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Case Report

Acute Hemorrhagic Edema of Infancy: A Two-Case Report

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Abstract

Acute hemorrhagic edema of infancy is a leukocytoclastic small vessel vasculitis of young children that is limited to the skin, generally has a benign course without systemic involvement, and does not require treatment. It is characterized by fever, edema of the lower extremities, and wide purpuric rash of the skin. It typically affects infants aged 6–24 months with a history of recent respiratory system illness. An 11-month-old and a 57-month-old cases with acute hemorrhagic edema of infancy who concurrently have a lower respiratory system infection are presented in this case report.

Keywords: Acute hemorrhagic edema of infancy; leukocytoclastic vasculitis; purpura.

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Acute infantile hemorrhagic edema (AIHE) is a rare leukocytoclastic vasculitis usually seen between 6 and 24 months old and involves the small vessels of the skin. In 1913 in the United States, Snow first described only skin involvement of Henoch–Schonlein purpura (HSP).[1] After being described by Finkelstein in Europe in 1938, the disease was also called "Finkelstein's disease" in European literature.[2] Although previously it was considered as a type of HSP, it is currently thought to be a separate entity due to the lack of organ involvement and the fact that accumulation of immunoglobulin A (IgA) in the vessel wall in skin biopsies is not encountered. Although it is frightening in terms of family and physician due to the large ecchymotic purpuric rash, the disease has a favorable course and heals spontaneously within a few weeks. Here, we present two cases with AIHE suffering from lower respiratory tract infection.

Case Reports

Case 1- A 57-month-old male patient was admitted with complaints of bruise and swelling on the legs and the hands. One day before admission, he had been referred to a family physician with complaints of earache and cough and was prescribed amoxicillin–clavulanate oral suspension and gentamicin-containing ear drops, but he did not receive his medications, yet. He did not use any other drugs or receive any vaccine in the near future. On physical examination (PE), the patient was in good health. His findings were as follows: axillary body temperature, 37.4 °C; heart rate, 104 beats/min; respiratory rate, 30 breaths/min; blood pressure, 100/60 mm Hg; body weight, 18 kg (50–75 p); and height 108 cm (25–50 p). The patient's legs and arms were densely packed with several purpuric and ecchymotic lesions elevated from the skin surface ranging from 1 to 4 cm in diameter with mild edema on the dorsum of the feet (Fig. 1). Systemic examinations of the patient were within normal limits except prolonged expiration and bilateral crepitant rales detected during respiratory system examination. Some remarkable laboratory test results were as follows: white blood cell count, 18.200/mm^3 (neutrophil, 72%; lymphocyte, 20%; monocyte, 5%; eosinophil, 1%; and basophil 1%); hematocrit, 38%; hemoglobin, 12.9 g/dl; platelet count, 452.000/mm^3; erythrocyte sedimenta-

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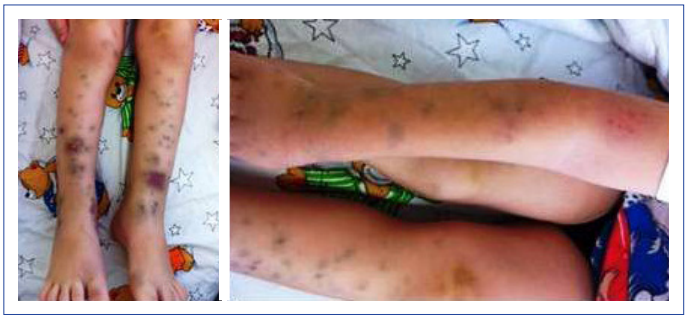

Figure 1. Ecchymotic purpuric rashes of the lower and upper extremities of Case 1.

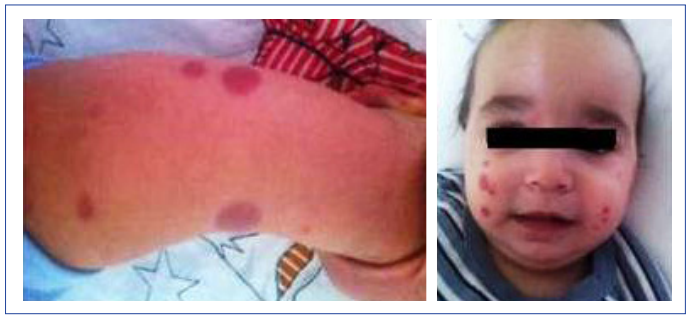

Figure 2. Ecchymotic purpuric rashes of the lower extremity and face of Case 2.

