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Cerebral Venous Sinus Thrombosis with Tentorial Haemorrhagic Infarctions in Combined Proteins Deficiency and Hyperhomocysteinemia Treated with Anticoagulation- Limited Evidence with Good Results: A Case Report

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Abstract

We are presenting a case of a 40-year-old lady who presented with sudden loss of consciousness. Computed Tomography scan of her brain revealed the presence of blood in her sub-arachnoid space on her right hemisphere, cerebral oedema, and cerebral venous sinus thrombosis later magnetic Resonance Imaging revealed extensive cerebral venous sinuses thrombosis formation associated with supra and infra-tentorial haemorrhages. Elevated levels of plasma homocysteine and deficient levels of protein S. Patient was anticoagulated with warfarin and INR was monitored. She recovered successfully with no complication of anticoagulation observed. The use of anticoagulation had a favourable outcome in our patient but the evidence of its use lacking to date.

Keywords: Cerebral venous thrombosis; Intracranial thrombosis; Stroke

Background

Cerebral venous sinus thrombosis (CVST) occurs due to a thrombus in the dural venous sinuses. Frequent headaches, abnormal vision, weakness of the face and limbs on any side of the body are some of the common presenting symptoms [1]. The diagnosis is usually established by computed tomography (CT) or magnetic resonance imaging (MRI) with the help of a radio contrast dye that aids in demonstrating the site of obstruction of the venous sinuses by the thrombus. CVST may be caused by a wide variety of acquired diseases, such as dehydration, infection, hematologic disorders, or congenital malformations [2,3]. One of the most common causes contributing to the formation of thrombi, are imbalances and deficiencies in the coagulation factors [4,5]. Deficiencies in protein C and S rank among the unusual causation factors [4-6]. Although possible, cases with combined deficiencies, as with our patient, are rare occurrence. We hereby report a case of adult Cerebral Venous Sinus Thrombosis and haemorrhagic infarctions with a combined abnormality of protein S deficiency and hyperhomocysteinemia.

Case Presentation

A 40 year lady, with no known co-morbid, presented to the emergency department with a history of sudden loss of consciousness. Her vitals upon arrival were heart rate of 91 bpm, blood pressure of 140/71 mmHg, oxygen saturation of 99% on room air, and a respiratory rate of 17 breaths per minute. She was received in an afebrile and unresponsive state with a Glasgow coma scale (GCS) of 3/15 and was intubated immediately to protect and secure her airway. An urgent CT scan of her brain revealed the presence of blood in her sub-arachnoid space on her right hemisphere, cerebral oedema, and cerebral venous sinus thrombosis. Nimodipine was started as her first dose in the emergency department and the patient was loaded with Levitiracetam. Neurology was consulted and a MRI with MRV of her brain was planned which revealed extensive cerebral venous sinuses thrombosis (CVST) formation associated with supra and infra-tentorial haemorrhages (Figure 1). She was admitted to the intensive care unit (ICU) for further management. A CVST diagnostic workup was done which revealed elevated levels of plasma homocysteine; 84.2 $\mu\text{mol/L}$

(reference range 5-12 $\mu\text{mol/L}$) and deficient levels of protein S; 46.8% (reference range 60-110%). Her INR and protein C levels were within their normal limits; 1.38 ratio and 101.9% (reference range 72-106%) respectively. No other abnormality was found.

Mannitol was started to relieve the cerebral oedema and the patient was started on vitamin supplements of methylcobalamin 20 mg once daily for 1 month, folic acid 5 mg once daily for 2 weeks and pyridoxine as 25 mg once daily for 1 month. Serial testing of her homocysteine levels showed a decreasing trend. The patient condition gradually improved and she was extubated after 6 days of ICU stay. A repeat CT scans revealed resolution in her cerebral oedema and tentorial haemorrhages. Warfarin was initiated for CVST and the patients INR was monitored regularly by repeat INR testing after every 48 hours once the INR came in the steady state of 2-3. She was discharged home after 20 days of hospital stay, in a stable condition with a GCS of 15/15.

