

Reversible Parkinsonism caused by deep cerebral venous sinus thrombosis

Hussein A. Algabani, MD, FRCPC, Ahmed A. Aldarmahi, M.Med, PhD, Mohammed W. Al-Rabia, MD, PhD, Wail N. Yar, MD.

ABSTRACT

أن التخثر الجيبي العرقي (الوريدي) الدماغية هو مرض خطير ونادر الحدوث وذو حضور سريري متغير ومتفاوت. على امتداد العقد الماضي تم تشخيص العديد من الحالات وذلك نتيجة لزيادة الإدراك والمعرفة بالإضافة إلى التطور في التقنية التشخيصية الغير اجتياحية. على خلاف الجلطات الشريانية، هذا المرض عادة ما يصيب صغار السن والبالغين مع نسبة عالية في الإناث. نحن هنا نقوم بدراسة وتقرير حالة باركنسون (الشلل الرعاشي) والتي حدثت كنتيجة ثانوية للتخثر الجيبي العرقي الوريدي العميق. هذه الحالة تم شفائها تماما بعد العلاج. أن التعرف على التخثر الجيبي العرقي الوريدي كسبب لباركنسون هو أمر بالغ الأهمية نظرا للنتيجة الإيجابية والتحسن الملحوظ إذا ما تم علاج المريض بشكل ملائم.

Cerebral venous sinus thrombosis (CVST) is an uncommon but serious disorder with highly variable clinical presentation. Over the past decade, more cases of CVST have been diagnosed more frequently and at an early stage of the disease process. This is mainly attributed to increased awareness by neurologists and the availability of sensitive non-invasive neuro-imaging techniques. Cerebral venous sinus thrombosis often affects children, adolescents, and young adults with female preponderance. We report a case of Parkinsonism secondary to deep CVST (DCVST), which recovered completely following treatment. Recognition of DCVST as a cause for Parkinsonism is of paramount importance due to its reversibility and favorable outcome when appropriately managed.

Neurosciences 2013; Vol. 18 (4): 378-381

From the College of Medicine (Algabani, Aldarmahi), King Saud bin Abdulaziz University for Health Sciences, and the College of Medicine (Al-Rabia, Yar), King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia.

Received 18th March 2013. Accepted 2nd June 2013.

Address correspondence and reprint request to: Dr. Hussein A. Algabani, Consultant Neurologist and Head of Neurology Section, Associate Dean, College of Medicine, King Saud bin Abdulaziz University for Health Sciences, PO Box 21483, Jeddah 21723, Kingdom of Saudi Arabia. Tel. +966 (2) 6240000 Ext. 21298/22070. Fax. +966 (2) 6240000 Ext. 22765. E-mail: gdrresearches@gmail.com

Cerebral venous sinus thrombosis (CVST) is a serious disorder with a remarkably wide spectrum of symptoms and signs. The deep venous system is affected in approximately 10% of patients with CVST, usually in association with other sinuses and cortical veins.¹ Headache and altered sensorium are the most common clinical presentations in deep CVST (DCVST). Deep CVST presenting as a movement disorder is extremely rare. In the current study, we describe a patient with DCVST who developed acute severe Parkinsonism and disturbed consciousness in association with MRI changes. The clinico-radiologic changes reversed completely on resolution of the venous thrombosis. The objectives in presenting this particular case are to report a rare cause of reversible Parkinsonism and to share with the readers interesting radiology and anatomy figures.

Case Report. A 45-year-old woman presented to a district hospital with a one-day history of progressive headache, nausea, and vomiting. Four days later she was referred to King Abdulaziz Medical City, Jeddah, Kingdom of Saudi Arabia because of tremor and poverty of movement. There was no history of fever, ear infection, intake of oral contraceptive pills, genital or oral ulcers, or recurrent deep venous thrombosis. She suffers from type II diabetes mellitus, hypothyroidism, and irritable bowel syndrome. She was on gliclazide and thyroxin. Systemic examinations, including vital signs, were normal. On neurological examination, she was conscious and oriented. She had a masked face with poverty of motion, bilateral rest tremors, rigidity, and bradykinesia. Her gait was slow and shuffling. One day later, her level of consciousness deteriorated and she developed bilateral papilledema, left central facial palsy, left side weakness, and bilateral Babinski signs.

Disclosure. The authors declare no conflicting interests, support or funding from any drug company.

