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Lower cranial neuropathy as a presentation of cerebral venous sinus thrombosis secondary to antiphospholipid syndrome: A case report

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ABSTRACT

Cerebral venous sinus thrombosis (CVST) is a rare cause of stroke especially among young adults. The clinical presentation of CVST is diverse, which makes the diagnosis to be challenging. Lower cranial neuropathy is a rare presentation of CVST, with few cases in literature. We are describing a case of 39-year-old male patient, presented with left occipital neuralgia, with left lower cranial neuropathies due to left transverse and sigmoid sinus thrombosis; secondary to antiphospholipid syndrome, with good response to anticoagulation.

Keywords: Antiphospholipid syndrome, Cerebral venous sinus thrombosis, Lower cranial neuropathy, Mastoid abscess

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INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is an uncommon condition characterized by the formation of blood clots in the cerebral venous system [1]. Its variable clinical presentation can result in a wide range of neurological symptoms and diagnostic challenges. This case study details an unusual case of cerebral venous sinus thrombosis in a patient who also had positive antiphospholipid antibody and underlying cervical spondylosis. There is a known association between antiphospholipid syndrome (APS) and CVST [2]. Antiphospholipid antibodies are a hallmark of APS, an autoimmune disease that raises the possibility of blood clot formation [3]. Antiphospholipid antibodies may play a role in the development of CVST in patients with APS. This correlation emphasizes how crucial it is to rule out APS as a possible underlying cause in patients who present with CVST, particularly when there are no other discernible risk factors. For patients with CVST and APS, early diagnosis and proper treatment—including anticoagulation therapy—are essential to improving outcomes [4].

CASE REPORT

A 39-year-old male, known case of cervical spondylosis for two years with no other previous illnesses, was referred from primary health center to the Emergency Department (ED) with severe headache and high C-reactive protein (CRP). The patient complained of a headache for the last three days. He denied difficulty of speech, vision, or gait. No abnormality was revealed in the computed

tomography (CT) brain which was done in the ED. He was treated with metoclopramide and tramadol injection in the ED and follow-up appointment was given in the Neurology clinic.

Next day he was seen in the Neurology clinic and on taking detailed history he complained of a severe headache for the last four days which started two days after heavy exercise. Headache was mainly in the occipital region radiating to the vertex on the left side associated with nausea, cough, profuse sweating, and numbness in the limbs. He denied blurring of vision, limb weakness, and gait disturbances. On physical examination he looked distressed and was wearing a solid neck collar. Cranial nerves were intact apart from left tongue deviation on protrusion but he could move it to both the sides. There was no fasciculation, no atrophy, uvula was central and intact gag reflex. There was also no focal weakness, no sensory deficit, and no cerebellar signs. Although plantar responses were left extensor and right downgoing. He was advised for admission for further investigation, but refused and asked to do a magnetic resonance imaging (MRI) brain to rule out subarachnoid hemorrhage and CT angiography head to rule out arterial dissection. Computed tomography angiography head with and without contrast showed no evidence of arterial dissection (Figures 1 and 2). Plain MRI examination of the brain incidentally noted a small left choroidal fissure cyst, and mild bilateral maxillary sinusitis with hypertrophied nasal turbinates.Otherwise, it was an unremarkable MRI examination of the brain (Figure 3). Three days later, he presented with the same complaints and was admitted to the hospital for further workup of headache. After admission he complained of dysphagia. On physical assessment there was uvula deviation to the right side,denoting left 9th cranial nerve injury, and tongue deviation to the right, denoting left 12th cranial nerve injury. There was no weakness in trapezius muscle or sternomastoid, no syncopal attacks, only hypoesthesia at C6 radicle distribution. There were also no signs of Horner syndrome and negative signs of meningeal irritation. He denied any ear pain or vesicles.

Some biochemical indications revealed mild abnormalities, such as elevated white blood cell (WBC) 13.03 × 10(3)/mcL (normal range, 4.0–10.0 × 10(3)/mcL), procalcitonin test (PCT) 0.11 ug/L (normal range, ≤0.10 ug/L), C-reactive protein (CRP) 116.4 mg/L (normal range, 0.0–3.0 mg/L), erythrocyte sedimentation rate (ESR) 52.00 mm/h (normal range, 0.0–15.0 mm/h). Since ESR was elevated, a vasculitic screen was done.

