Cerebral venous sinus thrombosis in patient of Immune thrombocytopenic purpura managed with mechanical thrombectomy: an anecdotal endovascular experience from Lower middle income country

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Abstract:

Key Clinical Message

The concurrent association of cerebral venous sinus thrombosis and immune thrombocytopenic purpura is one of the rarest occurrences. There exist very scarce evidence based medical literature regarding pathophysiology resulting cerebral venous sinus thrombosis in patients of immune thrombocytopenic purpura hence there lacks standard guidelines guiding prompt management in such cases.

Keywords: Cerebral venous sinus thrombosis, Immune thrombocytopenic purpura, Mechanical thrombectomy

INTRODUCTION:

Among the cerebrovascular diseases cerebral venous thrombosis is considered one of the uncommon disease which can present in any age group and accounts for only 0.5% of all stroke cases.(1) Majority of risk factors that are associated with cerebral venous sinus thrombosis mostly have a common pathophysiological ground of prothrombotic state either transient or permanent and immune thrombocytopenic purpura also falls under that category .(2) Among the several causes of isolated thrombocytopenia immune thrombocytopenic purpura (ITP) is an autoimmune disorder resulting from either increased destruction or decreased production of platelets associated with antibodies against platelets surface glycoproteins.(3)(4)The concurrent association of cerebral venou sinus thrombosis in patient of ITP is scarcely reported in medical literature along with it there is not any robust studied mechanism that explains the cause of CVST in patients of ITP. As far as from available evidences platelets microparticles (PMPs) which are tiny vesicles measuring less than 0.5 micrometer and stems from platelets membranes which further supports the formation of thrombus hence the chances of CVST. Studies have shown that the levels of PMPs are found to be in higher ranges in patient of ITP compared to other healthy individuals.(5)Regarding the management mostly the pharmacological modality such as IVIG, steroid therapy, platelet rich growth factors, anti coagulants and treatment of underlying cause are some of the major treatment means.(6)(7)There exist some studies (8)where mechanical thrombectomy have been done in CVST patients however in such rare cases where CVST resulted from ITP, the management from endovascular intervention have not been not noted well.This case has been written in accordance with SCARE guidelines .(9)

CASE SUMMARY :

A 25-year-old Asian Male was admitted to neuroscience department for headache. His past medical history was suggestive of diagnosed case of immuno thrombocytopenic purpura (ITP) under pharmacological treatment of Tab Dexamethasone 20 mg 4 days per week every alternate week since five months.Patient was also a known case of systemic hypertension but was not under regular anti hypertensive medications. Other medical and surgical history was unremarkable. . At arrival patient complaints of severe headache since 2 days, headache was diffuse in nature and more severe over bilateral frontal region, continuous, persisting, not relieved on taking over the counter medications and associated with sever bilateral periorbital pain. Vitals at the presentation were within normal range. There was no other history of dizziness, nausea,vomiting, weakness of limbs, abnormal body movement, slurring of speech, deviation of angle of mouth, bowel and bladder incontinence and trauma. On further examination neurologically GCS of the patient was 15/15, pupils were bilateral reactive to light and no other significant systemic findings. On Laboratory tests for full blood count, coagulation profile, and C-reactive protein, D-dimer remained normal limits except his platelets count was 67,500 .Patient still complained of persisting headache hence was initially managed conservatively with IV analgesics. On further investigation magnetic resonance venography (MRV) showed features suggestive of extensive dural sinus venous thrombosis i.e complete occlusion of superior saggital sinus, right transverse sinus, right straight sinus and right jugular vein . Furthermore venous congestion was also present along with venous drainage from bilateral superficial middle cerebral vein to cavernous sinus to inferior petrosal sinus to left jugular vein. A total body CECT was not done to rule out venous thrombosis in other sites however no symptoms suggesting thrombosis of other organs were apparent. Due to the clinical suspect of CVST , dexamethasone (40 mg i.v. daily for 4 days), and INJ Enoxaparin 60 mg subcutaneously twice day was started . A subsequent brain MR imaging further confirmed the diffuse cerebral venous thrombosis . The neuroradiologist suggested a neuroendovascular treatment and after a collegial discussion, we decided to proceed after platelet transfusion. Thrombectomy was performed both with aspiration using large bore aspiration catheter and with multiple embricated stent-retrievers. At the beginning of the procedure 6 vessel angio run off was done which was followed by thromobaspiration with cat-6 under 10 F guiding. After many passages, superior saggital sinus was completely opened, right transverse sinus, right straight sinus was also completely opened.Trolard and labbe vein appear draining to superior saggital sinus and right transverse sinus. Straight sinus was partly opened.At the end of the procedure, day 0, the patient was admitted in ICU where he stayed for 2 days. Screening tests for congenital and acquired thrombophilia was suggested to the patient. In the subsequent days his platelet levels fluctuated between 70,000 to 80,000.Symptomatically the severity of headache was on decreasing trend. CT head was repeated at the time of discharge which do not

