OMCR

Oxford Medical Case Reports, 2015;5, 284–287

doi: 10.1093/omcr/omv035
Case Report

CASE REPORT

Cerebral venous sinus thrombosis in heterozygous prothrombin G20210A mutation in Egyptian child, with an excellent outcome

Tarek Hamed Attia[1,*], Hisham Ahmed Fawzi[2], and Ibrahim Shahat Desouki[3]

[1]Pediatric Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt, [2]Clinical Pathology Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt, and [3]Radiology Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

*Correspondence address. Tel: +20-966532852660; Fax: +20-966112884536; E-mail: tareqhamed@live.com

Abstract

Prothrombin gene G20210A mutation is a risk factor for the development of deep vein thrombosis. We present a 6-year-old Egyptian boy who had vomiting associated with headache and dizziness. His conscious level was normal, with neither focal neurological signs nor papilledema. Brain computed tomographic scan, magnetic resonance imaging and magnetic resonance venography (MRV) revealed thrombosis of the superior sagittal and left transverse sinuses. The patient was heterozygous for prothrombin gene G20210A mutation. He received enoxaparin and warfarin. Brain imaging follow-up, after 1 month, showed complete resolution of the thrombus. The child was followed up for 1 year, and he was very healthy. Cerebral venous thrombosis must be considered in the differential diagnosis of any neurological symptoms, even mild symptoms, and prothrombin gene G20210A mutation must be considered in the screening of Egyptian children. Early diagnosis and treatment can be a good prognostic index.

INTRODUCTION

Predisposing factors can be identified in up to 80% of patients who develop cerebral venous thrombosis (CVT). In many patients, risk factors are acquired but 1015% of patients may have inherited tendencies to thrombosis. Deficiencies of protein C, protein S, antithrombin III and factor V Leiden mutation are reported in many cases.

Prothrombin is a precursor of the serine protease thrombin and is a key enzyme in the process of hemostasis. A single-nucleotide substitution (G to A) at position 20210 in the 3′ untranslated region of the gene encoding prothrombin has been identified. Its heterozygous state, 20210A, is a risk factor for the development of deep vein thromboses [1].

Here, we are reporting a case of heterozygous prothrombin gene mutation (20210A) in an Egyptian child who presented with superior sagittal and left transverse sinuses thrombosis and he was successfully treated.

CASE REPORT

A 6-year-old Egyptian boy presented with vomiting for 2 days associated with headache and dizziness. On examination, he appeared ill but afebrile, well hydrated, fully conscious and with negative meningeal signs. He had neither focal neurological signs nor papilledema. Complete physical examination, including heart, chest and kidney, was irrelevant. There was no family

Received: January 21, 2015. **Revised:** March 5, 2015. **Accepted:** April 10, 2015

© The Author 2015. Published by Oxford University Press.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

history of thrombosis, trauma or recent intracranial surgery. CBC, basic electrolytes, liver function, ammonia and C-reactive protein (CRP) were normal. Predisposing comorbid conditions associated with cerebral venous thrombosis (CVT), such as infection, iron deficiency, otitis media or mastoiditis, were investigated and excluded. Computed tomography revealed an image of superior sagittal sinuses thrombosis (Fig. 1a and b). Magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) confirmed the images of superior sagittal (especially posterior half) and left transverse sinuses thrombosis (Figs 2a and b and 3a and b).

D-dimmer, fibrinogen degradation products (FDPs) and fibrinogen level were done for diagnosis and follow-up of thrombotic activity (Table 1). Evaluation of thrombophilic state either genetic or acquired was done including searching for antithrombin III, protein C assay, protein S assay, sickle cell test, factor V Leiden, prothrombin G20210A mutation, lupus anticoagulant, anti-cardiolipin, anti-β2 glycoprotein antibodies, homocysteine and factor VIII levels. All investigations were within normal reference range, except a positive heterozygous prothrombin G20210A mutation (Table 2).

The child received enoxaparin and warfarin during first few days of admission and continued on warfarin, according to the American Heart Association guidelines [2].

His hospital stay was very satisfactory with progressive improvement in his clinical condition and normalization of FDP, D-dimmer and fibrinogen level (Table 1). MRI and MRV were repeated after 1 month, demonstrating complete recanalization of superior sagittal and left transverse sinuses (Figs 4a and b and 5a and b).

The child was discharged home on warfarin and followed up with INR (with a target level of 2–3 times of normal) for 6 months, and then he was followed up in the clinic for another 6 months. During the follow-up of 1 year, he was in a good health condition with no neurological deficit and with very high scholastic achievement.

