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Beware the Unexpected Infection: Disseminated Varicella Zoster Virus Mimicking A Drug Eruption

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Abstract

Adverse cutaneous reactions to medications are not uncommon and may resemble viral infection and vice versa, complicating diagnosis. We describe the case of a 79-year-old male with cholangiocarcinoma with liver and presumed lung metastasis who presented with abdominal pain and was admitted with ileitis with partial small bowel obstruction. He had a widespread papulovesicular rash with hemorrhagic center, mostly on his face, chest, and back. The rash was initially thought to be a drug eruption, but was eventually diagnosed via dermatopathological examination as disseminated varicella zoster virus (VZV) infection. Steroid treatment was discontinued, and airborne precautions were initiated. Polymerase chain reaction for VZV was obtained and intravenous acyclovir treatment was begun. This case of VZV, initially suspected to be an adverse drug reaction, highlights the importance of early identification of a highly infectious lesion and the importance of early infection control measures, given the implications of exposure to VZV for health care personnel.

Keywords

varicella zoster, herpes zoster, drug eruption, exanthem, infection control

Background

Adverse cutaneous reactions to medications are not uncommon; they occur in as many as 2% to 3% of hospitalized patients.[1-3] While most reactions are mild and self-limiting,[4] they can be severe in ≥2% of cases.[5] Eruptions can take many forms, some of which mimic viral infections; thus, prompt differential diagnosis is needed to ensure that the medication is withdrawn, or treatment for infection is begun as soon as possible.[6,7]

One such viral illness is varicella zoster virus (VZV).[8,9] VZV causes 2 main categories of illnesses: varicella (chicken pox) and herpes zoster (shingles).[10-12] VZV causes an acute viremia with incubation period ranging from 8 to 21 days after exposure. VZV is often a clinical diagnosis because of its characteristic diffuse multistage vesicular rash.

Varicella rash presents as papules and within days progresses to grouped vesicles or bullae then becomes pustular. In immunocompromised patients or the elderly, the lesions can be hemorrhagic and severe.[13,14] Rashes generally crust within 7 to 10 days in immunocompetent patients, but immunocompromised patients may develop new lesions more than a week after initial presentation. These lesions are infectious until the rashes have fully dried and crusted over.[10-12,15]

We describe a case in which the patient presented with what was initially thought to be a drug eruption, but was diagnosed via dermatopathological examination as disseminated VZV infection. In this case report, we identify the clinical features of VZV lesions and various laboratory tests used in its diagnosis, and note both infection control recommendations for hospitals for VZV and recommendations to establish immunity in health care personnel, including when and if titers should be checked.

Case Presentation

A 79-year-old gentleman presented with abdominal pain and was admitted with ileitis with partial small bowel obstruction (see Table 1, Case Timeline). He had an intraductal papillary neoplasm of the bile duct, a form of cholangiocarcinoma,

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Table 1. Case Timeline.

Hospital day	Symptoms and significant events
−56	Patient initiated capecitabine treatment
	Patient began experiencing papulovesicular rash with hemorrhagic center, mostly on his face, chest, and back, which continued to worsen with subsequent treatment
0	Patient presented with abdominal pain and was admitted with ileitis with partial small bowel obstruction
+2	Steroids were initiated
+3	Dermatology was consulted
	Biopsy was sent for histological staining along with direct immunofluorescence
	Capecitabine was discontinued
+10	Dermatopathology returned consistent with HSV/VZV
	Steroids were discontinued and IV acyclovir along with airborne precautions initiated
+11	Infectious disease was consulted and VZV PCR was obtained
+12	Patient improved, was transitioned to valacyclovir, and discharged

Abbreviations: HSV, herpes simplex virus; VZV, varicella zoster virus; PCR, polymerase chain reaction.

with liver and presumed lung metastasis. He had been on capecitabine, a pyrimidine analogue treatment, for 8 weeks prior to presentation. The patient also had a widespread papulovesicular rash with hemorrhagic center, mostly on his face, chest, and back, which started after his initial capecitabine treatment and progressed with 2 subsequent treatments. Hematologic studies did not initially suggest drug eruption or viral infection. The rash was initially suspected to be due to drug eruption; thus, capecitabine was discontinued and steroids were initiated. Dermatology was consulted. The lesions were biopsied and sent for histological staining and direct immunofluorescence (DIF). Differential diagnoses included paraneoplastic pemphigus, bullous pemphigoid, erythema multiforme (EM) spectrum lesions, and Stevens-Johnson syndrome (SJS). The slides were initially examined by general pathology with preliminary read of nonspecific findings with eosinophilia, seemingly supporting an adverse cutaneous reaction to capecitabine. Negative DIF excluded paraneoplastic pemphigus and bullous pemphigoid. Furthermore, the lesions were not consistent with SJS or EM spectrum rash. Additional dermatopathology review identified cytopathic effects on cells that were consistent with viral etiology: herpes simplex virus (HSV)/VZV. Steroid treatment was discontinued, and airborne precautions were initiated. Infectious disease was consulted and VZV polymerase chain reaction (PCR) was obtained. The patient was started on intravenous acyclovir.

At discharge, he was transitioned to valacyclovir to complete a 7-day treatment. The rash gradually resolved over several weeks. He followed up with his primary care physician, oncologist, and an infectious disease specialist. There were no observed cases of VZV spread to health care providers or their contacts.

Discussion

Capecitabine treatment is associated with adverse cutaneous reactions in the literature. As many as 50% of individuals receiving capecitabine chemotherapy experience hand-foot syndrome,[16,17] and this medication has been associated with skin eruptions in case reports, though dermatological manifestations are usually present in a lichenoid and/or palmoplantar distribution.[18-27]

Our patient presented with what was initially thought to be a drug eruption. Preliminary findings from his skin biopsy supported this diagnosis, but additional dermatopathological review detected disseminated VZV infection. Laboratory diagnosis for VZV is used when clinical presentation is uncertain or atypical. In these cases, PCR, direct fluorescent antibody (DFA), or enzyme-linked immunosorbent assay (ELISA) testing are used to confirm VZV infection. PCR testing is preferred as it can be used to test lesions of all stages and has a rapid turnaround time. PCR is also preferred as it can be used for noncutaneous specimens such as cerebrospinal fluid. DFA testing can be done on scrapings directly from infectious lesions. ELISA testing is used to determine susceptibility to infection and need for immunization. Viral culture can also be used to diagnose VZV, but is of low yield and requires a longer incubation period.

VZV is highly contagious because it is airborne; thus, infection control is key in health care facilities. Health care workers are at risk of exposure to VZV either via direct contact with infectious lesions or through airborne transmission; airborne precautions are thus advised.

Health care workers should be screened upon employment for immunity to VZV. Immunity is established by (1) 2 doses of varicella vaccine administered 4 to 8 weeks apart, or (2) documented previous diagnosis of varicella disease, or (3) laboratory evidence of immunity via evaluation of titers. Post immunization serology is not recommended after immunization of health care workers because commonly available commercial tests for VZV may not detect the lower antibody levels seen in vaccinated persons as compared with the higher antibody levels seen after natural infection.

This case of VZV, initially suspected to be an adverse drug reaction, highlights the importance of early identification of a highly infectious lesion. It also highlights

the importance of early infection control measures and the implications of exposure to VZV for health care personnel. Such exposures can require up to 21 days of monitoring, which can be logistically difficult; thus, infection control measures aim to extend protection to the patient and their contact exposures, as well as to the health care team, their exposures, and their loved ones.

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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