

A Case of Acute Hemorrhagic Edema of Infancy

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Acute hemorrhagic edema of infancy is an unusual form of leukocytoclastic vasculitis occurring in children from the age 4 months to 2 years. The etiology remains unknown. Numerous studies, however, suggest acute hemorrhagic edema of infancy as an immune-mediated vasculitis in response to a variety of antigenic stimuli. We report a case of an acute hemorrhagic edema of infancy; 11-month-old boy with a history of fever for 3 days and a history of purpuric rash on the extremities, trunk, buttock and oral mucosa for 2 days.

Key Words: Acute hemorrhagic edema of infancy (AHEI), leukocytoclastic vasculitis

INTRODUCTION

Acute hemorrhagic edema of infancy (AHEI) is an uncommon form of leukocytoclastic vasculitis occurring in infants and children younger than 2 years of age.¹ It was first described by Snow² in the United States in 1913. Since then, about 100 cases have been reported worldwide and 4 cases in Korea.³⁻⁶ It is clinically characterized by the acute development of typical rosette-like purpuric tender lesions within areas of pre-existing edema.⁷ The head and distal portions of the extremities are the favored sites.⁸ Clinical triad of AHEI is fever, tender edema and purpuric lesions. The vasculitis appears to be limited to the skin and the disorder follows a benign course with spontaneous resolution within a few weeks. It is important in the fact that AHEI should be regarded as a separate clinical entity of leukocytoclastic vasculitis, with a good prognosis for this generally benign disease

of infants. We report a case of acute hemorrhagic edema of infancy, which was diagnosed according to the clinical symptoms and the immunohistochemical characteristics.

CASE REPORT

An 11-month-old boy was referred to Yonsei University Severance Hospital with a 3-day history of fever and a 2-day history of purpuric rash. Physical examination showed multiple 1-2 cm sized violaceous to reddish colored, hemorrhagic tender purpuras on the upper and lower extremities, trunk and buttock (Fig. 1). The infant showed mild fever. On examination of the oral mucosa, tonsils were mildly injected with several erosions on buccal mucosa and lips. The infant had been in good health with the exception of coughs and rhinorrhea for the past 4 days. He did not receive any medication and was vaccinated according to the schedule.

Laboratory studies revealed a normal hemoglobin level and elevated leukocyte count. The platelet count and the CRP quantitation were within normal. The urine was negative for RBC. Tests for ASO and chemistry profile was normal. The level of immunoglobulin(Ig) A was 62.7 mg/dl that is below normal range. There was a slight rise in titers of Mycoplasma Ab(1:160 positive) but negative with EBV EA IgM. Blood cultures showed no growth of organisms. Chest X-ray was normal.

A biopsy with Direct immunofluorescence (DIF) was performed on the 3rd day of admission. The biopsy specimen of the purpuric lesion on the thigh showed normal epidermis and leukocytoclastic vasculitis with extravasated RBC in the

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Fig 1. Multiple 1-2 cm sized violaceous to reddish colored, hemorrhagic tender purpuras on thigh (A) and foot (B).

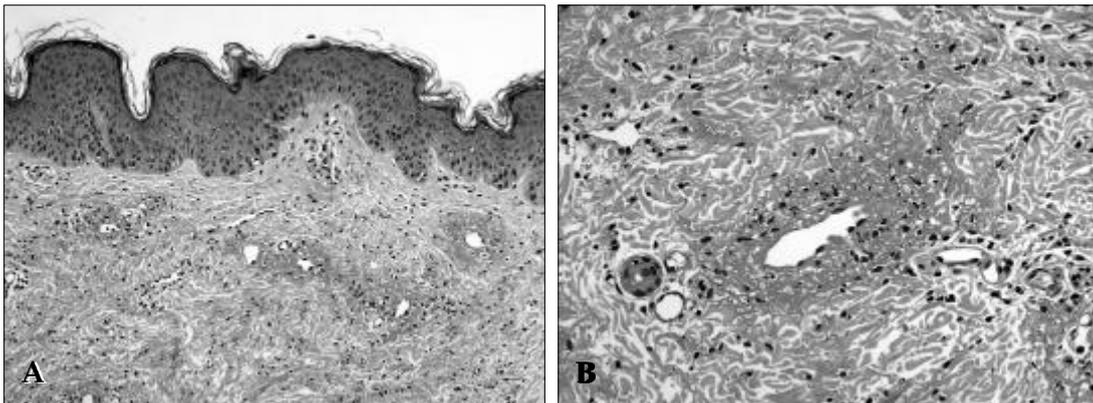


Fig 2. The biopsy specimen of a purpuric lesion on the thigh showed normal epidermis and leukocytoclastic vasculitis with extravasated RBC in the dermis (A, H&E $\times 40$). Fibrinoid necrosis was seen in the blood vessels (B, H&E $\times 100$).

