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Case Report

Herpes Zoster Virus Fulminant Hepatitis in an Immunocompetent Patient

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Abstract

Background: Herpes Zoster (HZ), resulting from varicella-zoster virus (VZV) reactivation, typically affects elderly or immunocompromised individuals. Rarely, HZ can cause severe complications like fulminant hepatitis, even in immunocompetent patients. This case highlights the need for awareness of atypical VZV presentations, particularly acute liver failure.

Case Presentation: A 57-year-old immunocompetent male presented with malaise, abdominal pain, gingivorrhagia, and purpuric skin lesions. Initial diagnostics included significant liver enzyme elevation (AST: 4303 U/L, ALT: 2503 U/L, LDH: 19,121 U/L) and thrombocytopenia. Imaging revealed hepatic steatosis, and serologic testing excluded common hepatitis etiologies. Rapid deterioration led to ICU admission and death within hours despite aggressive management. Postmortem liver biopsy confirmed viral hepatitis, suggesting VZV as the likely causative agent.

Discussion: Fulminant hepatic failure from VZV is rare in immunocompetent hosts. The absence of classic HZ rash in initial stages complicates diagnosis, emphasizing the importance of histopathology and clinical suspicion. Prompt antiviral therapy with acyclovir is crucial for favorable outcomes in suspected cases.

Conclusion: This case underscores the importance of considering VZV in acute liver failure cases regardless of immune status. It highlights the critical need for early recognition and treatment to mitigate poor outcomes. Further research is essential to understand VZV's pathogenesis in severe hepatic manifestations.

Keywords: *Fulminant Hepatitis; Varicella-Zoster Virus; Herpes Zoster; Immunocompetent; Liver Failure; Case Report*

Introduction

General background

Herpes Zoster (HZ), commonly known as shingles, results from the reactivation of the varicella-zoster virus (VZV). It typically manifests with a painful vesicular rash in elderly or immunocompromised individuals, though cases in healthy adults can occur [1,5]. Globally, the incidence of HZ has risen from 1990 to 2017, with an estimated 414.5 cases per 100,000 person-years, partially due a population aging and

increasing risk factors [6]. While HZ usually affects a single dermatome, it can lead to severe multi-organ involvement in rare instances, particularly in cases of viral dissemination.

Rare complications of herpes zoster

Fulminant hepatitis is a rare but life-threatening complication of HZ, characterized by massive hepatic necrosis and liver failure. The underlying pathophysiology involves viral reactivation, which triggers widespread hepatic inflammation and hepatocellular damage. Early recognition is key to improving prognosis; however, the rarity of this condition makes timely diagnosis challenging [3,5].

Significance of the case

This case report discusses a 57-year-old male without prior chronic illnesses who developed fulminant hepatitis due to HZ reactivation. This case highlights the need to consider HZ as an etiological agent in cases of acute liver failure, even in immunocompetent individuals. The clinical presentation, diagnostic process, and management strategies are analyzed, contributing to the limited literature on this rare clinical entity [1,4].

Differential diagnosis

The differential diagnosis for fulminant hepatitis includes a wide range of causes such as ischemic hepatitis, drug-induced liver injury, viral hepatitis (including HSV and VZV), and other less common etiologies. In HZ-induced hepatitis, the differential should also include herpetic encephalitis and hepatovirulent HSV strains [1,3,4].

Diagnostic challenges

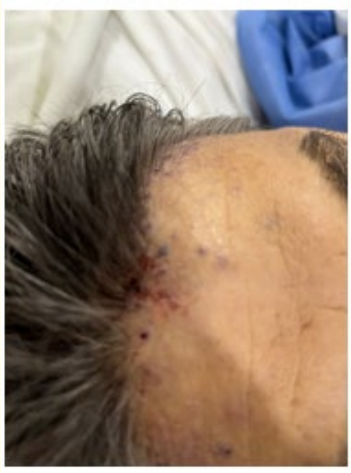
Diagnosing HZ-induced hepatitis is difficult, as its clinical presentation overlaps with other forms of acute hepatitis. Many cases do not present with the characteristic rash, complicating diagnosis. Furthermore, associated findings such as thrombocytopenia, leukopenia, and coagulopathy can mimic other viral infections. Laboratory abnormalities like elevated liver enzymes, combined with a detailed history, are critical for guiding the diagnostic process [3,5].

Pathophysiology of herpes zoster

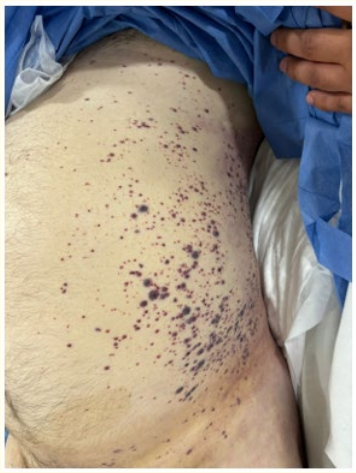
The varicella-zoster virus has two replication phases: lytic and latent. Following primary infection, the virus remains dormant in neurons, potentially reactivating years later to cause herpes zoster. Reactivation is typically triggered by immune suppression, although the mechanisms are not fully understood. In rare instances, systemic dissemination can lead to severe complications such as hepatitis [2,5].

