Systemic Varicella Zoster Infection Causing Cerebral Venous Thrombosis and Revealing Prothrombotic State

Ayman Mahmoud Alboudi
MD, MSc
Rashid Hospital , Dubai, UAE

- CVT is a rare disorder with incidence rate is around 1/100000[1]
- We are having about 6 cases per year in our hospital (Rashid hospital in dubai)

1. Ferro JM, Correia M, Pontes C, et al. Cerebral vein and dural sinus thrombosis in Portugal: 1980-1998. Cerebrovasc Dis 2001; 11:177.

- Heller et al found in his study on CVST in children that the majority of cases are multifactorial, as a combination of prothrombotic risk factors and/or underlying condition such as infection.[1]
- Even more, CVST can be precipitated by systemic infection.[2]

1. Heller C, Heinecke A, Junker R, Knofler R, Kosch A, Kurnik K,et.al. The Childhood Stroke Study Group. Cerebral venous thrombosis in children: a multifactorial origin. Circulation. 2003 ;108 :1362-67.
2. Sebire G, Tabarki B, Saunders D. E., Leroy I, Liesner R, Saint-Martin C, et.al. Cerebral venous sinus thrombosis in children: risk factors, presentation, diagnosis and outcome. Brain. 2005; 128 : 477-89

- Of the etiologic factors:
  - Prothrombotic conditions, either genetic or acquired
  - Oral contraceptives
  - Pregnancy and the puerperium
  - Malignancy
  - Infection
  - Head injury and mechanical precipitants

- previously it was thought that infections contributing in high percentage in the etiology, but nowadays it is recognized that they form 6-12 % only [1]
- The pathophysiology of CVT still not will known , even there was some theories [2]

1. Ferro JM, Canhão P, Stam J, et al. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke 2004; 35:664.
2. Schaller B, Graf R. Cerebral venous infarction: the pathophysiological concept. Cerebrovasc Dis 2004; 18:179.

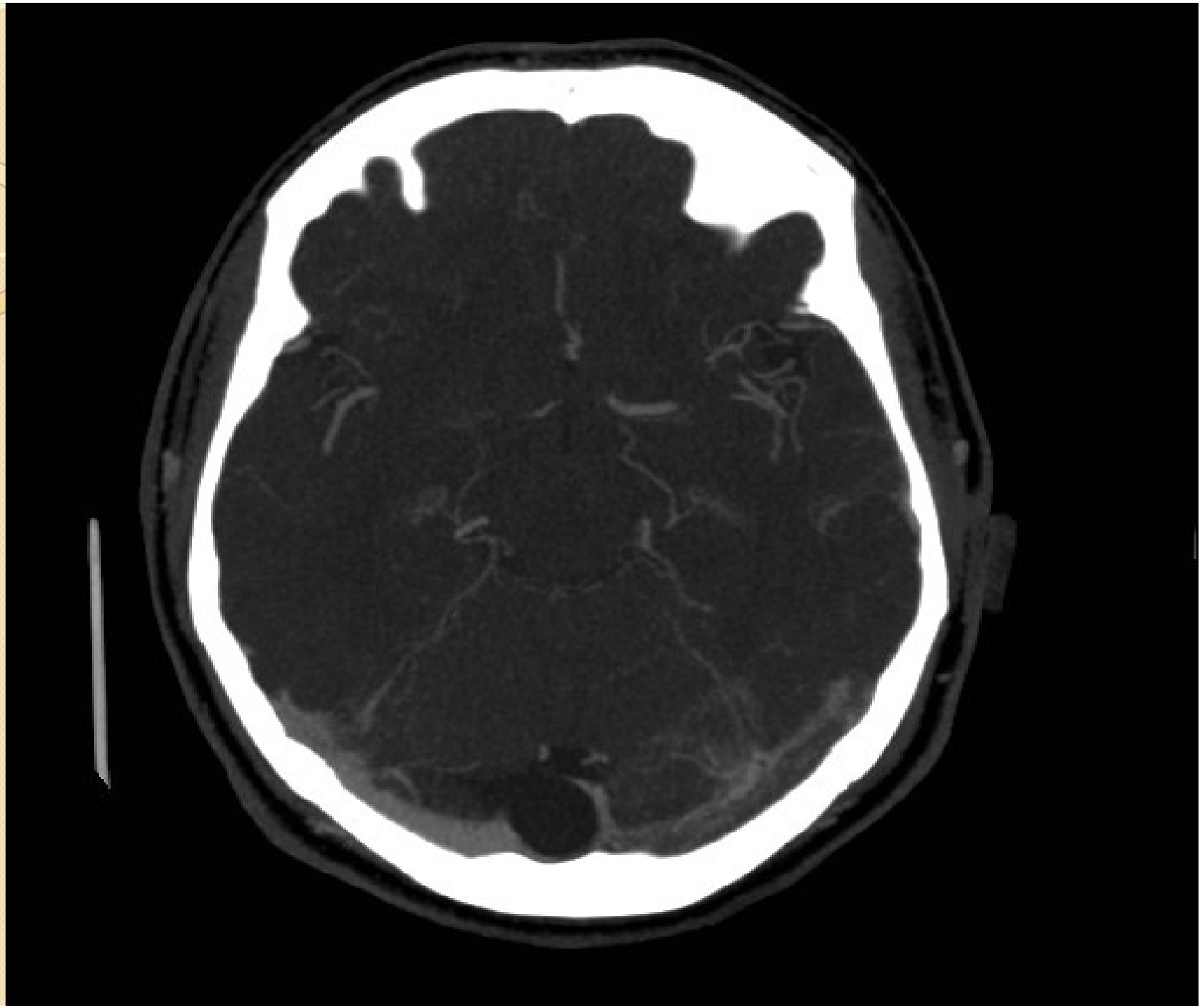
- Now speaking about our case:
  - This patient is 31y old male, previously healthy with no past medical history;
  - presented with a history of skin rash started 14d ago, accompanied with low grade fever at the first few days, with progression consistent with VZV.
  - 5d ago he started to have headache, holocephalic, accompanied with nausea and vomiting.
  - On the day of admission he had 2 GTCS.

