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Superior sagittal sinus thrombosis: a rare complication in a child with nephrotic syndrome

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Abstract A 2-year-old boy with new-onset nephrotic syndrome developed recurrent vomiting, apathy and papilloedema. Superior sagittal sinus thrombosis was diagnosed on cranial CT and MRI. He gradually recovered after treatment with heparin, fresh frozen plasma and warfarin with complete resolution of the thrombosis after 1 month. Superior sagittal sinus thrombosis is an extremely rare complication of nephrotic syndrome in children. Early diagnosis is essential for institution of anticoagulation therapy and a successful outcome.

Introduction

Nephrotic syndrome is characterised by proteinuria, oedema and hyperlipidaemia. In children, 90% of cases are idiopathic, of which minimal change disease is found in approximately 87%.

Thromboembolic complications have emerged as a major hazard of nephrotic syndrome. Renal vein thrombosis is particularly frequent and thromboses of the pulmonary artery, deep veins, inferior vena cava, femoral artery and mesenteric arteries have been described [1]. Superior sagittal sinus thrombosis is a rare complication that can be readily diagnosed by imaging. Early diagnosis is associated with successful outcome.

The medical literature contains only a few reports of the clinical [2–7] and radiological findings [8] of superior sagittal sinus thrombosis as a complication of nephrotic syndrome in children. In this report we describe the clinical and radiological findings of this rare complication.

Case report

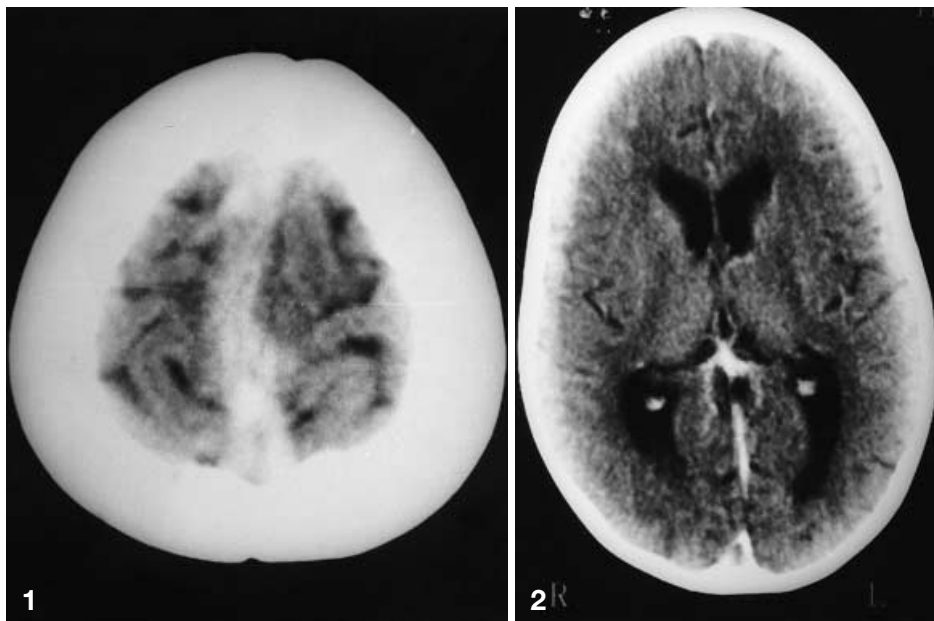
A 2-year-old boy developed marked proteinuria, peripheral, periorbital and scrotal oedema, hypoalbuminaemia (1.5 g/dl), hypertriglyceridaemia (429 mg/dl) and hypercholesterolaemia (513 mg/dl). Renal function tests and serological tests were normal. Abdominal US demonstrated slightly enlarged kidneys without hydronephrosis.

The initial therapy was prednisone, penicillin and a no-added-salt diet. Because of worsening oedema, elevated blood pressure and oliguria, furosemide and albumin were given intravenously with significant improvement. He was discharged from the paediatric ward.

Twenty-five days after discharge, he was readmitted because of recurrent vomiting, apathy and weakness. Physical examination revealed fever of 37.5°C, hypertension (141/76 mmHg), but no peripheral oedema. Neurological examination revealed a lethargic, but arousable child with papilloedema; there was no nuchal rigidity, no focal neurological signs and reflexes were normal. On the second day of admission, bilateral abducent nerve palsies developed. Serum electrolyte concentrations were: sodium 131 mEq/l, potassium 4.5 mEq/l, urea 13 mg/dl and creatinine 0.3 mg/dl. Serum albumin was 2.6 g/dl, cholesterol 373 mg/dl and triglycerides

Fig.1 Axial NCCT shows hyperdensity in the region of the superior sagittal sinus

Fig.2 Axial CECT shows a filling defect in the superior sagittal sinus in the region of the venous confluence – the ‘empty delta’ sign



128 mg/dl. The initial coagulation test results included platelets 183,000, PT 79%, APTT 54 s, INR 1.2, fibrinogen 377 mg/dl and antithrombin-3 levels 60% of normal. The levels of protein S and protein C were normal. A 24-h urine protein excretion was 8 g/day. EEG demonstrated diffuse slow waves.