Case Report

A 57 years old male presented to the Emergency department with 3 days history of malaise, abdominal pain and gingivorrhagia. 24 hrs prior admission was evaluated at another hospital reporting abdominal ultrasound with only hepatic steatosis Grade II, bloodwork relevance results Platelets 94, ALT, LDH and GGT slightly elevated (465, 138 and 1349 U/L) and Dengue test negative, he was discharged with symptomatic treatment. The day of admission purpuric lesions in abdomen, lower back, groins and head appeared with conjunctival hemorrhage of the left eye. Medical background with no allergies or chronic diseases, he was a farmer, consumption of tobacco and alcohol was denied, and had 3 children with active infection of Chickenpox. Physical exam with maculoerythematous and purpuric lesions on scalp, abdomen, lower back and groins (Picture 1 and 2); gingivorrhagia and conjunctival hemorrhage of the right eye. Blood results are presented in table 1.



Picture 1: *Maculo-papular lesions on scalp.*



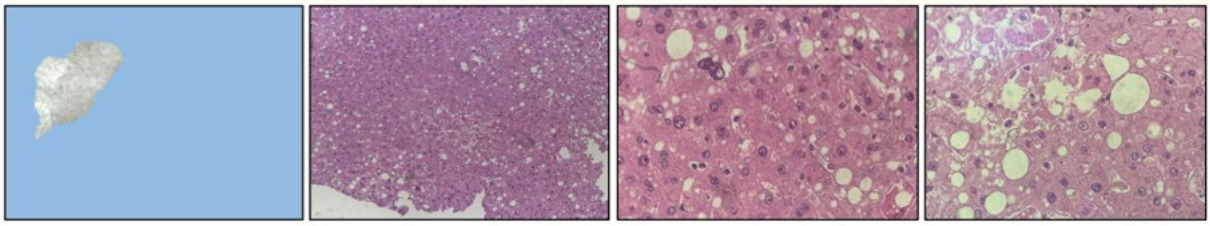
Picture 2: *Purpuric lesion on abdomen.*

	Result	Unit	Normal Range
White cells	8.1	x10*3mm^3	4-10
Neutrophils	73	%	37-73
Lymphocytes	23	%	20-40
Monocytes	3	%	3-9
Eosinophils	1	%	0.5-3
Basophils	0	%	0-2
PT	34.7	secs	10-15
Red cells	5.41	x10*3mm^3	3.5-5.5.

Hb.	16.4	g/dL	11-16
Hto.	48.3	%	30-46
MCV	89.2	fL	82-95
MCH	30.3	pg	27-31
RDW	16.4	%	11.5-14.50
Platelets	53	x10*3mm^3	150-400
PTT	49.4	secs	10-15
Glucose	177	mg/dL	75-99
Urea	40.0	mg/dL	10-50
Creatinine	1.0	mg/dL	0.6-1.4
Uric acid	10.2	mg/dL	2.6-7.2
Cholesterol	379	mg/dL	0-200
Triglycerides	408	mg/dL	35-135
LDL-c	332.8	mg/dL	0-150
TB	0.7	mg/dL	0.2-1.5
AST	4,303	UI/L	0-37
ALT	2,503	UI/L	0-42
LDH	19,121	UI/L	225-450
Amylase	98	UI/L	10-220
GGT	925	UI/L	9-39
Albumine	4.1	g/dL	3.5-4.8
Globulines	2	g/dL	2-3
Na	138.1	mEq/L	135-145
K	4.1	mEq/L	3.5-5.3
Cl	103.3	mEq/L	95-110
P	4.5	mg/dL	2.5-5,6
Ca	9.4	mg/dL	8.5-10.5
Mg	2.2	mg/dL	1.9-2.5
Urine sample, Erythrocytes	> 100	Per field	0
B Hepatitis, rapid test	Negative		
C Hepatitis, rapid test	Negative		
HIV, rapid test	Negative		
Abbreviations: PT: Prothrombin Time; Hb: Hemoglobin; Hto: Hematocrit; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; RDW: Red Cell Distribution Wide; PTT: Partial Thromboplastin Time; LDL-c: Low Density Lipoprotein-Cholesterol; TB: Total Bilirubin; AST: Aspartate-Aminotransferase; ALT: Alanine-Aminotransferase; LDH: Lactate Dehydrogenase; GGT: Gamma-Glutamyl Transferase; HIV: Human Immunodeficiency Virus			