dermis. Fibrinoid necrosis was seen in the blood vessels (Fig. 2). On DIF, C₃ deposition was shown on the blood vessels but no immunoglobulin was deposited.

The infant was treated with oral corticosteroid and antibiotics, which resulted in reduction of edema and tenderness of skin lesions. The infant was improved and discharged 5 days of admission. The initial prednisone dosage was 10 mg and was withdrawn after 5 days. At that time, most of the lesion resolved and did not recur afterwards.

DISCUSSION

AHEI is a rare acute vasculitis syndrome that affects young children primarily. Since Snow² first described the first case in 1913, approximately 100 cases were reported in the European and English literature. The prodromal period was observed in 75% of the cases, which is characterized by viral (e.g., mostly upper respiratory infections, otitis media or conjunctivitis) or bacterial infections (e.g., streptococcal, staphylococcal pharyngitis, pulmonary tuberculosis, bronchopneumonia, or urinary tract infections), the side effects of vac-

ination (measles, diphtheria-pertussis-tetanus, or combined), or the side effects of drug (eg, penicillin, cephalosporin, trimethoprim-sulfamethoxazole, paracetamol, cough syrup, or a combination of these).⁹ In our case the patient had prodromal period with fever and rhinorrhea of 3 days prior to the development of skin lesions. In the laboratory examination, mycoplasma Ab was positive.

Although the etiology of AHEI is unknown, its increased frequency during winter and its association with the upper respiratory infections suggest that it may be an immune complex mediated disease triggered by infectious agents as mentioned above.

The disease is clinically defined by more or less symmetrically distributed, large (1-5 cm) ecchymotic purpuric lesions, characteristically in a cockade pattern, and painful, nonpitting edema. The face, eg, the ears, eyelids, and cheeks, the scrotal area, and the extremities are most commonly affected. Our patient showed skin lesions primarily on the trunk, buttock and lower extremity. The skin lesion first appeared on the lower extremity and it spreaded to the upper extremity. Also erosions with violaceous purpura on mucous membrane of lips and buccal mucosa were seen. Usually mucosal involvement is uncommon. The mucosal lesion appeared and cleared simultaneously with cutaneous lesion in our patient. Although it was not confirmed by biopsy, this is the first report of AHEI occurring in the mucosa.

Besides fever and cutaneous lesions, children with AHEI are healthy. The involvement of viscera and joints is unusual. One case of gastrointestinal vasculitis followed by an intussusception with fatal consequences has been reported however.¹⁰

Laboratory studies usually show an elevated erythrocyte sedimentation rate and leukocytosis, thrombocytosis and mild eosinophilia. The patient in our case showed mild leukocytosis.

The typical histopathologic finding of AHEI is leukocytoclastic vasculitis of the dermal vessels with fibrinoid necrosis, extravasations of red blood cells, and a leukocytoclasia.¹¹ Direct immunofluorescence examination shows vascular deposition of C1q, C3 and fibrinogen.² Immunoglobulin(Ig) deposits in the vessels were found in the

following percentages: IgA in 30%; IgG in 20%; IgM in 80%; and IgE in 30%.² Our case showed normal epidermis and leukocytoclastic vasculitis with extravasated RBC in the dermis. Fibrinoid necrosis was seen in the blood vessels. On DIF, C₃ deposition was shown on the blood vessels but no immunoglobulin was deposited. The differential diagnosis includes acute febrile neutrophilic dermatosis, erythema multiforme, child abuse and other forms of leukocytoclastic vasculitis including Henoch-Schonlein purpura. Acute febrile neutrophilic dermatosis and erythema multiforme can be distinguished histologically as the former shows dense and diffuse neutrophilic infiltrate without vasculitis and the latter reveals interface dermatitis.

