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Cerebral Venous Thrombosis Complicated by Seizure Disorder in a Newly Diagnosed Hypertensive Patient with Nephrotic Syndrome: A Case Study Highlighting Alcohol and Smoking-Related Dehydration

[1]Dr.V. Ramachandra Rao, Junior Resident, Sree Balaji Medical College and Hospital, Chrompet, Chennai.

[2]Dr Suresh Kanna S, Associate Professor, Sree Balaji Medical College and Hospital, Chrompet, Chennai.

[3]Dr Arvind Raj, Senior Resident, Sree Balaji Medical College and Hospital, Chrompet, Chennai.

Corresponding Author: Dr. V. Ramachandra Rao, Junior Resident, Sree Balaji Medical College and Hospital, Chrompet, Chennai.

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Abstract

Dural Venous Sinus Thrombosis is an uncommon condition characterized by the formation of a blood clot within the cerebral sinus. Its clinical manifestations are diverse and often non-specific, encompassing symptoms such as headaches, papilledema, seizures, focal neurological impairments, and alterations in mental status. Various factors can predispose individuals to this condition, including genetic predispositions, acquired prothrombotic conditions, infections, inflammatory disorders, and trauma. Nephrotic syndrome (NS) is a kidney condition marked by changes in the glomerular capillary wall that lead to significant proteinuria, low levels of albumin, elevated cholesterol, lipid excretion, and swelling. A notable complication of NS is the heightened risk of both venous and arterial thromboembolic events, with about 27% of patients experiencing such complications — an eightfold increase compared to the general populace. The exact mechanisms underlying thrombus formation in NS remain not entirely clear but appear to be influenced by factors such as the specific underlying cause, notably common in membranous nephropathy, serum albumin levels (particularly when below 2 g/dl), prior thrombotic episodes, and genetic factors. Individuals with NS face elevated chances of developing conditions like deep vein thrombosis (DVT), renal vein thrombosis (RVP), and pulmonary embolism (PE). Although less common, cerebral venous thrombosis (CVT) is predominantly observed in pediatric populations. The definitive diagnostic modalities for this condition include Magnetic Resonance Imaging (MRI) combined with Magnetic Resonance Venography (MRV). We present a case of a patient who experienced dizziness followed by abrupt seizures and a sudden temporal headache, accompanied by disorientation. Additionally, the patient reported disturbed sleep over the past three days due to his mother's hospitalization in the same facility and had been experiencing toothache for the preceding three days. Radiological evaluations, including Computed Tomography (CT) and subsequent MRI/MRV studies, confirmed the presence of a thrombus in the right

transverse sinus, along with associated small venous infarcts in the right parietooccipital region and subarachnoid haemorrhage (SAH). Subsequently, the patient was managed with therapeutic anticoagulation initially using Low Molecular Weight Heparin, which was subsequently transitioned to Warfarin therapy.

Keywords: DVST, MRV, Nephrotic Syndrome, Seizures, Headache.

Case Report

A 31-years-old male who is a heavy smoker and alcoholic whose last binge was one hour prior to the presentation of about 500ml of Brandy presented in Emergency department of Sree Balaji Medical College and Hospital at 11.45pm with complaints of Giddiness followed by Seizures involving both upper limb a lower limb at 11:30 PM for 3 minutes. Seizures associated with Frothing, tongue bite and urinary incontinence. The headache was sudden in onset in left temporal, throbbing type, gradually progressive since hours. Patient had a history of disturbances in sleep since 3 days, patient had a history of tooth ache since 3 days. On examination, Patient is dehydrated, general condition was fair. There were no signs of pallor, icterus, lymphadenopathy, clubbing, oedema. The body temperature was 98°F, pulse 104 beats per minute, respiratory rate 11 times per minute, blood pressure 150/100 mmHg, oxygen saturation of 98% measured with pulse oximeter. His systemic examination was normal. Glasgow Comma Scale had score of E4, V4, M5. High mental function shows negative meningeal sign/neck rigidity. Kerning's sign was negative. On cranial nerve examination, the pupil showed bilateral 3mm reactive and cerebral sign were normal. The motor examination and reflex response were normal. The sensory response was intact. The investigations were done on intervals.

