

# Cerebral venous sinus thrombosis secondary to acute cytomegalovirus infection

Andrew J Martin 

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## ABSTRACT

**Background** Cerebral venous sinus thrombosis (CVST) is a potentially life-threatening disorder with a number of causes, including viral infections.

**Case presentation** A 25-year-old female patient presented with a non-specific febrile illness, headache and hepatitis. She was found to have right transverse sinus and cortical venous thrombosis in addition to acute systemic Cytomegalovirus (CMV) infection. She responded well to anticoagulation with warfarin for 6 months. CMV infection was treated conservatively.

**Conclusion** CVST is an increasingly prevalent condition often presenting with headache, focal neurological deficits and seizures. Despite extensive investigations, often no specific cause is found. CMV is a ubiquitous virus that can present with a non-specific febrile illness or a variety of organ dysfunction. CMV has been shown to be associated with predominantly venous thrombosis, most commonly lower limb deep venous thrombosis, pulmonary embolism and splanchnic vein thrombosis. The risk is highest in immunocompromised patients, though most patients are immunocompetent. There have been few reports of CVST related to CMV and all of these with a more tenuous link to acute CMV infection. Clinicians should be aware of this link, particularly in those who have CVST in the context of a febrile illness, or immunocompromised patients.

## CASE PRESENTATION

### Clinical presentation

A 25-year-old female patient presented with a 3-day gradual onset of a right-sided headache. There was no medical history. She was taking an oestrogen containing contraceptive pill (OCP) for the past few years. One month prior, she had received a second dose of Pfizer mRNA COVID vaccine. She was found to be febrile, though there were no other infectious symptoms. She had a focal-onset unaware seizure with left arm paraesthesia, followed by a few minutes of unresponsive staring while in the emergency department, for which she was commenced on levetiracetam. A neurological and systemic examination was normal.

## DIAGNOSTIC STUDIES

Imaging showed a small volume right central sulcus subarachnoid haemorrhage. CT, and later MR, venography confirmed both right cortical and right transverse venous sinus thrombosis (figures 1 and 2). A thrombophilia screen was negative, including antiphospholipid antibodies. She was commenced on therapeutic enoxaparin and later transitioned to warfarin.

The patient remained febrile for the first few days of admission. On presentation, white cell count was elevated at 14.5 (3.9–11), with lymphocyte count 8.8 (1–4). A blood film showed reactive lymphocytes only. Flow cytometry showed only a polyclonal T cell population. C-reactive protein was elevated at 35 mg/L. Liver enzymes were persistently elevated in a hepatocellular pattern (alanine transaminase 234 U/L, aspartate aminotransferase 211 U/L, gamma-glutamyl transferase 237 U/L, alkaline phosphatase 158 U/L). Albumin was mildly reduced at 31 g/L.



**Figure 1** Coronal MR venogram demonstrating thrombosis of the right transverse venous sinus.

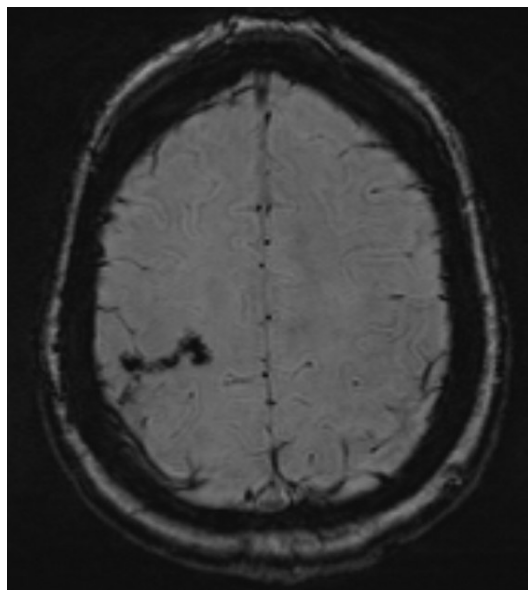


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Neurology Department, Blacktown Hospital, Blacktown, New South Wales, Australia

### Correspondence to

Dr Andrew J Martin;  
amar6353@alumni.sydney.edu.au



**Figure 2** Axial susceptibility-weighted image demonstrating focal areas of sulcal haemosiderin staining within the territory of the vein of Trolard.