showed any features of hemorrhage, infarction. Patient was discharged from our center after complete free of headache and without any neurological and motor deficits.

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DISCUSSION:

Thrombocytopenia, one of the major blood disorders can be defined as the level of platelets less than 1, 50,000 microliter in the blood. The cause behind such decrease in platelet count from blood can be categorized as either from decrease in production due to factors such as as viral infections, vitamin deficiencies, aplastic anemia, drugs or increase in destruction of platelets resulting from heparin-induced thrombocytopenia, idiopathic , pregnancy, immune system. Along with it sequestration due to splenomegaly, neonatal, gestational or pregnancy related sequestrations are the major culprits. (10)Associated with body's immune system, immune thrombocytopenic purpura (ITP) is an autoimmune disorder resulting from antibodies directed against the platelets surface glycoprotein such as GPIIb/IIIa,GP Ib/IX complexes along with certain role of T cell mediated cytotoxicity.(3),(4)Cerebral venous sinus thrombosis is one the rarest entity causing cerebral ischemia and is not mostly associated with blood disorders such as ITP. Based upon what minimal evidence that exist in the medical literature the cause behind the concurrent association of CVST in patient of ITP could be due to platelet microparticles, a nano vesicle causing increased thrombin formation,patient treated with IVIGs resulting in increased blood viscosity and increased levels of von willebrand factor antigen are some of the few studied fields.(11),(12)Regarding the certain group of risk factors that could potentially result in CVST are genetic thrombophilia, such as antithrombin deficiency, protein C deficiency, or protein S deficiency, factor V Leiden mutation, homocysteinemia, or acquired conditions like pregnancy and puerperium, oral contraceptive pills, malignancy, or infections.(2)In terms of patient presentation in cases of ITP , the patient usually presents with bleeding diathesis from low platelet count such as petechiae , purpura , and bleeding per mucosa along with platelet count less than 30×10^9/liter can result in fatal life threatening bleedings.(13)In cases of CVST patient usually presents with headache of various severity, nausea, vomiting, visual disturbances and in most cases also the optic disc changes have been seen.(14)

The diagnosis of ITP is considered after exclusion of all other possible secondary causes whereas the diagnosis of CVST is straightforward and radiological imaging mostly magnetic resonance venography (MRV) and MR imaging of the brain is the standard modality of diagnosis. Regarding the management of ITP the primary goal is to maintain adequate level of platelets and control the bleeding tendency. Prednisolone, dexamethasone, and methylprednisolone is considered the baseline management whereas in case of an emergency setting, intravenous immunoglobulin and anti-D plays vital role in acutely raising the platelets level and prevent patient deterioration.(15)Furthermore American Society of Hematology recommends thrombopoetion receptor agonist(TPO-RA) either romiplostim or eltrombopag as the second-line therapy for people suffering from ITP who are corticosteroid-dependent or resistant to corticosteroids for at least 3 months.(15)In case of CVST systemic anticoagulation with low molecular weight heparin and unfractionated heparin is considered standard modality of management which can bring about good prognosis in symptomatic improvement and drastic recanalization.(16),(17)In recent decade there has been rise in the cases of venous thrombotic events such as CVST but very less number of reports have talked about CVST in diagnosed cases of ITP.(14),(18),(19),(20) In majority of such cases where CVST and ITP co-exist pharmacological treatment has been prioritized but endovascular intervention such as mechanical thrombectomy in selected patients can also bring about fruitful prognosis.Furthermore a systematic review of CVST described emergency mechanical thrombectomy as an effective salvage therapy with a ratio of favorable outcomes (modified Rankin Scale scores 0–2) of almost 80%.(21)There exist several endovascular techniques for MT such as catheter thrombolysis, balloon-assisted thrombectomy, stent retrievers and penumbra aspiration system with no as such intervention guiding standard protocols to ascertain the superiority of the different endovascular interventions. Our patient was treated with a combination of stent retriever and direct aspiration thrombectomy known as "Solumbra" technique.(22),(23) Patient selection for such endovascular intervention is also a major dilemma and some of the established indicators are failure of systemic anticoagulation, extensive clot burden, cerebral edema, elevated intracranial pressure, altered mental status and progressive worsening of

