Acute hemorrhagic edema: uncommon features

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Acute hemorrhagic edema (AHE) of young children, also termed cockade purpura with edema or Finkelstein-Seidlmayer disease, is a rather rare small-vessel leukocytoclastic vasculitis. It characteristically occurs after a febrile illness or a vaccination and is sometimes considered a variant of Henoch-Schönlein purpura [1, 2]. The diagnosis is made clinically in not-ill appearing children, who present with erythematous annular skin lesions and diffuse non-pitting and often tender body edema with a predilection for cheeks, ears, and extremities. Petechiae, purpuric lesions or ecchymoses also sometimes occur. It is widely held that this vasculitis typically affects children 4 weeks to 23 months of age, is skin-limited, remits within 3 weeks and does not recur [1-3].

To investigate the characteristics of uncommon features and the prevalence of recurrences, we employed the **A**cute **H**emorrhagic **E**dema **BI**bliographic **D**atabase AHEBID. This database includes 270 original reports addressing 458 individually documented cases (313 males and 145 females) published between 1970 and 2019 [4, 5].

We analyzed the following uncommon features: 1) systemic features such as articular (joint pain with or without swelling), abdominal (such as pain, vomiting, intestinal bleeding, and intussusception), or kidney involvement (proteinuria or hematuria); 2) eruptions such as blistering lesions, Köbner phenomenon, or extensive skin necrosis; 3) production of tears partially composed of blood (i.e. hemolacria); 4) compartment syndrome of the extremities; 5) positive family history (AHE or another vasculitis in a first-degree relative of a patient) ~~(one family member affected by AHE hemorrhagic edema and at least one further first-degree relative affected by another vasculitis)~~.

Uncommon features were detected in 109 of the 458 cases (table 1): a systemic involvement in 66 (61%), uncommon eruptions in 24 (22%), hemolacria in seven (6.4%), compartment syndrome in three (3.3%), and a positive family history in nine (8.2%) cases (table 1). Patients with articular or kidney involvement were significantly older than those without uncommon features. The disease duration was ≤3 weeks in 107 out of the 109 cases with

uncommon features. The diagnosis was supported by a skin biopsy in 39 (36%) of the 108 cases with uncommon features (including 21 of the 22 cases with blistering eruptions and the patient with extensive skin necrosis).

Nine AHE cases occurred within five families. In three families one case each of AHE and Henoch-Schönlein purpura were observed. In the remaining families, two and four family members were affected by AHE.

Recurrences (reappearance of eruption after a recovery for ≥4 weeks) were observed in 21 (4.5%) of the 458 cases (10 in cases without and 11 in cases with uncommon features; $P<0.01$; Fisher exact test).

This analysis confirms the excellent prognosis of AHE: it normally resolves spontaneously within ≤3 weeks without recurrences and is skin-limited in approximately 85% of cases. On the other hand, this analysis provides new insights into the condition: one-fifth of cases presents with a systemic involvement, uncommon eruptions, or a compartment syndrome. Furthermore, the family history is sometimes positive.

References

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Figure 1 – Legend

Characteristic erythematous annular skin lesions

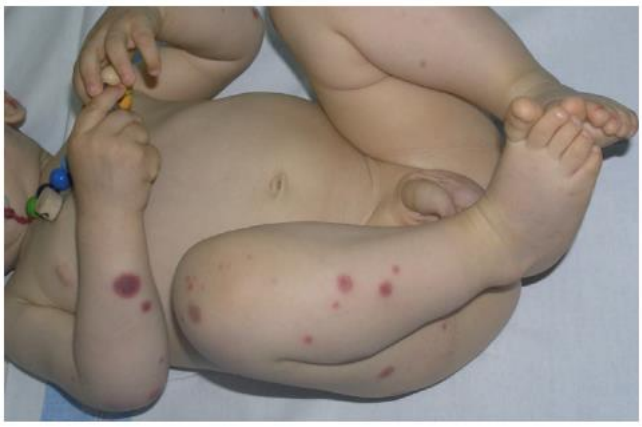

Table 1: Patients affected by acute hemorrhagic edema without and with uncommon features.

	N	Gender (males : females)
Without Uncommon Features	349	228 : 120
With Uncommon Features	109	84 : 25
Systemic Features♦	66	51 : 15
Articular involvement	34	25 : 9
Abdominal involvement	26	20 : 6
Kidney involvement	13	11 : 2
Uncommon Eruptions*	24	22 : 9
Blistering lesions	22	18 : 4
Köbner ~~sign~~ phenomenon	3	2 : 1
Extensive skin necrosis	1	0 : 1
Hemolacria	7	4 : 3
Compartment Syndrome	3	3 : 0
Positive Family History	9	8 : 1

▪median and interquartile range (≥10 cases) or individual values (<10 cases); *one systemic feature in 59 and two in seven cases;

*one uncommon eruption in 22 and two in two cases; ǂinformation not available in one case; ⁺P<0.05 versus cases without uncommon features (Kruskal-Wallis test with Dunn post-test).

Table 1: Uncommon features in 109 patients (84 males and 25 females) affected by acute hemorrhagic edema of young children. Results are given as relative frequency, as median and interquartile range (≥10 cases) or as individual values (<10 cases).

	N	Gender (males : females)	Age (months)
Uncommon eruptions*	31	22 : 9	9 [7-15]
Blistering lesions	22	18 : 4	9 [6-16]
Hemolacria	7	4 : 3	5, 6, 7, 10, 11, 12, 13
Köbner sign	3	2 : 1	5, 11, 27
Extensive skin necrosis	1	0 : 1	7
Compartment syndrome	3	3 : 0	11, 19, 25
Extracutenous features◆	66	51 : 15	15 [10-21]
Articular involvement	34	25 : 9	19 [12-23]
Abdominal involvement	26	20 : 6	11 [9-18]
Renal involvement	13	11 : 2	17 [13-19]
Familiarity	9	8 : 1	birth (N=4), 8, 11, 12, 42‡

*One uncommon eruption in 29 and two in two cases; ◆One extracutaneous feature in 59 and two in seven cases; ‡information not available in one case.