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CASE REPORT OPEN ACCESS

CEREBRAL VENOUS SINUS THROMBOSIS WITH GOOD RESPONSE TO HEPARINIZATION THERAPY: TWO CASE REPORT AND DIAGNOSTIC ALGORITHM

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ABSTRACT

Cerebral venous sinus thrombosis (CVST) is an uncommon condition of cerebral venous sinus thrombosis with a varied clinical presentation that can be diagnostically challenging. Intravenous heparin is the optimal immediate anticoagulant according to the European Academy of Neurology (EAN) guideline 2017. This report aims to describe highly suspicious CVST clinical features and suggest a diagnostic algorithm based on two cases of CVST found in our center. The first case is a 52-year-old man who presented with serial seizures preceded by subacute headache and diparesis. Non-contrast head CT (NCCT) showed multifocal haemorrhages and cord signs. The second case is a 19-year-old woman who presented with slowly decreased consciousness, headache, and a history of upper respiratory infection. Diffuse cerebral edema was revealed in NCCT. Both of these patients had thrombosis in superior sagittal sinus, right transverse, and sigmoid sinus. Heparinization was conducted and continued with rivaroxaban with a good response. CVST is rare case and often unrecognized; since it has serious complications, early diagnosis and treatment improve prognosis and survival.

Keywords: Cerebral venous sinus thrombosis, heparinization, venous occlusion, algorithm

Introduction

Cerebral venous sinuses thrombosis (CVST) is a rare condition of cerebral venous sinuses thrombosis estimated to be 1,3 in 100.000 persons; however, it may be caused by unrecognized due to its varied clinical features that mimic other conditions.[1–3] The most common symptom of CVST is headache (80-90%), followed by seizures (39,3%), paresis (37.2%), motor deficit (19,1-39%), papilledema (28,3-84,6%), aphasia (19-24%), visual impairment (13,2%), altered consciousness (20-30,6%), and cranial nerve palsy (12%).[4–6] This variety of clinical features of CVST depends on thrombosis sites caused by underlying pathological conditions due to an imbalance of prothrombotic and fibrinolytic processes.[2,7–9]

According to the EAN 2017 guideline for CVST, acute anticoagulation treatment with heparin or low-molecular-weight (LMWH) heparin is recommended for all types of CVST, including intracerebral haemorrhages.[10] Herein, we report two cases of CVST with different clinical features, one of them had intracerebral haemorrhages; however, both cases received heparinization and showed recovery.

Case Report

Case 1

A 52-year-old man is presented with a serial seizure, preceded by a one-week history of headache and diparesis with unremarkable past medical history. He had global aphasia, left facial nerve palsy, and bilateral weakness, predominantly on the right side. Emergency NCCT revealed multifocal haemorrhages in the left frontoparietal, hyperdense sign, cord sign, and brain swelling (Figure 1a), with a high D-dimer level (8.919 ng/mL). Thorax X-ray was normal. The next day, head CTV was conducted since he had an uncontrolled serial seizure. It revealed cerebral oedema, bilateral multifocal bleeding spot, cord sign, empty delta sign, and filling defect in the superior sagittal sinus, right transverse, and sigmoid sinus concerning cerebral venous thrombosis (Figures 1b-c).