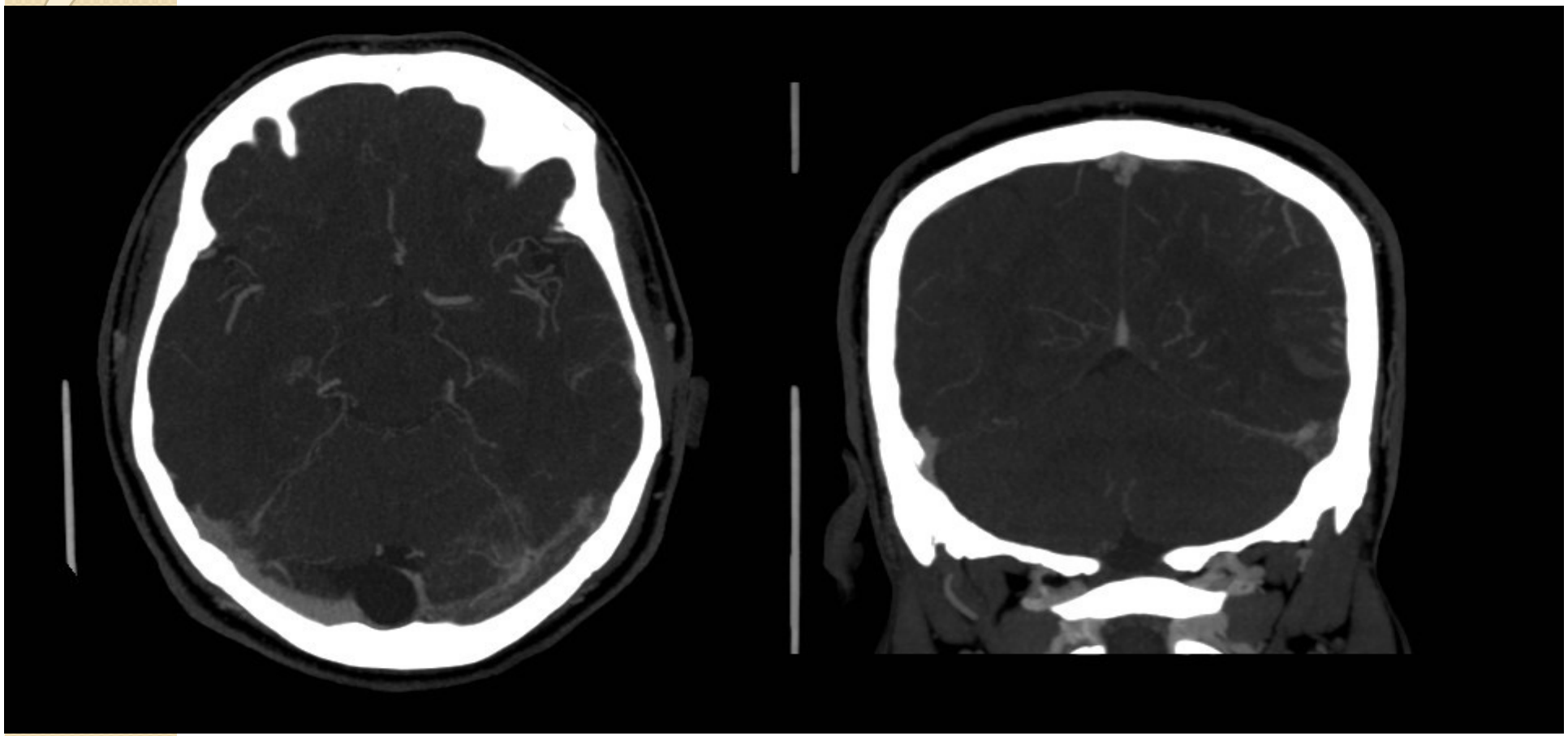
- The neurological exam was totally normal apart from mild bilateral pupil edema.
- General examination showed skin rash in crusting stage. There was no fever or meningeal signs.

