Acute Hemorrhagic Edema of Infancy after Vaccination: A Case Report

Hikmet Tekin Nacaroğlu[1], Solmaz Saygaz[1], Özlem Saraç Sandal[1], Canan Şule Ünsal Karkıner[1], Hülya Tosun Yıldırım[2], Demet Can[1]

[1]Department of Pediatric Allergy, Dr Behcet Uz Children's Hospital, *İzmir, Turkey*
[2]Department of Pathology, Dr Behcet Uz Children's Hospital, *İzmir, Turkey*

Abstract

Acute infantile hemorrhagic edema (AIHE) is a benign form of cutaneous leukocytoclastic vasculitis that usually occurs in children younger than 2 years of age. Although the etiology is unknown, AIHE often follows infections, drug treatment, or vaccination. The onset of AIHE is often dramatic with petechiae, ecchymoses, and annular, nummular or targetoid purpuric lesions usually appearing on the extremities, face, or ears. In this report we aimed to present a case with AIHE in whomvaccination was considered the etiologic cause. *(J Pediatr Inf 2014; 8: 40-3)*

Keywords: Acute infantile hemorrhagic edema, leukocytoclastic vasculitis, immunization

Introduction

Acute infantile hemorrhagic edema (AIHE) is a benign cutaneous leukocytoclastic vasculitis characterized by fever, palpable purpura and edema usually occurs in children younger than two years (1). It is claimed that mostly differentiation from Henoch-Schönlein Purpura (HSP) is difficult, in fact it is a different presentation of HSP (1, 2). With unknown etiology it is observed that infection, drugs and vaccines play a role in 75% of the cases (1, 2). A 7. 5 month old female with AIHE after vaccination was presented.

Case Report

A seven-and-half month female presented initially with a purplish rash and swelling especially on the face, hands and legs. The lesions began to fade one week after. In her story there was no infection or drug, it was learned that the third dose of Hepatitis B (Hep B), DaBT-IPA-Hib, oral polio vaccine (OPV) and Pneumococcal conjugate vaccine (PCV) were performed two weeks ago before the start of the lesions. The patient had no special feature in her personal and family history, had no known history of drug allergy and dermatosis. In her physical examination, her body weight was 7 kg (25-50p), length: 65 cm (25-50p), body temperature 36.7°C, pulse rate 110/min, respiratory rate: 28/min, arterial blood pressure: 90/60 mmHg. There was a puffy, purpuric rash that did not blanch on applying pressure in various sizes on face, arms and legs with edema but not accompanied by mucosal involvement on examination (Figure 1a, b). In her laboratory investigation, white blood cell count was 17.500/mm^3, hemoglobin 10.4 g/dL, hematocrit 31.4%, platelet count 346.000/mm^3, erythrocyte sedimentation rate 3 mm/h, C-reactive protein was 0.35 ng/dL. Biochemical parameters and bleeding profile, Anti-streptolysin O titre, immunoglobulins, C3 and C4 levels, urinalysis were normal. No abnormality was found in the investigation for etiologic diagnosis, hepatitis, HIV, and TORCH infection. Also, *Mycoplasma pneumoniae*, and *Parvovirus B19* infection were negative in serological tests. Punch biopsy of the lower limb lesions revealed mixed inflammation with infiltrating polymorphonuclear and nuclear cells and fibrinoid material infiltration around the walls of blood vessels in the dermis. IgG, IgA, IgM and C3 were negative, fibrinogen staining

Received: 29.10.2012
Accepted: 22.03.2013
Available Online Date: 12.10.2013

Correspondence Address:
Hikmet Tekin Nacaroğlu
Dr. Behcet Uz Çocuk Hastanesi, Çocuk Allerji Bilim Dalı, İzmir, *Türkiye*
Phone: +90 232 411 63 19
E-mail: tekin212@gmail.com