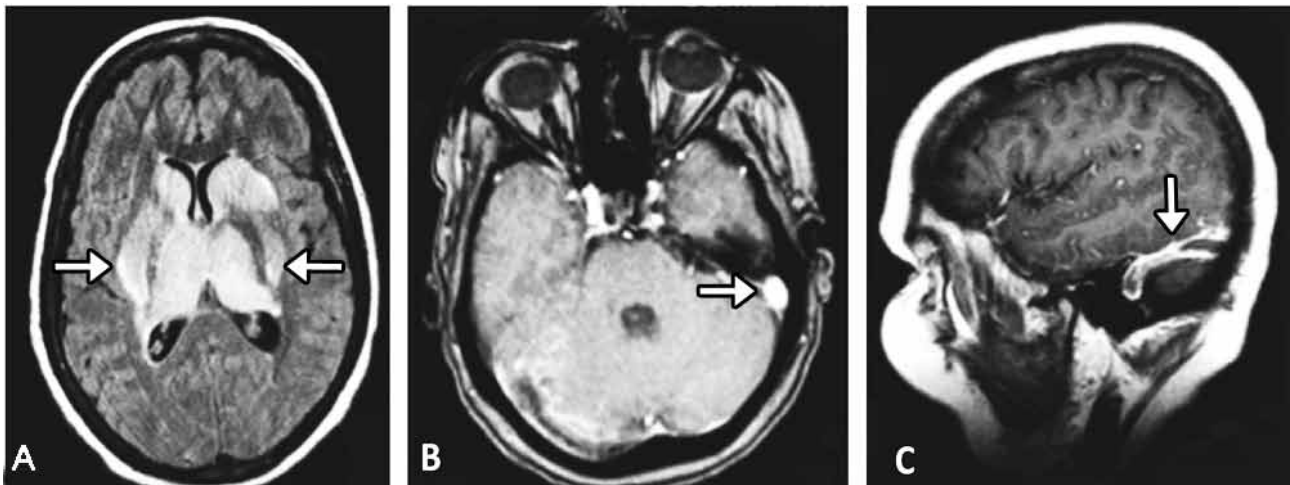


Figure 1 - Patient MRI showing A) Flair (T2-WI) image demonstrating bilateral increased signal intensity in the basal ganglia, thalami, and heads of caudate nuclei (arrows). B) Post Gadolinium T1-WI gradient echo showing filling defects in right lateral sinus (arrow). C) Post gadolinium T1 spin echo sagittal plane midline cut demonstrating extension of filling defect to the torcular herophili (arrow).

Investigations revealed normal complete blood count, erythrocyte sedimentation rate, and biochemistry. Screening for hypercoagulable disorders revealed an elevated anticardiolipin antibody titre (IgG 86.6 GPL, IgM 5.1 GPL, IgA 3.3 GPL).

A brain CT showed hypodense regions in the basal ganglia and thalami bilaterally with loss of gray-white matter differentiation and hyperdense right transverse sinus. An MRI and venography showed low signal intensity lesions in the basal ganglia on axial T1-weighted images, which were of high signal intensity on FLAIR images (Figure 1A). The gradient echo MRI (GRE) with contrast showed a filling defect reflecting dural sinus thrombosis in the right internal jugular vein, transverse and sigmoid sinuses (Figure 1B), extending to the torcular herophili in the midline sagittal plane (Figure 1C). She was managed with heparin and high pulse intravenous steroids. She gradually improved, and 3 days later could talk. Within 2 weeks, she had a complete resolution of her Parkinsonism. She was discharged on citalopram, carbamazepine, and coumadin with an international normalization ratio of 2.5. Follow-up MRI and MR venography 2 months later showed complete resolution of the changes seen in the basal ganglia and thalami bilateral with improvement in the obstruction noticed in the large veins. She remained normal at follow-up 2 years later.

Discussion. Although CVST is considered a relatively rare cause of stroke, it can be more challenging to diagnose.¹ In a multicenter Canadian registry of infants and children aged less than 18 years, the

incidence of CVST was 0.67/100,000 per year.² Due to the widespread use of sophisticated neuroimaging modalities and rising clinical awareness, the incidence of CVST is expected to increase. A significant female predominance has been noticed in young adults with CVST (70-80%), but not among children and elderly persons.¹⁻³ There is a definite increase in the incidence of CVST during pregnancy and the postpartum period. In a hospital discharge registry in the United States, the incidence of CVST affecting pregnant women was 11.6/100,000 deliveries.⁴ Because of its diverse causes and clinical presentations, CVST may be encountered by

