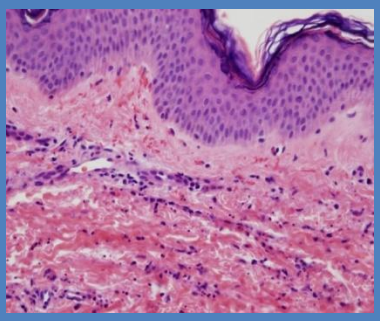
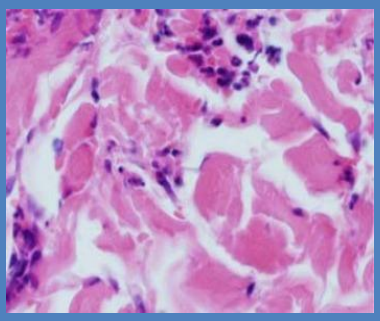
Dermatopathology

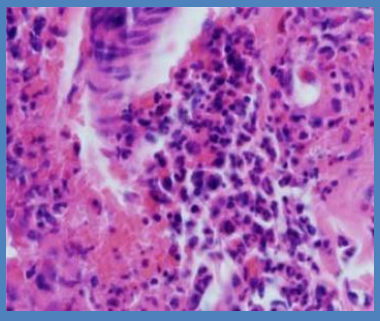
Weill Cornell Medical College

Case Presentation 6

ACUTE HEMORRHAGIC EDEMA OF INFANCY







This educational series for physicians is presented by the Weill Cornell Comprehensive Dermatopathology Service

Case author: Cynthia M. Magro, MD

Clinical History

The patient was a 2 year old male who developed a very striking rash involving the trunk, arms, feet, and thigh two weeks following immunization for hepatitis A(figure 1). The patient was otherwise asymptomatic. Laboratory work revealed a peripheral blood thrombocythemia and lymphocytosis. A biopsy was performed. Tissue was submitted for both direct immunofluorescent studies as well as routine light microscopy. A rather striking interstitial and angiocentric neutrophilic infiltrate was present. There was concomitant leukocytoclasia along with focal mural fibrin deposition(figure 2a-d). Overall there was somewhat of a disparity between the extent of tissue neutrophilia and relative lack of fibrin deposition resulting in a morphology closely recapitulating urticarial vasculitis. Direct immunofluroescent studies demonstrated granular deposits of IgM and IgA in vessels(figure 3a and 3b). The staining intensity was prominent and co-dominant for both. The patient was treated with prednisone which did not improve the rash. He was then commenced on colchicine. Resolution of the rash occurred within 2 months from its onset.

Discussion

The case represents a classic example of Acute Hemorrhagic Edema of Infancy (AHEI) also known as Finklestein's disease, Seidlmayer syndrome and postinfectious cockade pupura. This condition is a benign leukocytoclastic vasculitis seen in infants. The disease is self-limiting and usually resolves without treatment without any sequelae. Infants affected are usually aged between two months and two years although there are some documented cases of outbreaks at the age of three. There is a very high male to female ratio at 4.64 to 1 (1-5).

The three clinical features that characterize AHEI are fever, purpura and edema. The onset of these symptoms typically occurs after temporal exposure to a causative antigenic trigger most commonly of infectious, antibiotic and or vaccine based etiology anywhere from as short as two days to as delayed as one month. The fever can range from mild to severe although there are cases unassociated with fever. The non-pitting edema often affects the face, ears, and extremities. Less often the eyelids, lips, penis and scrotum are affected including cases with severe orbital and scrotal swelling. The most consistent manifestation is purpura. The lesions undergo morphologic evolution from an erythematous macular eruption at is inception to the fully evolved large (i.e. up to 5 centimeters) distinctive annular, cockade, or rounded deeply pupuric lesions most striking on the ears, cheeks, gluteal area and hands, the latter well exemplified by figure 1. Eruptions often occur symmetrically and extracutaneous symptoms rarely occur although have been reported including in the context of gastrointestinal bleeding and hematuria(1-2).

Whereas the features of AHEI sometimes overlap with that of Henoch-Schönlein purpura (HSP), immunofluorescent (IF) studies of AHEI suggest that AHEI and HSP are separate entities. IF studies of those with AHEI demonstrate deposition in the vessel wall of fibrinogen, C3, IgG, IgM, IgA, IgE and C1q. Although HSP also shows reactivity with fibrinogen, C3 and IgM, activation of the classic complement pathway as revealed by significant deposits of C1q is not apparent. IgM is rarely codominant with IgA and is typically of much weaker intensity compared to IgA (3). IgA deposition is not as consistent in AHEI patients and rarely defines a dominant pattern of vascular immunoglogulin deposition (2,4); C1q deposits are frequent.

In summation AHEI is a benign self limited Arthus type III Immune complex mediated vasculitic syndrome. Somewhat analogous to cocaine induced retiform purpura, it is one of the rare dichotomous vasculitic syndromes where impressive cutaneous involvement is in contradistinction to the noticeable lack of signs and symptoms related to extracutaneous vasculitis.

Case References

1. AlSufyani MA. Acute hemorrhagic edema of infancy: unusual scarring and review of the English language literature. Int J Dermatol. 2009 Jun; 48(6): 617-22.

2. Karremann M, Jordan AJ, Bell N, Witsch M, Dürken M. Acute hemorrhagic edema of infancy: report of 4 cases and review of the current literature. Clin Pediatr (Phila). 2009 Apr;48(3):323-6.

3. da Silva Manzoni AP, Viecili JB, de Andrade CB, Kruse RL, Bakos L, Cestari TF. Acute hemorrhagic edema of infancy: a case report. Int J Dermatol. 2004 Jan;43(1):48-51.