neurological symptoms.(21)In our case the major indicator was extensive clot burden over multiple site and severe persisting headache. With appropriate patient selection and timely intervention the desired prognosis was achieved in our case.

CONCLUSION:

There exist a draught in terms of clinical reported cases where ITP and CVST have co-existed and furthermore scarce are the endovascular intervention done in such rare concurrent cases .The aim of medical management in CVST is early recanalization of the thrombosed sinuses and thereby preventing complications. Anticoagulants are considered the standard therapy but considering the low complication rate and the clinical and radiological success, our study provides evidence supporting the efficacy and safety of MT in selected cases. More multicenter academic trials with a large sample size are needed to perform multivariable regression analyses on such low incidence rare cases with large pathophysiological heterogeneity, in order to provide reliable data on efficacy and safety of MT to guide prompt clinical decision.

Consent to participant

Written informed consent was obtained from the participant.

Consent to publish

The participant has consented to the submission of the case report to the journal.

Ethical approval

Not applicable.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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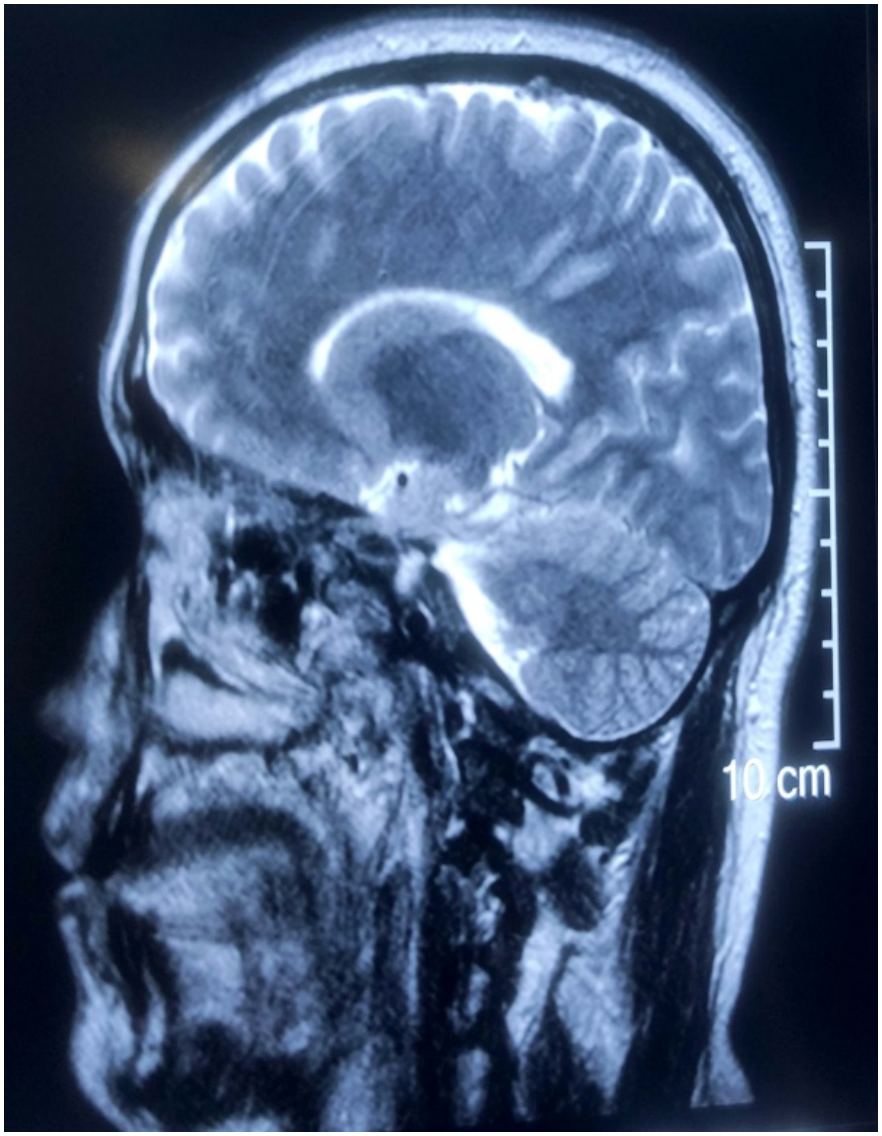

