

Case Report

Acute Hemorrhagic Edema of Infancy with Extensive Necrosis-A Rare Presentation

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Abstract

Observations: Acute hemorrhagic edema of infancy (AHEI) is a rare acute cutaneous vasculitis usually affecting children between 4 and 24 months of age. The disease is characterized by the acute appearance of hemorrhagic lesions, edema, and fever. Sometimes necrotic lesions may develop, as well. However most of the cases reported in literature describe local necrosis limited to a part of a body site. A 7 months- old baby developed extensive necrotic ulcers as the dominant lesion of AHEI. As we know such a presentation has not been reported in English literature.

Introduction

Acute hemorrhagic edema of infancy (AHEI) is a well known but rare cutaneous vasculitis affecting the children aged 4-24 months [1]. Initially it was considered to be a variant of *Henoch Schölein Purpura* (HSP) but evidences later on established it as a separate entity. It is a self limiting condition manifesting as purpuric lesions involving face and extremities, sparing trunk. Besides necrotic lesions are known to develop at times [1]. However necrotic lesions are generally localized as reported in literature [2, 3]. The condition is self limited and have excellent prognosis. It usually resolves spontaneously in 1-3 weeks without any sequelae [1]. Recognition of this benign self limiting condition is important as it allows an appropriate prognosis to be made for this rare disease in children.

Case Report

A 7 months- old breastfed female, immunized for age, presented with widespread necrotic lesions for

20 days. The baby had developed fever with cough and cold 2 days prior to onset of skin lesions for which her parents consulted a nearby Homeopathic doctor. She was given some medicines. On day 2 of taking medicines the baby developed necrotic lesions all over her body. The lesions started as erythematous plaques over face and extremities. Within few hours lesions darkened and became necrotic. The parents attended a child hospital. She was admitted and was given intravenous ceftriaxone along with oral prednisolone syrup for 7 days. After that she was discharged with necrotic lesions which have started to heal. During this period she did not develop any new lesions. After few days baby was brought to us by her parents. On examination the baby was playful and was not toxic despite having extensive necrotic ulcers. Vitals were stable and there were no systemic features. There were multiple necrotic ulcers covered with black eschar involving the face, including nose, and lateral part of extremities. Scalp, trunk, palm, soles and mucosa were spared. The nasal cartilages were destroyed. Most of the lesions were confluent with few being discrete. Lesions were bilateral and had a tendency to symmetry. Most of the lesions were in healing stage. Black eschar was getting detached under which healthy ulcer floor



Figure 1. Extensive necrotic lesions over face and extremities. Note sparing of trunk.

was visible. There was no central/peripheral cyanosis. All peripheral arteries were normally palpable. However there was bilateral pitting edema of all four limbs. There was no history of similar episode in past (**Figure 1, 2**).

All routine blood investigations except for raised ESR were within normal limits. Screening tests for coagulation factors i.e. platelet count, bleeding time (BT), clotting time (CT) and aPTT were within normal limits. Serological tests for Antinuclear antibody (ANA) as well as C-ANCA and P-ANCA were negative. Skin biopsy was taken from the margin of the lesion over right arm and was sent for histopathological examination and direct immunofluorescence. Histology (H&E stain) showed an epidermal necrosis with underlying perivascular and periappandageal infiltration at mid and lower dermis. Dilated blood vessels were present with almost completely destroyed endothelium. Perivascular and periappandageal mononuclear infiltrate were seen. There were evident neutrophilic dust near the upper part of vessels (**Figure 3, 4**).



Figure 2. Close up of lesions over face. Necrotic ulcer covered with black eschar. Lesions have started to heal from periphery. Note destruction of nasal cartilages.

