Dermatology Online Journal
UC Davis

Persistent varicella as the initial manifestation of systemic lymphoma

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Dermatology Online Journal 14 (2): 24

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Abstract

Varicella is a common benign childhood disease that often presents in adolescents and adults in a more severe form. We report a previously healthy 50-year-old man who developed multiple necrotic cutaneous ulcers associated with fever, asthenia and anorexia. Physical examination revealed few tense hemorrhagic vesicles on the trunk and necrotic cutaneous ulcers scattered over the entire cutaneous surface. After the diagnosis of varicella with varicella pneumonia was established, treatment with acyclovir was instituted. His poor response to treatment was indicative of immune compromise; an underlying peripheral T-cell lymphoma was discovered.

Primary varicella-zoster virus (VZV) infection results in chickenpox, characteristically a benign disease of childhood. Complications such as pneumonia, hepatitis, and encephalitis are rare in healthy children but more common in adolescents, adults, and immunocompromised patients [**1**]. Additionally, in immunocompromised patients, varicella may present the atypical form of disseminated ulcerative or necrotic skin lesions [**2**]. Also, the duration of replication and virus shedding can be extended and result in protracted disease [**3**]. While this is well-described for advanced stages of leukemia and lymphoproliferative disorders, mainly after chemotherapy, it is rarely described as the first manifestation of such diseases.

Clinical synopsis

A previously healthy 50-year-old man presented with a 6-week history of cutaneous vesicles, ulcers, fever, asthenia, and anorexia. Tense sero-hemorrhagic vesicles and multiple necrotic ulcers were observed (Figs. 1 and 2). Mucosal surfaces were free of lesions; there was no enlargement of lymph nodes, liver, or spleen.

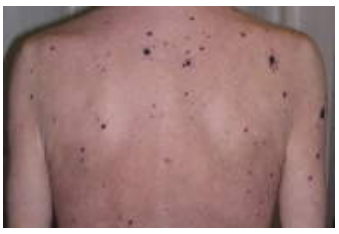

Figure 1

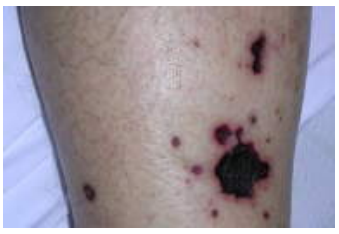

Figure 2

trunk
Figure 2. Close view of ulcers and surrounding petechiae on the leg

The skin biopsy revealed intraepidermal vesiculation with ballooning degeneration and multinucleated giant cells. Oral acyclovir (800 mg five times a day) was started. Further investigations showed an elevation of immunoglobulin G and M for varicella-zoster virus. After 7 days on acyclovir there was sustained fever with the development of new cutaneous lesions, hypotension, peripheral edema, and abdominal distension with hepatomegaly. Laboratory tests revealed pancytopenia and cholestasis, a marked decrease on T-cells ($170/mm^3$), an inverted CD4/CD8 ratio. Acyclovir treatment was changed to the intravenous route. Bone marrow biopsy was consistent with chronic myelofibrosis. Computed tomography revealed a diffuse interstitial infiltrate of the lungs and lymphadenopathy at multiple sites. On broncho-alveolar lavage, DNA of VZV was detected by polymerase chain reaction and confirmed VZV pneumonia.

A polymorphic cellular infiltrate on lymph node biopsy, including basophilic cells expressing CD3 and CD5 antigens and CD7 negativity corroborated the diagnosis of a peripheral T-cell lymphoma, unspecified (PTCL-u). It was classified as an IV-B lymphoma by the Ann-Arboisr classification, falling into the unfavorable International Prognostic Index category 3. The patient began chemotherapy with the regimen cyclophosphamide, vincristine, doxorubicin and prednisone after resolution of the varicella (after 28 days on intravenous acyclovir). Oral acyclovir was maintained prophylactically (400 mg twice a day); however, 3 episodes of ophthalmic zoster occurred. Rapid progression of the lymphoma occurred in spite of treatment and the patient died after 8 months.

Discussion

The patient described had a severe varicella-zoster infection prior to any visible sign of immunosuppression. His disease was classified

as persistent varicella because new lesions continued to develop for more than 1 month [**4**]. Typically, this occurs in patients with very low CD4 cell counts at the time of infection [**5**]. Literature reports point to cellular immunity as the principal factor for resolution of the acute infection and convalescence. However, the exact role of cell-mediated and humoral immunity is not completely understood [**5**]. Our patient had no evidence of immunosuppression or complications at presentation but further investigation resulted in the diagnosis of varicella pneumonia and PTCL-u. This type of lymphoma represents 5-7 percent of all non-Hodgkin lymphomas, is usually aggressive, and commonly relapses, especially when there is an unfavorably high score according to the International Prognostic Index [**6**]. There are no rigorous treatment guidelines for persistent VZV infection. Intervention regimens have varied tremendously. Recommendations include continuing acyclovir treatment for 7 days or until no new lesions have appeared for at least 48h, followed by lifelong suppressive therapy [**7**]. Long-term acyclovir is controversial. It has been used to prevent life-threatening complications and recrudescent infection, but development of drug resistance is a possibility [**8**, **9**]. Moreover, there is no evidence that prophylactic acyclovir prevents herpes zoster. Indeed, in this patient there was occurrence of herpes zoster while he was continued on prophylactic acyclovir.

This case is intriguing because persistent varicella was the initial manifestation of an undiagnosed peripheral T-cell lymphoma in an adult man who had appeared healthy.

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