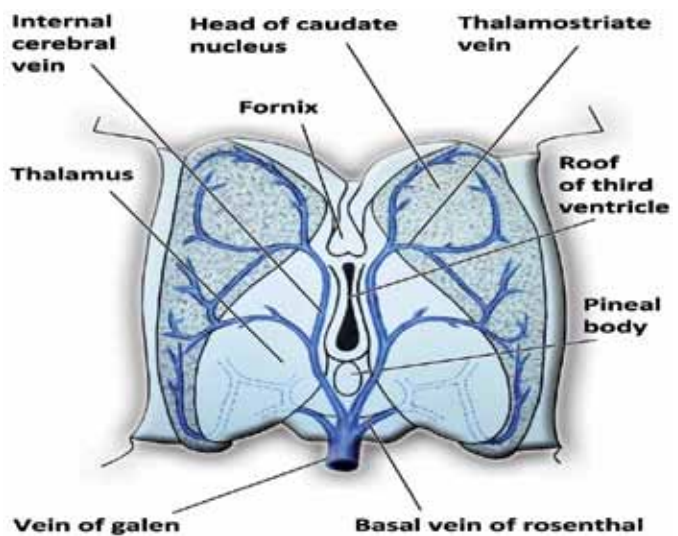


Figure 2 - Superior view of deep cerebral veins.

several specialties including neurologists, neurosurgeons, internists, oncologists, hematologists, obstetricians, pediatricians, and family practitioners. In around 85% of patients, a prothrombotic risk factor or a direct cause can be identified.¹ Inherited hypercoagulable disorders include antithrombin III deficiency, protein C and protein S deficiency, factor V Leiden mutation, prothrombin mutation (the substitution of A for G at position 20210), and homocystinemia (caused by gene mutations in methylene tetrahydrofolate reductase). Acquired prothrombotic states include nephrotic syndrome, antiphospholipid antibody syndrome, pregnancy, and puerperium.⁵⁻⁷ Other causes include oral contraceptives, malignancy, infection, head injury, and mechanical precipitants.

The deep cerebral veins drain the deepest parts of the white matter, the basal ganglia, and the diencephalon (Figure 2). The septal veins receive blood from the genu of the corpus callosum, the septum pellucidum, and the anterior part of the caudate nucleus. They drain into the thalamostriate veins, which also receive blood from the basal ganglia and the internal and external capsules. Then, they pass through the roof of the third ventricle, cross in the interventricular foramen of Monro, and end into the internal cerebral veins. The internal cerebral veins run parallel beneath the choroidal vein of the third ventricle to join their counterpart and form the vein of Galen. The vein of Galen runs from the posterior part of the diencephalon up to the straight sinus, between the cerebellum and the splenium of the corpus callosum. Early in its course, it receives the paired basal veins of Rosenthal, which drain the bottom parts of the basal ganglia, temporal, frontal and occipital lobes. It also drains the insula and medial part of the temporal lobe.

The clinical presentation of CVST can be non-specific and highly variable, and the onset can be acute, subacute, or chronic. Headache, focal neurologic deficits, partial or generalized seizures, and encephalopathy with altered mental status, stupor or coma are the most common clinical presenting features.^{5,6} Although DCVST usually present with bilateral venous infarction of thalami and sometimes basal ganglia, unilateral involvement can also be seen. When the deep cerebral venous system (namely, the straight sinus and its branches) is occluded, the signs and symptoms are generally severe and bilateral. The radiological diagnosis of deep cerebral venous thrombosis may be difficult due to the lack of a characteristic radiological appearance including the delta sign of the superior sagittal sinus thrombosis on contrast enhanced CT scan. Cerebral angiography may still be necessary when the diagnosis is not clear.

Parkinsonism is a syndrome characterized by rigidity, tremor, bradykinesia, and postural instability. Idiopathic Parkinson's disease is the usual cause, being responsible for approximately 80% of cases. Reversible structural causes of Parkinsonism including DCVST are extremely rare.⁸ In 2 retrospective studies, 37 cases of DCVST have been analyzed and no extrapyramidal features were seen.^{6,9} Murray et al¹⁰ were the first to report such manifestations as a consequence of thrombosis of the internal cerebral vein, vein of Galen, straight sinus, left transverse sinus, left sigmoid sinus, and left internal jugular vein. Their patient recovered on anticoagulation treatment. In another case report,¹¹ Parkinsonism was attributed to thrombosis in the vein of Galen, straight sinus and left transverse sinus. This patient's MRI showed high signal intensities in the thalami and basal ganglia suggesting a pathophysiological basis for the syndrome. Here, the neurological and MRI findings reversed with anticoagulation. A recent study¹² proposed that some clinical features of Parkinson disease (particularly resting tremor) are due to involvement of both the basal ganglia and the cerebro-thalamo-cortical circuit.

