Bahrain Medical Bulletin, Vol. 35, No. 4, December 2013

Cerebral Venous Thrombosis and Cerebral Infarction: A Rare Disease with a Rare Cause

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We present a case of cerebral venous thrombosis and cerebral infarction associated with diabetic ketoacidosis. The patient presented with vomiting, headache, lethargy and altered sensorium. CT venography provided the final diagnosis; therefore, anticoagulant was used, which resulted in the improvement of neurological outcome. Neurological deterioration during an episode of diabetic ketoacidosis is usually assumed to be caused by cerebral edema. Neuroimaging should always be performed in suspected cerebral edema associated with diabetic ketoacidosis in order to exclude other pathologies.

Bahrain Med Bull 2013; 35(4):

Cerebral venous sinus thrombosis (CVT) is a blood clot formation in the dural venous sinuses, which drain blood from the brain. This could result into impaired venous drainage and consequently lead to intracranial hypertension and/or cerebral infarcts.

CVT is an uncommon condition. It often affects young to middle aged patients and more common in women. More than hundred causes of cerebral venous sinus thrombosis have been identified in the scientific literature[1]. However, even with extensive investigation, no cause is identified in 20-25% of cases[1]. Clinical presentation can be extremely varied and symptoms can evolve over hours to few weeks. The most frequent symptoms and signs are headache in 70-90% of cases, focal seizures with or without secondary generalization, paresis (uni or bilateral), papilledema, and impairment of consciousness or coma[1,2].

Investigations should focus on establishing the diagnosis and searching for underlying causes[3]. Magnetic resonance imaging (MRI) combined with magnetic resonance venography (MRV) is the gold standard investigation to diagnose this rare condition and has largely replaced invasive cerebral angiography and conventional computed tomography (CT). The prognosis of cerebral venous sinus thrombosis is generally favorable if diagnosed in time[4].

The aim of this report is to present a case of cerebral venous sinus thrombosis associated with DKA and to raise awareness among physicians about this rare but difficult condition and to have high index of suspicion.

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THE CASE

A thirty-eight-year-old female who had been previously fit and well presented to the Emergency department with 12 hours history of vomiting, headache, lethargy and altered sensorium.

On admission, she was pale, afebrile, moderately dehydrated, and slightly confused. She was stable hemodynamically. No infective focus was found on clinical examination and no focal neurological manifestations were found. Admission laboratory studies revealed increased random blood glucose of 27 mmol/L, with a compensated metabolic acidosis (pH 7.24, pCO2 3.4 KPa, bicarbonate 14 mmol/L, base excess-12 mmol/L). Anion gap was calculated as 28 mmol/L. Urinalysis showed ketones of 21 mmol/L. Renal, liver and electrolyte profiles were within normal range. Chest X-ray was normal with clear lung fields bilaterally. A diagnosis of diabetic ketoacidosis (DKA) with moderate dehydration was made and the patient was transferred to the intensive care unit (ICU) for further management.

In ICU, standard treatment for DKA was started with intravenous fluids and insulin but the patient became more irritable. She was immediately intubated to secure the airway and commence mechanical ventilation. Remifentanil infusion was started for sedation but the patient remained agitated despite an improvement in ketoacidosis.

An urgent CT scan of brain and chest was performed which revealed diffuse bilateral cerebral edema, which was immediately treated with mannitol (0.5 g/kg). Piperacillin/Tazobactam 4.5g was given every 8 hours as the CT chest showed left lower lobe infiltrates. The patient remained intubated and sedated for the next 2 days and showed little signs of improvement of her agitation despite improved metabolic elements. Follow-up CT brain was arranged on the third day, which revealed brain edema with suspicious venous sinus thrombosis associated with prominent cortical veins. Therapeutic dose of enoxaparin (1 mg/kg/12h) was given. CT brain venogram was performed on the fourth day, which confirmed venous sinus thrombosis involving the superior sagittal sinus, straight sinus, transverse sinus, confluence of sinus and right sigmoid sinus. Figure 1 revealed empty delta sign, which is the most frequently seen CT sign of sagittal sinus thrombosis[5].

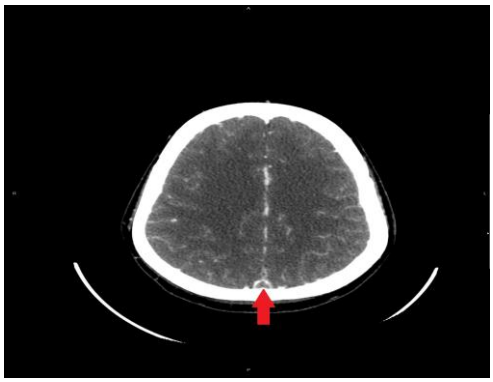

Figure 1: CT Brain with IV Contrast: Empty Delta Sign

On day seven, the patient showed neurological improvement and started to have purposeful movements. She was weaned successfully from mechanical ventilation. On day ten, right-sided weakness was noted with no change in pupillary response. MRI and MR angiogram (MRA) of the brain were performed, which revealed cerebral venous sinus thrombosis

involving the superior sagittal and both transverse and right sigmoid sinuses, with acute infarction involving the left frontal and left temporo-occipital region, see figure 2. She remained in ICU for another 3 days and was discharged to the ward where she made a full motor recovery of her involved limb. The patient was discharged from hospital with prophylactic dose of Warfarin for 3 months with target international normalized ratio (INR) of 2-2.5.