On admission, non-contrast-enhanced cranial CT (NCCT) revealed hyperdensity along the superior sagittal sinus (Fig. 1). Contrast-enhanced CT (CECT) demonstrated the ‘empty delta’ sign (Fig. 2). There was no mass effect, midline shift or acute haematoma. Abdominal US showed enlarged kidneys with no evidence of renal vein thrombosis. Following the diagnosis of superior sagittal sinus thrombosis, heparin therapy was commenced, in combination with fresh frozen plasma. The nephrotic state was treated with prednisone 60 mg/m² IV and cyclophosphamide was added when the protein disappeared from the urine. Complete renal response was achieved 7 weeks from treatment initiation.

Within 1 week of initiation of anticoagulant therapy there was also marked improvement in neurological status, conjugate eye movement and normalisation of blood pressure.

On the tenth day of admission, T1-weighted (T1-W) cranial MRI, gadolinium-enhanced T1-W MRI and MR venography (MRV) revealed increased signal intensity in the superior sagittal sinus compatible with thrombosis (Fig. 3), and irregular flow in the superior sagittal sinus with multiple venous collaterals. There was normal flow in the other dural sinuses and there was no cerebral infarction or haemorrhage. CECT performed 1 month after admission demonstrated a normal superior sagittal sinus.



Fig.3 Sagittal T1-W image reveals increased signal intensity within the superior sagittal sinus, indicative of thrombosis

Discussion

Arterial and venous thromboses are frequent and serious complications in patients with nephrotic syndrome [9]. Intracranial venous thrombosis, however, appears to be very rare. There are isolated case reports in children aged 2–12 years old [2–7]. In a review of 52 children with acute neurological symptoms that were

caused by cerebrovascular disease, only 2 cases had thrombosis of dural sinuses and one of these occurred in a 3-year-old boy as a complication of nephrotic syndrome [10]. Divekar et al. [5] reported only 1 case of dural sinus thrombosis out of 700 children with nephrotic syndrome followed over a period of 17 years.

The signs and symptoms of dural venous thrombosis are nonspecific and include headache (in 75%), papillo-

edema (45%), seizures (37%), mental status change or coma (33%) and motor or sensory deficit (%) [11].

Nephrotic syndrome causes a hypercoagulable state. Among the alterations there is abrupt urinary renal loss of antithrombin-3. An increased incidence of thromboembolic complications is generally observed when antithrombin-3 levels are below 75% of normal, such as in our case [1, 12]. The hypercoagulable state has also been related to abnormalities of other coagulation factors: low level of zymogene factors (factor 9 and 11), increased level of procoagulatory cofactors (factors 5 and 8), altered fibrinolytic system (2-antiplasmin increased, plasminogen decreased) and increased platelet reactivity [1]. Excessive risk of thromboembolic complications is associated with low serum albumin (less than 2.5 g/dl), high rate of protein excretion (more than 10 g/day), low antithrombin-3 levels and hypovolaemia [1].

Because the clinical picture of superior sagittal sinus thrombosis is nonspecific, the diagnosis is dependent on imaging. NCCT can show the thrombosis directly, as hyperdensity along the affected sinus or as linear hyperdensities consistent with thrombosed cortical veins – the 'cord' sign [13]. Oedema, infarct or haemorrhage can often occur. On CECT, the central portion of the thrombosed superior sagittal sinus will remain hypodense relative to the intensely enhancing venous collaterals within the leaves of the falx – the 'empty delta' sign.

MRI, because of its noninvasiveness and high sensitivity, is the preferred modality for diagnosis and follow-up of cerebral venous thrombosis. The normal flow void seen in veins and sinuses on non-contrast-enhanced MRI is replaced by signals that are hyperintense or iso-intense to brain, depending on the sequence utilized

and the age of thrombus. The most striking and reproducible finding is high-signal intensity of methaemoglobin on T1-W imaging [14]. Contrast enhancement has limited ability to aid the diagnosis of thrombosis.

The high-signal thrombus can be mimicked by flow-related enhancement caused by entry of saturated protons into the imaging volume. MR angiography can differentiate flow from thrombus, either by the less time consuming time-of-flight techniques or by phase-contrast techniques which are limited by high signal substances, such as fat or methaemoglobin [15].

The treatment of choice is heparin, followed by oral anticoagulation, administered as long as the patient has proteinuria and albumin level below 2 g/dl or both [1]. Anticoagulation was difficult to achieve in our case, possibly because of loss of antithrombin-3, the heparin anticoagulant cofactor, in the urine. Fresh frozen plasma was given to correct antithrombin-3 levels. Similar problems with anticoagulation in a nephrotic child with dural sinus thrombosis have been reported before [5, 6]. There is one case report of treatment of sinus thrombosis with low-molecular-weight heparin which has a longer plasma half life, better bioavailability and lower haemorrhage risk than standard heparin [4, 12].

The present case illustrates a rare complication of nephrotic syndrome in children that should be considered in all nephrotic patients who develop any unexplained neurological symptoms. MRI or cranial CT should achieve prompt diagnosis of cerebral sinus or vein thrombosis, since immediate institution of treatment with anticoagulation and control of the nephrotic syndrome can lead to a successful outcome.

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