Atypical hydroa vacciniforme mimicking dermatomyositis: A case report in a Lebanese girl

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Key words: dermatomyositis; EBV-associated T-/natural killer cell lymphoproliferative disorder; hydroa vacciniforme.

INTRODUCTION

Atypical hydroa vacciniforme (HV) is a rare vesiculopapular eruption reported mainly in patients from Asia and Latin America[1-3] and presents with similar but more severe cutaneous manifestations than classic HV. In addition, systemic findings may be present.[1] Distinguishing between classic and atypical HV is essential, as the latter carries a worse prognosis and may progress to HV-like lymphoma.[1,2] Involvement of muscle resulting in a picture similar to dermatomyositis (DM) is a rarely reported presentation of atypical HV.[4,5] Herein, we present the first case, to our knowledge, of a 9-year-old Lebanese girl with atypical HV presenting with a picture of DM.

CASE REPORT

A 9-year-old Lebanese girl presented with a 6-year history of recurrent fevers, headache, fatigue, facial edema, orogenital ulcers, and facial "vesicles" that ulcerated and healed with scars. She was treated with numerous courses of oral steroids and colchicine for presumptive diagnosis of Behcet disease. Results of full blood and endoscopic workup to rule out connective tissue and inflammatory bowel diseases were normal. Physical examination found dry crusted vesicles on the face, lips, and ears and facial edema mostly in the periorbital and perioral areas (Fig 1). Multiple aphthous ulcers were present on the upper gingiva, the buccal mucosa, and the vulvar and peri-anal areas. Neurologic examination found generalized proximal and distal muscle weakness most pronounced in the lower extremities with muscle strength of 3 of 5. Severe hoarseness was noted. No lymphadenopathy or hepatosplenomegaly was present. Juvenile DM was strongly suspected. Blood tests found elevated creatine kinase (1845 U/L; normal value, 60-400 U/L). A vastus lateralis muscle biopsy found severe myositis. Immunohistochemistry highlighted a predominantly T-cell infiltrate positive for CD45 and CD4 with only a few cells positive for CD8, findings consistent with the diagnosis of DM (Fig 2). Facial skin biopsies found reticular epidermal degeneration and a bland dense dermal lymphoid infiltrate (Fig 3). Immunoperoxidase studies found most of the infiltrate to stain with CD3 with only scattered CD20+ cells, and the T-cell component to be composed of a mixture of $CD4^+$ and $CD8^+$ T-cells. In light of the clinical presentation, these findings were suggestive of atypical HV. The lack of cytologic atypia excluded frank HV-like lymphoma at that point. Results of other studies, including anti-Ro(SS-A), anti-La(SS-B), anti—topoisomerase 1 antibodies, anti-Sm, antiribonucleoprotein antibodies, anti—Jo-1 antibodies, anti—double-stranded DNA, antinuclear antibodies, and anticardiolipin antibodies, were negative. Results of tests for human leukocyte antigen (HLA)-B27, HLA-B5, and HLA-B51 were negative. Computed tomography scan of the

Abbreviations used:

CAEBV:	Chronic active Epstein-Barr virus infection
DM:	Dermatomyositis
EBV:	Epstein-Barr virus
HLA:	Human leukocyte antigen
HV:	Hydroa vacciniforme

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Funding sources: None.
Conflicts of interest: None declared.

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JAAD Case Reports 2015;1:63-5.
2352-5126

http://dx.doi.org/10.1016/j.jdcr.2015.01.001

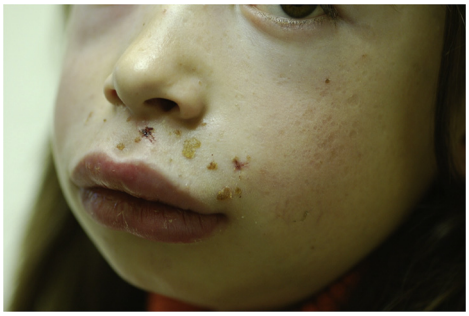

Fig 1. Atypical HV. On initial presentation, multiple mainly perioral crusted vesicles, facial scars, and aphthous ulcers of the upper lip associated with periorbital and lip swelling.

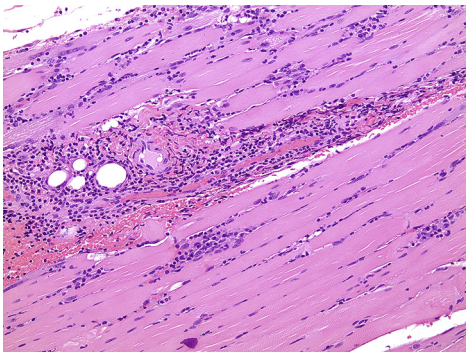

Fig 2. Severe myositis. Multiple fibers with regenerative changes and lymphocytic inflammatory infiltrate streaming between myocytes and focally clustering around destroyed fibers. (Hematoxylin-eosin stain; original magnification: ×200).

chest, abdomen, and pelvis found bilateral widespread tiny patches of alveolar infiltrate but was otherwise unremarkable. This atypical presentation raised the possibility of a chronic active Epstein-Barr virus (EBV) infection (CAEBV). IgG antibody titers to EBV capsid antigen (>200 RU/mL; normal, <1 RU/mL) and EBV nuclear antigen (28 RU/mL; normal, <1 RU/mL) were highly elevated. EBV DNA was detected in the blood by polymerase chain reaction. EBV-encoded small RNA was detected in skin by in-situ hybridization. The patient was thus confirmed to have CAEBV. Her condition progressed rapidly (Fig 4) despite an acyclovir trial (10 mg/kg intravenously 3 times a day for 14 days) and respiratory and renal failures developed. Her last computed tomography scans showed several prominent lymph nodes along the chains of the neck, consolidations and nodules in both lung fields, hepatosplenomegaly, and signs of renal failure. Given these findings and the fulminant course of her disease, the cause of death was presumed to be HV-like lymphoma with secondary multiorgan failure.