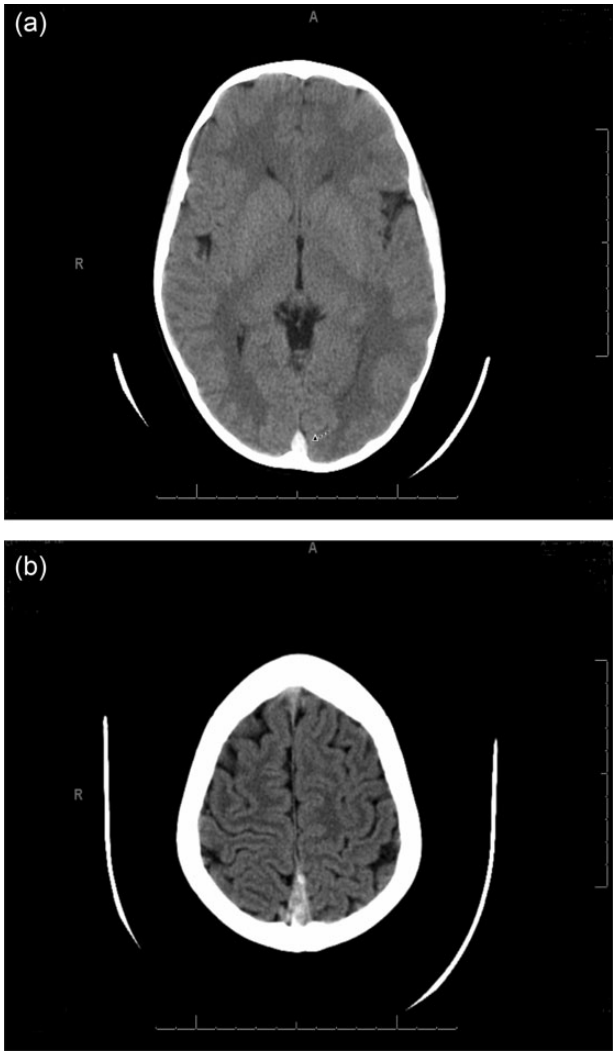

Figure 1: (**a** and **b**) CT brain showing prominent and hyperdense superior sagittal sinus, with no mass effect or cerebral changes around, denoting sagittal sinus thrombosis.

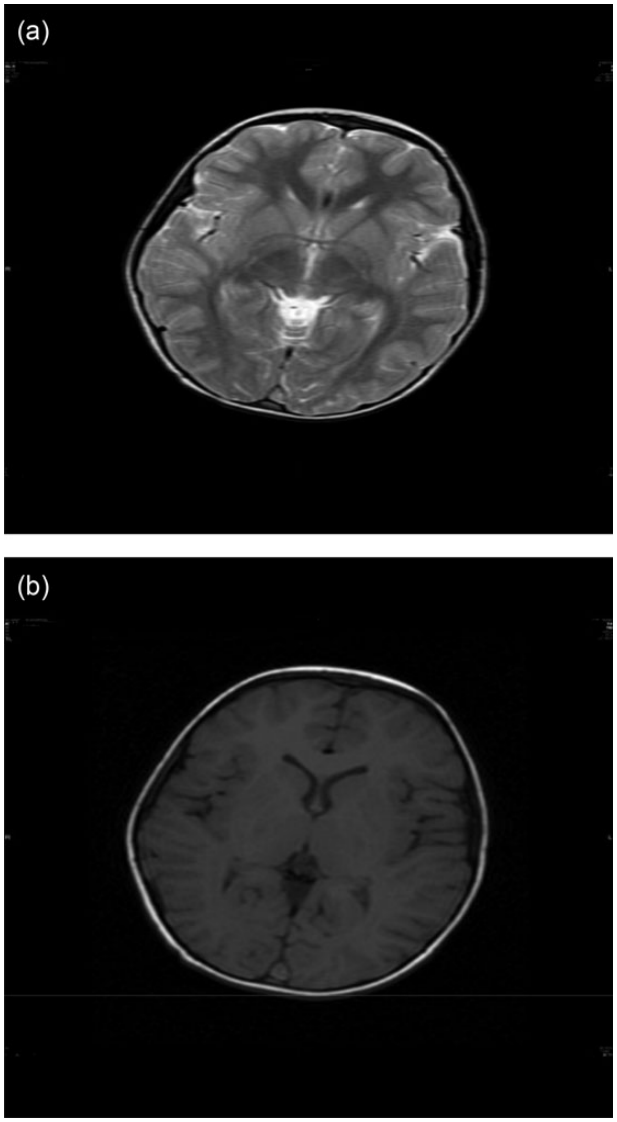

Figure 2: (**a** and **b**) MRI brain before treatment showing high signal intensity of the superior sagittal sinus till confluence of sinus and left transverse venous sinus, denoting venous sinus thrombosis.