4. 3. Lai-Cheong JE, Banerjee P, Hill V, Kenny P, Ross J. Bullous acute haemorrhagic oedema of skin in infancy. Clin Exp Dermatol. 2007 Jul;32(4):467-8.

5. Savino F, Lupica MM, Tarasco V, Locatelli E, Viola S, Cordero di Montezemolo L, Coppo P. Acute Hemorrhagic Edema of Infancy: A Troubling Cutaneous Presentation with a Self-Limiting Course. Pediatr Dermatol. 2012 Nov 21. doi: 10.1111/pde.12004.

Figure Legend

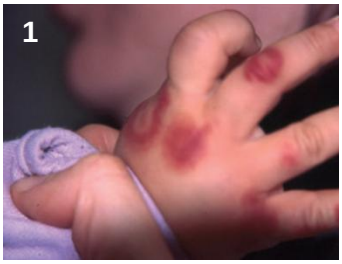


Figure 1 : This 10 month old child shows the typical purpuric lesions of acute hemorrhagic edema of infancy. The photograph is courtesy of Dr. Savino and is from the fifth referenced article (Savino et al). Permission to use this picture has been provided by the authors.

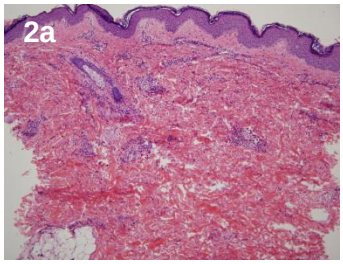
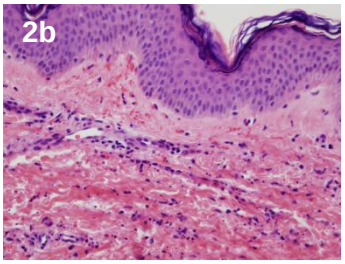
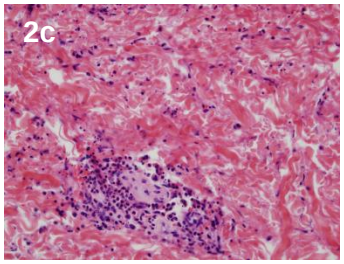


Figure 2a : This low power view shows a perivascular and interstitial neutrophil predominant infiltrate.





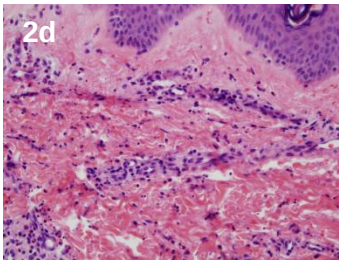


Figure 2b,c, and d: The infiltrate is associated with leukocytoclasia and hemorrhage. Despite the intensity of the infiltrate, fibrin eposition was minimal resulting in a pattern that closely recapitulates urticarial vasculitis.

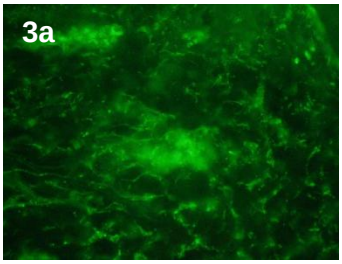


Figure 3a: Direct immunofluorescent studies show a granular deposits of IgM within the cutaneous vasculature.

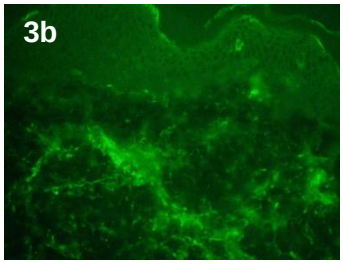


Figure 3b: A similar extent of deposition is observed with IgA. Hence by direct immunofluorescent assessment the pattern recapitulates IgA associated vasculitis/Henoch Schonlein purpura, leading some authors to consider acute hemorrhagic edema of infancy a form of IgA vasculitis.

Under the direction of Dr. Cynthia M. Magro, the Weill Cornell Comprehensive Dermatopathology Service is a leading edge consultation service and CAP-accredited laboratory for dermatologists, plastic and general surgeons and other dermatopathologists. Dr. Magro is an internationally renowned dermatopathologist, educator and author. She is a Professor of Pathology and Laboratory Medicine at the Weill Cornell Medical College in Manhattan, and is board certified in anatomic pathology, dermatopathology and cytopathology. Dr. Magro is an expert in the diagnosis of complex inflammatory skin diseases. Her areas of expertise include cutaneous manifestations of auto-immune disease, systemic viral disease and vasculitis, atypical drug reactions, benign, atypical and overtly malignant lymphocytic infiltrates of the skin, and diagnostically difficult melanocytic proliferations.The award-winning author of ***The Melanocytic Proliferation: A Comprehensive Textbook of Pigmented Lesions***, Dr. Magro has recently completed her second book, ***The Cutaneous Lymphoid Proliferation, a comprehensive textbook on benign and malignant lymphocytic infiltrates***. She has co-authored over 250 peer reviewed papers and several textbook chapters. Dr. Magro frequently presents courses on inflammatory skin pathology and difficult melanocytic proliferations to the American Academy of Dermatology, the United States and Canadian Academy of Pathology, and the American Society of Clinical Pathology. Dr Magro has consistently been recognized in Who's Who in America®, Castle Connolly's renowned America's Top Doctors – New York Metro Area® edition and in the Super Doctors® list published in The New York Times Magazine.

For more information, consultation, or patient referral please contact:

Cynthia M. Magro, MD, Director
Weill Cornell Comprehensive Dermatopathology Service
Tel. 212-746-6434
Toll-free 1-800-551-0670 ext. 66434
Fax. 212-746-8570
www.weillcornelldermpath.com