Table 1: Investigations

Investigations	
Haemoglobin	17.2
Total WBC	15430
ESR	14
Urea	27
Creatinine	1.4
OT/PT	23/21
GGTP	50
Urine Albumin	+++
24 hr Urine Protein	7612
PT/INR	11.9/1.00
Serum Albumin	2.9
Serum Homocysteine	18.01
Factor V	115 (50-150)
Anti-Thrombin III	70(80-120)
Protein C	143
Protein S	69.3
Factor V	115
Thyroid Profile	Normal

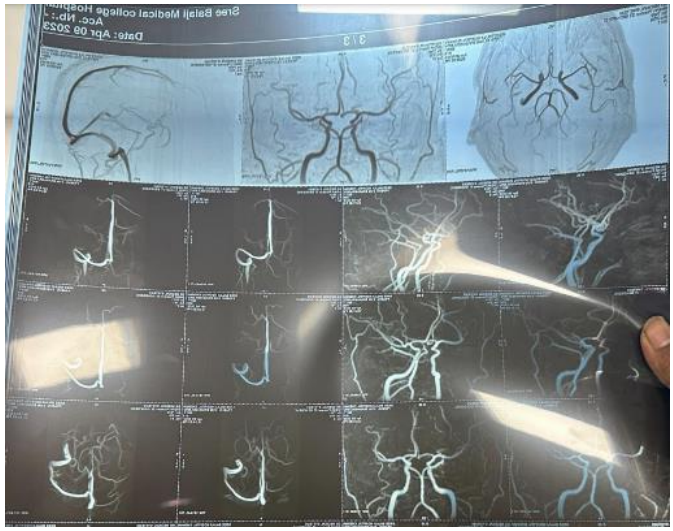
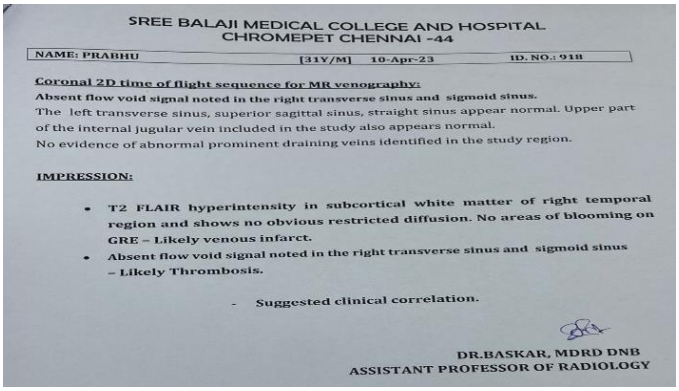


Figure 1: MRV Brain



SREE BALAJI MEDICAL COLLEGE AND HOSPITAL
CHROMEPET CHENNAI -44

NAME: PRABHU [31Y/M] 10-Apr-23 ID. NO.: 918

Coronal 2D time of flight sequence for MR venography:

Absent flow void signal noted in the right transverse sinus and sigmoid sinus.

The left transverse sinus, superior sagittal sinus, straight sinus appear normal. Upper part of the internal jugular vein included in the study also appears normal.

No evidence of abnormal prominent draining veins identified in the study region.

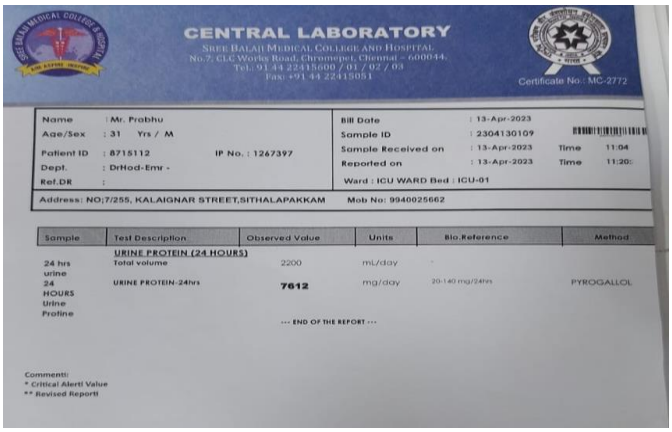
IMPRESSION:

- **T2 FLAIR hyperintensity in subcortical white matter of right temporal region and shows no obvious restricted diffusion. No areas of blooming on GRE – Likely venous infarct.**
- **Absent flow void signal noted in the right transverse sinus and sigmoid sinus – Likely Thrombosis.**

- **Suggested clinical correlation.**

DR.BASKAR, MDRD DNB
ASSISTANT PROFESSOR OF RADIOLOGY

Figure 2: MRI Report



CENTRAL LABORATORY
SREE BALAJI MEDICAL COLLEGE AND HOSPITAL
No.7, CLC Works Road, Chromepet, Chennai - 600044.
Tel.: 91 44 22415000 / 01 / 02 / 03
Fax: +91 44 22415051
Certificate No.: MC-2772

