Case Report

Role of systemic steroids in acute hemorrhagic edema of infancy: report of two cases

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ABSTRACT

Acute hemorrhagic edema of infancy (AHEI) is an unusual form of leukocytoclastic vasculitis with dramatic distinguishing skin lesions that occurs in infants who age 4 to 24 months old. Clinical presentation at onset requires clinical and, less often, histological evaluation to distinguish it from more serious diseases and other vasculitis. Treatment of AHEI remains controversial; and since it is a self-limiting disease, a conservative approach should be considered first. Although some authors have reported that the use of steroids may be beneficial if started early on, we think their use, based on our presented cases here, may accelerate the healing and improves the color of preexisting skin lesions but does not significantly alter the course of the disease. Authors reported here two clinical Cases of AHEI (Diagnosed based on characteristic skin lesions and confirmed with Histological evaluation) who were treated initially with systemic steroids, besides we reviewed the role of systemic steroids in the treatment of AHEI.

Keywords: Acute, Edema, Hemorrhagic, Infancy, Steroids, Vasculitis

INTRODUCTION

Acute Hemorrhagic Edema of Infancy (AHEI) is a rare form of cutaneous vasculitis that affects male children mainly between 4 months and 2 years of age. It was initially described in the United States by Snow, in 1913, under the name of “Purpura, urticaria and angioneurotic edema of the hands and feet in a nursing baby”. Since then, increasing number of cases had been described in the European literature, as Finkelstein’s Disease and Seidlmayer Syndrome. It is rarely reported in American literature, maybe because in the United States AHEI is given the name Henoch-Schönlein Purpura (HSP). The etiology is largely unknown, however around two thirds of cases are related to infectious etiology with upper respiratory tract infections being the most common, others include drugs and vaccines. The skin lesions present suddenly with rapidly evolving urticarial, targetoid plaques that later become hemorrhagic. These lesions frequently present on the checks, ears and acral areas with the trunk being less favoured site. The lesions are typically asymptomatic; however, few patients report mild itching and tenderness. The disease course is completely benign with complete recovery without any complications is expected within 1 to 3 weeks. Although recurrences are seen, once the episode has lasted 2 weeks, the disease is unlikely to recur.

The association of fever and purpuric rash in small children usually poses a diagnostic dilemma to the physician. In the light of diseases that develop with this association, we should always keep in mind Henoch-
Schönlein Purpura, meningococcemia and septicemia, the main differential diagnosis of AHEI.

The study shows report of 2 clinical cases of AHEI seen at King Fahad Medical City in Riyadh, Saudi Arabia, treated with systemic steroids then we discuss the role of systemic steroids in the treatment of AHEI.

**CASE REPORT**

**Case 1**

An 8-month-old baby boy was referred to the emergency room at King Fahad Medical City in Riyadh, Saudi Arabia, from a local nearby hospital with 4-day history of fever and runny nose that was followed by an abrupt onset of erythematous rash over the face and the gluteal area. The cutaneous eruption was characterized by edema and purpura. The patient had been in an otherwise good health status apart from his skin lesions, fever, and mild irritability. Physical examination revealed mild fever (38.7°C, rectal), multiple symmetrical, 1–5 cm sized, edematous purpuric plaques over the face, ears, and extremities. Some lesions showed a cockade pattern (Figure 1).

![Figure 1: Multiple well defined, coin shaped, targetoid hemorrhagic plaques.](image)

Complete blood count; renal, liver, coagulation profiles; and urinalysis were normal. Erythrocyte sedimentation rate, C-reactive protein, complement factors (C3, C4 and CH50), antistreptolysin O (ASO) titers and antinuclear antibodies were all within normal limits. Serology for adenovirus, herpesvirus 1, 2, and 6, Chlamydia and Mycoplasma pneumonia were all negative. Two days after admission, the patient developed lesions over both hands and feet, and the cutaneous lesions increased in number and size, becoming more edematous with pronounced inflammatory component. Skin biopsy and direct immunofluorescence studies were performed and confirmed the diagnosis. Oral prednisolone therapy was started based on pediatric rheumatology recommendation and then was discontinued after 4 days because of improvement in skin lesions (Figure 2) and edema after 2 days only of starting the therapy. Complete resolution with no relapse occurred within 10 days.

![Figure 2: Multiple, less well defined, faintly erythematous, thin plaques.](image)

**Case 2**

A 3-month-old baby boy presented to our hospital with reddish skin lesions for 3 days. The patient had prodromal symptoms of an upper respiratory infection 4 days before his skin eruption. His mother noticed small erythematous spots initially on the lower limbs which gradually increased to involve the face, knees and arms. There was no recent history of vaccination or new medication. The father mentioned a history of runny nose and nonproductive cough the previous week. On examination the child was mildly irritable with low grade fever (38.7°C, rectal). The cutaneous examination revealed many symmetrically distributed, well-defined and circular, ecchymotic, purpuric plaques localized on the cheeks and extremities. The ears appeared edematous bilaterally. Some of the plaques showed the characteristic circle in circle pattern. The mucosal surfaces were all free. There were no signs of systemic involvement. Blood work revealed low hemoglobin (9.5 g/dL; normal range 10.5-13.5 g/dL), leukocytosis (21,000/ L; normal range 6,000-17,000/ L), with neutrophilia (10,860/ L), and a C-reactive protein level of 18 mg/L (normal range 0.1-10.0 mg/L). Erythrocyte sedimentation rate was normal. Occult blood testing was negative. Complement levels, coagulation profile, immunoglobulins, antinuclear antibodies, ASO titer, antineutrophil cytoplasmic antibodies, and lymphocyte subtypes were all normal. Adenovirus antibody titers were high, and Adenovirus deoxyribonucleic acid was detected using reverse transcriptase polymerase chain reaction (RT-PCR; 250,350 copies/mL). Cytomegalovirus (CMV), herpesvirus 1, 2, and 6, parvovirus B19, coxsackievirus, Chlamydia, and M. pneumoniae serologies and RT-PCR were all negative. Nasal swab culture for bacteria was negative as well. A few hours after admission, the patient developed new lesions mainly over the right ear (Figure...
3), and lift check, new sharply demarcated hemorrhagic edematous lesions also appeared over the extensor surface of the right elbow (Figure 4). Skin biopsy and direct immunofluorescence studies were performed and confirmed the diagnosis. The infant was treated with IV Methylprednisolone (1 mg/kg) for 7 days, with an improvement in cutaneous lesions seen within 2 days after the first dose.

