Varicella Pneumonia With Immune Thrombocytopenic Purpura: A Patient With Multiple Complications

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GOAL

To understand varicella infection and immune thrombocytopenic purpura to better manage patients with these conditions

LEARNING OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Assess the impact of varicella infection on the adult population, particularly immunocompromised patients.
2. Evaluate treatment options for varicella infection in high-risk patients and patients with complications.
3. Discuss immune thrombocytopenic purpura in patients with primary varicella infection.

INTENDED AUDIENCE

This CME activity is designed for dermatologists and generalists.

CME Test on page 414.

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Viral syndromes can present with various cutaneous manifestations, from the morbilliform eruption of measles to the papular lesions of molluscum. The systemic manifestations of viral illness can be similarly varied, with different presentations in each individual. We describe a patient with recently

diagnosed AIDS who presented to the emergency department with hemorrhagic papules and shortness of breath. She was found to be severely thrombocytopenic, and a Tzanck smear revealed multinucleate giant cells. She received a diagnosis of immune thrombocytopenic purpura (ITP) and primary varicella pneumonia. Acyclovir and intravenous immunoglobulin (IVIG) were initiated. Her respiratory status improved after 5 days of treatment and her cutaneous lesions healed, with some scarring. We believe the rapid resolution and benign outcome of this patient's varicella infection may have been attributed to the concomitant initiation of IVIG with antiviral therapy.

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Case Report

A 33-year-old woman who recently received a diagnosis of AIDS presented to the emergency department with a cough productive of green, blood-tinged sputum and the acute onset of a diffuse skin eruption of 10 days' duration. Physical examination demonstrated multiple 3- to 5-mm hemorrhagic vesicles surrounded by an erythematous rim located on all skin surfaces and the hard palate (Figures 1 and 2). Lesions ranged from fresh vesicles to crusts to erosions. Soon after presentation, she developed respiratory distress requiring intubation. A Tzanck smear displayed multinucleate giant cells (Figure 3) and primary varicella pneumonia was diagnosed. The patient also had a platelet count of $4\times10^3/\mu L$ (reference range, $150–350\times10^3/\mu L$), which led to the concomitant diagnosis of immune thrombocytopenic purpura (ITP). Acyclovir and intravenous immunoglobulin (IVIG) were initiated. She was extubated after 5 days of treatment and her cutaneous lesions have since resolved, with some scarring.

Comment

Primary varicella is a serious infection with higher rates of complications in the adult population than in children.[1] In patients who are substantially immunocompromised, such as patients with AIDS, both hemorrhagic lesions and viremia leading to hematogenous disseminated disease are common. Even in an immunocompetent host, the disease can be fulminant and severe with associated encephalitis, pancreatitis, hepatitis, and pneumonia.[2] Pneumonia is the most serious complication and leading cause of death in adults with primary varicella infection, regardless of their immune status; in one study, the mortality rate for patients with advanced immunosuppression who developed pneumonia was found to be 43% (3/7).[3]

The diagnosis of varicella infection often is clinical, especially when patients present with the typical cutaneous manifestations, including multiple pruritic macules that rapidly progress to papules and vesicles before beginning to crust in 1 to 2 days. The crusts typically fall off in 1 to 2 weeks and often leave an area of hypopigmentation.[4] The lesions tend to be concentrated on the trunk and face and appear in crops, with lesions present at the various stages of disease progression. The exanthem is frequently accompanied by fever, malaise, headache, and anorexia. If uncertain of the diagnosis, a positive Tzanck smear showing multinucleate giant cells will indicate an α-herpesvirus infection, but it is not specific for varicella-zoster virus (VZV). Other confirmatory methods include serologic tests detecting IgA and IgM against the virus. This test may be positive for varicella infection within 24 to 28 hours of symptom onset, but a negative test result does not rule out the infection. Indirect methods of viral detection, such as polymerase