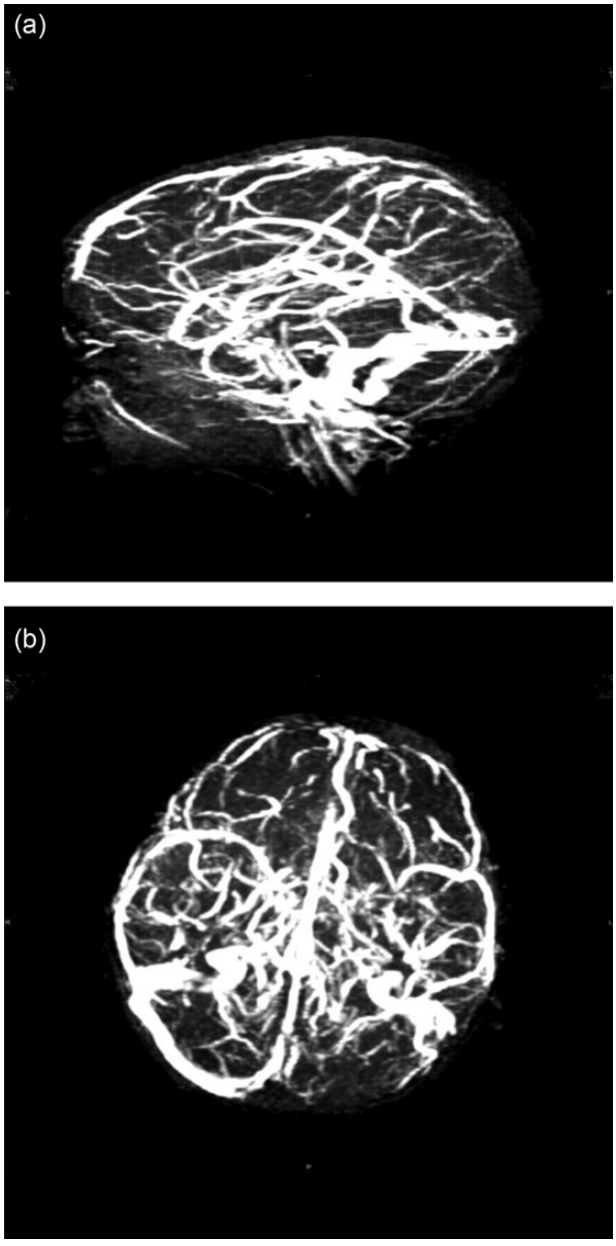

Figure 3: (**a** and **b**) MRV brain before treatment showing non-visualization of the superior sagittal sinus (especially posterior half) and left transverse venous sinus, denoting venous sinus thrombosis.

Table 1: Workup done to follow-up activity of thrombosis

Laboratory test results upon admission		Laboratory test results during follow-up in hospital	Reference range
APTT	31.9 s		26–40 s
Prothrombin time	12.1 s		11.5–14 s
INR	1.14	2–3 times of normal (target level)	0.65–1.17
FDP	20 µg/ml	3 µg/ml	0–5 µg/ml
D-Dimmer	4.3 µg/ml	0.4 µg/ml	0–0.5 µg/ml
Fibrinogen	0.8 g/l	2.96 g/l	1.8–4 g/l

Table 2: Workup done to diagnose etiology of thrombosis

Test	Result	Reference range
Protein C assay	66%	65–110%
Protein S assay	72%	44–92%
Sickle cell test	Negative	
Factor V Leiden	Absence of mutation	
Homocysteine	8.6 µmol/l	<15 µmol/l
Antithrombin III assay	120%	80–120%
Anti-cardiolipin IgG	3.9 GPL/ml	(negative) <10 GPL/ml
Anti-cardiolipin IgM	2 MPL/ml	(negative) <10 MPL/ml
Anti-beta 2 glycoprotein IgG	<5 U/ml	(negative) <10 U/ml
Anti-beta 2 glycoprotein IgM	<5 U/ml	(negative) <10 U/ml
Prothmbin gene mutation	Heterozygous for G20210A mutation	