Then the decision to do Lumbar puncture was taken and cerebrospinal fluid (CSF) analysis showed high protein 904.3 mg/L (150.0–450.0 mg/L) and lymphocytes. Gram stain and acid fast bacillus (AFB) were unremarkable and polymerase chain reaction (PCR) for Herpes simplex virus (HSV) negative results came after a few days. Viral screening showed Epstein–Barr virus (EBV) capsid antigen IgG and EBV nuclear antigen IgG positive. Epstein–Barr virus capsid antigen IgM was negative, and Varicella zoster virus antibodies IgG was 953 (normal range, <100). Based on this report he was started on acyclovir 10 mg/kg TID.

At this point, differential diagnoses were: acute onset headache with progressive lower cranial neuropathy, arterial dissection (excluded by CT angiography), and subarachnoid hemorrhage (excluded by CT brain and MRI).

After admission, magnetic resonance venography (MRV) examination of the brain was done which was unremarkable. Magnetic resonance imaging brain with contrast showed: small left choroidal fissure cyst, bilateral anterior inferior cerebellar artery vascular looping; chavda III classification, and a left sigmoid and adjacent internal jugular vein intraluminal filling defect most probably representing venous thrombosis (Figure 4). Based on the symptoms and the investigation results, final diagnosis of cerebral venous sinus thrombosis was made.

Until the rest of the results were yet to come, Dexamethasone 4 mg ter in die (TID), Oxcarbazepine 300 mg bis in die (BID), Paracetamol 500 mg/ Orphenadrine 35 mg BID, and Tramadol 50 mg pro re nata (PRN) were given.

Vasculitis workup showed positive antiphospholipid antibody and positive cardiolipin IgG. Whereas IgM, lupus anticoagulant, antinuclear antibody (ANA), and double stranded DNA (DSDNA) were negative. He was consulted by rheumatologist and planned to repeat antiphospholipid antibodies after three months. Seven days after admission he was discharged home on anticoagulant warfarin, gabapentin, Paracetamol Orphenadrine tablets.

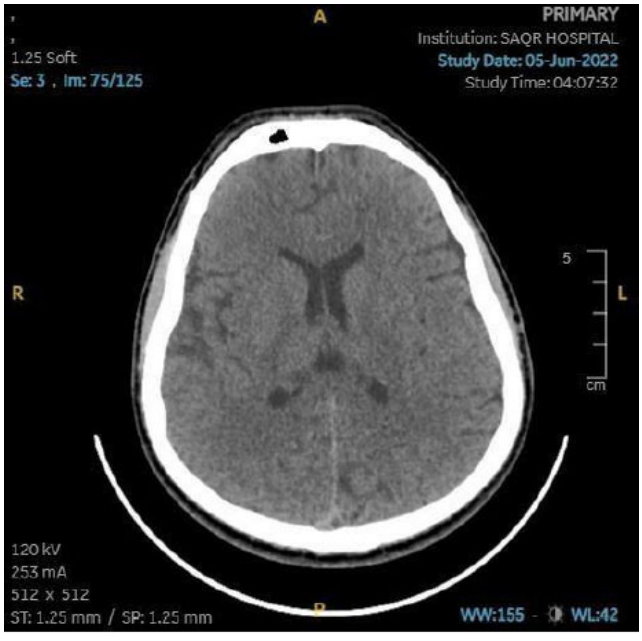

Figure 1: CT head or brain w/o contrast results of the patient, showing normal density of the gray and white matter with no definite focal or diffuse pathology. No intracranial bleed or hematoma. No intracranial space-occupying lesions.

