

# Hydroa Vacciniforme: A Case Presentation and Discussion

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## Abstract

*Hydroa vacciniforme (HV) is a sunlight-induced dermatosis hallmarked by fluid-filled (hydroa) lesions that resolve with vacciniform, pox-like scarring. Primarily affecting Caucasian children, HV ranges from simple to complex or severe disease. While the more common simple variant is typically benign and resolves by young adulthood, complex cases can progress to lymphoproliferative disorders. The clinical presentation of HV is expansive, mandating a wide differential. Patients report a significant impact on lifestyle, as the foundation and only universal mode of treatment is strict sun avoidance. Herein, we describe the case of a 9-year-old female who presented with a vesicular and papular eruption with crusting on sun-exposed skin that developed following short periods of being outdoors, identified as hydroa vacciniforme.*

## Introduction

First described by Bazin in 1862, hydroa vacciniforme is a rare and recurrent photodermatosis characterized by vesicular crops that crust and ulcerate, leaving permanent scarring.<sup>1,2</sup> The exact pathophysiology of HV remains unknown, though studies indicate a causative link with Epstein-Barr virus (EBV).<sup>3,4</sup> While adult-onset disease has been reported, most cases present in children, with a predilection for the light-skinned.<sup>1,5,6</sup>

Common or “simple” HV displays cutaneous or mucocutaneous symptoms without internal complications.<sup>7</sup> The literature also describes a “complex,” “severe” or “HV-like” disease in which systemic manifestations develop; these cases are much more serious and often precede malignancy.<sup>8</sup> Despite the physical and psychosocial effects of HV, the disease process is considered benign, with spontaneous remission typically occurring by adolescence.<sup>2</sup>

## Case Report

We present a case of a 9-year-old African American-Caucasian female brought in by her mother for a rash that had been present since the age of 3 years. The patient’s mother said the rash developed after sun exposure of a 10- to 15-minute duration and evolved into a welt that crusted over. The rash was limited to areas exposed to the sun: face, dorsal arms, dorsal hands, and tops of ears. The patient’s mother denied any concerns or history of lupus with her daughter, herself or in the immediate family. The mother stated that the use of sun block did not prevent the rash. The child had no past medical, surgical, or family history and was not taking any medications. The patient was allergic to hazelnuts, apple flavor and wheat dextrin.

On clinical exam, the child had multiple, pink to flesh-colored papules on the dorsal forearms and dorsal hands as well as areas of post-inflammatory hyperpigmentation in areas of previous lesions (Figures 1,2). She also had crusted plaques on her ears and left cheek along with areas of post-inflammatory hypopigmentation on her face (Figures 3, 4a, 4b). On further examination, photo-onycholysis and a mild conjunctivitis was noted (Figures 4b, 5). There was no involvement of mucosal membranes, and the rest of the exam was benign.

The differential diagnosis included discoid lupus, systemic lupus erythematosus, erythropoietic protoporphyria and hydroa vacciniforme. The workup for the patient included protoporphyrins, a hepatic function panel and an ANA with reflex.

ANA with reflex was negative, and hepatic-function panel was within normal limits. Free erythrocyte protoporphyrin (FEP) was 36ug/dL, and zinc protoporphyrin was 40ug/dL, both within normal limits and verified by repeat analysis. Given the results of the lab tests along with clinical correlation, the patient was diagnosed with hydroa vacciniforme. The patient was started on 15 mg of beta carotene twice daily and was advised to avoid UV light as much as possible and wear a zinc-based sunblock when outdoors. At four-week follow-up,



Figure 1



Figure 2



Figure 3



Figure 4a



Figure 4b



Figure 6

the patient was responding well to vigorous sun protection and beta carotene, with no active lesions.

## Discussion

### Epidemiology

Hydroa vacciniforme is an exceptionally rare condition often considered a scarring variant of the photodermatosis family, which includes polymorphous light eruption (PMLE) and actinic prurigo.<sup>1,7</sup> Approximately one in 300,000 people is affected, though non-specific diagnostic criteria render this prevalence questionable.<sup>1,9</sup> The disease process occurs with a bimodal distribution at ages 1 year to 7 years and 12 years to 16 years, with males affected more frequently and more severely than females.<sup>2,9</sup> Most HV is sporadic, although familial cases have been described.<sup>10</sup>

### Pathophysiology

While HV's exact pathophysiology is unknown, sunlight is known to trigger eruptions, a fact substantiated via artificial UV exposure in controlled settings.<sup>7</sup> The mechanism behind lesion formation is unclear, though many studies have identified EBV within cutaneous vesicles, suggesting an association.<sup>4,8,11</sup> Further, titer levels of EBV-encoded BZLF1 mRNA in peripheral blood appear to correlate with disease severity.<sup>5,12</sup> Transcription factor BZLF1 triggers EBV reactivation by activating the lytic cascade responsible for viral gene expression.<sup>5,13</sup> One study showed that 33% of patients with systemic symptoms were BZLF1-positive, 80% of whom died during study follow-up.<sup>8</sup>