Direct immunofluorescence (DIF) with the same tissue sample was done. It was negative for IgA, IgG, IgM, C3 and fibrinogen. Considering age, history of infection, clinical and histopathological features diagnosis of AHEI with necrotic lesions was made due to diagnostic criteria suggested by *Krause and Lazarov et al* [4]. Parents were counseled and asked to attend Department of Plastic surgery and to come for follow up. They were specifically asked to come if baby develops new lesions. On the first visit (45 days following onset of

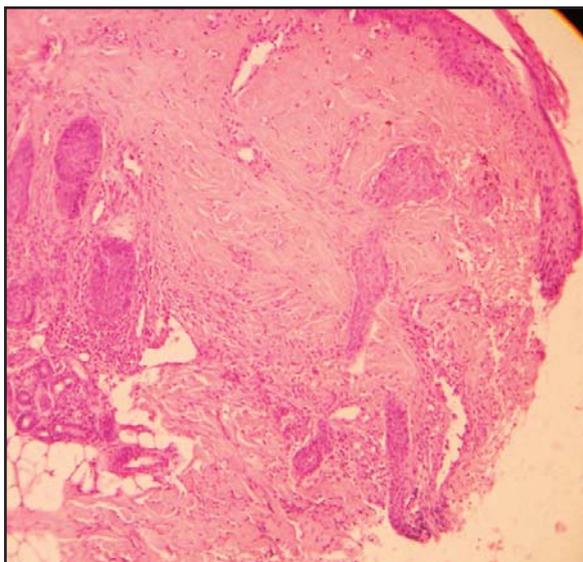


Figure 3. - Epidermal necrosis with underlying perivascular and periappandageal infiltration at mid and lower dermis (H & E stain, X40)

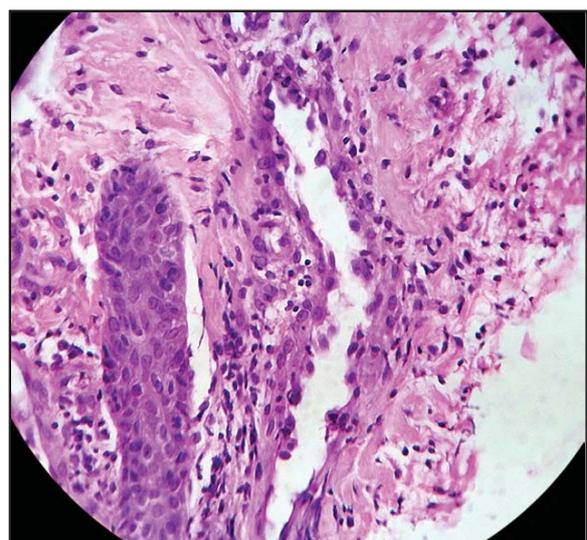


Figure 4. Dilated blood vessel with almost completely destroyed endothelium. Perivascular and periappandageal mononuclear infiltrate. Note neutrophilic dust near the upper part of vessel.

lesions), most of the necrotic tissue were detached leaving behind ulcers. Smaller ulcers had healed. Larger ones were in the process of healing; the floor of the ulcers was improving and was covered with granulation tissue.

Ulcers healed completely by 3 months (following onset of lesions), though with scarring, both hypertrophic and atrophic (**Figure 5, 6**).

Baby is still under follow up. She is doing fine and is gaining weight normally. She did not develop any similar lesions.

Discussion

The age of the baby, prior history of respiratory infection, dramatic onset, characteristic distribution of lesions, histopathological finding of leukocytoclastic vasculitis and benign self limiting nature of the condition were strongly in favour of diagnosis of AHEI [4]. However DIF findings were non contributory. It is to be noted that these findings are not universally positive- IgM deposition has been reported in 78 %, IgG in 22% while IgA in only 33% cases. However C3 and fibrinogen deposition has been reported in 100% of cases [5]. The absence of C3 and fibrinogen deposition in this case may be because of late presentation (on 20th day). One more unusual finding in this case was development of extensive necrotic lesions which have not been reported in literature. Necrotic ulceration is known to develop in this condition but most of the case reports show necrotic ulceration of localized area like only ear [2].

Acute hemorrhagic edema of infancy (AHEI), also known as post infectious cockade purpura, *Seidlmayer's* disease and *Finkelstein's* disease, and was first described in 1913 by *Snow* [6]. It was initially thought as a variant of HSP, but evidences have shown it to be a separate condition. It is an acute cutaneous leukocytoclastic vasculitis affecting children less than 24 months of age and is characterized by a triad of fever, purpuric skin lesions, and edema [7]. Only few cases have been reported in English literature.