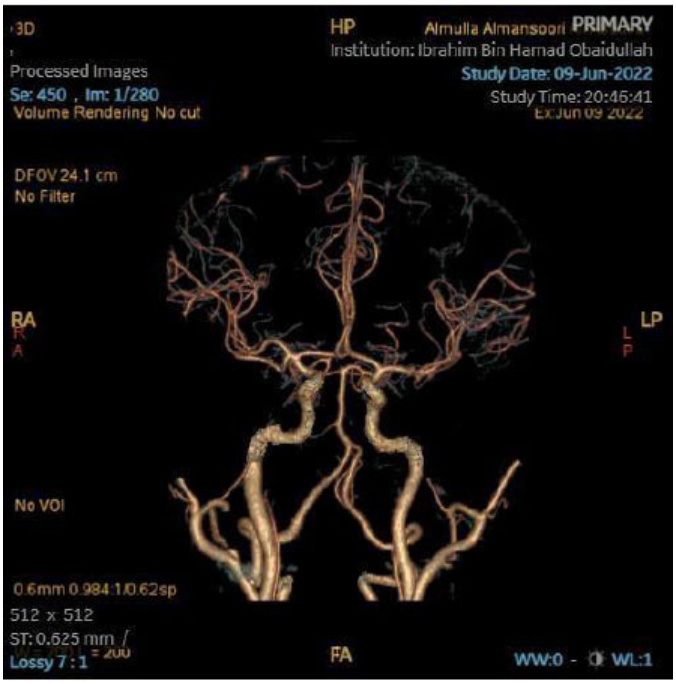

Figure 2: CT angiography head w/ + w/o contrast results of the patient, showing normal CTA angiography of the extra and intracranial carotid and vertebrobasilar arterial systems study with no evidence of arterial dissection.

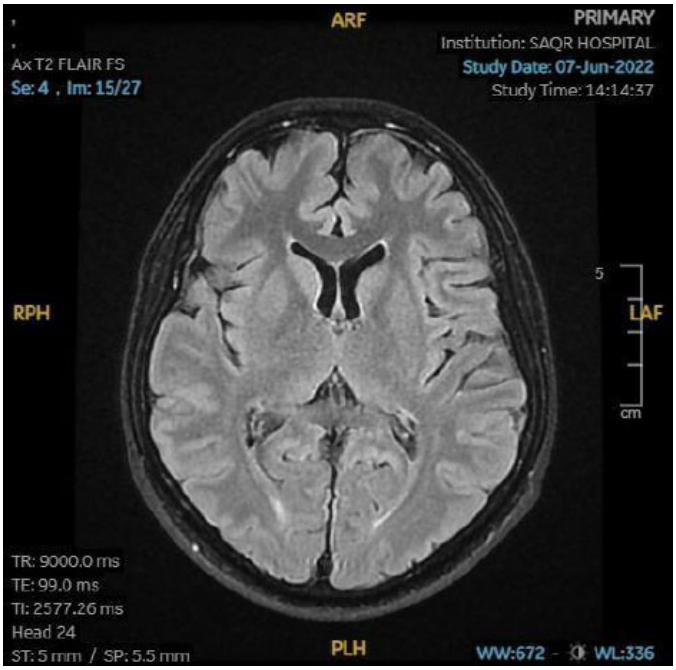

Figure 3: MRI brain w/o contrast result of the patient, showing small left choroidal fissure cyst, mild bilateral maxillary sinusitis with hypertrophied nasal turbinates. Otherwise, an unremarkable MRI examination of the brain.

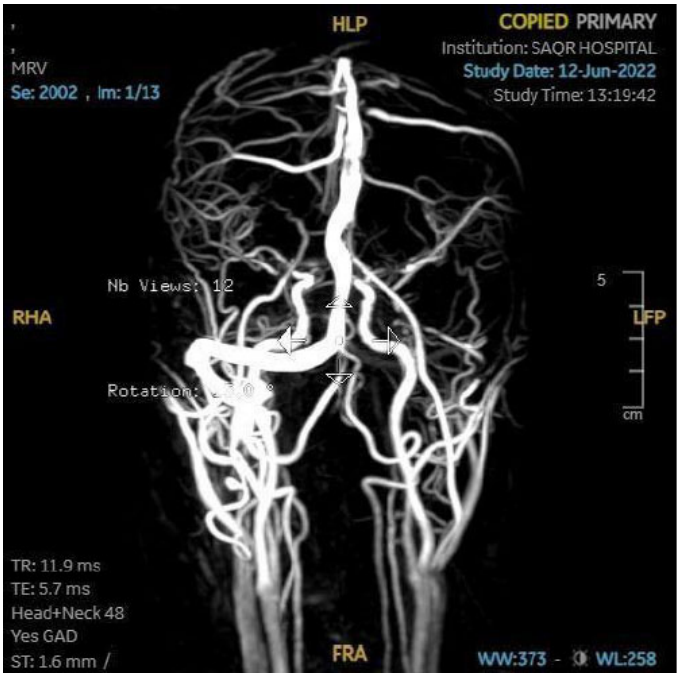

Figure 4: MRV examination of the brain result of the patient showing hypoplastic left transverse and left sigmoid venous sinuses (normal variant). Unremarkable MRV of the brain.