Name	: Mr. Prabhu	Bill Date	: 13-Apr-2023
Age/Sex	: 31 Yrs / M	Sample ID	: 2304130109
Patient ID	: 8715112 IP No. : 1267397	Sample Received on	: 13-Apr-2023 Time 11:04
Dept.	: DrHod-Env -	Reported on	: 13-Apr-2023 Time 11:20:
Ref.DR	:	Ward : ICU WARD Bed : ICU-01	

Address: NO;7/255, KALAIGNAR STREET,SITHALAPAKKAM Mob No: 9940025662

Sample	Test Description	Observed Value	Units	Bio.Reference	Method
	URINE PROTEIN (24 HOURS)				
24 hrs urine	Total volume	2200	mL/day	-	
24 HOURS Urine Protine	URINE PROTEIN-24Hrs	7612	mg/day	20-140 mg/24hrs	PYROGALLOL

--- END OF THE REPORT ---

Comments:
* Critical Alert! Value
** Revised Report!

Figure 3: 24 – Hour Urine Protein

The patient was recently diagnosed with hypertension and subsequently initiated on antihypertensive medications following routine blood pressure monitoring. Given findings suggestive of venous infarcts and thrombosis involving the right transverse and sigmoid sinuses, a consultation with neurosurgery was sought. The neurosurgical team recommended a conservative approach without surgical intervention. Consequently, the patient received intravenous anticoagulants initially, transitioning to oral anticoagulants during the hospital stay. Additionally, due to the presence of nephrotic range proteinuria, a nephrology consultation was arranged. The nephrology team emphasized the importance of stringent blood pressure management and initiated treatment with oral prednisolone. Furthermore, in light of the cerebral venous thrombosis (CVT) diagnosis, a neurology evaluation was conducted, and the recommended therapeutic measures were implemented. A thorough ophthalmic assessment was performed to evaluate the fundus, revealing no signs of papilledema. Upon achieving clinical improvement, the patient was discharged on oral anticoagulants with a target international normalized ratio (INR) range of 2–3. Additionally, a gradual tapering regimen for prednisolone, a statin, a low-dose angiotensin-converting enzyme (ACE) inhibitor, and dietary modifications were prescribed. The patient continues to be monitored with regular follow-up visits.

Discussion

Dural Venous Sinus Thrombosis (DVST) is a significant neurological condition, accounting for approximately 1-3% of all strokes. Predominantly, the superior sagittal sinus is affected in 70-80% of cases, followed by the transverse and sigmoid sinuses. In the current case, the patient manifested thrombosis within the right transverse sinus, accompanied by infarcts in the parietooccipital vein. Various underlying factors contribute to DVST, encompassing genetic and acquired prothrombotic conditions, pregnancy-related states, infections like sinusitis and meningitis, oral contraceptive use, trauma, inflammatory conditions, among others. Notably, certain genetic factors such as deficiencies in Antithrombin III, protein C and S, mutations in factors like V and prothrombin, and hyperhomocysteinemia have been linked to DVST. In this instance, alcohol consumption is suspected as a potential trigger. Clinical presentations of DVST are multifaceted, with headaches being the most prevalent symptom (88.8%), followed by seizures (39.3%), paresis (28.3%), and alterations in mental status (22%). The nature of the headache can sometimes be misleading, resembling conditions like migraine or subarachnoid haemorrhage. Additionally, seizures are more frequently observed in DVST compared to arterial