Figure A: MRI brain saggital veiw showing loss of T2 flow void, single arrow suggestive of superior saggital sinus thrombosis, double arrow suggestive of transverse sinus thrombosis.

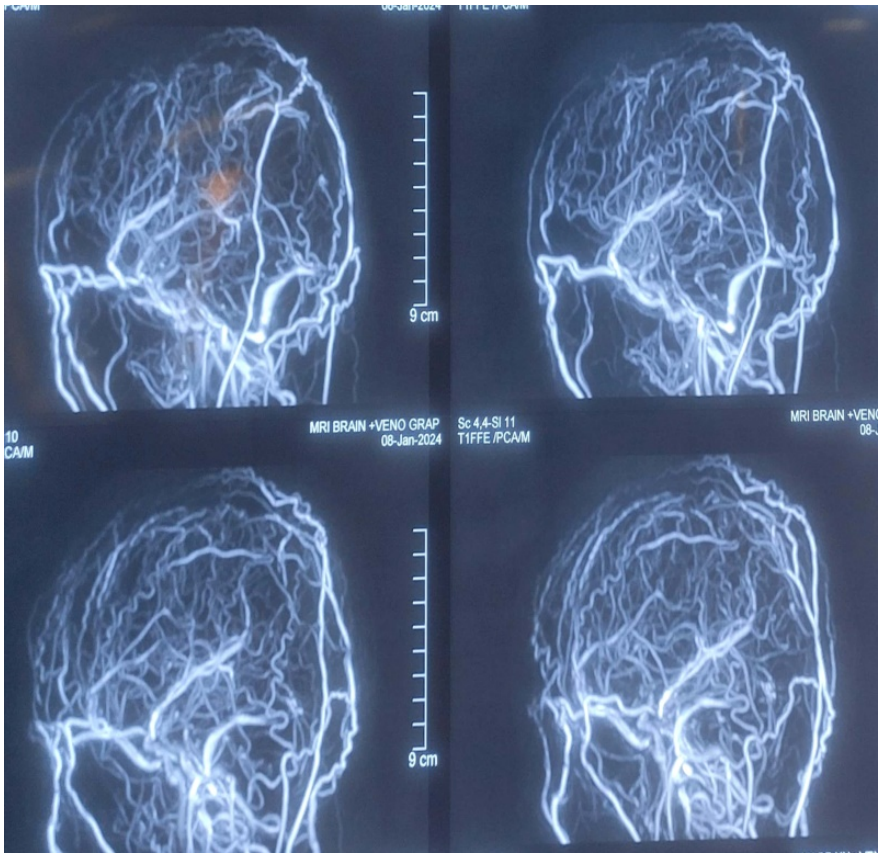

Figure B : MRV brain showing drainage from secondary channels, superior saggital sinus draining into superior middle cerebral vein which draining into cavernous sinus then to inferior petrosal sinus then to jugular vein