AHEI, however, is histologically indistinguishable from other form of leukocytoclastic vasculitis, especially Henoch-Schonlein purpura, drug hypersensitivity and viral hypersensitivity. Although AHEI shares similar clinical features with Henoch-Schonlein purpura, there are some differences. The young age of patients, the rare involvement of internal organs, the rarity of recurrence and the absence of IgA deposition in vessel walls distinguish AHEI from Henoch-Schonlein purpura.¹² But since there was a report of an overlap of the two diseases in a child,¹ it is therefore suggested that AHEI is not a distinct entity but a variant of HSP occurring in younger children. But others⁹ believe that the two diseases are separate entities. The difference between the two disorders is secondary to the age-related developmental changes in the IgA immune system. In HSP, perivascular IgA is found in almost 100% but only occasionally in AHEI. Since most of the patients diagnosed as AHEI are under the age of 2, we suggest that the physiologic or functional immaturity of the IgA immune system may play a role in the pathogenesis. In our patient, serum level of IgA was below normal, which confirms the diagnosis of AHEI rather than HSP. Some authors also suggest that IgA have a central role in the pathogenesis of visceral involvement in HSP.¹³

Despite the critically ill-looking cutaneous lesions, the disease course of AHEI is benign. Complete resolution occurs within one to three weeks. No treatment is necessary, but careful follow up

is recommended.¹⁴ Systemic corticosteroids and antihistamines have shown to be ineffective on resolution of cutaneous lesions.¹⁰ Treated with corticosteroids, the general condition of our patient improved within 5 days of hospital stay.

In conclusion, we report a rare case of acute hemorrhagic edema of infancy (AHEI).

REFERENCES

1. Shah D, Goraya J, Poddar B, Parmar V. Acute Infantile Hemorrhagic Edema and Henoch-Schonlein Purpura Overlap in a Child. *Pediatr Dermatol* 2002;19:92-3.
2. Snow IM. Purpura, urticaria and angioneurotic edema of the hands and feet in a nursing baby. *JAMA* 1913; 61:18-9.
3. Lee YJ, Lee CH, Park CW. A case of Acute Infantile hemorrhagic Edema. *Korean J Dermatol* 1994;32:332-6.
4. Kim JK, Park JH, Park SD. Infantile Acute Hemorrhagic Edema of the Skin. *Korean J Dermatol* 1995;33:1143-7.
5. Lee HJ, Lee DW, Kim SY. A Case of Infantile Acute Hemorrhagic Edema. *J Korean Pediatr Soc* 1996;39: 1168-72.
6. Park JY, Choi YB, Kim KH, Cho KH. A Case of Acute Hemorrhagic Edema of Childhood. *Korean J Dermatol* 2002;40:999-1001.
7. Gattorno M, Picco C, Gambini C, Buoncompagni A, Castagnola E, Pistoia V, et al. Erythema multiforme-like manifestations and arthritis in a 3-year-old child with leukocytoclastic vasculitis. *Clin Exp Rheumatol* 1997;15:329-32.
8. Dubin BA, Bronson DM. Acute hemorrhagic edema of childhood: an unusual variant of leukocytoclastic vasculitis. *J Am Acad Dermatol* 1990;23:347-50.
9. Smitt J, Vermeer M, Faber W. Acute Hemorrhagic edema of Infancy(AHEI). *Clin Dermatol* 2002;20:2-3.
10. Legrain V, Lejean S, Taieb A, Guillard JM, Battin J, Maleville J. Infantile acute hemorrhagic edema of the skin; study of ten cases. *J Am Acad Dermatol* 1991;24: 17-22.
11. Capputo R. Acute hemorrhagic edema of the skin of the newborn (Finkelstein's disease). *Pediatr Dermatol* 1990;7:323.
12. Morrison R, Saulsbury F. Acute hemorrhagic edema of infancy associated with Pneumococcal bacteremia. *Pediatr Infect Dis J* 1999;18:832-3.
13. Goraya J, Kaur S. Acute hemorrhagic edema and Henoch-Schonlein purpura: Is IgA the missing link? *J Am Acad Dermatol* 2002;47:801.
14. Serna MJ, Leache A, Sola A. Targetlike lesions in an infant. *Arch Dermatol* 1994;130:1055-60.