- CT brain was done and showed small haemorrhagic infarction on the left occipital area (fig 1),



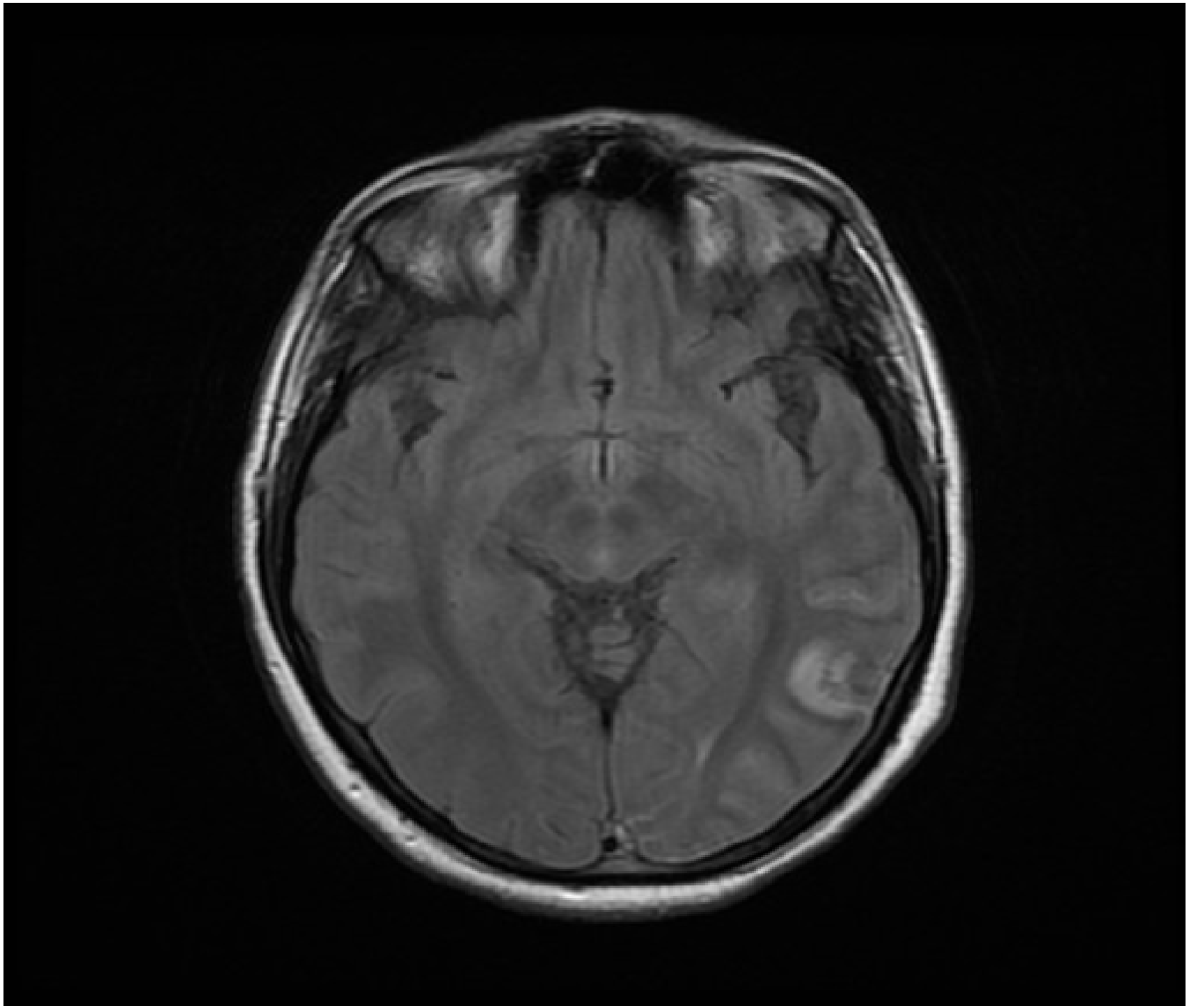
- CT venogram showed CVST on the left transverse, lateral sinuses and superior sinus (fig 2).