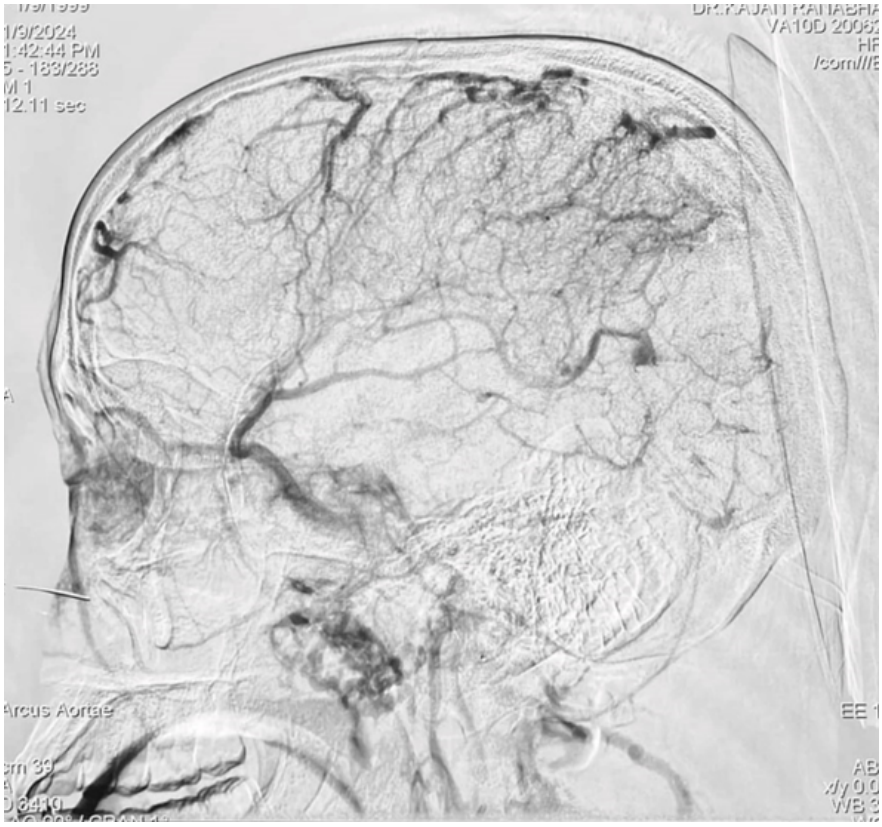

Figure C: Pre procedure venous run off showing thrombosed superior saggital vein, inferior saggital vein, transverse vein and drainage through secondary channels as depicted in figure D