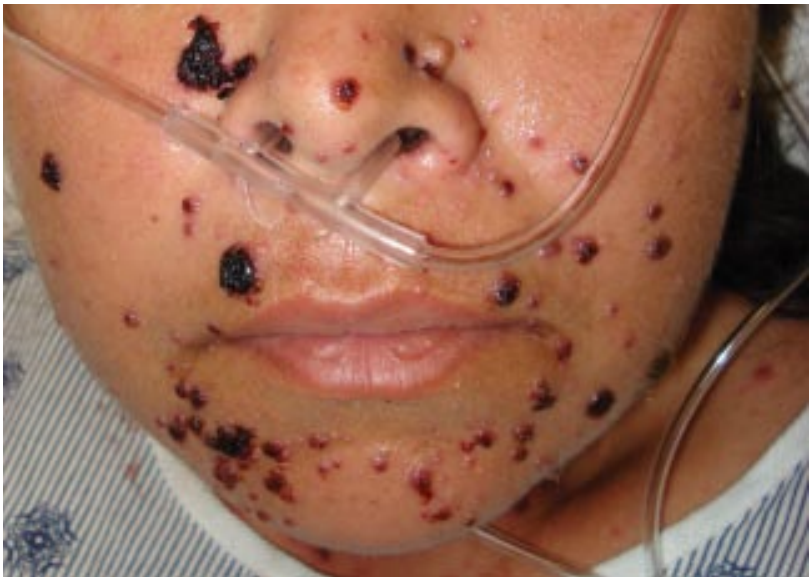

Figure 1. The patient presented with multiple hemorrhagic papules, crusts, and erosions on the skin surfaces and the hard palate.

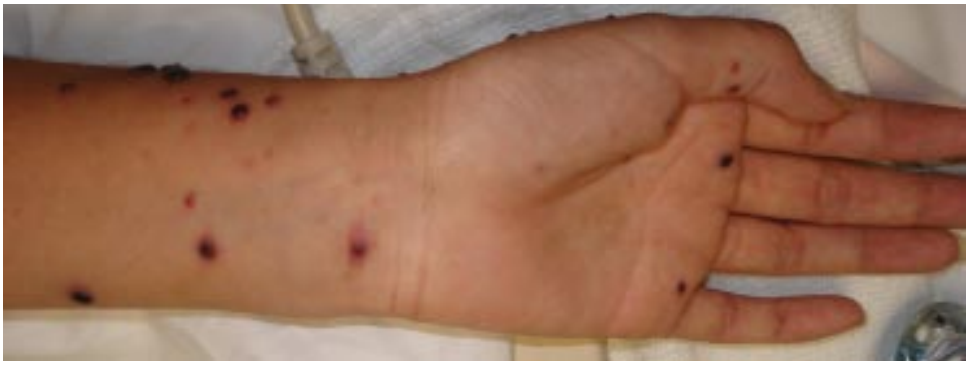

Figure 2. Physical examination of the papules revealed tense hemorrhagic bullae on an erythematous base involving the skin, including the palms and soles.

chain reaction and rapid antigen immunofluorescence techniques, are more useful and are typically reserved for confirming severe or unusual presentations of disease.[4]

Treatment of varicella infection is necessary in high-risk patients, including immunocompromised hosts, and patients with complications such as pneumonia, encephalitis, or ocular involvement. For immunocompromised hosts, the treatment is acyclovir 30 mg/kg (in 3 divided doses) administered intravenously within 72 hours of disease onset.[4] Despite the widespread use of valacyclovir hydrochloride in immunocompetent patients, this medication has a relative contraindication for the treatment of patients with advanced human immunodeficiency virus (HIV) disease. The use of high doses of valacyclovir hydrochloride in patients with HIV has been associated with the development of hemolytic uremic syndrome and increased mortality.[5] Because other hematologic disorders such as thrombocytopenia are common in patients with either HIV or varicella infection, this potential side effect must be kept in mind when treating patients with complications.