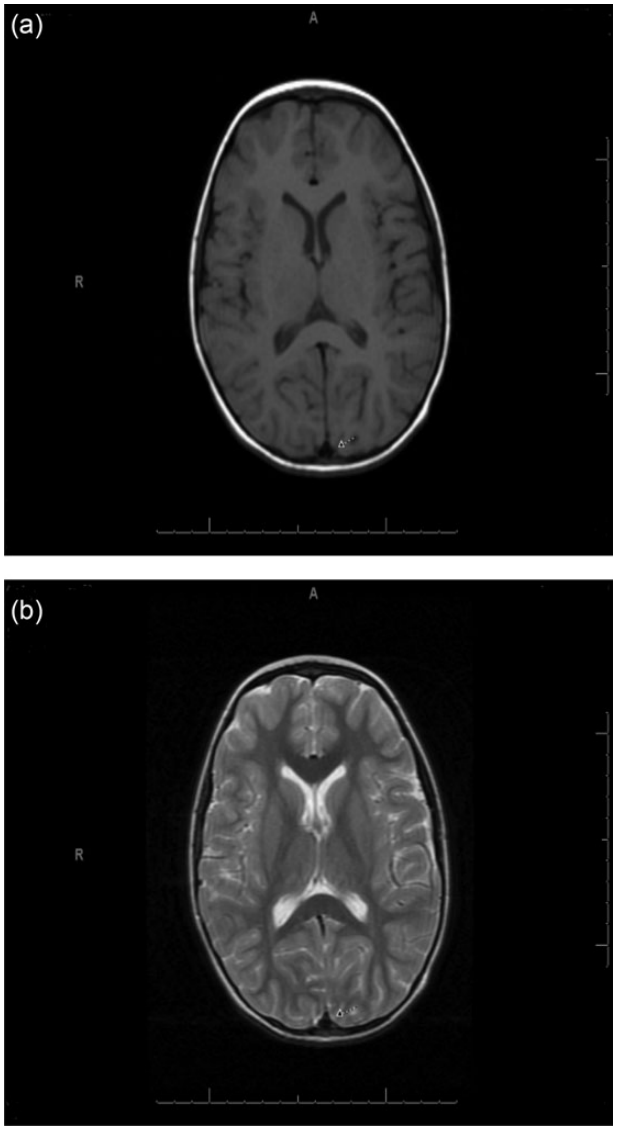

Figure 4: (**a** and **b**) MRI brain after treatment showing complete recanalization of the superior sagittal and left transverse venous sinuses.

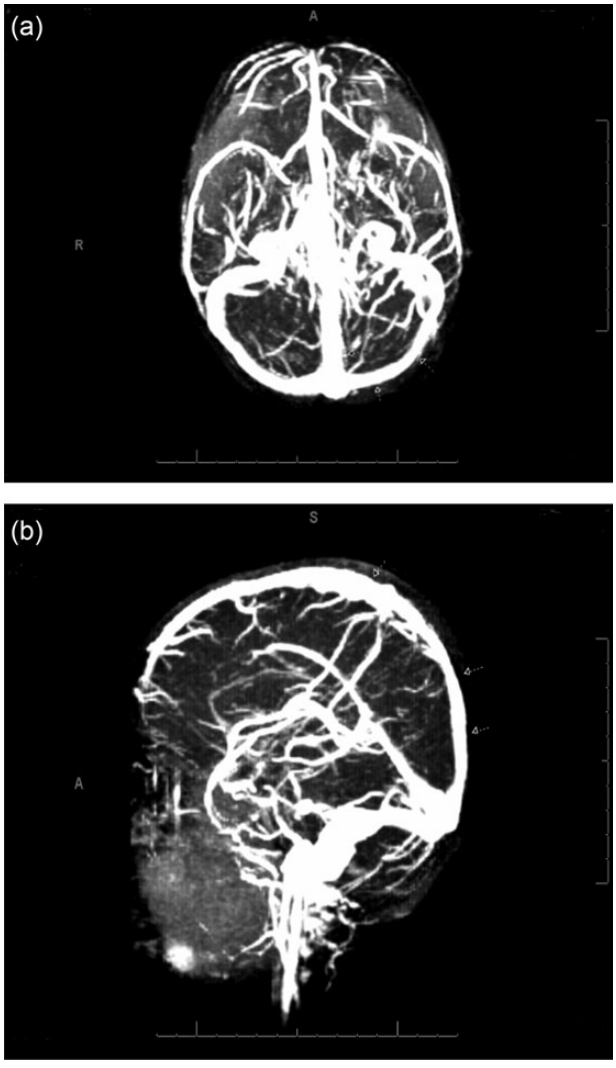

Figure 5: (**a** and **b**) MRV brain after treatment showing complete recanalization of the superior sagittal and left transverse venous sinuses with no detectable filling defect.

