An Accidental Pox Party:
A Preventable Case of Fatal Disseminated Varicella in an Elderly Immunocompromised Female

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Abstract

Varicella zoster virus (VZV) infection represents a highly preventable yet extremely contagious array of infectious disease states with a broad range of clinical manifestations ranging from self-limiting local or diffuse dermatological eruptions to severe ophthalmological eruptions accompanied by blindness, bilateral multifocal pneumonia, meningoencephalitis, and even fulminant hepatitis. The degree of severity is often proportional to degree of immunosuppression, either inherited or acquired, with immunocompromised patients exhibiting greater morbidity and mortality associated with acute infections. We present an interesting and unfortunate case report involving an 86-year-old female with a history of rheumatoid arthritis on chronic methotrexate therapy who presented with acute hypoxic respiratory failure secondary to disseminated VZV infection with pulmonary involvement, likely acquired by exposure to her husband with active shingles. Unfortunately, the patient left against medical advice at the time of initial presentation to the ED, only to return the following day with worsening respiratory failure requiring intubation and mechanical ventilation. This likely resulted in a delay in initiation of appropriate antiviral therapy, which may have improved her eventual outcome if started sooner in her presentation. The patient was also unfortunately not vaccinated for either primary varicella infection or shingles, either of which would have likely helped to prevent the development of disseminated disease, if not the fatal complications observed in this case. We include an overall review of the current literature with respect to the epidemiology, clinical presentation, diagnosis, prevention, and management of VZV including pertinent clinical information regarding management of disseminated disease, such as post-exposure prophylaxis and antiviral therapy. Although this patient's presentation was potentially worsened by post-mortem findings indicating mycobacterium avium complex (MAC) coinfection, the case serves as a strong reminder for encouraging universal VZV vaccination, particularly in patients with inherited or acquired immunodeficiency. This is particularly relevant in the setting of rising vaccine hesitancy, which is increasing even for non-COVID vaccines, largely in the wake of widespread misinformation surrounding vaccination during the COVID19 pandemic.

Background

- Disseminated varicella (DV) is primarily a disease of immunocompromised, and varicella zoster virus (VZV) rarely leads to severe or fatal disease [1-3]
- Primary VZV is self limiting diffuse dermatological eruption, followed by extended period of latency with the virus remains dormant in sensory nerve ganglia [1]
- Reactivations manifest most commonly as shingles, an often-painful vesicular rash in dermatomal distribution, potentially followed by post-herpetic neuralgia [2]
- Shingles typically occurs in patients over 50 years, often due to age-related reduction in immunity (immunosenescence), or other acquired immunodeficiency [2,3]
- DV may have a wide variety of presenting symptoms, including rash, abdominal pain, bilateral hypoxic varicella pneumonia, meningoencephalitis, and fulminant hepatitis [3]
- Severe complications are relatively rare, with 1% - 4% of all cases requiring hospitalization, of which 30% involve immunocompromised patients [4]
- Mortality for DV approx. 9% - 50%, with higher mortality in immunocompromised [3,4]
- Diagnosis can be made clinically or using highly sensitive serological markers (IgM), or less commonly skin biopsies, Tzanck smears, bronchial washing, or IHC staining [4]
- Prevention is by far the most efficacious approach to management
  - Primary: VZV vaccine or MMRV vaccine (all ages) [5]
  - Shingles: recombinant zoster vaccine or zoster live vaccine (>50yrs) [5]
- Unless severe or disseminated, treatment is supportive +/- oral acyclovir (or equiv.)
- DV requires *prompt* administration of antivirals (acyclovir, valacyclovir, famciclovir)
  - Severe cases may benefit from parenteral therapy with acyclovir [6,7]
  - Consideration for varicella zoster immune globulin for immunocompromised patients (i.e., post-exposure prophylaxis) [8,9]
  - Antivirals should be initiated before crusting or within 1 week of onset [10]

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Figures

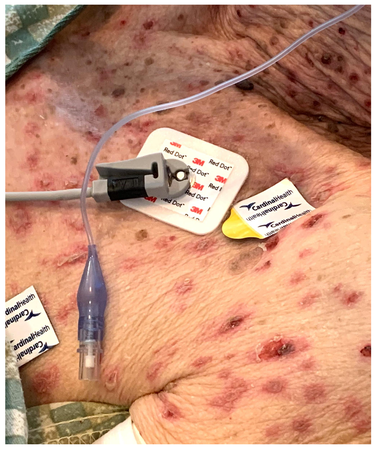

Figure 1: *Diffuse crusted vesicular rash throughout arms, legs, chest, neck and face of patient, present on initial presentation*

Figure 2: *Chest X-ray performed on admission demonstrating diffuse bilateral alveolar and interstitial opacities, consistent with extensive viral pneumonia vs. pulmonary edema*