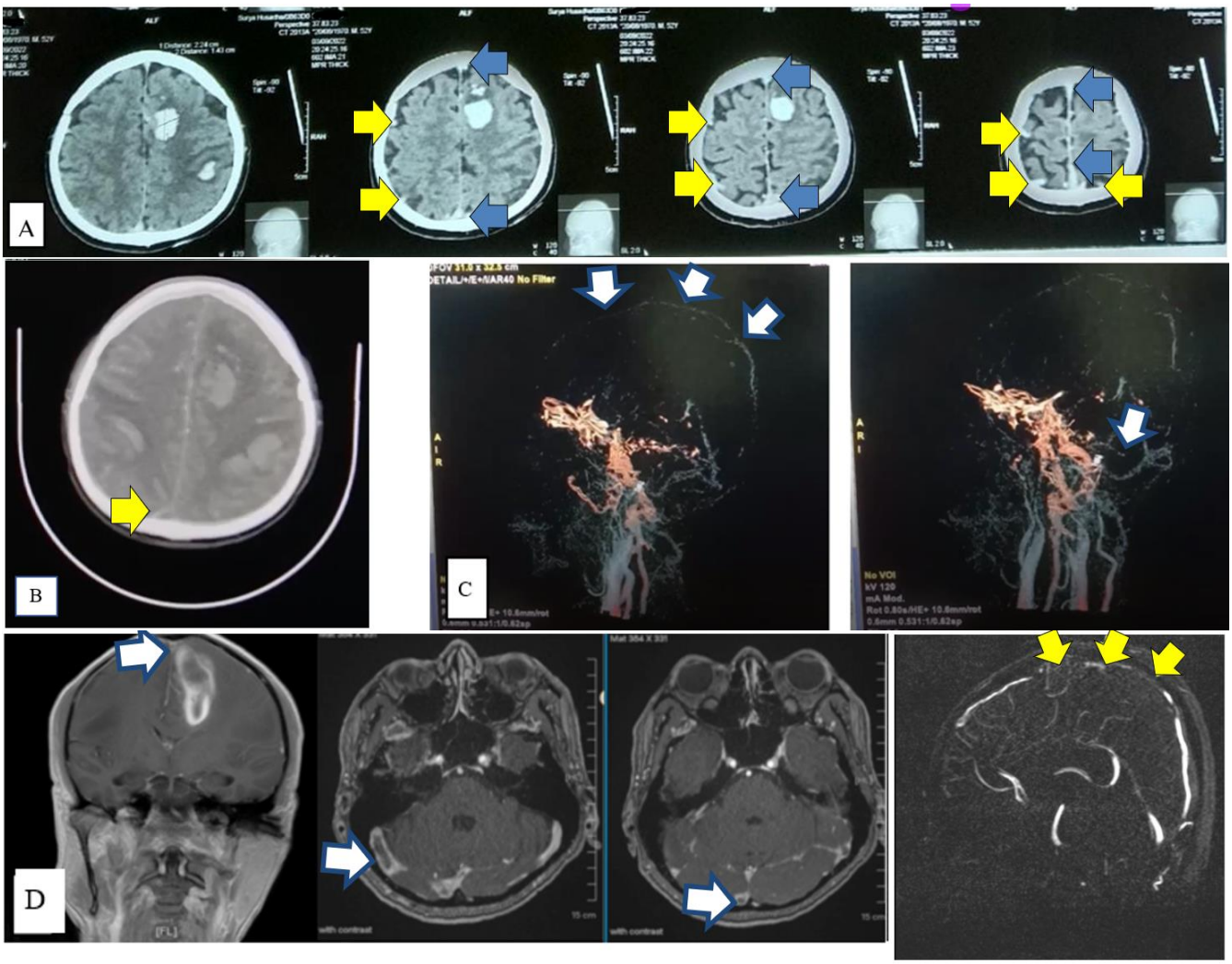

Figure 1. Case 1. **(a)** First Axial NCCT shows multifocal haemorrhages in the left frontoparietal, hyperdense sign (blue arrow), and "cord sign" (yellow arrow). **(b, c)** CTV shows an "empty delta sign" in the superior sagittal sinus (yellow arrow) and a filling defect in the superior sagittal sinus, right transverse, and sigmoid sinus (white arrow). **(d)** Follow-up MRV 1-month onset reveals an empty delta sign in the superior sagittal sinus, right transverse, and sigmoid sinus (white arrow) and a filling defect in the superior sagittal sinus (yellow arrow)

Case 2

A 19-year-old woman is presented with an altered consciousness, preceded by delirium to semicoma and history of throbbing bilateral headache three days before onset. She had an upper respiratory infection two weeks before unconsciousness.

She had no relevant past medical history. In the emergency department, the patient was semicoma, febrile (100.580F), tachycardia, and tachypnea with peripheral oxygen saturation of 96%. There is no stiff neck or abnormal neurological deficits. The routine laboratory examinations demonstrated leukocytosis (18.500 cells/uL) with neutrophilia, increased liver function, and respiratory alkalosis. The serum electrolyte was standard. The D-dimer level was increased (2657 ng/ml). Emergency NCCT demonstrated diffuse cerebral oedema (Figure 2a). Lumbar puncture was routine. On the fourth day after admission, CT venography showed thrombosis of the right transverse sinus and sigmoid sinus (Figure 2b). ANA-IF test showed a negative result.