tion rate (ESR), 26 mm/h; C-reactive protein (CRP), 7.03 mg/dl; hemoglobin concentration; activated partial thromboplastin time (aPTT), 24.5 s; prothrombin time (PT), 12.4 s; and international normalized ratio (INR), 1.2. In addition, blood electrolyte, liver enzyme, renal function test, urinalysis result, antistreptolysin O (ASO) (51 IU/ml; N<200 IU/ml), complement 3 (C3) (135 mg/dl; 90–180 mg/dl), and complement 4 (C4) (30.7 mg/dl; 10–40 mg/dl) values were within normal limits. There was no bacterial growth in the blood culture obtained at the beginning of the treatment. On chest X-ray, paracardiac infiltration was detected. The patient whose clinical and laboratory findings suggested AIHE had also lower respiratory tract infection. Thus, he was hospitalized in the children's health and diseases clinic, and treatment with intravenous cefuroxime sodium (150 mg/kg/day) and maintenance doses of intravenous fluid and nebulized salbutamol (0.15 mg/kg/dose) were administered. Since the age of the patient was far advanced for the typical age of AIHE, skin biopsy was performed for differential diagnosis, revealing leukocytoclastic vasculitis. Since his respiratory findings resolved and his rashes somewhat regressed, the patient was discharged after a week-long follow-up. His rashes regressed within 2 weeks, and completely disappeared within 4 weeks. During 6 months of follow-up, his rashes did not recur, or nephrologic involvement was not detected.

Case 2- An 11-month-old male patient was admitted presenting with cough, bruises, and swelling on the legs and arms. The patient who started exhibiting cough 2 days ago had no history of drug use. On PE, his general condition was good. His findings were as follows: body temperature (axillary), 36.7 °C; heart rate, 112 beats/min; respiratory rate, 28 breaths/min; blood pressure, 90/60 mm Hg; body weight, 10 kg (50–75 p); height, 74 cm (50–75 p); and head circumference, 47 cm (50–75 p). On respiratory system examination, prolonged expirium and bilateral crepitant rales were present. On his legs, arms, and face, ecchymotic purpuric rashes of 1–4 cm in size with distinct contours and elevated from the skin surface, associated with edema, were detected (Fig. 2). Other systemic examination findings were unremarkable. Some laboratory test results were as follows: hemoglobin, 9.9 g/dl; platelet count, 615.000/mm^3; ESR, 23 mm/h; leukocyte count, 12.300/mm^3 (neutrophil, 34%; lymphocyte, 56%; monocyte, 6%; and eosinophil, 3%); CRP, 0.5 mg/dl; aPTT, 14.9 s; PT, 11.9 s; and INR, 1.1. Blood electrolyte, liver enzyme, and renal function test results were within normal limits, together with ASO (51.7 IU/ml; N<200 IU/ml), C3 (140 mg/dl; 90–180 mg/dl), and C4 (52.6 mg/dl; 10–40 mg/dl). Bilateral paracardiac infiltration was detected on chest X-ray. The patient was hospitalized with an indication of AIHE and lower respiratory tract infection. Examination for viral etiology was not possible. There was no bacterial growth in the blood culture obtained at the beginning of the treatment. Treatment with intravenous ampicillin–sulbactam (100 mg/kg/day) and maintenance treatment with hydration and nebulized salbutamol (0.15 mg/kg/dose) were started as the bacterial or viral agent could not be identified precisely. Skin biopsy was not performed because of the typical clinical findings of the patient. His extremity edema completely disappeared, rash resolved partly, and respiratory findings improved completely; thus, he was discharged on day 10. His rashes completely disappeared within 4 weeks. During 6 months of follow-up, his rashes did not recur, or nephrologic involvement was not detected.

Discussion

AIHE is a vasculitic disease characterized by fever and acral edema and accompanied by extensive purpuric, ecchymotic rash also called postinfectious cockade purpura, Finkelstein's disease, or Seidlmayer's disease.[3, 4] The exact incidence of the disease is unknown. It is more common in infants between the ages of 6 and 24 months; however, it may occur earlier and later. According to Fiore et al., the age range of 294 patients was between 2 and 60 (median 11) months.[5] In the literature, a case detected at birth was reported.[6] It is more common in boys.[5] Both of our cases were boys. Since our first case was older than the typical

age of onset of the disease, diagnosis was confirmed by skin biopsy.

The most prominent clinical finding in AIHE is sudden onset and symmetrical skin rashes with distinct contours in the form of palpable purpuric, ecchymotic plaques ranging in size from 1 to 5 cm in diameter with a configuration of medallion or annular target board and is more frequently localized on the face, earlobe, arms, and legs.

Lesions may be painful and edematous and generally tend to merge. Rash may develop on the scrotum while the trunk is generally spared.[3, 7, 8] A typical finding is that patients are healthy. Fever is usually present. Edema may start from the back of the hand and foot and spread to the proximal and may be seen on the scalp, ears, and eyelids. It can be painful and generally does not leave a pitting edema.[3, 9, 10] In our cases, skin findings were similar to those reported in the literature.