DOI:10.5152/ced.2013.41

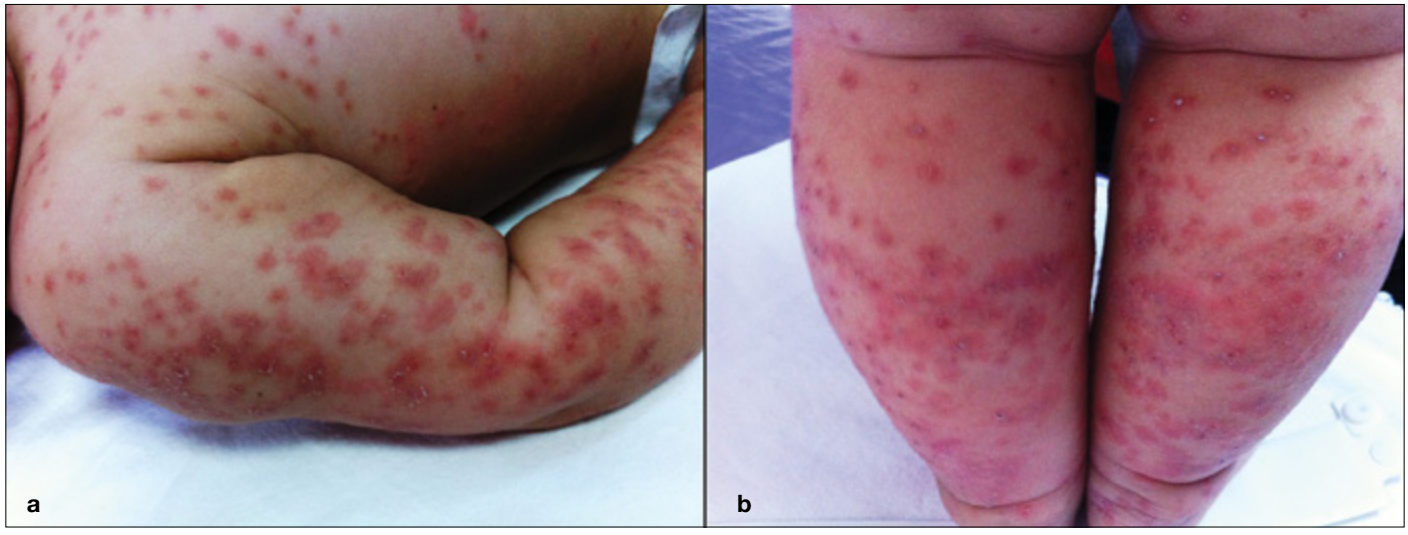

Figure 1. a, b. Edema and purpuric rash in the arms and legs

was positive in the direct immune fluorescence examination (Figure 2, 3). Results were reported compatible with leukocytoclastic vasculitis. AIHE were diagnosed according to the current age of the patient, with clinical and histopathological findings. The lesions disappeared gradually within 10 days of clinical follow-up of the patient who was started on anti-histamine. The patient is currently being monitored and is asymptomatic.

Discussion

Acute infantile hemorrhagic edema (AIHE) is a benign leukocytoclastic vasculitis, usually self-limiting with skin involvement, rarely includes visceral organs and other systems. It was described firstly by Snow (3) in 1913, as purpura, urticaria, angioneurotic edema on hands and feet, later different definitions such as Finkelstein disease (4), Seidlmayer disease (5) have been reported. This disease is seen rarely, but is especially seen in children under 2 years of age and a 4.64/1 ratio is observed more frequently in males (6).

Etiopathogenesis is not clearly understood, and there is infection, drug use and history of vaccination in 75% of the cases (1, 2-7). Various infections such as upper respiratory and urinary tract infections, conjunctivitis, otitis media, bronchitis, pneumonia, tuberculosis, and viral infections (Coxsackie B4, Cytomegalovirus, Rotavirus and Herpes simplex virus) have been reported in association with this disease (2, 6, 7). Various antibiotics (penicillin, erythromycin, cefaleksin), anti-inflammatory and antipyretic drugs and cases of the diphtheria-pertussis-tetanus-polio, and *Haemophilus influenza* type b (Hib), measles, rubella, H1N1 vaccine is reported as a precipitating factor (2, 7). After encountering factors which cause immunological response, the average time of