After discharge, on his first follow-up in the clinic he still complained of headache. On physical examination swallowing was better and his tongue weakness decreased significantly. His international normalized ratio (INR) was 8 thus warfarin was stopped for time being then resumed warfarin 4 mg daily when INR reached 1.77 on the next visit.

After three months, he presented with similar complaints. On extensive investigations that were done in a tertiary hospital, a left mastoid bone abscess was found and a biopsy was taken. Cultures were negative. He was started on ceftriaxone and metronidazole for four weeks treatment and continued warfarin 6 mg daily. A follow-up MRV report showed complete resolution of the sigmoid sinus thrombosis (Figure 5). He was kept on anticoagulant therapy with warfarin and regular blood tests to monitor the effect of anticoagulation.

Follow-up blood tests for antiphospholipid antibodies at three and six months for lupus anticoagulants were repeatedly positive. There was mild residual left tongue weakness persistent. But there was no other focal deficit, speech difficulty, or swallowing defect. He was regularly following-up in the neurology clinic without any new complaints and is on 5 mg warfarin. Follow-up after six months showed complete recanalization of sigmoid sinuses.

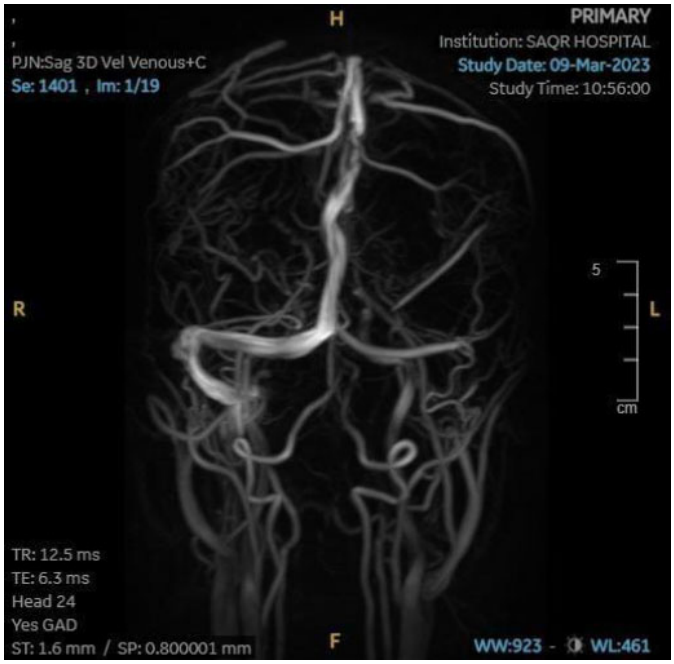

Figure 5: Enhanced MRI and MRV examination of the brain result of the patient in follow-up showing remarkable regressive course regarding the extent of the previously depicted intraluminal sizeable filling defect within left sigmoid venous sinus and scanned left internal jugular vein only remaining minute intraluminal filling defect within left sigmoid venous sinus in the current study.

DISCUSSION

About 5 people per million suffer from cerebral venous sinus thrombosis (CVST), which makes up 0.5–1% of all strokes. It is a rare and often undiagnosed form of stroke [5]. It is more prevalent in younger people. As per the findings of the largest cohort study, the International Study on Cerebral Venous and Dural Sinuses Thrombosis (ISCVT), patients under 50 years of age accounted for 487 (78%) out of 624 cases [5, 6]. Due to its nonspecific and variable clinical manifestations, which include a wide range of symptoms like headache, focal neurological deficits, seizures, and altered mental status, it is still very difficult to diagnose CVST early and accurately in clinical practice [7].

Antiphospholipid syndrome (APS) is a systemic autoimmune disease that can leadto cerebral venous and arterial thrombosis. This condition can develop early in the course of the disease or as a presenting symptom [8]. Our case study includes comprehensive clinical features, radiological findings, laboratory results, treatment plans, and CVST outcomes for a 39-year-old male patient with APS. The patient initially presented with a chronic occipital headache, which later progressed to the development of specific neurological symptoms like tongue deviation on protrusion.

