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Widespread Rash in an Immunocompromised 31-year-old Female: Case Report and Literature Search

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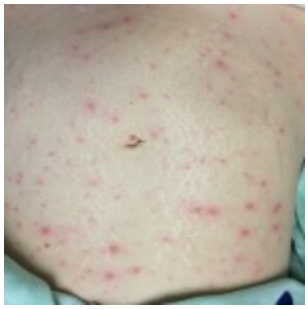
CASE REPORT

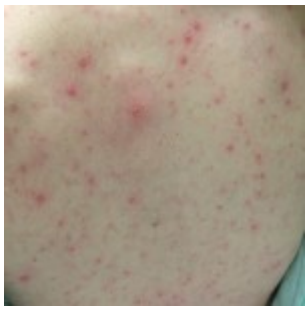
History: A 31-year-old female presents with a widespread vesicular and papular rash involving her anterior and posterior trunk, proximal extremities, neck, and face with sparing of soles and palms. Her past medical history is significant for Philadelphia chromosome and BCR-ABL positive chronic myelogenous leukemia (CML) diagnosed in 2011 and now s/p allogenic hematopoietic stem-cell transplant (HSCT) and subsequent CNS recurrence. Five days before presenting, the rash initially began around her vagina and coccyx and spread laterally to the left and onto her medial buttock and is associated with significant pernineal swelling. In addition, the rash is present in all dermatomes of the trigeminal nerve with lesions also present in her oropharynx on the soft palate. She has had no relief or improvement of the rash with monostat, triple antibiotic cream, or valacyclovir 500 mg qDay received from the Primary Care Physician. Her past medical history is also notable for health-care associated pneumonia 6 weeks ago at the end of January requiring ICU admission and ventilator support. Her only surgery was for Ommaya reservoir placement. She is not sexually active, smokes 1 pack of cigarettes per day, and lives at home with her two daughters.

Exam: Vitals are temperature 37.1C, heart rate 91, respiratory rate 18, blood pressure 91/66 mmHg, and SpO2=90% on 2L O2 by nasal canula. Physical exam reveals a notably thin Caucasian female, moderately injected and watery conjunctiva, no lymphadenopathy, unremarkable cardiac exam, lungs clear bilaterally without crackles, and a soft, nontender abdomen without hepatosplenomegaly. Skin exam confirms a dermatomal rash extending from her coccyx and left labia, wrapping around laterally on the left, and extending onto the buttock with diffuse macular papules on torso, back, and face interspersed with vesicles. The oral mucosa has some vesicles on the palate. The rash spares her palms and soles. She has no focal neurologic deficits.

Lab results demonstrate a normal white blood cell count, hemoglobin level, platelet count, basic electrolytes, total bilirubin, and AST. Elevated results include: MCV = 107.4 fL, alkaline phosphatase 192 unit/L, and AST 45 unit/L. Labs demonstrate decreased: total protein 6.0 g/dL and albumin 3.3 g/dL. A pregnancy test is negative.



Papular rash on patient's abdomen



Papular rash on patient's back

WHAT IS YOUR DIFFERENTIAL DIAGNOSIS AND WHAT COMPLICATIONS MUST YOU BE ALERT TO? HOW WOULD YOU MANAGE THIS PATIENT?

Concerns in immunocompromised patients: Immunocompromised patients are at increased risk of a multitude of infections. Patients who have undergone allogenic HSCT are immunologically naïve to almost all diseases and at greater risk of reactivation of many viral illnesses, even if they had previously completed all recommended childhood and subsequent vaccinations. Among the most common reactivations are cytomegalovirus (CMV), herpes simplex virus (HSV), varicella-zoster virus (VZV), and hepatitis B virus (HBV). The respiratory viruses, and in particular influenza virus also cause significant morbidity and mortality in the HSCT population.

Differential diagnosis: For this patient, the differential diagnosis include varicella-zoster virus (VZV), herpes zoster virus-1 or herpes zoster virus-2 (HSV-1,2), acute on chronic graft-versus-host disease (GVHD), other viral exanthems, eosinophilic folliculitis, and Sweet syndrome. The patient's prior history of chicken pox infection and of oral herpes strongly suggests the possibility of reactivation of either VZV or HSV. Furthermore, the initial localized start to the rash prior to subsequent dissemination to involve nearly the entire skin is further suggestive of viral reactivation. In conjunction with mostly unremarkable basic labs not concerning for bacterial infection, CML recurrence, or other hematologic cancer the most prudent approach would be to evaluate for ZVZ and HSV infection while initiating empiric therapy. The other aspects of the differential mentioned above are: (a) less likely given the situation, or (b) would be unusual timing for presentation, e.g. Sweet syndrome.

