

## CASE REPORT

# Cutaneous necrotizing small-vessel vasculitis induced by acute hepatitis E

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## Abstract

Hepatitis E virus is a new emergent virus causing acute self-limiting hepatitis, but may also cause extrahepatic manifestations. Hepatitis E virus should be systematically considered in patients with cutaneous small-vessel vasculitis and cytolytic hepatitis.

## KEYWORDS

cutaneous vasculitis, fibrinoid necrosis, hepatitis E virus, leukocytoclastic vasculitis

## 1 | INTRODUCTION

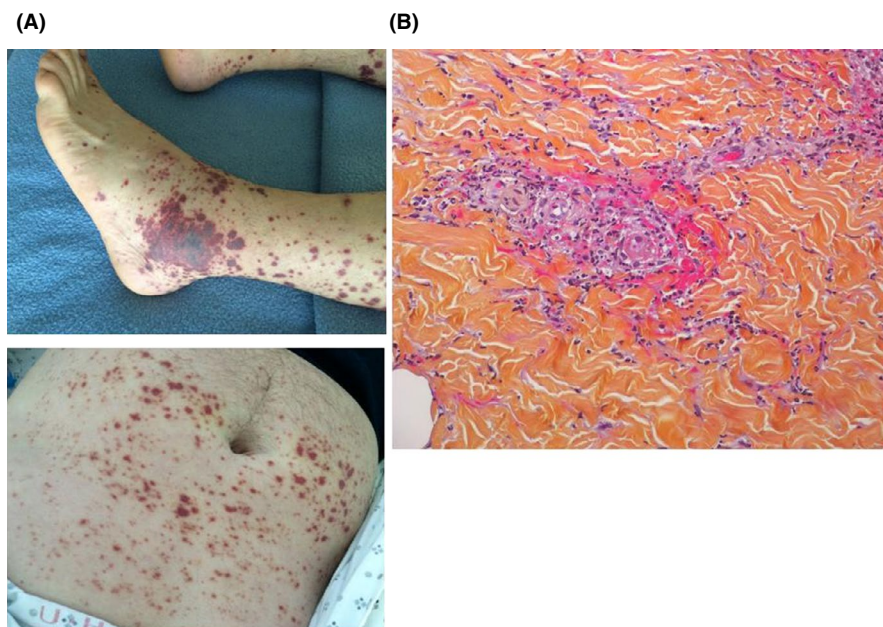
A 54-year-old male was referred to our Department of Internal Medicine for palpable purpura on the lower limbs, associated with a high fever (39°C) that had suddenly appeared 5 days earlier, in a context of arthritis of the knees and ankles. He had no recent travel history or sexual risk behaviors. He had no prior chronic liver disease or illicit drug abuse and was not taking medications.

At consultation, his temperature was 38.8°C, blood pressure 120/85 mm Hg and other vital signs were normal. Physical examination revealed bilateral extensive palpable purpura (Figure 1A) on the lower extremities and abdomen, and marked swelling of the knees filling the suprapatellar pouch. He was oriented, without any signs of meningitis, encephalopathy, or endocarditis. Routine laboratory tests showed elevated C-reactive protein (109 U/L; normal <5 U/L) and predominant hepatic cytolysis (aspartate aminotransferase 457 U/L, normal 7–40 U/L; alanine aminotransferase 680 U/L, normal 5–50 U/L), with

moderate cholestasis (alkaline phosphatase 123 IU/L, normal 40–130 U/L;  $\gamma$ -glutamyl transpeptidase 248 U/L, normal 5–38 U/L). Blood counts and renal function were normal, and the patient had no proteinuria and/or microhematuria.

First, we excluded thrombopenic and infectious purpura. Echocardiography showed no signs of infectious endocarditis. The chest radiograph was normal and hepatic ultrasonography showed normal gallbladder, absence of biliary duct obstruction, and normal hepatopetal blood flow. Blood and urine cultures grew no microorganisms; blood alcohol and acetaminophen levels were negative. Serological tests for hepatitis A, B, and C viruses, HIV-1 and -2, rickettsiae, *Coxiella Burnetii*, and *Toxoplasma gondii* were negative, but anti-cytomegalovirus and Epstein-Barr virus immunoglobulins (Ig) (IgG but no IgM) were found.