The etiology of CVST is complex, just like that of any thrombosis. At least one risk factor is found in 85% of patients, the interaction of multiple risk factors causes 50% of events, and a small percentage of cases are still idiopathic [6, 9]. The primary pathophysiological mechanism of CVST is the disproportion between fibrinolytic and venous thrombosis mechanisms. Cerebral venous sinus thrombosis may result from any illness that causes the blood to become hypercoagulable, abnormal venous blood flow, or an inflammatory reaction in the venous wall. A variety of factors, both infectious and non-infectious, contribute to the multifactorial and diverse etiology of CVST [10].

Meningitis, mastoiditis, otitis media, sinusitis, and infections of the skin and gums are the main infectious factors associated with CVST. Non-infectious factors include autoimmune diseases (such as systemic lupus erythematosus, Behçet's disease, and vasculitis), malignancies, nephrotic syndrome, hematological diseases, and oral contraceptives.

Hereditary prothrombotic conditions include protein S deficiency, protein C deficiency, and antithrombin III deficiency. There have been numerous reports of COVID-19 infections leading to intracranial venous sinus thrombosis recently [11–15]. When COVID-2019 infection results in endothelial dysfunction, platelet adhesion, leukocyte aggregation, complement activation, and cytokine release occur, all of which contribute to microvascular thrombosis [14]. Antiphospholipid antibody syndrome (APLS) was the risk factor in this patient.

A consequence of APS is CVST, which is primarily caused by prothrombotic states and decreased clot dissolution. About 6–17% of patients with CVST are caused by APS [16]. Most of the pathogenesis of CVST in APS is still unknown. Research indicates that the synthesis of APLS, which target cerebral venous and platelet in APS, is linked to CVST [13–17].

The identification, diagnosis, and treatment of CVST depend more and more on diagnostic imaging. Further MRV screening is necessary when the results of the head CT and cranial MRI are normal, as CVST cannot be completely ruled out [18]. Both the MRV and cranial MRI exams are easy to use and can make up for each other's shortcomings. Our patient underwent a combined cranial MRI and MRV examination, which has been shown to be an effective tool for the clinical diagnosis and prognosis of CVST [19].

Throughout the acute phase, anticoagulation serves as the primary therapeutic option and standard of care for patients with CVST [20, 21]. Anticoagulation therapy works well to stop the spread and progression of thrombosis, lower systemic hypercoagulability in CVST patients, and stop CVST from recurring. Guidelines for CVST state that regardless of whether they have experienced intracranialhemorrhage, patients with CVST who do not have a contraindication to anticoagulation should begin anticoagulation treatment as soon as possible [22]. Regular heparin and low molecular weight heparin (LMWH) are anticoagulants that are frequently given

to CVST patients during the acute phase. Subcutaneous LMWH doses that are adjusted based on patient weight have been shown to be more effective and have a lower riskof bleeding than plain heparin [23].

Patients with CVST should usually continue long-term treatment with oral anticoagulants, most commonly warfarin, after the acute phase of anticoagulation. Theoretically, LMWH should be discontinued after maintaining an INR of two tothree, and warfarin should be repeated with it for three to five days. In accordance with the INR, the warfarin dosage should also be changed on a regular basis to keepthe INR between two and three [24].

Nevertheless, individual genetic factors, triggers, recurrence, follow-up, and potentialbleeding risk should all be taken into account when determining the length of oral anticoagulant therapy. Our patient responded to treatment very well. Thus, one of the study's main strengths is the patient's excellent treatment outcome. However, since this is a case study of a single person, no generalizations or suggestions can be made, which means that our study has certain limitations as well.

Neurologists, neurosurgeons, emergency physicians, internists, oncologists, hematologists, pediatricians, obstetricians, and family practitioners may all encounter CVT. Therefore, for the quick diagnosis and treatment of such cases, amultidisciplinary approach is needed.

CONCLUSION

This case study highlights the significance of ruling out cerebral venous sinus thrombosis as a possible diagnosis in patients who exhibit severe acute headaches, neck pain, and related neurological symptoms. It also emphasizes how crucial a thorough assessment is for the best possible patient care and successful results, along with the importance of extensive investigations, imaging studies, and prompt multidisciplinary interventions. To fully understand the underlying mechanisms and potential, more research is necessary.

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Author Contributions

Aaisha Mohammed Rafi – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Karuna Khan – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Ammar Alomar – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Aya AlSayyad – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Nahla Yousef – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.