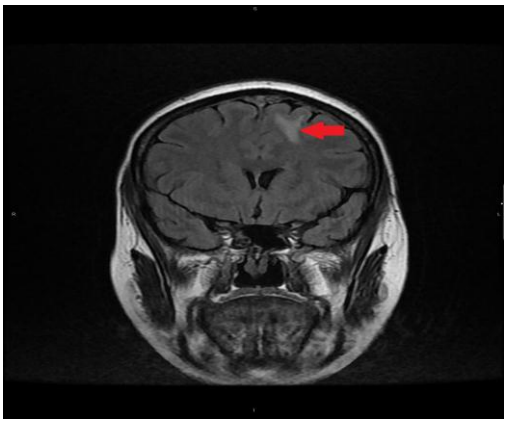

Figure 2: MRI Brain Acute Left Temporo-occipital Infarction

DISCUSSION

This is the first published report of central venous sinus thrombosis occurring in association with DKA in the Middle East. Cerebral venous sinus thrombosis (CVT) is a blood clot formation in the dural venous sinuses, which drain blood from the brain.

Cerebral venous sinus thrombosis is not an easy condition to diagnose as it can present with varying signs and symptoms. It is more prevalent in young pregnant females in puerperium and those on oral contraceptive pills. Any age group can be affected by this condition but other studies have found that the mean age is between 37 and 38 years[1,2].

The main cerebral venous sinuses affected by CVT are the superior sagittal sinus (72%) and the lateral sinuses (70%). In about one-third of cases more than one sinus is affected[3]. In a further 30-40%, both sinuses and cerebral or cerebellar veins are involved[1,3].

Predisposing factors can be identified in up to 80% of patients[4]. Numerous conditions can cause or predispose to CVT and often more than one cause will be found in an individual patient. Causative factors can be categorized as infective and non-infective. There has been a decline in infective causes because recent studies showed that they are responsible for only 8% of the cases[1,2]. Cavernous sinus is typically affected followed by *staphylococcal* infection of the face[1]. Systemic conditions such as connective tissue diseases, malignancies and dehydration are most common among the non-inflammatory causes[1,5]. It is estimated that Bechet's disease may be responsible for up to 25% of cases in the Middle East[6].

CVT presents with a wide range of symptoms and signs. Headache is the presenting symptom in 70-90% of cases[1,2,4]. Focal deficits such as hemiparesis and hemisensory disturbance, seizures, impairment of level of consciousness and papilloedema occur in one-third to three-quarters of cases[1,7].

Investigations should focus on establishing the diagnosis and searching for underlying causes. Conventional CT scan has been largely replaced by MRI combined with magnetic resonance venography (MRV). The latter will, however, often remain the first imaging modality to be used simply due to availability and also to exclude other conditions such as intracerebral hemorrhage or abscess. CT is entirely normal in 10-20% of cases with proven CVT[1].

Intravenous heparin should be the first-line of treatment, even in the presence of hemorrhagic infarction, provided there are no general contraindications to its use[1,8]. If the patient deteriorates despite adequate heparinization or presents in comatosed condition, selective catheter-guided local thrombolysis may be an option, in spite of the increased hemorrhagic risk. This should be followed by 3-6 months of oral anticoagulation[8,9].

Between 57% and 86% of patients have complete functional recovery[2]. Mortality ranges from 5.5% to 18% in recent series[1,2,10]. Twelve percent of patients suffer a recurrence of CVST and 14% present with different forms of venous thrombosis[11].

The prognosis of cerebral venous sinus thrombosis is generally favorable. Physicians should have high index of clinical suspicion to diagnose this rare disease particularly among patients with diabetic ketoacidosis who develop neurological symptoms.

CONCLUSION

Physicians should have high index of suspicion for cerebral venous sinus thrombosis if the DKA patient developed any neurological signs or symptoms. Neuroimaging should always be performed in suspected cerebral edema associated with DKA in order to exclude other pathologies.

Author contribution: All authors share equal effort contribution towards (1) substantial contribution to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of manuscript version to be published. Yes.

Potential conflicts of interest: None.

Competing interest: None. **Sponsorship:** None.

Submission date: 20 June 2013. **Acceptance date:** 26 September 2013.

Ethical approval: Research and Ethical Committee, King Hamad University Hospital, Bahrain.

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