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**Case Report**

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# Cerebral venous sinus thrombosis in JAK2 V617F positive polycythaemia vera presenting as a haemorrhagic stroke.

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**Abstract**

**Background:** Cerebral venous sinus thrombosis (CVST) has been reported to present with intracranial haemorrhage (ICH) due to its varying effects on cerebral circulation. Polycythaemia rubra vera (PRV) is one of the rare causes of CVST.
**Case Report:** We present a 53-year-old gentleman with vascular dementia who presented with right upper and lower limb weakness. His NCCT brain revealed an ICH involving the left internal capsule. His FBC revealed polycythaemia. A cerebral CT venogram revealed thrombosis of cerebral venous sinuses. JAK-2 V617F mutation was detected confirming primary polycythaemia which was treated with antithrombotic and cytoreductive therapy.
**Discussion:** This is a rare case of PRV presenting with CVST as the initial presentation. It is important to recognize the underlying cause which requires specific management to prevent future recurrences.

*Keywords: cerebral venous sinus thrombosis, polycythaemia rubra vera, JAK-2 V617F mutation*

## INTRODUCTION

Dural venous sinuses in the skull carry the venous drainage from the brain to the internal jugular veins bilaterally. Therefore, thrombosis of these venous sinuses results in various neurological manifestations, some resulting from rare instances where there is a haemorrhagic stroke. This entity, which is termed cerebral venous sinus thrombosis (CVST) is a rare but important cause of mortality and morbidity. Many risk factors play a role in causing thrombosis of these dural venous sinuses. However, among these identified risk factors polycythaemia rubra vera (PRV) is a very rare cause. We came across a patient with JAK2 V617F mutation positive polycythaemic patient who presented with a haemorrhagic stroke as a result of CVST.

## CASE REPORT

A 53-year-old gentleman presented with sudden onset right upper and lower limb weakness which had lasted for one day. He carried a diagnosis of "vascular dementia" previously and had discontinued his medications. He was confused with a reduced level of consciousness. His weakness mounted to an NIHSS score of 10 with the disability resulting in an mRS score of 5. On





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examination he had reduced power of his right upper and lower limbs with a GCS of 12/15. He had dysphagia with no other cranial nerve palsies. He had neither cardiac murmurs nor an irregularly irregular pulse. There were no bruits heard over the carotids. He was not clinically plethoric. His blood pressure was 140/90 mmHg.

An NCCT brain revealed an intracranial haemorrhage involving the left capsular region with intraventricular extension. His haemoglobin level was 18 g/dl with a haematocrit of 60%. True polycythaemia was confirmed by repeating the full blood count following hydration. CT venography of cerebral vessels was arranged due to the presence of significant polycythaemia in a patient with a cerebral haemorrhage as CVST was highly possible. The CT venogram which is shown in figure 1, showed thrombosis of the left transverse, bilateral sagittal sinuses and the confluence of sinuses.

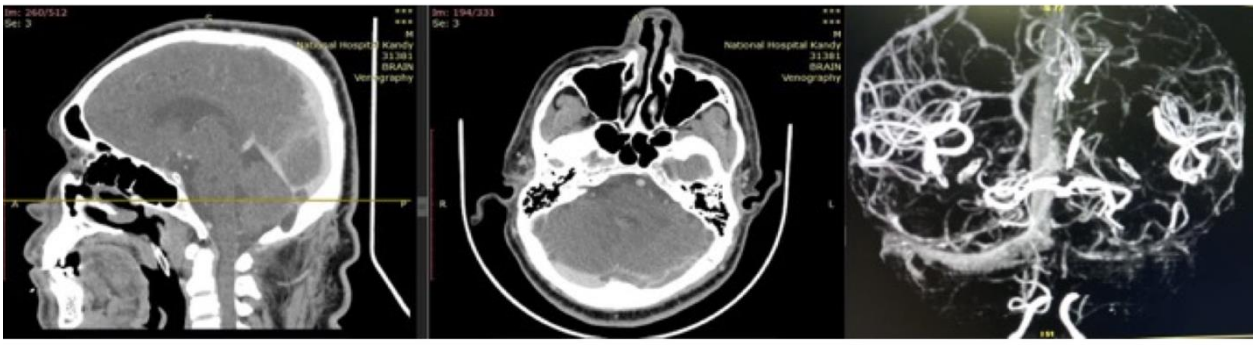

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**Figure 1: CT venogram of the brain revealing thrombosis of the left transverse sinus and the confluence of sinuses**