Potential complications and management: Complications that must be watched for involve both the presumed diagnosis and the empiric therapy. Unusual complication of VZV include herpes zoster ophthalmicus, trigeminal zoster with keratitis, acute retinal necrosis, encephalitis, aseptic meningitis, pneumonia, Ramsey-Hunt syndrome (herpes zoster oticus), secondary bacterial and yeast infections, post-herpetic neuralgia, and visceral involvement of the liver or gastrointestinal tract. The latter may actually lack significant or any skin lesions. Involvement of the lungs, gastrointestinal tract, or central nervous system carries significant morbidity and mortality. Involvement of the lungs may require intubation and mechanical ventilation.

Empiric management of both VZV and HSV in immunocompromised individuals involves early antiviral therapy with valacyclovir, acyclovir, or famciclovir. In the immunocompromised patient or if the patient that is hospitalized, Intravenous acyclovir is the standard therapy for the duration of 7 days. This treatment protocol is also indicated in any complicated cases which includes herpes zoster ophthalmicus, Ramsey-Hunt syndrome, or involvement of internal organs. Intravenous immunoglobulin and systemic corticosteroids are proven of no benefit. Corticosteroids are only indicated in herpes zoster ophthalmicus as topical drops to abort the inflammatory response and minimize the keratitis and iritis that arises due to the inflammatory response.

PATIENT COURSE IN THE HOSPITAL

The patient was placed on airborne precautions and started on empiric intravenous acyclovir therapy along with symptomatic management included hydroxyzine . Tests ordered included quantitative IgM (immunoglobulin M), serum PCR (Polymerase chair reaction) for HSV and VZV, serum HIV(human immunodeficiency virus) antigen/antibody, and serum RPR (rapid plasma reagin). Chest radiograph done for a lone episode of desaturation the night of admission showed streaky bibasilar opacities, atelectasis versus trace pneumonia.

Dermatology was consulted the day after admission and was found to be in agreement with the differential and current plan. The patient now reported decreased urination and a sensation of a full bladder. Further refinement of management at their recommendation included avoiding any use of corticosteroids and swab of left perineum vesicle for VZV and HSV polymerate chair reaction.
Ophthalmology consult was prompted the day after admission due to Hutchinson's sign, involvement of the lateral side and tip of the nose and complaint of blurry vision. Ophthalmologic exam found moderate to severe dry eye syndrome but no evidence of ocular infection, infection, or malignancy on exam and recommended use of preservative free artificial tears (lacrilube) at night and restarting restasis once discharged.

Hematology-oncology was also consulted given the patient's history of CML.Hematology deemed continued holding of dasatanib reasonable at this time. The patient had stopped her dasatanib at onset of the rash and had most recently received chemotherapy involving methotrexate and cytarabine.

Lab results came back with nonreactive HIV and RPR, quantitative IgM within normal range, serum and perineum swab negative for HSV-1,2 by PCR and both serum and perineum swab positive for VZV by PCR.

On day 3 of admission the patient was switched to oral valacyclovir therapy. After lesions were deemed crusted over and she was discharged home to complete the oral valacyclovir therapy and follow-up with her primary care physician.

DISCUSSION

VZV is part of the herpes viruses. Initial infection causes varicella, or what is commonly known as chickenpox. After recovery, the virus becomes latent in dorsal ganglion cells and may reactive many years later, often during times of waning immunity or during a time of increased physical or mental stress. In the average person who is immunocompetent, the reactivation as shingles is typically a vesicular rash limited to one or perhaps two dermatomes and is almost exclusively a cutaneous disorder.

Although the majority of VZV reactivation is limited to the skin, disseminated infection is also possible. In particular, immunocompromised patients of any cause have both higher chances of reactivation of more extensive disease. HSCT patients used to have a VZV reactivation rate of nearly 50% within 6 months of transplantation. Prophylaxis has cut that rate and in non-HSCT patients, reactivation rates vary from 2% to 25% depending on the original cancer and the type of therapy. CML patients receiving imatinib have recurrence rates averaging 2%. Our patient reports no exposure to individuals with an active VZV infection so there was no indication for varicella immune globulin or antiviral prophylaxis. Use of the varicella or the zoster vaccine for prevention of disease is currently contraindicated for HSCT recipients as are other live viral vaccines. Therefore, these patients must take care to avoid infected persons and active infection, primary or secondary. Prophylaxis after exposure is still debated but may include administration of varicella immunoglobulin or short term antiviral therapy.

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