### Presentation

Commonly, HV first manifests as symmetric macular crops in a photodistribution within minutes to hours of sun exposure.<sup>1</sup> These macules, which can be painful or pruritic, evolve into papules, vesicles, or plaques that go on to form hemorrhagic, necrotic crusts.<sup>7,14</sup> Healing occurs over one week to six weeks, resulting in atrophic and often telangiectatic, umbilicated scarring.<sup>1,15</sup> Mucosal involvement is uncommon, presenting in 6% to 26% of cases with symptoms such as stomatitis, ulcerative gingivitis, photophobia, or inflammation of various ophthalmic structures. Extracutaneous manifestations indicate more severe or HV-like disease.<sup>2,16,17</sup>

### Histology

While EBV titers and BZLF1 expression have been used to predict disease prognosis, there exists no pathognomonic test for HV.<sup>8,11</sup> With appropriate clinical suspicion, however, biopsy can provide characteristic histologic findings. Early lesions show intraepidermal spongiosis and focal keratinocyte degeneration with associated perivascular lymphoneutrophilic infiltration.<sup>2,7</sup> Later, there is epidermal vesiculation with confluent necrosis and ulceration that may extend into the upper dermis.<sup>1,14</sup> Infiltrate density and subcutis extension are indicative of more severe disease.<sup>8,14</sup> While the direct immunofluorescence assay (DFA) is often non-specific, immunohistochemistry typically demonstrates cytotoxic T-lymphocytes and monoclonal T-cell receptors.<sup>2,11,18</sup>

### Differential Diagnosis

The differential diagnosis for HV is wide and includes both photodermatoses and blistering disorders, including PMLE, actinic prurigo, solar urticaria, erythropoietic protoporphyria (EPP), porphyria cutanea tarda (PCT), systemic lupus erythematosus (SLE), and herpes simplex eruption,

among others.<sup>1,4,7</sup> Distinguishing between these conditions requires a detailed history coupled with clinical, laboratory, and histopathologic evaluation. A history of non-scarring lesions is suggestive of PMLE or solar urticaria, while actinic prurigo is more common in Native American and Latin American populations.<sup>2</sup> EPP and PCT display abnormal urine, blood, and stool porphyrin levels.<sup>2,15</sup> Herpes simplex eruptions and SLE can be ruled out via viral culture and antinuclear antibody panel, respectively.<sup>7,18</sup> Aside from routine blood work, these studies should be ordered to rule out other disorders and to confirm diagnosis in suspected HV.

### Prognosis and Treatment

The prognosis for simple HV is generally very good. Though significant scarring remains, most cases resolve by adolescence with a near-100% survival rate.<sup>8</sup> Because of this, the detrimental psychosocial and emotional tolls of active and persistent disease are often understated. In one study of diagnosed children, 54% to 64% reported sadness, anger, or embarrassment due to clothing limitations and an inability to play outside.<sup>2,19,20</sup> More than half of adults endorsed difficulty completing daily tasks like shopping or gardening out of apprehension for being in public.<sup>19,20</sup> When compared to psoriasis and atopic dermatitis using the dermatology quality of life index (DLQI), HV was considered the most life-altering and impactful.<sup>19</sup>

In the rare refractory and chronic cases, certain factors indicate a poorer overall prognosis, most notably systemic manifestations like fever, weight loss or hematologic abnormalities.<sup>12</sup> When these symptoms are present and age of onset is greater than 9 years old, risk of mortality surpasses 80%.<sup>8,12</sup> Exceptionally high levels of EBV titers or BZLF1 expression also correlate with more severe disease and eventual progression to lymphoproliferative malignancies.<sup>4,8,18</sup>

Treatment for HV follows the trend of other light-induced disorders. Sun avoidance is the foundation of management, with photoprotective clothing and liberal application of zinc-based sunblock recommended for times when avoidance is impossible.<sup>8,15,21</sup> Remission or control has been noted with multiple therapies, including hydroxychloroquine, thalidomide, corticosteroids, beta-carotene, PUVA and fish oil.<sup>4,19,21</sup> One study reported indirect treatment success by suppressing EBV replication with acyclovir/valacyclovir/ganciclovir.<sup>4</sup> Unfortunately, no therapeutic modality has shown widespread success, making sun abstinence the only universal recommendation.

## Conclusion

Hydroa vacciniforme is a frustrating disease for patient and provider alike. Patients experience significant worsening in quality of life due to disfiguring scars and limitations on daily activities. Without universally effective therapies, providers must resort to recommending strict sun avoidance and treatments that have variable success rates. Besides limiting sun exposure, other frequent practices include referrals to oncology for systemic investigation and to ophthalmology for monitoring of ocular involvement.<sup>2,4,16,17</sup> Supportive efforts via psychological care or group therapy may also be prudent, when appropriate. With ongoing research into the pathophysiology of HV, providers will have more effective treatment modalities at their disposal, translating into improved care and a better quality of life for the patient.

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