Further investigations were arranged to evaluate the cause of polycythaemia. An arterial blood gas did not reveal hypoxia. His renal and liver profiles were within normal limits. His basic imaging which included a chest radiograph and an ultrasound scan of the abdomen were normal. A blood picture confirmed polycythaemia with absence of atypical cells or an increase in other cell lineages. A bone marrow aspiration was performed and the appearance was more in favour of primary polycythaemia. JAK-2 V617F mutation was detected in blood confirming the diagnosis of polycythaemia rubra vera.

Despite having an intracerebral haemorrhage after the opinion of the Neurology and the Haematology teams, he was commenced on anticoagulation (subcutaneous Enoxaparin followed by Warfarin) as the thrombotic risk was considered higher. A nasogastric tube was in situ initially to prevent aspiration. However before discharge a swallowing assessment revealed improvement of dysphagia and the nasogastric tube was removed. Physiotherapy was initiated and there was a marked improvement with regard to the disability (mRS score of 2). Multiple phlebotomies were done for the polycythaemia with a target haematocrit of equal or less than 45. Hydroxyurea was started with allopurinol and he was referred to be seen at the routine clinic.

## DISCUSSION

Cerebral venous sinus thrombosis (CVST) is a rare occurrence and is due to thrombosis of the dural venous sinuses which carries the venous drainage of the brain. Its annual incidence is estimated to be three to four cases per million. CVST, even though rare, can result in various disabling neurological manifestations. These manifestations can range from headache, focal neurological deficits, transient visual disturbances, focal as well as generalized seizures to altered level of consciousness and memory impairment. CVST results in mechanical effects on the circulation of the cerebral vessels. Therefore, cerebral oedema, venous infarcts and intracerebral haemorrhage occur as a result of CVST (Neurology). Intracerebral bleeds are due to the increased venous and capillary pressure. [1]

Many risk factors have been identified in the development of CVST. Prothrombotic states, both inherited and acquired, can lead to thrombosis of the venous sinuses. Among females the use of oral contraceptive pills, pregnancy and post-partum state increase the risk of CVST. Protein C, S deficiency, antithrombin deficiency, factor V Leiden, hyperhomocysteinaemia are the identified inherited thrombophilic conditions which result in CVST. In the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) it was discovered that 34% of cases with CVST was the result of a thrombophilic condition. Only 2.8% accounted for polycythaemia as a cause of CVST. [2]

Polycythaemic patients have an increased risk of thrombosis due to hyperviscosity. The incidence of venous thromboembolism in myeloproliferative neoplasms is reported to be 1.7% per patient/year. Out of these, 55.6% were found to be involving uncommon sites such as cerebral and splanchnic veins. [3] British Society for Haematology and the European Collaboration on Low-Dose Aspirin in Polycythemia Vera (ECLAP) study has identified age (65 years or more) and prior thrombosis, as the main clinical risk factors for thrombosis in PRV. [4,5] The incidence of thrombosis increases linearly in patients with PRV when the haematocrit (HCT) is more than 45%. Our patient had a HCT of 60% with no past incidents of thrombosis. [6]

The JAK2 V617F mutation is an acquired genetic mutation seen in patients with myeloproliferative neoplasms. 97% of patients with PRV were found to carry this mutation. [7] A high JAK2 V617F allele burden was found to have an association with thrombosis in patients with PRV. [8] According to literature PRV is not a commonly associated condition with CVST. According to a study conducted by Passamonti S et al., only 6.6% of patients with CVST were found to carry the JAK2 V617F mutation. [9]

## CONCLUSION

This case illustrates the importance of having a high index of suspicion to diagnose cerebral venous sinus thrombosis when a patient present with an intracerebral haemorrhage and that PRV with JAK2 positivity, should be sought after as a cause in order to prevent further episodes of thrombosis.

**Author declaration**

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**Author contributions**

NTW under the supervision of PJPP and JS managed the patient referred to, in the case report. NTW drafted the manuscript and JS revised the final version.

**Conflicts of interest**

Not applicable.

**Funding**

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**Consent for participation**

Informed written was obtained from the patient for the publication of case details.

**Availability of data**

Not applicable.

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