Although the precise etiology of the disease is unknown, it may reportedly be an immunocompetent vasculitis associated with bacterial and viral infections (often upper respiratory tract infections and urinary tract infections), vaccinations, and medications used (penicillin, cephalosporin, trimethoprim–sulfamethoxazole, paracetamol, thiazides, and nonsteroidal anti-inflammatory drugs).[3, 7, 11, 12, 16] The most well-known pathogens associated with leukocytoclastic vasculitis are streptococci, staphylococci, mycobacteria, Escherichia coli, Herpes simplex virus, varicella zoster virus, hepatitis B virus, hepatitis C virus, human immunodeficiency virus, cytomegalovirus, and rotavirus.[11, 13, 14, 15, 16] In our cases, there was no history of drug use or vaccination. Though tests to identify a specific etiological agent could not be performed, it was thought that the infection developed due to the presence of lower respiratory tract infection. In addition, lack of drug use and vaccination history suggested the diagnosis. The diagnosis of AIHE is usually based on history and typical clinical findings. Laboratory test results are usually normal or not specific. Transient abnormalities may be seen in ESR and CRP levels, leukocytosis, lymphocytosis, thrombocytosis, eosinophilia, and liver function tests. Some patients may develop hypocomplementemia (low C4, C1q, and CH50).[3, 10] Skin biopsy may be performed in cases with suspected diagnosis. Histopathological examination reveals leukocytoclastic vasculitis and fibrinoid necrosis involving venules and postcapillary venules in the upper and middle dermides.[8] Direct immunofluorescence studies have shown accumulation of fibrinogen, C3, and immunoglobulins in the walls and veins of the small vessels. Perivascular immunoglobulin accumulation is observed in 10%–35% of the cases.[12, 18] Saraçlar et al.[17] reported that in 10 out of 13 cases with amyotrophic lateral sclerosis, immunofluorescence examination reveals C3 and fibrinogen accumulation in the dermal vessel wall.

On differential diagnosis, HSP, meningococcal disease, septicemia, purpura fulminans, urticaria, Kawasaki disease, trauma-related purpura, Sweet's syndrome, and erythema multiforme should be considered.[16] There are some clinical and laboratory characteristics that can be used in the differential diagnosis of HSP, which is the most common leukocytoclastic vasculitis in childhood. AIHE is more frequently seen between 4 and 24 months old, whereas HSP is frequently seen between 3 and 6 years old. In HSP, palpable swollen purpuric lesions are observed on the outer surface of the legs and on the hips, whereas in AIHE, wider purpuric lesions associated with edema are observed on the face and distal parts of the extremities.

Immunofluorescence tests reveal more intensive accumulation of IgA, C3, and fibrin in the lesions of HSP, whereas in only 10% and 35% of the patients with AIHE, perivascular accumulation of immunoglobulin is observed. The duration of the disease is usually 12 days in AIHE, and generally, recurrences are not seen. In HSP, the average duration of the disease is 30 days, and recurrence may be seen.[3, 8, 18] In both of our cases, diagnosis was made based on the presence of typical rash, good general health condition of the patient, edema on the extremities, and slight fever, apart from mild leukocytosis and increased ESR in both cases and increased CRP in Case 1. Any remarkable finding was not detected. In Case 1, diagnosis of leukocytoclastic vasculitis was confirmed by skin biopsy, and immunofluorescence analysis was not performed. In our patients, arthritis and gastrointestinal or renal involvement were not observed. AIHE has no specific treatment. In some case reports, the potential use of steroids[16, 19, 22, 23] and antihistamines[8, 16, 20, 21] has been reported, but the general opinion is that the treatment does not alter the clinical course of the disease. Since the disease has a good prognosis, spontaneous recovery is expected within 1–3 weeks, systemic involvement is not seen, and generally, systemic treatment other than supportive treatment is not required. If infection is present, antimicrobial therapy is administered. In our cases, antibiotherapy (cefuroxime sodium and ampicillin–sulbactam IV) was administered because discrimination between viral and bacterial agents of lower respiratory tract infections could not be made. No specific treatment was given for AHRS. Rash and extremity edema regressed within 1 week, whereas full recovery was observed within 4 weeks. No recurrence was observed during the follow-up of both cases.

In conclusion, AIHE, which is a rarely seen leukocytoclastic vasculitis of the skin, is a more frequently encountered disease especially within 6–24 months of infancy. However,

it can be seen earlier or later. It resolves spontaneously within a few weeks and does not require special treatment. In small children, purpura should be considered in the differential diagnosis.

Disclosures

Informed consent: Written informed consent was obtained from the parents of the patient for the publication of the case report and the accompanying images.

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Conflict of Interest: None declared.

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