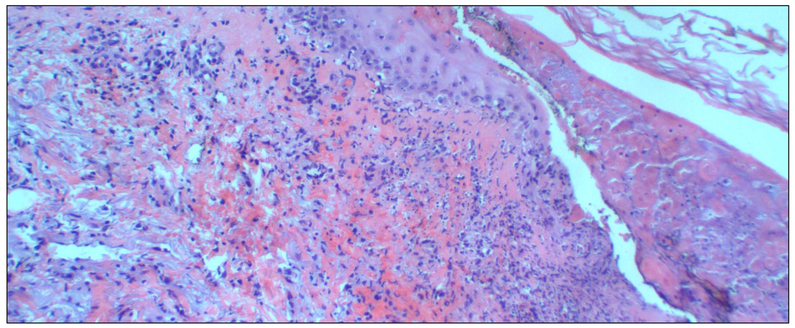

Figure 3: *H&E staining of skin punch biopsy reveals vesicular forming dermatitis with necrosis.*

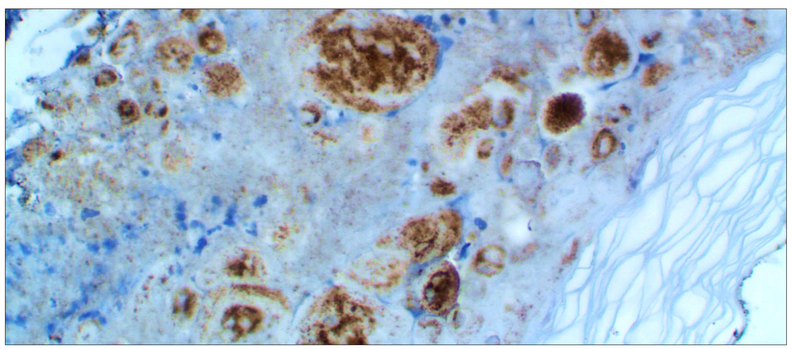

Figure 4: *Punch biopsy from leg rash enhanced with Anti-VZV IHC staining to reveal areas of focal reactivity.*

Case Presentation and Clinical Course

- 82 F with PMH of rheumatoid arthritis (on chronic MTX) who presented with hypoxic respiratory failure and disseminated vesicular rash
- Patient was seen in ED two days prior, had left AMA without starting antiviral therapy
- Patient had no prior VZV or vaccination, exposed to husband with active shingles
- She immediately required intubation for hypoxic respiratory failure, taken to ICU
  - **Vitals**: T 99.7F, HR 89 bpm, BP 142/89, RR 22, O_2 88% (on BIPAP, 70L 100% FiO_2)
  - **Exam**: diffuse crusted vesicular rash (Figure 1) with harsh lung sounds throughout
  - **CXR**: diffuse bilateral alveolar and interstitial opacities (Figure 2)
  - **Labs**: WBC 7.1, HGB 12.0, PLT 172, normal CMP, CRP 24.1 (elevated)
- Started on IV acyclovir given high suspicion for DV alongside ceftriaxone and azithromycin for empiric CAP coverage, with negative influenza & COVID PCR
- Respiratory status initially improved allowing extubation, but was reintubated on day 3 due to worsening hypoxic respiratory failure
- Bronchoscopy performed at the time of reintubation noted for large mucus plugs and severely inflamed bronchial mucosa with vesicular appearance
- Skin biopsies revealed vesicular dermatitis with necrosis (Figure 3), with positive IHC showing areas of focal anti-VZV reactivity (Figure 4)
- Patient was extubated again, but after several days on NIPPV/HFNC family decided to transition to comfort focused care, after which she rapidly declined
- Bronchial washings resulted post-mortem, with growth of mycobacterium avium complex (MAC), and insufficient sample to perform cultures for VZV

Discussion

- DV is not diagnostically challenging, with the greatest hurdle being prompt and aggressive initiation of parenteral antiviral therapy +/- VZV immune globulin
- Outcome was negatively impacted by patient leaving AMA at initial presentation, delaying initiation of antiviral therapy
- Potentially complicated by undiagnosed MAC pneumonia, likely unmasked by DV co-infection
- Case may have been prevented entirely if patient (and husband) were adequately vaccinated for primary VZV and/or shingles
- COVID has led to increased vaccine-hesitancy, leading to reduction in compliance for other routine vaccines such as shingles and VZV [12]

Conclusions

- Efforts should focus on vaccination to prevent primary VZV, shingles and DV
- Immunocompromised patients should be screened regularly for vaccine status and counselled regarding vaccination for preventable illnesses
- Efforts to improve public access to reliable information regarding vaccines, including risks and benefits, side effects, and complications (if unvaccinated)

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