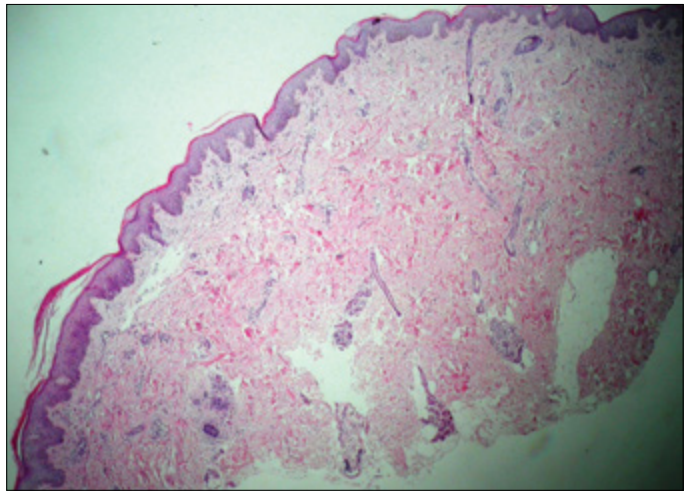

Figure 2. Parakeratosis, epidermis minimal acanthosis in a focal area of the surface (HEX40)

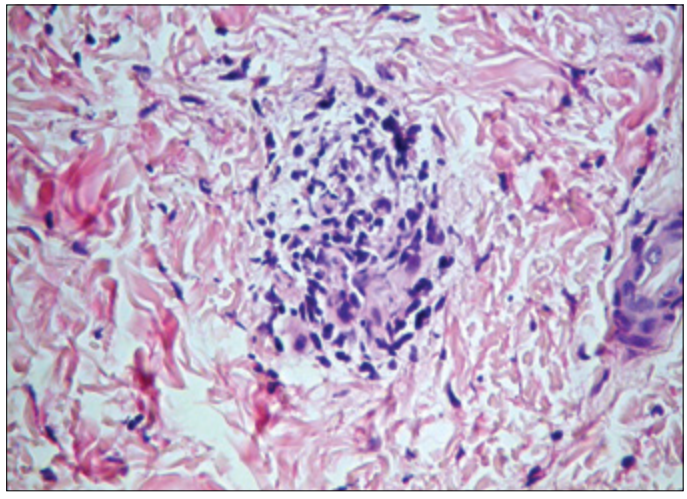

Figure 3. Perivascular polymorphonuclear leukocytes infiltration, accumulation of fibrinoid material and mixed inflammation including nuclear cell debris were observed in the dermis (HEX400)

appearance of clinical signs is 7-15 days but some cases have been reported in the literature which are protracted by 2 days to 1 month (7). In our case, due to multiple vaccination 15 days prior to the development of AIHE and lack of any other evidence of infection or medication, immunization was thought to be a precipitating factor. Although the clinical picture has a rapid start and dramatic progress, patients have generally no toxic appearance, and clinical recovery occurs within 1 to 3 weeks. The general clinical appearance is characterized by a triad of fever, edema and purpura. Fever may change from low to high temperatures and also afebrile cases have been reported (2, 5-7). Usually edema is seen on the ear, face and legs, rarely can be seen on the penis and scrotum. The most important finding is purpura, which usually begins as maculopapular urticarial plaques, within a few days, size of the lesions increases and takes the form of medallion like annular, sharp-edged targetoid-shaped purpuric lesions.

Generally, symmetric distribution is seen on the face, ears and extremities, and also the trunk, buttocks, perineum, penis and scrotum may be involved. Extracutaneous involvement is rarely seen in AIHE. Cases that involve oral petechiae, conjunctival hyperemia and mucosal involvement such as the soft palate and glomerulonephritis symptoms, abdominal pain, elevated transaminase levels, intussusception, intestinal bleeding, and arthralgia-arthritis have been reported in the literature (6, 7). In our case, although there was a similar involvement of the face and extremities, mucosal involvement and systemic involvement was not observed.

There is no diagnostic value of laboratory investigations in the diagnosis of AIHE. In some cases, lymphocytosis, eosinophilia and leukocytosis, thrombocytosis, and elevated erythrocyte sedimentation rate and C-reactive protein level can be found. Bleeding profile is always normal. Although urinalysis is normal, microscopic hematuria and proteinuria have been reported. Anti-streptolysin O titer, antinuclear antibody (ANA), anti-deoxyribonucleic acid (antiDNA) and rheumatoid factor (RF) is almost always negative. Immunoglobulin levels are usually normal, but cases of increased IgG, IgM, IgA, and IgE levels have been documented (2-7). In our case, no specific laboratory examination findings were not detected.

