CASE REPORT

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

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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 10–15% 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
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-dimer, 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-dimer 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                                                | 0.65–1.17       |
| FDP                                     | 20 µg/ml                                             | 0–5 µg/ml       |
| D-Dimmer                                | 4.3 µg/ml                                            | 0–0.5 µg/ml     |
| Fibrinogen                              | 0.8 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  | 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              |
| Prothrombin 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.
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.

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