DISCUSSION

Since the discovery of the prothrombin G20210A mutation, which is associated with an increased risk of deep vein thrombosis and pulmonary embolism, cases associated with CVT in adults have been reported [3]. A 10-year-old boy with basilar artery thrombosis who was heterozygous for prothrombin G20210A mutation was described, suggesting that this mutation may be a risk factor for arterial ischemic stroke in children [4]. In Argentina, among 23 cases with sinovenous thrombosis, one child had combined PT20210A and an inherited protein C deficiency [5]. CVT in children is often multifactorial in etiology, with a predisposing comorbid condition identified in up to 95% of affected patients. Prothrombotic states have been identified in 24–64% of children [6]. In our patient, no predisposing factor for CVT other than prothrombin gene mutation was detected. Pérez-Dueñas *et al*. reported a case of CVT in a 4-year-old girl who was admitted to hospital with drowsiness and progressive sensorial depression. Within 24 h, her clinical condition deteriorated with partial seizures of the right side of the body and right hemiparesis [7]. Our patient had vomiting for 2 days associated with headache and dizziness. His conscious level was normal with negative meningeal signs. He had neither focal neurological signs nor papilledema. The difference in the clinical presentation between our case and the reported case by Pérez-Dueñas *et al*. is the highly variable clinical presentation of CVT, from isolated signs of increased intracranial pressure to combination of focal signs and/or encephalopathy [8]. Our patient was followed up in the clinic for 1 year, and he was very healthy. In The International Study on Cerebral Vein and Dural Sinus Thrombosis study in adults, complete recovery at last follow-up was noted in 57% of patients [9]. In children, CVT-specific mortality was <10% but neurologic deficits were present in 17–79% of survivors at the time of discharge or follow-up examination [6]. The good prognosis in our case may be due to early diagnosis and treatment. A high index of suspicion is necessary to effect earlier detection and therapeutic strategies [6].

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Kellett MW, Martin PJ, Enevoldson TP, Brammer C, Toh C. Cerebral venous sinus thrombosis associated with 20210A mutation of the prothrombin gene. *J Neurol Neurosurg Psychiatry* 1998;**65**:611–2.
2. Monagle P, Chan AK, Goldenberg NA, Ichord RN, Journeycake JM, Nowak-Göttl U, *et al*. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;**141**(2 Suppl):e737S–e801S.
3. Biousse V, Conard J, Brouzes C, Horellou MH, Ameri A, Bousser MG. Frequency of the 20210 G—a mutation in the 3′-untranslated region of the prothrombin gene in 35 cases of cerebral venous thrombosis. *Stroke* 1998;**29**:1398–1400.
4. Hüdaoglu O, Kurul S, Yis U, Dirik E, Cakmakçi H, Men S. Basilar artery thrombosis in a child heterozygous for prothrombin gene 20210A mutation. *J Child Neurol* 2007;**22**:329–31.
5. Bonduel M, Sciuccati G, Hepner M, Pieroni G, Torres AF, Mardaraz C, *et al*. Factor V Leiden and prothrombin gene G20210A mutation in children with cerebral thromboembolism. *Am J Hematol* 2003;**73**:81–6.
6. Diamini N, Billinghurst L, Kirkham FJ. Cerebral venous sinus (Sinovenous) thrombosis in children. *Neurosurg Clin N Am* 2010;**21**:511–27.
7. Pérez-Dueñas B, Cambra-Lasaosa FJ, Noguera-Julian A, Palomeque-Ric A, Toll-Costa T, Campistol J, *et al*. Cerebral venous thrombosis in a girl carrier of the prothrombin gene mutation G20210A treated by local fibrinolysis of the superior sagittal sinus. *Rev Neurol* 2002;**35**:913–7.
8. Bousser MG, Russell RR. Cerebral venous thrombosis. In: Warlow CP, Van Gijn J, eds. *Major Problems in Neurology*. London: WB Saunders, 1997: p. 27, 104.
9. Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke* 2004;**35**:664–70.