Acute Infantile Hemorrhagic Edema: A Case and Literature Review

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Abstract

Acute infantile hemorrhagic edema is a cutaneous leukocytoclastic vasculitis, clinically characterized by symptoms of fever, large purpuric skin lesions, and edema. We report the case of an infant with acute infantile hemorrhagic edema and discuss the clinical, laboratory, and histopathological features of the disease.
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Keywords: Acute infantile hemorrhagic edema, leukocytoclastic vasculitis, infant

Introduction

Acute infantil hemorrhagic edema (AIHE) is a cutaneous leukocytoclastic vasculitis generally seen in children under two years of age (1). Although the etiology of the disease is not exactly known, the drugs and vaccines are considered as the triggering factors (2). It is clinically characterized by symptoms of fever, ecchymotic and large purpuric skin lesions in the face and extremities, and subcutaneous edema (3). Although acute infantile hemorrhagic edema is a cutaneous tends to progress fast, it heals spontaneously within one to three weeks by leaving postinflammatory hyperpigmentation; recurrence is rare.

In the article, a 15-month-old male infant who developed rashes was diagnosed with acute infantile hemorrhagic edema after ampicillin-sulbactam treatment upon the diagnosis of otitis media was presented and the relevant literature was reviewed.

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Case Report

A 15-month-old male infant was admitted to our hospital due to red and purple rashes that had initially began on the hands two days earlier and spread all the way to cheek area, the arms, legs and hips. In his history, it was learnt that the patient was ampicillin-sulbactam treatment that was started upon the diagnosis of otitis media at the external medical center he was admitted to; that he developed rashes that initially began on the hands and then spread fast to arms and legs and swellings developed on the hands and legs on the day of admittance. There was no specificity in the personal and family history of the patient.

In the physical examination of the patient, the axillary body temperature was: 36°C, pulse: 112/min, respiratory rate: 20/min, blood pressure: 90/60 mmHg. In the physical examination, the patient had sharp edged palpable purpura 3-4 cm in diameter in both malar regions on the face, on the arms, and legs and hips (Figures 1a, b), and edema on the hand and back of the foot with redness and puffiness in the right eardrum; no specificity was detected in the other system examinations.

In the laboratory examinations; White blood count was: 12,170/mm^3, Hb: 8.2 gr/dL, platelet: 170,000/mm^3, erythrocyte sedimentation rate (ESR): 65 mm/hour, CRP: 0.1 mg/dL. No specificity was detected in the complete urinalysis. Active partial thromboplastin time was 25.4 sec., prothrombin time: 12.8 sec., INR: 0.96, C3, C4, Protein C, Protein S and Antithrombin III levels were normal.

Considering the patient's age, past otitis history, past history of antibiotic use, the edema that developed on the hands and feet, the patient was diagnosed with acute infantile hemorrhagic edema, and single dose of ceftriaxone and ibuprofen as anti-inflammatory was started. On the sixth day his admittance, the rashes started to heal fast by leaving pigmentation and the patient

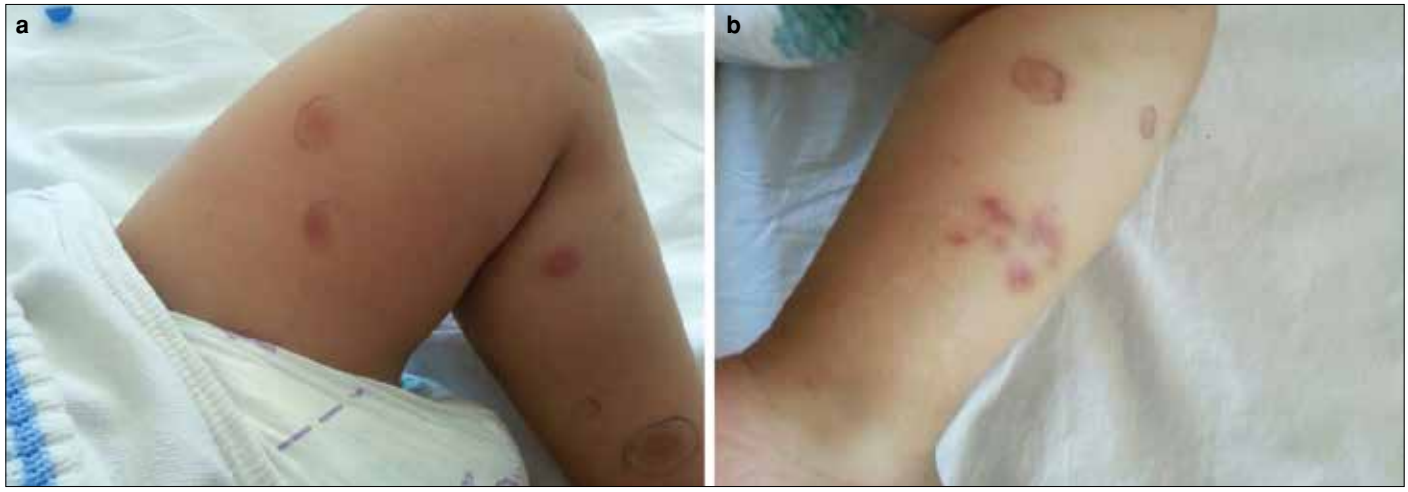

Figure 1. a, b. Sharply edged palpable purpura in the legs

was observed to have complete recovery. The patient was discharged on the basis of outpatient follow-up.