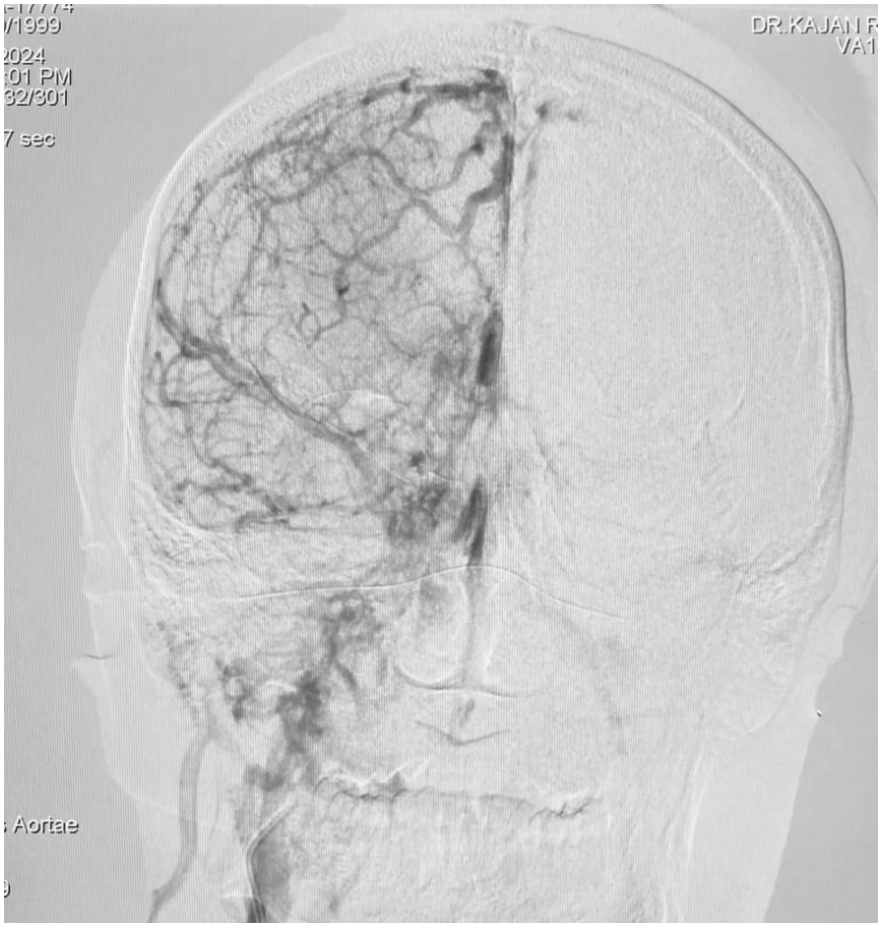

Figure D: Pre procedure venous run off shows absent superior saggital sinus, transverse sinus and drainage from secondary venous channels , superior middle cerebral vein draining into cavernous sinus then to inferior petrosal sinus then to inferior jugular vein. Visible venous strain indicative of parenchymal venous congestion.