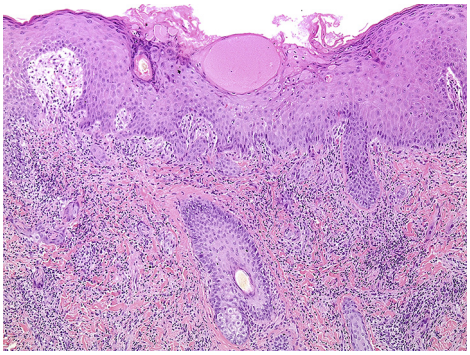

Fig 3. Atypical HV. Punch biopsy from an early facial papulovesicle exhibiting scale crust with inspissated serum, mild spongiosis, and a dense dermal perivascular and interstitial lymphocytic infiltrate. (Hematoxylin-eosin stain; original magnification: ×100).

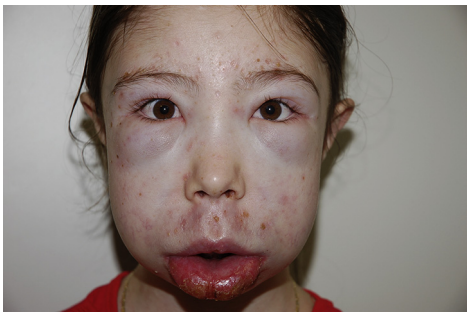

Fig 4. Atypical HV. Rapid progression of her condition 1 year after presentation. Multiple dried up and crusted vesicles over the face, crusted lip ulcers, and severe periorbital and lip swelling.

DISCUSSION

Atypical HV presents similarly to HV with recurrent vesiculopapules in children and adolescents that ulcerate and crust leaving atrophic vacciniforme scars.[1,2,6] Atypical HV, however, presents with more severe skin lesions, a more extensive distribution beyond sun-exposed areas, and systemic manifestations such as fatigue, fever, facial edema (particularly perioral and periorbital), oral or genital aphthosis,[1] hepatosplenomegaly, and lymphadenopathy. In contrast to the self-limited classic HV which resolves by early adulthood, atypical HV lesions tend to become more severe with age and may progress to HV-like cutaneous lymphoma.[1,2] Histologically, both classic and atypical HV are characterized by reticular degeneration, epidermal necrosis, and a perivascular T-cell infiltrate. Atypical HV-like eruptions may comprise a denser infiltrate with a few atypical cells reaching the subcutaneous tissue. However, it is difficult to distinguish between classic and atypical HV based on histology alone.[2,3,7] In HV-like lymphoma, the dense atypical pleomorphic T-cell

infiltrate extends to the subcutaneous tissue with evidence of angiodestructive/angiocentric patterns.[2,8] The histologic features may mimic other aggressive cutaneous T-cell lymphomas. Clinicopathologic correlation remains important for appropriate diagnosis of these entities.[8]

Classic and atypical HV are considered to belong to the same disease spectrum of EBV-associated T-/natural killer cell lymphoproliferative disorder.[1-4,8] The latter represents a rare disorder of immunocompetent patients resulting from the clonal expansion of EBV-infected T or NK cells. Defects in EBV-specific cytotoxic responses have been implicated.[2,3,6] In fact, both HV and atypical HV are associated with infiltration of EBV-infected lymphocytes. However, an overt EBV T-/natural killer cell lymphoproliferative process is only seen in atypical HV and HV-like lymphoma, which probably explains the more aggressive clinical outcomes of these entities.[2,4] Atypical HV represents one of the best-known cutaneous manifestations of CAEBV, a category including several conditions associated with EBV infection, some of which have skin involvement.[1] HV-like lymphoma is an exceedingly rare peripheral T-cell lymphoma manifesting with skin lesions clinically similar to but more severe than those in HV and may represent the malignant edge of the spectrum of EBV-associated HV. Its development is possibly influenced by genetic and environmental factors such as excessive solar exposure.[8] Although infection with EBV has been implicated in the pathogenesis of HV, atypical HV, and HV-like lymphoma,[3,8] not all patients were shown to have EBV infection.[7] This may be attributed in part to the limited sensitivity of the methods used to diagnose EBV infection or to the incomplete nature of the workup done.

To the best of our knowledge, atypical HV presenting as DM has only been reported in 3 patients.[4,5] Facial swelling and eyelid edema are known features of atypical HV and HV-like lymphoma.[2,4] In particular, periorbital involvement may create diagnostic confusion with DM, particularly in the presence of a T-cell–mediated myositis. The absence of the heliotrope rash and of the other cutaneous stigmata of DM may further help avoid misdiagnosis. Primarily reported in East Asia and Latin America, this is the first report, to our knowledge, of CAEBV from Lebanon.[1-3] This entity should always be considered in the differential diagnosis of atypical presentations of DM.

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