ACUTE HEMORRHAGIC EDEMA OF INFANCY - CASE REPORT

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ABSTRACT

Acute hemorrhagic edema of infancy (AHEI) is a rare vasculitis of small dermal vessels with characteristic presentation in infants aged up to 24 months. It manifests as a sudden occurrence of palpable purpuric skin lesions, swellings in hands, feet, face and auricles, and mild fever. The children affected with AHEI are almost always in good general health and with normal laboratory parameters. Approximately 400 cases have been described in the literature so far. However, the etiology is still unknown. Most evidence suggests infections or vaccination as the principal triggers. Extra cutaneous manifestations are recorded in only about 10% of AHEI patients. The majority of the affected children undergoes recovery spontaneously and without any complications within 1-3 weeks, with or without any treatment. AHEI is usually diagnosed on the clinical grounds only and the diagnostic procedure rarely requires a skin biopsy. The current literature indicates the use of corticosteroids and/or antihistamines as a therapy, but there is still a lot of controversy about these therapeutic measures. This paper presents the case of AHEI with its typical clinical manifestations that resolved in a rapid spontaneous recovery without the use of any treatment within a week. AHEI is a rare syndrome that pediatricians should be well familiar with in order to differentiate it from other potentially severe diseases that have similar cutaneous manifestations, but also to avoid unnecessary investigations and therapy.

Keywords: *Acute hemorrhagic edema, infancy.*

INTRODUCTION

Acute hemorrhagic edema of infancy (AHEI) manifests as a sudden onset of painless, non-itching, localized, palpable, purpuric oval skin lesions on extremities, face and auricles, limb and facial swelling and mild fever. It affects children aged up to 24 months who are otherwise found to be in good general condition [1, 2]. AHEI is a rare form of leukocytoclastic vasculitis of small dermal vessels that involves inflammation and endothelium fibrinoid necrosis, and consequently also the presence of perivascular infiltrates and erythrocytes extravasation [3, 4]. The etiology of the syndrome is still unknown even though the certain causal correlations with recent bacterial or viral infections, immunization or drug intake have been reported [5, 6]. In the majority of the patients, most of the laboratory analysis have been recorded as normal [7-9].

The disease has a benign, self-limiting course and usually resolves without any further complications [1, 2, 5-13]. The presence of extra cutaneous manifestations, such as glomerulonephritis, abdominal pain with gastrointestinal bleeding, arthralgia, testicular torsion, intussusception, scarring and hyperpigmentation has been recorded in less than 10% of the patients [12-15]. The current literature indicates the use of corticosteroids and/or antihistamines as a therapy, but there is still a lot of controversy about these therapeutic measures [10, 11, 16, 17]. Most authors find it unnecessary because patients generally recover spontaneously within 1-3 weeks [5-9, 11-14].

This paper will describe one case of AHEI that manifested with its typical clinical presentation and that resolved in spontaneous full recovery without any treatment in a week. Since the syndrome has dramatic manifestations, it is a great source of panic, anxiety and concern to parents. Thus, it is extremely important to recognize it promptly and point out its benign nature [7-9, 11].

CASE REPORT

Patients consent

From parents of patient was obtained written and informed consent for taking data and publishing scientific article. All procedure were described and manuscript was done in according to the *CaRe* guidelines.

Case presentation

A seven-month-old male infant, with no prior health issues reported, was referred to a hematology department on the first day of illness onset. The child had been born after the second full-term pregnancy with normal vaginal delivery. His psychomotor development was evaluated as adequate for his age. The child had had a mild fever (37.8°C) during the previous day and the bruises had appeared on the various body parts. The baby was active, playful, and with stable vitals. However, numerous small hematomas (up to 2 cm in diameter) were present on the lower legs and forearms, as well as on the dorsum of his hands and feet. The mild swelling was detected on the right feet (Fig. 1). There were also several small hematomas on the knees, elbows and cheeks that soon formed larger surfaces whose diameter ranged from 5 to 8cm (Fig. 1-3). All the lesions were purple, irregular, circular, skin-leveled and had well-defined peripheral edges. The child also had an associated mild nasal congestion. Except for the symptoms described above, the complete systematic examination showed no abnormalities.

The parents reported that the baby had been upset on the day of the admission and that they had administered Paracetamol. The child was being breastfed. Reportedly, he had had an infection of the middle ear a month before treated with Amoxicillin ®. The baby had been vaccinated regularly with the last vaccination against Diphtheria, Tetanus and Pertussis, Hemophilus influenza type B and Polio taking place the previous month. Negative family history of bleeding disorders was reported. The possibility of child abuse was eliminated.

All the laboratory tests were in the normal ranges - complete blood count (CBC) and hemostasis examinations, including a test for congenital and acquired thrombophilia, fibrinogen, C-reactive protein, erythrocytes sedimentation rate, liver and kidney function tests, electrolytes, serum proteins and albumins, immunoglobulins, complements, hormones and antibodies of the thyroid gland, antinuclear antibodies, anti-streptolysin O, cellular and perinuclear anti-neutrophilic cytoplasmic antibodies and rheumatoid factor, and urine analysis and culture. The ultrasound of the abdomen and brain appeared normal for the given age. All the available virusology analyses were negative. The only laboratory parameter that was beyond the proscribed level was D-dimer that equaled 6.30 ng/mL and that normalized as the illness regressed.