Discussion

One of the earliest descriptions of thrombosis of the cerebral sinuses and veins is attributed to the French physician [7]. Until the latter half of the 20th century; CVST remained a diagnosis that was established only after death [8]. CVST is a rare disease with an annual estimated incidence of 4 cases per million in adults. Although it may occur in all age groups, it is most common in the third decade of life with preponderance in the female gender [9,10].

Coagulation factor imbalances are predominately responsible for causing thrombophilia, with factor V Leiden being the most common

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Figure 1: Post contrast MRV shows filling defect representing extensive thrombus involving the superior sagittal sinus, straight sinus, confluence of the sinuses.

of them all [2-6,11]. Dehydration and the use of oral contraceptives also play a major role in the development of thrombosis in several women. Isolated deficiencies of protein C and protein S are of one of the uncommon presenting causes for CVST [5,6,12]. These deficiencies usually tend to occur as a secondary manifestation of syndromes that cause a haematological disorder like SLE. Our case was unique because it presented with two co-existing hyper-coagulable states of protein S deficiency and simultaneously hyper-homocysteinemia.

The veins of the brain empty into the dural venous sinuses that carry blood to the heart. In cerebral venous sinus thrombosis, blood clots usually form in the veins of the brain, both superficial and deep, and the venous sinuses. The thrombosis of the veins themselves causes venous infarction that causes damage to brain tissue due to an insufficient blood supply which leads to cerebral oedema, and eventually results in small petechial haemorrhages that may merge into large haematomas. Sinus thrombosis is the main mechanism that results in elevated intracranial pressures due to decreased resorption of the cerebrospinal fluid (CSF). However, hydrocephalus does not occur because no difference in pressure is found between the different regions of the brain [9]. Formation of any blood clot is due to an imbalance between coagulation and fibrinolysis. Most cerebral venous sinus thrombosis cases are due to hypercoagulability [9,10].

Protein S deficiency is estimated to occur in 1 in 20000 individuals approximately. Severe protein S deficiency is rare; however, the exact prevalence is unknown. Protein S deficiency can also be an inherited autosomal dominant disorder of the PROS1 gene. Individuals inheriting two altered copies have an increased severity of the disease. The genetic analysis was not conducted in our patient in order to understand the cause of the combined disorder. The presentation of the patient with coma is a scarcity, which we find in the medical literature also the combined involvement of the supra-tentorial and infra-tentorial regions with hemorrhagic infarctions, is something that we find in rarity.

Several studies have found that the hyperhomocysteinemia is associated with a several fold-increased risk of CVT [13-15]. In the case of our patient, the elevated homocysteine levels were brought down by treatment with pyridoxine, methylcobalamin and folic acid supplementation, similarly described in another case by Hassan et al. [16].

A coagulation factor abnormality, anti-phospholipid antibodies and thrombophilia screening, is the recommended diagnostic work up in patients with CVST [6]. It is suggested that screening of plasma homocysteine levels should be included in the thrombophilia diagnostic work up as demonstrated by a study performed by Martinelli et al., Ventura et al. and Cantu et al. among a few [11,14,17]. It is also suggested that the correction of hyperhomocysteinemia with vitamin

supplementation therapy may help to reduce the high risk of recurrent CVST should be tested in proper studies.

The American Heart Association 8 favours the anticoagulation treatment in cerebral venous sinus thrombosis but the literature published in Cochrane in 2011 showed few randomized trials, which are favouring the anticoagulation treatment with significant results. Our patient was benefitted with this treatment but we didn't find any good cases in-patient who has associated hemorrhagic infarctions [18].

Conclusion

Cerebral venous sinus thromboses with tentorial hemorrhagic infarction are a rare clinical entity. The use of anticoagulation has a favourable outcome in our patient but the evidence is lacking to date.

Consent

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal

Competing interests

The authors declare no conflict of interest and there are no competing interests between the authors.

Author's Contribution

MWK was involved in the writing of the manuscript. MAB was involved in the care of the patient, literature search and manuscript writing, SW was involved in the writing of the manuscript, literature search and final review. MK was the consultant on call and was involved in the final review of the manuscript.

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