Discussion

Acute infantile hemorrhagic edema usually common in children under two is the leukocytoclastic small vessel vasculitis of the skin; it was characterized for the first time by Snow (4) in 1913 as 'purpura, urticarial and angioneurotic edema on the hands and feet'. In the European literature, it was reported by the definition of Finkelstein's disease and Seidlmayer purpura or purpura 'en cocarde avec edema' (5). Until preset day, nearly 350 cases have been reported in the literature (2); Also many cases were reported in our country (6, 7). The disease is generally observed between 4-24 months. However, apart from this age group, neo natal cases have also been reported (4). Male/female ratio is nearly 2:1 (2). Although the etiology of the disease is not exactly known, the drugs and vaccines are considered as the triggering factors. Out of the infections, upper respiratory tract infections caused by the viral and bacterial agents, otitis media, conjunctivitis, pharyngitis, tuberculosis, pneumonia, cytomegalovirus infection and urinary tract infection are the most frequently reported infections (8). Middle ear infection in our patient and the subsequent use of antibiotic were considered to be the triggering factors. Diarrhea was common during the attacks of the disease; Coxsackie virus and Campylobacter were detected in the stool samples in some studies; a relationship was reported between the rotavirus-linked diarrhea and AIHE. Regarding the drugs, it was proved that the disease was related with antibiotics such as penicillin, cephalosporin, sulfonamide, thiazides and some nonsteroidal anti-inflammatory drugs as well (9). Some of the cases have the story of active immunization. The combined vaccines (diphtheria-tetanus-pertussis), varicella and H1N1 vaccines are the vaccines linked to the disease (2). No mycoplasma or streptococcus-related acute hemorrhagic edema cases were reported. It is though that this particular situation is to do with the fact that factors are mostly seen in school-age children.

There is no defined diagnostic criterion of the disease; however, there are important distinguishing features (Table 1) (4). Patients generally do not have toxic appearance. Fever is usually subfebrile and seen in 50% of the patients. The first lesions on the skin are in the form of urticaria, macule, papules, and purpura; the purpuras are round and sharp-edged, typically in the form of colorful medallion plaque dark in the middle with lighter edges. Usually the lesions are located outside of the body. Internal organ involvement is rare. If the gastrointestinal system has been affected, bloody stool and scrotal edema may be seen. Abnormal proteinuria and hematuria can be seen in the urine tests of the patients; however, no hypertension is observed in patients and kidney functions are normal (2). While spontaneous and complete recovery is seen within 1-3 week in the course of the disease, no relapses have usually been reported. Despite the fast progress of the lesions, it heals spontaneously within 1-3 weeks leaving hyperpigmentation postenflamatuvar and no recurrence is seen. The disease may rarely recur. Our patient had the story of fever as well as widespread purpuric lesions on the face. There was no internal organ involvement and the lesions remitted fast within a week and clinical recovery was observed. It took 30 days for the disease to heal and had the typical characteristics of the AIHE clinical features.

Routine laboratory tests are not important in the diagnosis of acute infantile hemorrhagic edema. In some cases, a leukocytosis, an increase in erythrocyte sedimentation rate, and thrombocytosis can be seen (10). In our own case, increase in the sedimentation rate and anemia existed; leukocyte count was normal. In general, the punch taken from the skin region with purpura and the leukocytoclastic vasculitis identified in the biopsy are the invariant histopathological findings (11). Skin biopsy has been applied to nearly 50% of the cases in the literature. In direct immunofluorescence staining, it was reported that there were C3 and fibrinogen depositions on the vessel wall, and perivascular IgA deposition was rare. In a previous

Table 1. Diagnostic criteria for acute infantile haemorrhagic edema (4)

Being younger than 24 months
Purpuric or ecchymotic target lesions and edema on the face, ear and extremities without mucosal involvement
Nontoxic appearance, systemic disease or lack of visceral involvement signs
Spontaneous healing within few days or weeks

study, while perivascular C3 and fibrinogen depositions in all of the patients, IgG was reported in 22%, IgM in 78%, and IgA and IgE depositions in 33% of the cases (11).

Even though acute infantile hemorrhagic edema is considered to be a variant of Henoch Schonlein Purpura (HSP) due to its cause and histopathology by some authors, most of the authors argue that acute infantile hemorrhagic edema should be regarded as a separate entity. The most important characteristics that distinguish acute infantile hemorrhagic edema from the Henoch Schonlein Purpura are that; the disease is common in children under 2; cutaneous lesions are relatively larger; there was no renal and gastrointestinal involvement; and the probability of recurrence of the disease is low. In a case series carried out in France, it was reported that all the patients were 4-24 months old; they did not have visceral involvement; leukocytoclastic vasculitis was detected in the skin biopsy of all cases whose spontaneous recovery period was 1-3 week; in some of the cases aged 2-4 months, the disease had similarity with HSP (12).

The differential diagnosis of the disease included erythema multiforme, erythema multiforme, drug reactions, meningococcal diseases and very rarely *Pseudomonas aeruginosa* sepsis and Sweet syndrome (13-15).

There is no specific treatment of the acute infantile hemorrhagic edema and steroids and antihistamines are known not to change the clinical course of the disease (2, 11). In two-60 day- period, all the patients spontaneously heal. Paracetamol may be prescribed to painful lesions. As our case had the story of otitis, single-dose antibiotic and anti-inflammatory treatment were implemented.

Conclusion

In conclusion, acute infantile hemorrhagic edema is a disease that should be born in mind in children under two years old admitted with exanthematous lesions.

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