Then, we thought anti-neutrophil cytoplasm antibody (ANCA)-associated vasculitis might be possible but serum ANCA were not detected, including with enzyme-linked immunosorbent assay (ELISA). Serum antinuclear antibodies and circulating cryoglobulins were negative, as was screening



**FIGURE 1** Hepatitis E virus-induced HSP: clinical observations and histology. A, Extensive purpura on the lower extremities and the abdomen. B, Histological section of a purpuric lesion on the leg showing evidence of leukocytoclastic vasculitis with fibrinoid necrosis of small blood vessels in the upper dermis. There is accompanying nuclear dust, extravasated erythrocytes, and infiltrated lymphocytes and neutrophils. (Hematoxylin-eosin staining, original magnification  $\times 20$ )

for autoimmune liver disease, and complement levels were within normal ranges. A skin biopsy showed leukocytoclastic vasculitis with fibrinoid necrosis of the vessel wall (Figure 1B). Immunofluorescence labeling and IgA labeling of vessels were negative. Serum IgA levels were normal (2.21 g/L), with no evidence of IgA paraprotein.

Because the association of skin purpura and cytolytic hepatitis was strongly suggestive of a viral etiology, tests for emergent viruses were run. Hepatitis E virus (HEV)-IgM ELISA (WANTAI, Eurobio, Courtaboeuf, France) was reactive, and polymerase chain reaction for HEV RNA was positive. The purpuric rash disappeared spontaneously within 2 weeks. Liver function tests returned to normal within 4 weeks. Two months postdiagnosis, physical examination and laboratory findings were normal.

## 2 | DISCUSSION

Cutaneous small-vessel vasculitis (CSVV) is often idiopathic (45%-55%) but may be caused by autoimmune conditions, hypersensitivity drug reactions, lymphoproliferative disorders or malignancies, and infections (15%-20%).<sup>1,2</sup> Our patient's skin biopsy showed leukocytoclastic vasculitis with fibrinoid necrosis of the vessel wall, but without ANCA, or cryoglobulin or IgA deposits. The patient was not taking any medication, thereby ruling out hypersensitivity vasculitis. Cutaneous polyarteritis nodosa was excluded because necrotizing vasculitis was not observed in the lower dermis and/or subcutaneous fat.

Viruses are well-recognized triggers of CSVV which can occur as a consequence of the inflammation of vessel walls due to direct infection, type II or immune

complex-mediated reaction, or cell-mediated hypersensitivity. Then, it is important to point out all new emergent pathogen that may cause CSVV. Our case is unusual because CSVV, although reported with other hepatotropic viruses, especially during the acute phase of hepatitis A, has not been reported as an isolated association with acute HEV infection.<sup>3</sup> HEV infections occur worldwide but, in developed countries, it is an emerging disease, particularly in southwest France, where the disease is considered to be hyperendemic.<sup>4,5</sup> Usually, HEV causes acute self-limiting hepatitis, which is zoonotic, with pigs as the primary host. However, extrahepatic manifestations have been described, mostly acute pancreatitis, neurological disorders with predominantly peripheral nerve involvement, cytopenia, glomerulonephritis, or mixed cryoglobulinemia.<sup>6</sup> Medical community should be aware of new entities related with this emerging virus.

## 3 | CONCLUSION

Hepatitis E virus is a new emergent virus which should be now systematically considered in patients with CSVV and elevated transaminase levels.

## CONFLICT OF INTEREST

None declared.

## AUTHOR CONTRIBUTION

JFV, CG, EL, and JLP: took care of the patient. BV: analyzed the cutaneous biopsy and performed the histological Figure.

JFV: wrote the manuscript. All authors have read and corrected the manuscript.

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