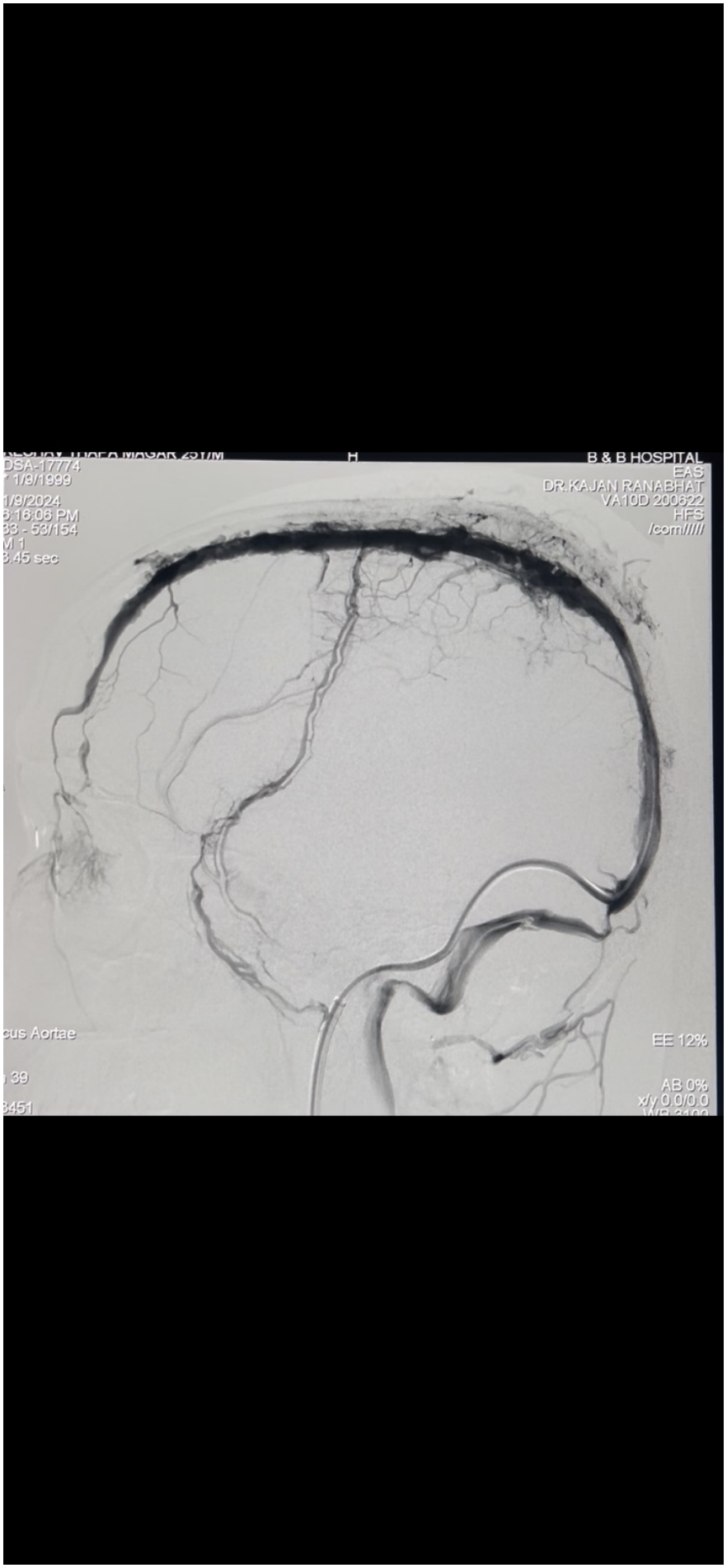

Figure E: Post mechanical thrombectomy lateral view venous run off showing opened up superior saggital sinus, transverse sinus, sigmoid sinus,torcula, patent vein of trolard and labbe and drainage to interior jugular vein.

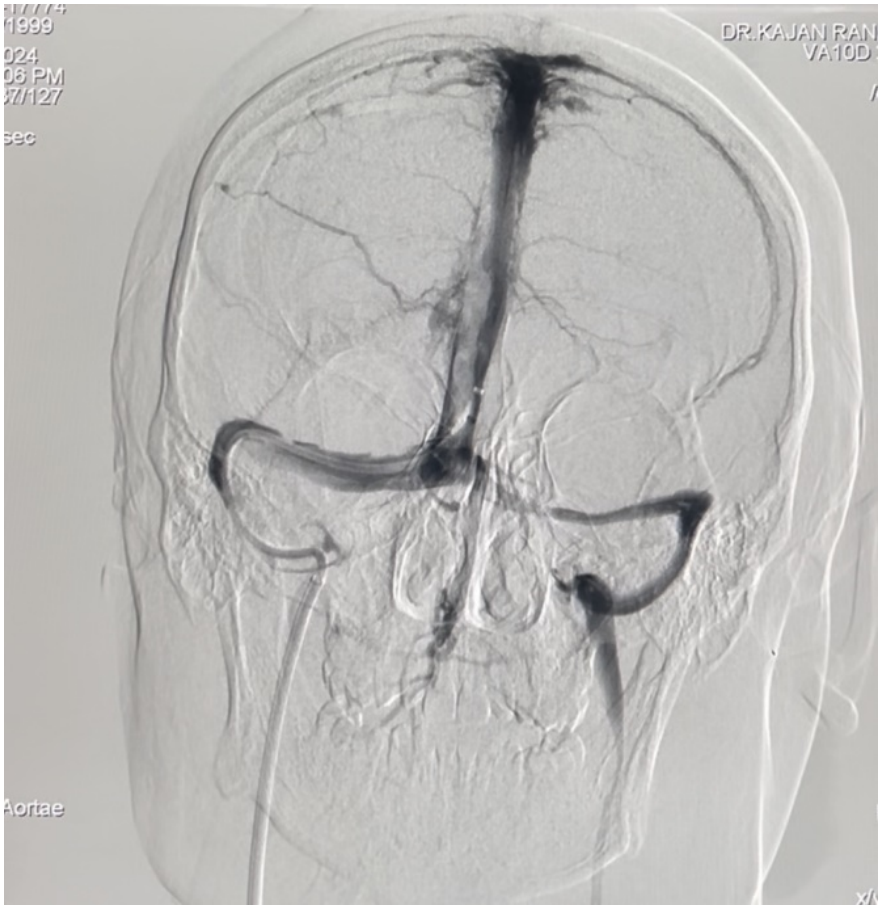

Figure F : Post mechanical thrombectomy AP view venous run off showing patent superior saggital sinus, transverse sinus,sigmoid sinus and internal jugular vein.