strokes, while focal neurological deficits are attributable to venous infarctions. Diagnostic modalities encompass laboratory evaluations such as complete blood profiles, thrombophilia assessments, and D-Dimer assays, alongside neuroimaging techniques like CT/CTV, MRI/MRV, and cerebral angiography. Specifically, MRI/MRV stands out as the gold standard for DVST diagnosis due to its ability to visualize thrombi and assess flow dynamics. Treatment strategies for DVST primarily involve supportive care, anticoagulation, and occasionally, endovascular thrombolysis. Anticoagulation, a cornerstone in DVST management, typically commences with subcutaneous heparin followed by oral anticoagulants like warfarin to maintain INR levels between 2 to 3.8. In our case, the patient was initially treated with weight-adjusted Low Molecular Weight Heparin before transitioning to Warfarin, showing promising recovery. Despite complications like pneumonia, the patient exhibited an 80% recovery rate over a variable period. In summary, our case underscores the imperative of comprehensive imaging investigations for the accurate diagnosis and management of the rare condition, Dural venous sinus thrombosis. DVST constitutes a relatively small fraction, approximately 1-3%, of overall stroke occurrences. This underlines its rarity compared to other stroke subtypes. With timely and appropriate management, the prognosis for DVST is generally favourable. Studies indicate an overall recovery rate of approximately 80%, though the recovery timeline can vary significantly, spanning several weeks to months. Nonetheless, vigilance is essential during follow-up due to potential complications, including seizures and recurrent thrombotic events. While DVST predominantly affects adults, its presentation in neonates and children exhibits similarities but may be associated with a higher incidence of neurological deficits and seizures. Apart from the primary neurological manifestations, patients with DVST may experience complications like pneumonia, emphasizing the need for comprehensive care and management strategies tailored to individual patient needs. Individual cases may present unique challenges, such as identifying specific triggers like alcohol consumption, necessitating a tailored diagnostic and therapeutic approach based on comprehensive evaluation and assessment.

DVST and Its Relationship with Nephrotic Syndrome

Hyper coagulation arises from an imbalance between clotting activators and inhibitors within the body. In patients with nephrotic syndrome, urinary excretion of regulatory proteins like anti-thrombin III and plasminogen is believed to be a primary mechanism promoting clot formation. Additionally, heightened platelet activity along with increased levels of fibrinogen, factor V, and factor VIII contribute to this hypercoagulable state. Although the liver produces more haemostatic proteins to offset some of these effects, the overall equilibrium still leans toward increased clotting tendencies. Factors such as advanced age and severe hypoalbuminemia amplify the risk of thrombosis, with severe hypoalbuminemia standing out as a significant biochemical indicator for clot formation. Thromboembolic events are most common during the initial months of the disease onset and during relapses. This timing is possibly due to significant losses of clotting factors and acute reduction in blood volume. Deep vein thrombosis (DVT) of the extremities is the predominant thrombotic event in nephrotic syndrome patients, followed by renal vein thrombosis (RVP). Cerebral venous thrombosis (CVT) is a less common but severe complication of nephrotic syndrome, typically affecting the superior sagittal sinus more frequently. Women face a higher risk, attributed to factors like

pregnancy, post-childbirth, and oral contraceptive use, resulting in a 3:1 female-to-male ratio in CVT cases. Additionally, females generally have a more favourable prognosis. While rare, there have been instances linking CVT to nephrotic syndrome. However, most cases of cavernous sinus thrombosis stem from infections in nearby areas like the paranasal sinuses or face. The clinical signs of CVT can vary, often presenting with non-specific symptoms that may delay diagnosis. Headaches are a prevalent symptom in a majority of CVT patients and may be the sole indicator in some cases. However, rapid neurological decline is also commonly observed. Cavernous sinus thrombosis specifically leads to varying degrees of dysfunction in specific cranial nerves. Any nephrotic syndrome patient exhibiting neurological symptoms should undergo imaging tests. MRI venography stands out as the most effective diagnostic tool for identifying CVT, as there's no singular laboratory test specifically for this condition.

Conclusion

In conclusion, the patient presented with a complex clinical scenario marked by right-sided transverse sinus thrombosis, leading to right parietooccipital small venous infarcts accompanied by a subdural hematoma (SDH). The manifestation of seizures and headaches underscores the severity and multifaceted nature of this condition. Notably, contributory factors such as alcohol-induced dehydration and insomnia may have exacerbated the thrombotic event and subsequent neurological manifestations with presenting risk factors such as Hypertension and Proteinuria. This case underscores the importance of recognizing and addressing potential risk factors like alcohol consumption and sleep disturbances, as they can significantly influence the development and progression of thromboembolic events. Prompt diagnosis and management are crucial to mitigate complications and improve patient outcomes. Close monitoring, multidisciplinary care, and addressing underlying predisposing factors are essential to guide therapeutic interventions and prevent recurrence of such intricate cerebrovascular events. Thromboembolic complications arising from nephrotic syndrome (NS) are significant and demand a heightened level of awareness to detect certain manifestations of the condition. Our understanding of the thrombotic mechanisms associated with NS remains limited, and to date, no specific biomarker of clinical significance has been identified. It is imperative that future research focuses on pinpointing biomarkers that can help ascertain which patients would derive the most benefit from preventive anticoagulant therapy.

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