It also is recommended by the Centers for Disease Control and Prevention to administer varicella-zoster immunoglobulin (VZIG) prophylactically to immunocompromised children and adults without a history of varicella infection or immunization within 96 hours of a notable exposure.[6] As of February 2006, however, the supply of VZIG was nearly depleted because it has not been produced in the United States since October 2004. A newer VZIG product is only available under an investigational new drug application protocol.[7] Although the use of IVIG for the treatment or prophylaxis of varicella infection is not a standard recommendation, there have been several reports of the success of IVIG in addition to acyclovir for the treatment of disseminated varicella infection complicated by pneumonia and respiratory distress, with or without encephalitis.[8-10] In addition to this anecdotal evidence, it also has been shown via in vitro studies of commercially produced IVIG preparations that they contain high levels of antibodies against VZV, indicating that IVIG is highly active against this pathogen.[11] Because there is not an officially licensed supply of varicella-specific immunoglobulin currently available in the United States, IVIG may become an important option in the treatment of complicated varicella infections.

In addition to a diagnosis of varicella pneumonia, our patient was complicated by thrombocytopenia, a finding seen in as many as 30% of adults with a primary varicella infection[12] and up to 40% of patients with HIV infection sometime during the course of their disease.[13] The mechanism of ITP in viral infections is multifactorial involving direct infection of megakaryocytes, absorption of virus or preformed immune complex directly onto the platelet surface, and antibodies produced against a viral epitope cross-reacting with normally occurring platelet glycoproteins.[14]

Although thrombocytopenia often is asymptomatic in patients with HIV infection and therefore may not require intervention, the first-line treatment of thrombocytopenia in this population is antiretroviral therapy.[15] Treatment of ITP in patients without HIV infection includes corticosteroids, IVIG, anti-D immunoglobulin, or splenectomy. These treatments also are used in HIV-infected individuals when antiretroviral therapy fails or is not tolerated; of these treatments, anti-D immunoglobulin has been shown to have a substantially longer duration of effect on platelet count compared with IVIG.[16] Corticosteroids tend to be avoided due to the concern for additional immunosuppression, and although splenectomy can lead to decreased immunity, it has a 50% cure rate for refractory thrombocytopenia in patients with HIV.[15]

We believe the rapid resolution and benign outcome of this patient's varicella infection may have been due to the concomitant initiation of IVIG for the treatment of ITP along with antiviral therapy. As more cases are reported of successful use of IVIG in the treatment of primary varicella pneumonia, this therapy may become more widely used in clinical practice.

Conclusion

Immune thrombocytopenic purpura can be seen in patients with both HIV and VZV infections; some

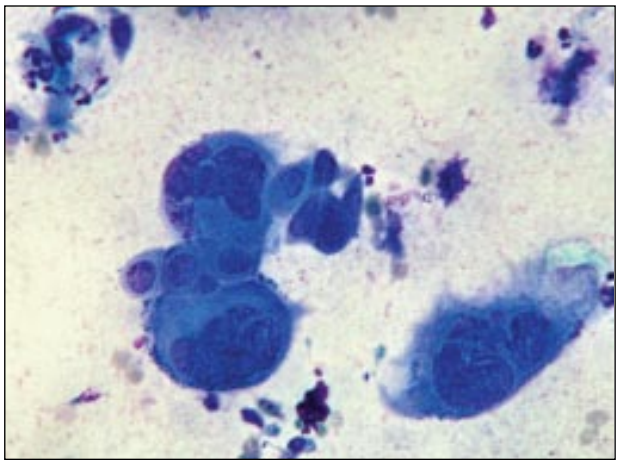

Figure 3. Giemsa stain of a Tzanck smear from the base of a hemorrhagic vesicle revealing multinucleate giant cells (original magnification ×40).

patients may present with all 3 simultaneously. The vesicular eruptions of primary varicella may appear hemorrhagic, especially when the patient is thrombocytopenic, leading to an atypical presentation of illness. Rapid diagnosis is essential to initiating the appropriate therapy in a timely manner. Treatment of ITP may include corticosteroids, IVIG, anti-D immunoglobulin, and splenectomy, though contraindications may exist for some patients. Therapy for varicella infection includes antiviral medications along with VZIG or IVIG. The rapid resolution of VZV and ITP in our patient treated with IVIG illustrates an increasingly useful therapy for these patients with complications.

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