At first, we suspected the *Henoch-Schönlein* purpura. After consulting the relevant literature, we concluded that we are dealing with AHEI. Skin biopsy and immunofluorescence study were not performed because the child was soon afebrile and the changes on the skin started spontaneously to regress. No therapy was administered; the patient only underwent the elimination diet for vasculitis. He did not have any systemic complications and the skin lesions completely healed in five days. No sequelae were detected or reported during the follow-up visits that took place in the year to follow.

DISCUSSION

AHEI (also known as Finkelstein-Seidlmayer disease, rosette form purpura, medallion-like purpura or infantile postinfectious iris-like purpura) was initially considered to be a variant of Henoch-Schönlein purpura [18]. Later on, it became recognized as a separate clinical entity [3, 4, 19]. There are no exact data on its incidence. According to the systematic review of the recorded AHEI cases conducted by Fiore et al. [13] in 2008, approximately 300 cases of AHEI have been reported, with male patients being predominant (2:1

ratio). The sex of our patient follows this trend. The authors also claim that the number of the described cases has increased to approximately 400 in the following years, probably due to better knowledge on the issue.

All the consulted authors recognized AHEI as a condition which manifests through the specific triad of symptoms. A low-grade fever occurs in the prodrome and is followed in the next few hours by the onset of red macules or urticarial lesions and then by symmetrically arranged large palpable ecchymotic lesions on the skin. Finally, asymmetrical swelling appears on auricles, face and extremities (most frequently dorsum of hands and feet). In all the cases described in the literature, the general condition of the patients was evaluated as good [1-11]. The onset and the further course of the disease in our patient completely corresponded to the typical clinical form described in the literature. Fortunately, except for the mild edema on the right foot, no edema was found elsewhere. The skin lesions did not progress and necrosis or bullas were absent in our case although they reportedly occur in AHEI [12].

The literature source we have consulted have argued that AHEI can be associated with viral infections (Coxsackie, Cytomegalovirus, Rota virus, Hepatitis A), bacterial infections (Escherichia coli, Campylobacter, Streptococcal and Staphylococcal), vaccination (MMR, DTP) or drug intake (antibiotics, non-steroidal anti-inflammatory drug, cough syrup) [3-5, 17, 20]. In 10% of the described cases, it could be linked to immunization [7, 19]. According to Chesser et al., in 75% of the patients infectious agents could be seen as triggering factors, which is further supported by the fact that AHEI occurs more frequently during the winter months [20]. Our patient had had a history of middle ear inflammation for two months and the last vaccination had taken place a month before the onset of the disease. Consequently, we cannot make confident claims about causal factors and what triggered the immune process.

The AHEI diagnosis is initially made on the clinical basis without the necessity for a skin biopsy [3, 4, 12-14]. However, there are a lot of diseases with similar dermatological manifestations, but potentially more severe clinical presentations, which must be promptly differentiated and eliminated. The following diagnoses that should be also considered: meningococcemia, Kawasaki disease, purpura fulminans and skin lesions in septicemia, drug eruptions, Henoch-Schönlein purpura, rheumatoid purpura, Sweet syndrome, erythema multiforme, angioedema, child abuse, idiopathic thrombocytopenia, nephrotic syndrome and acute hemorrhagic urticaria [7, 19]. When skin biopsy is performed, it shows a leukocytoclastic vasculitis of small dermal blood vessels with perivascular infiltrates composed of neutrophils, and occasionally eosinophils [3, 4]. The direct immunofluorescence testing shows vascular deposits of C1q, C3, fibrinogen and immunoglobulins. IgM deposits are the most common of all immunoglobulins while IgA, the most common finding in Henoch-Schönlein purpura, is present in approximately one-third of the patients [3, 4, 18].

According to the majority of the consulted authors, skin biopsy should be performed only if the disease keeps progressing, the further complications start occurring or the diagnosis appears unclear [3, 4, 12-15]. The similar stand has been taken by numerous authors when it comes to not introducing any therapy [8-11, 16]. However, the rapid progression of the syndrome could be an indication for the introduction of the systemic steroid therapy and/or antihistamines [16]. In cases of extensive bullous lesions, secondary infections of ruptured bullae or similar, patients should be treated with local and systemic antibiotics, and also monitored for any signs of infant dehydration [15]. The opinions about putting patients on the elimination diet are also contradictory and thus controversial. Despite all the disagreements, we introduced the elimination diet for vasculitis [21] and intravenous hydration, but decided not to administer any therapy and not to perform skin biopsy given the good clinical course of the disease in our patient.

CONCLUSION

Although AHEI is a rare syndrome, pediatricians should be well informed about its presentation and proper management. The early diagnosis of AHEI is important in order to avoid unnecessary and/or invasive medical investigations and therapy. Due to the dramatic clinical image of AHEI, parents may seek medical help in emergency departments where the condition should be also promptly recognized and adequately treated.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

From parents of patient was obtained written and informed consent for taking data and publishing scientific article. All procedure were described and manuscript was done in according to the CaRe guidelines.

CONFLICT OF INTEREST

The authors declare that there is no potential conflict of interest regarding this manuscript.

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