Anticoagulation with heparin is the mainstay of treatment even in the presence of hemorrhagic infarction. Direct thrombolysis with urokinase or tissue plasminogen activator (tPA) is also useful, and lyses of the thrombus with persistent recanalization of deep veins can be achieved. It has been shown that the time window of the thrombolytic may be extended from 3 to 4.5 hours.¹³ In a high risk group, the presence of non-specific symptoms and an altered level of consciousness should alert the neurologist to suspect the diagnosis of DCVST. If detected, immediate therapy should be started to avoid a devastating outcome. With prompt treatment prognosis can be favorable as in our case. Although the use of steroids in CVST is controversial and considered by some experts and small studies to be detrimental, in our case this type of treatment might be justified. It was found to be of help in this case to reduce the swelling (edema) in view of rapid deterioration of neurological status.

In conclusion, our patient would be the third case report of DCVST manifesting with Parkinsonism. The reversibility of the venous infarction changes on MRI seen in our patient are believed to be due to an increase in transcapillary and interstitial pressure secondary to venous thrombosis, which caused cellular swelling, but little or no cellular injury.¹⁴ What makes our case interesting is not only its rarity, but also the excellent response to the treatment with full clinical and radiological recovery. Although rare, DCVST should be included as a structural

cause of Parkinsonism worthy of consideration, given the favorable response to anticoagulation.

Acknowledgments. *The authors thank Dr. Sattam Lingawi for his review of the radiological figures for clarity and correctness.*

References

1. Khatri IA, AlKawi A, Ilyas A, Ilyas MS. Unusual causes of cerebral venous thrombosis. *J Pak Med Assoc* 2006; 56: 501-506.
2. deVeber G, Andrew M, Adams C, Bjornson B, Booth F, Buckley DJ, et al. Cerebral sinovenous thrombosis in children. *N Engl J Med* 2001; 345: 417-423.
3. Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F; ISCVT Investigators. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke* 2004; 35: 664-670.
4. Lanska DJ, Kryscio RJ. Risk factors for peripartum and postpartum stroke and intracranial venous thrombosis. *Stroke* 2000; 31: 1274-1282.
5. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. *Lancet Neurol* 2007; 6: 162-170.
6. Woods CA, Foutch PG, Kerr DM, Haynes WC, Sanowski RA. Collagenuous sprue as a cause for malabsorption in a patient with myotonic dystrophy: a new association. *Am J Gastroenterol* 1998; 83: 765-766.
7. Pfefferkorn T, Crassard I, Linn J, Dichgans M, Boukobza M, Bousser MG. Clinical features, course and outcome in deep cerebral venous system thrombosis: an analysis of 32 cases. *J Neurol* 2009; 256: 1839-1845.
8. Ameri A, Bousser MG. Cerebral venous thrombosis. *Neurol Clin* 1992; 10: 87-111.
9. Jankovic C. The Extrapyramidal Disorders. In: Bennet JC, Plum F, editors. *Cecil Textbook of Medicine*. 20th ed. Philadelphia (PA): WB Saunders Co; 1996. p. 2042-2046.
10. Murray BJ, Llinas R, Caplan LR, Scammell T, Pascual-Leone A. Cerebral deep venous thrombosis presenting as acute micrographia and hypophonia. *Neurology* 2000; 54: 751-753.
11. Jenkins M, Hussain N, Lee D, Jog MS. Reversible parkinsonism and MRI diffusion abnormalities in cortical venous thrombosis. *Neurology* 2001; 57: 364-366.
12. Helmich RC, Hallett M, Deuschl G, Toni I, Bloem BR. Cerebral causes and consequences of parkinsonian resting tremor: a tale of two circuits? *Brain* 2012; 135: 3206-3226.
13. Bansal S, Sangha KS, Khatri P. Drug treatment of acute ischemic stroke. *Am J Cardiovasc Drugs* 2013; 13: 57-69.
14. Forbes KP, Pipe JG, Heiserman JE. Evidence for cytotoxic edema in the pathogenesis of cerebral venous infarction. *Am J Neuroradiol* 2001; 22: 450-455.

Related articles

Algahtani HA, Abdu AP, Shami AM, Hassan AE, Madkour MA, Al-Ghamdi SM, et al. Cerebral venous sinus thrombosis in Saudi Arabia. *Neurosciences* 2011; 16: 329-334.

Kajtazi NI, Zimmerman VA, Arulneyam JC, Al-Shami SY, Al-Senani FM. Cerebral venous thrombosis in Saudi Arabia. *Clinical variables, response to treatment, and outcome. Neurosciences* 2009; 14: 349-354.

Al-Said Y. Management of cerebral venous thrombosis. *Neurosciences* 2004; 9 (Suppl 2): 62.