Figure 3: Acute ill-defined hemorrhagic plaque over the right ear pinna in this 3 months old boy.

Figure 4: Typical purpuric dusky red plaques over the right elbow.

DISCUSSION

The described cases are classical presentations of AHEI, also called Finkelstein’s disease.

AHEI is an uncommon type of cutaneous leukocytoclastic vasculitis predominantly affecting male children who age from 4 to 24 months old. Around 75% of the affected patients have presented with a prodromal symptoms suggestive of infectious etiology, such as upper respiratory infection, gastrointestinal, bronchopneumonia and urinary tract infection. Medications (antibiotics and paracetamol) and vaccines have been also described to be triggering factors, suggesting a possible link with type two hypersensitivity reaction. In both of our patients, a history of upper respiratory tract infection preceded the development of AHEI.

Authors have described a concurrent adenovirus infection in this second case; to our knowledge, few cases have had described this association. Skin lesions usually start with large (1-5 cm), symmetrically distributed, well-defined, hemorrhagic plaques. The lesions typically prefer the acral extremities, face (specially the ears and cheeks) and genital area. The lesions may assume medallion, annular, iris, or targetoid configuration. Mucous membranes are usually not involved. Low grade fever is a common feature.

The hallmark of the disorder is that, although it has acute clinical presentation, affected patients usually present with good health status and generally look well. Although internal organ involvement is unusual, reports of gastrointestinal pain and arthralgia have been described. Two patients have had gastrointestinal involvement followed by intussusception. Transient renal involvement with microscopic hematuria, proteinuria, and decrease in complement levels up to full picture of glomerulonephritis has also been reported. Laboratory investigations are usually nonspecific. Most of the affected patients have a normal erythrocyte sedimentation rate and C-reactive protein level. Slight increase in the leukocytic count with lymphocytic line shift, neutrophilia or eosinophilia can be seen. The coagulation profile is almost always normal. Urinalysis and stool sample are often negative for blood. ASO titer, antinuclear antibodies, antideoxyribonucleic acid, and rheumatoid factor are usually negative. High serum levels of gamma globulins and immune complexes have been described. Complement levels are usually normal in most of patients. In a recent case report, transient decrease in C1q, C4, and CH50 levels have been described.

In both of these cases, histopathologic analysis demonstrated the typical features of leukocytoclastic vasculitis of the deep dermal vessels. Vascular wall fibrinoid necrosis and dermal neutrophilic infiltrates are characteristic features. Ig deposits in the dermal vessels are found in different proportions: IgA in 30%, IgG in 20%, IgM in 80%, and IgE in 30%. Krause et al, have introduced the described diagnostic criteria as age less than 2 years old, purpuric or ecchymotic skin eruption, with edema of the face, ears and extremities with or without mucosal involvement, lack of internal organ involvement and spontaneous recovery within a few days or weeks. Early recognition of this uncommon, self-limiting disease is important to differentiate it from other disorders that require specific therapy.

The main differential diagnosis of AHEI is HSP. The two disorders have many overlapping cutaneous findings, and even some authors suggest that AHEI is a benign
cutaneous type of HSP occurring in younger children. Saraclar et al, demonstrated perivascular IgA deposition in almost all cases of HSP, whereas IgA deposits are seen only in a few cases of AHEI. Some authors have demonstrated that these differences can be explained by the immaturity of the immune system in younger children, especially for IgA production, who are more likely to be affected by AHEI.

Other important clues to differentiate AHEI from HSP are uncommon involvement of internal organs, male predominance and lower rate of recurrence and complications in AHEI. HSP presents classically with polymorphic skin eruption in the form of palpable purpura on the extensor surfaces of the lower limbs mainly, with a tendency to spare the face, scalp and upper trunk, whereas in AHEI, larger purpuric, ecchymotic lesions are evident on the face, head, wrists, and specially over the ears with extensive edema. Despite the acute evolution of skin eruption, the disease has a favorable prognosis with complete spontaneous recovery and no sequelae in 1–3 weeks. In both of our cases we used systemic steroids early on and we had clearly observed that the skin lesions are becoming less inflammatory and color is fading significantly over the next 48 hours with no new lesions noted after the first dose.

CONCLUSION

Authors have reported here two prototypical cases of AHEI, one related to adenovirus infection, that both showed complete recovery without complications. AHEI is rare, often under recognized disease that is commonly mistaken with HSP because of their similar skin manifestations, but they are different clinical entities, and they can be distinguished according to age of onset, absence of internal involvement in AHEI, and time of resolution.

Treatment of AHEI remains largely conservative; although some authors have recommended the use of short-term oral steroids, their use, based on our presented cases here, may accelerate the healing of pre-existing skin lesions, improves the color and halt the formation of new lesions but does not significantly alter the course of the disease.

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