The pathogenesis and etiology is largely unknown, but it is reported to be frequently preceded by a prodromal period, which is characterized by a bacterial or viral infection, drugs side effects, or immunization side effects [8, 9]. AHEI has been categorized as an immune complex hypersensitivity reaction in

response to the previously mention factors. Antigen-antibody complexes are deposited within blood vessels and lead to the activation of the complement cascade, which results in endothelial damage, typically of the postcapillary venules [10]. Complement deficiency [11] too has been implicated in pathogenesis.

AHEI is more frequently seen in winter. There is slight male preponderance [1]. It starts abruptly with development of large cockade, annular or targetoid purpuric lesions almost entirely limited to extremities and face, with sparing of trunk [1, 6]. Fever and painful edema of the distal extremities, ears, and eyelids are associated features of AHEI [6]. The disease is mostly limited to the skin. Visceral involvement is rarely reported. The kidneys and intestines involvement leads to hematuria, mild proteinuria, and bloody diarrhea [12]. Mucosa is reported to be affected in rare cases [13]. Trunk involvement is reported in one case [8].

Light microscopy examination of skin biopsies typically show normal epidermis or ulcer depending on lesion, leukocytoclastic vasculitis of the dermal vessels with extravasated red blood cells in the dermis, and fibrinoid necrosis in the blood vessel. Direct immunofluorescence on skin biopsies specimens have revealed vessel wall deposition of fibrinogen (100 %), C3 (100 %), IgG (22 %), IgM (78 %), IgA (33 %), and IgE (33 %) [5]. Laboratory tests typically show normal results. Elevated erythrocyte sedimentation rate, leukocytosis, thrombocytosis, and eosinophilia have been seen in AHEI. The disease is often self limiting with spontaneous recovery in 1-3 weeks without any sequale [1]. Relapses, though very rare, have been documented [5, 6]. The treatment is supportive and antibiotics are recommended when there is evidence of infection. Systemic corticosteroids and antihistamines have not demonstrated to alter the course of disease [5].

The differential diagnosis of AHEI includes *Henoch-Schönlein* purpura (HSP), *Sweet's* syndrome, acute febrile neutrophilic dermatosis, erythema multiforme, septic vasculitis, drug induced vasculitis, meningococemia, and trauma-induced purpura. All these disorders are differentiated by the clinical presentation, history, physical examination, laboratory tests, and histopathology of the



Figure 5. Healing of the lesions over leg by hypertrophic scars. Some lesions have healed by atrophic scars are seen as hypopigmented areas.

skin lesions. The main entity in the differential diagnosis of acute hemorrhagic edema of infancy is *Henoch-Schönlein* purpura. AHEI patients are 4 to 24 months-old with male predominance, while HSP patients range between 3 to 10 years-old [1, 3]. AHEI is almost always confined to the skin, whereas HSP usually shows renal, joints, and gastrointestinal tract involvement [1, 3, 6]. HSP is characterized by polymorphic skin lesions in the form of palpable purpura on the extensor surfaces of the lower extremities with a tendency to spare the face [3].

In AHEI, larger purpura and ecchymoses are found on the face, head, ankle, wrists, auricles, with more extensive edema and fever. Moreover, AHEI does not commonly contain the perivascular IgA deposition that is seen in 100 percent of HSP cases [3, 5]. Recently a diagnostic criteria for AHEI has been proposed by Krause and Lazarov et al [4]. It is as follow:

- An age less than 2 years
- Purpuric or ecchymotic targetoid lesion with edema of face, auricle and extremities with or without mucosal involvement
- Lack of systemic disease and visceral involvement
- Spontaneous recovery within a few days or weeks

Usually no active treatment is needed [5]. Corticosteroids do not alter the course of disease [5, 6]. Parents must be reassured and explained the nature and prognosis of the condition [14]. Symptomatic treatment may be given.



Figure 6. Healing of lesions over face with both hypertrophic and atrophic scars. Note destruction of part of the nose and deformity of upper lip.

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