Both patients were diagnosed with CVST and immediately treated with intravenous Unfractionated Heparin/UFH. Heparinization was started with bolus doses (50-70 IU/kg), a maintenance dose of 10-15 IU/kg for five days, and continued with rivaroxaban 20 mg twice daily. Follow-up imaging was performed. Patient 1 had a one-month onset of Magnetic Resonance Venography (MRV) revealed incomplete recanalization (Figure 1d). Even the follow-up CTV 15 days onset of patient 2 did not show any recanalization; however, the patients were markedly improved clinically. Patient 1 had no recurrent seizures one day after treatment. Patient 2 was extubated, then fully conscious and alert without neurological deficits on the fourth-day post-heparinization. Digital Subtraction Angiography (DSA) was considered in patient two. Thrombocytopenia was noted in patient 1 (114.000 cells/uL); however, no significant bleeding occurred.

Both patients were diagnosed with CVST and immediately treated with intravenous Unfractionated Heparin/UFH. Heparinization was started with bolus doses (50-70 IU/kg), a maintenance dose of 10-15 IU/kg for five days, and continued with rivaroxaban 20 mg twice daily. Follow-up imaging was performed. Patient 1 had a one-month onset of Magnetic Resonance Venography (MRV).

Discussion

CVST commonly affects young patients, especially females; however, it can be found in all age and gender groups with acute, subacute, or chronic clinical onset.[2,11] Clinical manifestations of CVST and its severity can be seen depending on the venous and sinuses involved, brain injury, and intracranial pressure.[2]

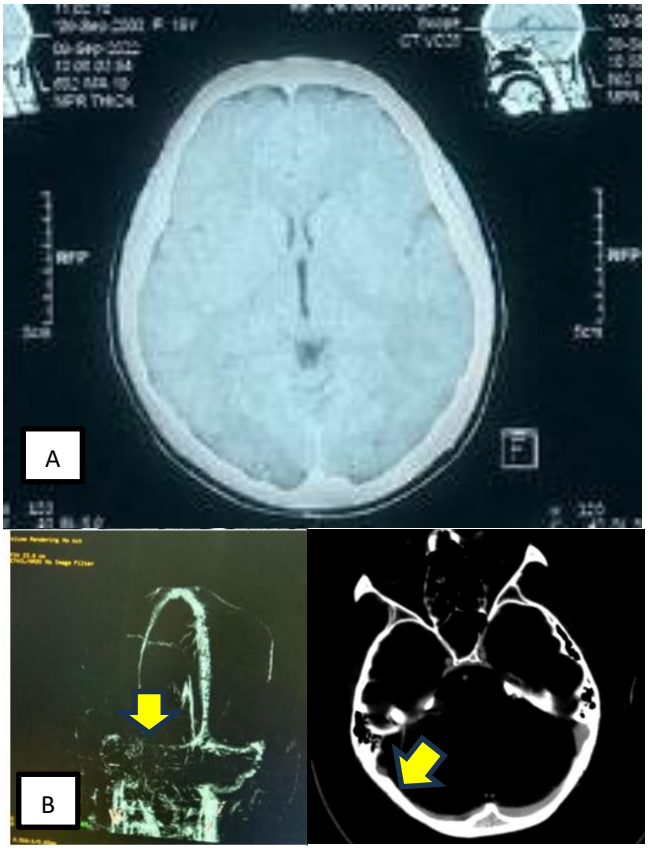

Figure 2. Case 2**.** Axial NCCT shows **(a)** diffuse brain oedema. Early CTV **(b)** reveal: a filling defect in the right transverse and sigmoid sinus (yellow arrow) and inhomogenous enhancement right transverse sinus (yellow arrow).

Khan et al. (2020) conducted a descriptive study on 54 patients with CVST. They revealed that the most common thrombosis site was the transverse sinus (54,5%), sigmoid sinus (51,5%), superior sagittal sinus (45,5%), and straight sinus (15,1%); however, 66.6% of patients had multiple sinuses involved.[11]

Some clinical considerations, such as the patient's characteristics, any risk factors, clinical onset and manifestation, head CT features, and supporting examinations, help neurologists to identify CVST. Some clinical features are red flags for CVST, such as new or different pattern headaches, papilledema, stroke-like focal deficits, altered consciousness, and seizures.[2,4,8] CVST risk factors should be identified, such as oral contraceptives, pregnancy or puerperium, malignancy, anaemia, infection, chronic inflammation, trauma, or heritable thrombophilia.[1,2] There is at least one risk identified in 85% of cases of CVST; however, the hypothesis of multiple hits might be considered.[1,12] Emergency head CT can visualize thrombosis in around 70% of cases, such as direct (dense clot sign, string or cord sign, empty delta sign) and indirect features (cerebral oedema, mass effect, venous infarction, cortical, juxtacortical, or subarachnoid hemorrhagic, or infarct hemorrhagic).[2,4,8]