Table 1: *ER blood results at admission.*

The patient was admitted to the ICU with the diagnosis of fulminant hepatitis, he requested no invasive mechanical ventilation, high flow nasal cannula with 45 L and 50 - 80% was initiated, treatment with antibiotic and antimycotic therapy (Ceftriaxone, azithromycin, metronidazole and fluconazole), transfusions with fresh frozen plasma, K vitamin and hydrocortisone. During ICU stay he developed a shock state, severe hypoglycemia, VT and VF that required advanced cardiovascular support for 30 minutes with no return to spontaneous circulation, the patient was deceased 10 hours after hospital admission. With the informed consent of the relative post-mortem puncture liver biopsy was performed (Picture 3) with the report of acute ischemic-necrotic liver injury with histological changes consistent with viral hepatitis. The morphological picture observed in the liver tissue suggests ruling out the presence of viruses of the family of Herpes (herpes simplex virus, human herpes virus and varicella-zoster) as well as adenovirus. Other findings: 30% macrovesicular steatosis; without periportal fibrosis or fibrosis.



Picture 3: *Post-mortem puncture liver biopsy.*

Discussion

This case describes a healthy, immunocompetent man who presented with fulminant hepatic failure due to VZV infection. This case demonstrates that severe hepatic complications can occur in both immunocompromised and immunocompetent hosts. It represents a rare form of VZV infection presentation, involving an immunocompetent adult male farmer who developed disseminated cutaneous herpes and fulminant liver failure. This pathology is commonly seen in immunosuppressed patients, with a prevalence of around 40%, whereas cases in immunocompetent patients are rare [7]. The patient had no recent history of travel, illicit drug or alcohol use, or herbal medicine intake.

Varicella infection is most commonly observed in children under 10 years of age, who account for more than 90% of cases. Varicella is a highly contagious disease transmitted via respiratory route and direct contact. The incidence of herpes zoster (HZ) increases with age, with an estimated 2.5 cases per 1,000 in those aged 21 to 50 years, and 10.1 cases per 1,000 in individuals over 80 years [8]. Herpes zoster results from reactivation of latent VZV and occurs most frequently in the elderly and immunocompromised individuals, where it poses a higher risk of visceral dissemination and complications such as pneumonia, hepatitis, or CNS disease [9].

The patient's initial blood tests showed normal counts, renal function, liver function, serum electrolytes, and urine microscopy. Glucose levels were within normal limits, and markers for hepatitis B, hepatitis C, and HIV were negative. Histopathological examination of postmortem liver tissue revealed changes consistent with viral hepatitis. The observed morphological characteristics ruled out other herpesviruses (e.g. herpes simplex virus, human herpesvirus, and varicella-zoster virus) [10]. Liver involvement has been documented in adults with varicella infection, typically as an asymptomatic and self-limited condition [11].

Diagnosis and treatment for visceral varicella are often delayed, and diagnosis is frequently made postmortem. Biopsy-proven visceral hepatic involvement with varicella is uncommon, typically affecting immunosuppressed hosts, and has a high mortality rate when it occurs [12].

A literature search on PUBMED (1990-2023) using the keywords "Varicella" and "liver" yielded few additional cases, mostly in immunocompromised individuals. Only a few cases of fulminant hepatic failure secondary to VZV infection have been reported. In children, several cases of varicella with clinical signs of hepatitis have been associated with Reye's syndrome [13].

The clinical diagnosis of fulminant hepatitis was confirmed postmortem, with varicella identified as the causative agent. Serology can assist in diagnosis, showing positive IgG antibodies in reactivation cases and positive IgM antibodies during primary infection. However, treatment should not be delayed while awaiting these results. Diagnosis can be confirmed through clinical presentation, VZV serology, skin biopsy, and histopathological findings. According to literature, intravenous acyclovir at a dosage of 10 mg/kg every 8 hours is recommended if varicella hepatitis is suspected, with a typical treatment duration of 7 to 10 days [14].

Timely identification is essential for rapid initiation of acyclovir treatment. A multidisciplinary team approach, including experts in hepatology, infectious diseases, critical care, the molecular adsorbent recirculating system (MARS), and transplantation, is vital for management of such cases.

Conclusion

This case underscores the importance of considering varicella-zoster virus (VZV) as a potential etiological agent of fulminant hepatitis, even in immunocompetent patients. Although severe hepatic complications from VZV infection are rare, especially in immunocompetent individuals, the rapid progression observed in this case emphasizes the need for early diagnosis and timely antiviral treatment with agents like acyclovir, which has proven effective in other presentations of disseminated VZV infection. Post-mortem histopathological findings, including acute hepatic necrosis and morphological changes consistent with viral hepatitis, provided evidence of viral invasion as the underlying cause of hepatic failure. This case contributes to the limited literature on visceral VZV manifestations in otherwise healthy adults, supporting the recommendation for a multidisciplinary approach to managing fulminant hepatitis, involving hepatology, infectious disease, and critical care specialists to optimize patient outcomes.

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