A Young Man with Cerebral Venous Thrombosis and Hyperhomocystinemia

Md Enayet Hussain1,*, Afzal Momin1, Mahmudul Islam1, Sk Rezaul Haque1, Sharmin Jahan2, Md Azharul Hoque1

1National Institute of Neurosciences (NINS), Agargaon, Dhaka, Bangladesh
2Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka
*Corresponding author: enayetdmc@yahoo.com

Abstract  Cerebral venous sinus thrombosis is an uncommon condition and can be precipitated by various conditions. Here we report a case of cerebral venous sinus thrombosis in a young man in whom the serum homocysteine level was found to be elevated. A 36-year-old man was admitted with sudden severe headache, vomiting and visual obscuration. Investigations revealed widespread cerebral venous sinus thrombosis. All investigations to find out the etiology came out normal except the serum homocysteine level which was found to be elevated. Further studies are required to evaluate the importance of estimation of serum homocysteine level in cases of CVST, especially where a clear risk factor has not been identified and where other investigations failed to find out any known etiological factor.

Keywords: cerebral venous sinus thrombosis, hyperhomocysteinemia


1. Introduction

Cerebral venous sinus thrombosis (CVST) is a rare form of stroke that can be precipitated by a variety of conditions. [1,2,3] It often affects young-to-middle-aged patients, and more commonly women. It is associated with infections, neoplasm, pregnancy, puerperium, systemic diseases, dehydration, oral contraceptives (OCPs), and coagulopathies. In 30% of the patients, underlying pathology could not be identified. In young to middle-aged adults, CVST is much more common in women than men with a ratio of three to one. This women preponderance is attributable to gender-specific risk factors (GSRF) such as OCPs, pregnancy and hormone replacement therapy (HRT). In the Middle East countries (Persian Gulf region, Turkey and North Africa) Behcet disease is mostly reported as the causative risk factor (33-36%). The superior sagittal sinus (SSS) and the transverse sinuses are mainly affected with a rate of 72% and 70%, respectively. More than one sinus is affected in nearly one-third of patients. CVST has a wide spectrum of clinical presentation. In 70-90% of the patients, the presenting symptom is headache. In 25-75% of the patients, focal neurologic deficits (FND) are present. In many patients, symptoms develop over days or weeks. In some patients, clinical presentations are nonspecific. Therefore, there is not a defined clinical syndrome [10].

We present a young male who developed widespread cerebral venous sinus thrombosis in whom all the investigations related to the etiological factors were found to be normal except a moderately elevated serum homocysteine.

2. Case Report

A 35-year-old, right-handed male, sanitary worker by profession got admitted into National Institute of Neurosciences & Hospital (NINS & H), Dhaka on the 22nd April 2014 with the complaints of severe headache for 8 days. The headache started suddenly at around 9:30 pm on 13th April reaching its maximum intensity within few minutes. It was very severe, throbbing in nature and was confined to the right fronto-temporal area. It was associated with nausea but not with vomiting, photophobia and phonophobia. The patient stated that he never had headache of such nature & severity in his life. With these complaints he consulted a local registered practitioner who prescribed him some medications which gave him some but not complete relief of the headache. On 17th April he continued to suffer from the headache with one episode of vomiting. He then went to one government hospital and was admitted there. A Noncontrast CT scan was done (on 17th April) which was interpreted as normal and was treated symptomatically. The patient did not find any satisfactory improvement and he got himself admitted to NINS & H on 22nd April 2014 with the complaints of severe headache for 8 days. The headache started suddenly at around 9:30 pm on 13th April reaching its maximum intensity within few minutes. It was very severe, throbbing in nature and was confined to the right fronto-temporal area. It was associated with nausea but not with vomiting, photophobia and phonophobia. The patient stated that he never had headache of such nature & severity in his life. With these complaints he consulted a local registered practitioner who prescribed him some medications which gave him some but not complete relief of the headache. On 17th April he continued to suffer from the headache with one episode of vomiting. He then went to one government hospital and was admitted there. A Noncontrast CT scan was done (on 17th April) which was interpreted as normal and was treated symptomatically. The patient did not find any satisfactory improvement and he got himself admitted to NINS & H on 22nd April. On admission the patient had a moderately severe headache in the right fronto-temporal area with visual obscuration of both eyes without any nausea, vomiting, photophobia & phonophobia. On examination the patient was fully conscious and oriented, the pulse rate was 88 beats/min and the BP was 140/100. His higher psychic function and speech was normal. The cranial nerves examination revealed no abnormality except papilledema. There was no other focal deficit. Careful assessment of his CT scan
revealed a dense triangle sign of the superior sagittal sinus and a hyper density of the straight sinus (Figure 1). A provisional diagnosis of cerebral venous sinus thrombosis was made and an MRI with MRV was advised. MRI T1, T2 & FLAIR images all revealed a hyper intensity along the right transverse sinus and MRV revealed irregularity of outline of superior sagittal sinus (SSS), right transverse sinus, right sigmoid sinus & left transverse sinus (suggestive of thrombi) (Figure 2). The diagnosis of cerebral venous sinus thrombosis was established. To find out the underlying etiology all relevant investigations (CBC, ESR, PBF, ANA, antiphospholipid antibody, Protein C, Protein S, antithrombin III, serum homocysteine, prothrombin time, APTT, VDRL) were done. All were found to be normal except the serum homocysteine level which was found to be moderately elevated (27μmol/L, N: 5-15 μmol/L).