- And because there is systemic viral infection, encephalitis was a concern
- Unfortunately the patient refused LP
- MRI was done

- MRI showed no signs of encephalitis, there was only signs of the infarction already seen on CT



- On blood tests the patient was found to have:
  - positive IgG, IgM Ab for VZV, also
  - positive :
    - Antinuclear sntibodies
    - phosphatidyl serin
    - Anticardiolipin antibodies
    - B2 microglobulin.
  - Other investigations as Anti dsDNA, HCV ab, HBV ag, ANCA p,c all were negative. Normal urine test.

- Thrombotic profile of :

  Prothrombine ,

  Protein C deficiency

  Protein S deficiency

  Antithrombin deficiency

  Factor V Leiden mutation

  G20210A prothrombin gene mutation

  All were negative

- The patient was treated as CVT and anticoagulation started
- Negative MRI in VZV encephalitis was described [1]
- That is why antiviral treatment was started with acyclovir

1. De Broucker T et al, Clin Microbiol Infect. 2012 Aug;18(8):808-19. doi: 10.1111/j.1469-0691.2011.03705.x. Epub 2011 Nov 15.

- VZV is a commonly seen infection as febrile illness with a vesicular rash, especially in pediatric population.
- However, the neurological complications in adults specifically, are not commonly encountered, but include arterial vasculopathy, which can cause ischemic strokes, aneurysms, subarachnoid or cerebral hemorrhages, and carotid dissection[1-3].

1. Gilden D, Cohrs RJ, Mahalingam R, et al. **Varicella zoster virus vasculopathies: Diverse clinical manifestations, laboratory features, pathogenesis, and treatment.** *Lancet Neurol*. 2009;8:731–740
2. Takeoka M, Takahashi T. **Infectious and inflammatory disorders of the circulatory system and stroke in childhood.** *Curr Opin Neurol*. 2002;15:159–164
3. Massano J, Ferreira D, Toledo T, et al. **Stroke and multiple peripheral thrombotic events in an adult with varicella.** *Eur J Neurol*. 2008;15:e90–e91.

- Our patient was like Saddiqi et al patients [1], without any signs of purpura fulminans, but he was unique in the fact that he has positive antinuclear, phosphatidyl serin, anticardiolipin antibodies, B2 microglobulin, and VZV IgG, IgM (which were negative in Saddiqi patients).

1. Siddiqi SA, Nishat S, Kanwar D, Ali F, Azeemuddin M, Wasay M. Cerebral venous sinus thrombosis:association with primary varicella zoster virus infection. J Stroke Cerebrovasc Dis 2012;21:917.

- Those lab tests were repeated after 3 months when the patient was seen in the clinic , and they came positive again
- The anticoagulation was recommended for the patient for life

Take home messages

- Encephalitis is a major concern in infectious diseases, but CVT is very important treatable complication to think about it
- Thrombotic profile should be evaluated in all CVT patients, as this can change the patient's management
- Multifactorial etiology is a possibility in CVT, and should not be ignored

Thank You