CTV/MRV helps confirm thrombosis since it has a high sensitivity to visualize thrombus as lumen-based; however, DSA, a flow-based neuroimaging, is a gold standard. D-dimer can be increased in CVST, but it has a high negative predictive value in patients with isolated headaches, so it is necessary to exclude CVST in its condition.[2,4]

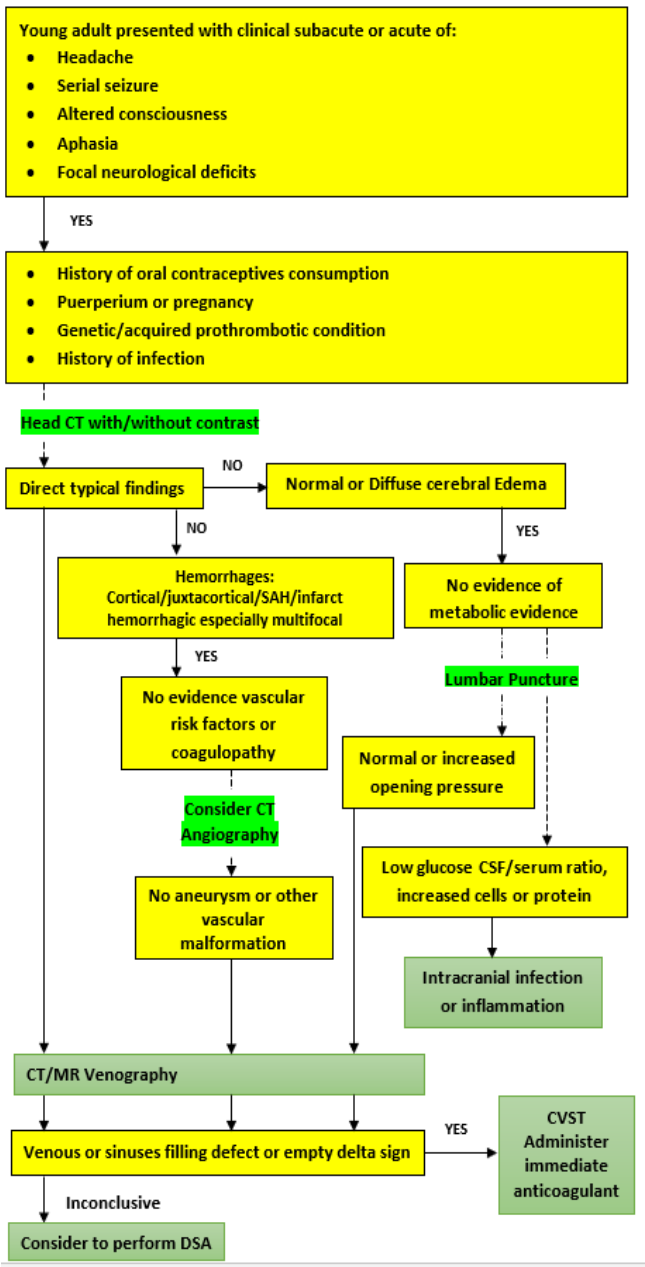

Figure 3. Suggested diagnostic algorithm of CVST. CVST, cerebral venous sinuses thrombosis; SAH, subarachnoid haemorrhages; CSF, cerebrospinal fluid; MR, magnetic resonance; CT, computed tomography; DSA, Digital Subtraction Angiography.

Our cases of CVST presented different characteristics and significant clinical features, such as serial seizure, decreased consciousness, and history of headache and infection, then reinforced by standard lumbar puncture and increased D-dimer level. Even though both cases had different features, especially intracerebral haemorrhage in case one, the new guideline of the EAN 2017 recommends acute anticoagulation for immediate therapy of CVST and

applies to CVST with hemorrhagic. LMWH was suggested; however, UFH was preferred in these cases because it can be titrated on the target and has an antidote. The patient had a favourable clinical outcome, meaning a good prognosis if treated immediately and appropriately.[8,10] The lack of thrombophilia examination due to its availability is the limitation of this report. According to this report and previous clinical evidence, a diagnostic algorithm of CVST have been made to help clinicians in suspicious case (Figure 3).

Conclusion

CVST can be unrecognized due to its varied clinical features. Diagnosis of CVST is made using clinical onset and manifestation, any risk factors, reinforced with neuroimaging. CT/MR venography has a high sensitivity to confirm thrombosis. Immediate diagnosis and treatment provide a favourable prognosis and survival rate.

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