Bilirubin levels were normal. Coagulation profile on presentation was normal. CT imaging of the liver was unremarkable; specifically, there was no evidence of portal or hepatic vein thrombosis. Extensive autoimmune serology was negative. Copper, ceruloplasmin and alpha-1 antitrypsin levels were normal. Hepatitis (A, B, C, E), Human Immunodeficiency Virus (HIV), Epstein-Barr Virus (EBV) and Varicella Zoster Virus (VZV) serology was negative. CMV IgM, but not IgG was positive. CMV PCR in blood was positive with a viral load of 5072 copies/mL, consistent with acute CMV infection. A repeat test 2 months later showed no evidence of viraemia. The patient was well, and her liver function tests improved, and so no lumbar puncture or antiviral treatment was undertaken.

### MANAGEMENT AND FOLLOW-UP

She completed 6 months of warfarin therapy without any residual symptoms. Repeat imaging showed near complete recanalisation of the right transverse sinus. The OCP was ceased.

### DISCUSSION

CMV infection is common in the general population and may be asymptomatic, present with a non-specific viral illness, or with various organ dysfunction, including hepatitis. CMV itself has been well linked to thrombosis, predominantly venous, in the past. Any thrombosis was found in 6.4% of acute CMV infections,<sup>1</sup> and in those presenting with acute venous thrombosis acute CMV infection was found to be present in 7.4%.<sup>2</sup> Venous thrombosis is most common, with lower limb deep venous thrombosis (DVT) and pulmonary embolism being most

common, followed by splanchnic and portal vein thrombosis. The risk is higher in immunocompromised individuals, though most patients are immunocompetent.<sup>3</sup> Other predisposing factors to thrombosis, such as the OCP, are present in only 63% of patients, though it is generally thought that CMV acts a precipitant to thrombosis in a susceptible individual, rather than being directly causative.<sup>3</sup> The mechanism of CMV-related thrombosis is not entirely clear, though it is thought to relate to a transient elevation in antiphospholipid antibodies (which this patient did not have), enhanced platelet and leucocyte adhesion to endothelium, and to an increase in activating factor X and FVIII levels.<sup>4</sup> Antiviral treatment is typically only recommended in immunosuppressed patients and is otherwise as per usual cerebral venous sinus thrombosis (CVST) treatment.<sup>3</sup>

There have been three prior reports of CVST related to acute CMV infection.<sup>5</sup> Two of these patients had evidence of encephalitis, however, and one patient had comorbid acute HIV infection.<sup>6</sup> Only one patient was shown to have CMV viraemia, with the other two patients being diagnosed with acute CMV infection based on serology. This is the first case with clear evidence of acute CMV infection, with a febrile infectious illness associated with hepatitis, and positive acute IgM serology and viraemia. The temporal relation between CMV infection and CVST in this patient is also closer than in previous reported cases. The OCP may be considered here a predisposing factor for CVST, though a recent meta-analysis has shown an odds ratio (OR) of 5–7,<sup>7</sup> indicating that there are likely other contributory factors, such as CMV infection. Other herpesviridae infections, particularly VZV and rarely EBV, can also be rarely reported to cause CVST and a more widespread vasculopathy.<sup>8,9</sup> In such cases with CVST and systemic inflammation, a lumbar puncture and viral multiplex PCR may be revealing.

In short, this is a case of CVST related to acute CMV infection. Clinicians should be aware of this link, particularly in cases of CVST associated with fever and hepatitis, or CVST in immunocompromised individuals.

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## ORCID iD

Andrew J Martin <http://orcid.org/0000-0002-9198-7511>

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