Histopathological findings are characterized by leukocytoclastic vasculitis of capillaries and postcapillary venules and perivascular, interstitial inflammation and fibrinoid necrosis caused by extravasation of erythrocytes. Although immunofluorescence studies are often negative, fibrinogen, C1q, IgM, IgG, IgE, even IgA deposits can be seen in different proportions (2, 7, 8). Saraçlar et al. (9) detected 100% perivascular C3 deposition, 100% fibrinogen deposition, 22% IgG deposition, 78% IgM deposition, 33% IgA deposition, 33% IgE deposition in their study. In our case, histopathologic examination was compatible with leukocytoclastic vasculitis. IgG, IgA, IgM and C3 was determined as negative, staining of fibrinogen was positive in Immunofluorescence examination.

Usually AIHE is diagnosed clinically by experienced clinicians. It is focused on four main criteria supporting diagnosis in the literature (8);

1. To start before the age of 2
2. To be purpuric rashes on the face and extremities with edema
3. Lack of systemic and visceral involvement
4. Lesions heal without sequelae within a few days or weeks

As is seen, AIHE is similar to HSP but it is differentiated from HSP by its occurrence during the infantile period, not showing systemic and visceral retention, mostly being retained in the face and extremities and rarely showing relapse. It is observed that, although both diseases have a leukocytoclastic vasculitis table, perivascular IgA retention is seen in only 10-35% in the cases which are AIHE (9, 10). Meningococcemia, Kawasaki disease, purpura fulminans, Sweet syndrome, erythema multiforme, urticarial vasculitis and child abuse should be considered in the differential diagnosis (7-10).

The use of antihistamines and systemic corticosteroids is disputable in AIHE which has no treatment (2, 7-10). Generally, lesions recover within 1 and 3 weeks without sequelae. In our case, ithad been only antihistaminic treatment was implemented and lesions recovered within 10 days. She is currently being monitored and at the same time no relapse have been observed.

Conclusion

It should be kept in mind that AIHE is rarely seen as a vaccine complication in the childhood period, and it is usually difficult to discriminate from HSP.

Informed Consent: Written informed consent was obtained from patients who participated in this case.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.N., D.D.; Design - H.N., S.S.; Supervision - D.D.; Funding - H.N., Ö.S.; Materials - H.N., H.Y.; Data Collection and/or Processing - H.N., Ö.S.; Analysis and/or Interpretation - H.N., D.D.; Literature Review - H.N., Ö.S.; Writing - H.N, S.S.; Critical Review - D.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this case has received no financial support.

References

1. Sites LY, Woodmansee CS, Wilkin NK, et al. Acute hemorrhagic edema of infancy: case reports and a review of the literature. Cutis 2008; 82: 320-24.
2. Ferreira O, Antunes I, Cruz MJ, et al. Acute hemorrhagic edema of childhood after H1N1 immunization. Cutan Ocul Toxicol 2011; 30: 167-69. [CrossRef]
3. Snow I M. Purpura, urticaria and angioneurotic edema of the hands and feet in a nursing baby JAMA 1913; 61: 18-9. [CrossRef]
4. Long D, Helm F. Acute hemorrhagic edema of infancy. Finkelstein's disease. Cutis 1998; 61: 283-84.
5. Cox NH. Seidlmayer's syndrome: postinfectious cockhade purpura early childhood. J Am Acad Dermatol 1992; 26: 275. [CrossRef]
6. Fiore E, Rizzi M, Ragazzi M, et al. Acute hemorrhagic edema of young children (cockade purpura and edema): a case series and systematic review. J Am Acad Dermatol 2008; 59: 684-95. [CrossRef]
7. Al Sufyani MA. Acute hemorrhagic edema of infancy: unusual scarring and review of the English language literature. Int J Dermatol 2009; 48: 617-22. [CrossRef]
8. Krause I, Lazarov A, Rachmel A, et al. Acute hemorrhagic edema of infancy, a benign variant of leucocytoclastic vasculitis. Acta Paediatr 1996; 85: 114-17. [CrossRef]
9. Saraçlar Y, Tınaztepe K, Adalıoğlu G, et al. Acute hemorrhagic edema of infancy (AHEI) - a variant of Henoch-Schönlein purpura or a distinct clinical entitiy? J Allergy Clin Immunol 1990; 86: 473-83. [CrossRef]
10. Legrain V, Lejean S, Taieb A, et al. Infantile acute hemorrhagic edema of the skin: studies of ten cases. J Am Acad Dermatol 1991; 24: 17-22. [CrossRef]