![Figure 1. CT scan (axial & coronal section) showing dense triangle sign of the superior sagittal sinus and a hyper density of the straight sinus](image1.png)

![Figure 2. Left-MRI FLAIR image showing hyper intensity along the right transverse sinus. Right- MRV showing nonvisualized right transverse sinus](image2.png)

![Figure 3. Papilledema (27/04/2014); Near normal optic disc (07/05/2014)](image3.png)

Anticoagulation was started on the day following admission with subcutaneous Enoxaparin 60 IU twice daily along with Acetazolamide, 250mg bd. The patient started to notice an improvement of headache and visual
obscuration 5 days after admission. The optic disc margin began to reappear. On 08/5/2014 (25 days after the onset of headache) the patient was discharged with complete relief of headache and visual obscuration along with a near normal optic disc (Figure 3). He was prescribed tab warfarin, 5mg once daily, tab folic acid, 5mg bd, vitamin B6, B12 and was advised for follow up after one month in the department.

3. Discussion

Cerebral venous sinus thrombosis is a serious but treatable condition with a diagnostic challenge due to its nonspecific symptoms, remarkably wide spectrum of signs and mode of onset. The diagnosis is even more challenging in the underdeveloped countries where the investigation facilities are not easily available. So even when diagnosed, many a times the underlying cause remains unidentified.

Many causative conditions have been described. These may be seen alone or in combination. Among the various causes are sinusitis, trauma and surgery, hypercoagulable states (Antiphospholipid syndrome, protein C and protein S deficiency, antithrombin deficiency, vasculitis, pregnancy, puerperium, use of oral contraceptive pills, nephrotic states (Antiphospholipid syndrome, protein C and protein S deficiency), intracranial hypotension, lumbar puncture etc.

A correlation between hyperhomocystinemia and arterial vascular disease is well established. Several studies have investigated the role of hyperhomocysteinemia in venous thromboembolism. [4,5,6,7] There are however very few reports of cerebral venous sinus thrombosis and hyperhomocysteinemia. Researchers’ have found that hyperhomocysteinemia is associated with a 4-fold increase risk of cerebral venous sinus thrombosis; whether or not its correction with vitamins reduces the risk of the disease remains to be determined [8].

Homocysteine, a non-protein α-amino acid, primarily comes from methionine. Methionine is a by-product of protein catabolism. There are two distinct pathways whereby homocysteine is metabolized:

- Transulfuration pathway requires cystathione beta synthetase. This converts homocysteine to cystathionine and then to cysteine, which is excreted in the urine. Vitamin B6 is required as a co-factor in this pathway. Deficiency of the enzyme causes homocysteinuria, an inborn error of metabolism.
- Remethylation pathway requires methylene tetrahydrofolate reductase (from folate metabolism) which helps methionine synthetase to convert homocysteine back to methionine. Vitamin B12 is a co-factor in this reaction. Pathology in this pathway is responsible for hyperhomocysteinemia.

High levels of auto-oxidation of homocysteine reacting with highly reactive oxygen species cause lipid peroxidation which in turn leads to vascular damage and smooth muscle proliferation leading to atherogenesis. The same phenomenon also causes vascular endothelial injury and is responsible for prothrombogenesis [9].

4. Conclusion

The case we reported had moderately elevated homocysteine level. Other investigations done to search for aetiology were normal and the patient did not have other risk factors for CVST. Further studies are required to evaluate the importance of estimation of serum homocysteine level in cases of CVST, especially where a clear risk factor has not been identified.

References