapy for necrotic lesions in the ears and he responded well with complete remission of the picture.

Acute hemorrhagic edema can be considered a variant of HSP. It is a pediatric entity with benign course, no systemic involvement and rare recurrence. Its diagnosis is clinical, based on cutaneous involvement located particularly

in the face. The association of URTIs preceding the clinical manifestations is frequent. Treatment with corticosteroids is only indicated in the presence of necrotic lesions.

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