Case Report

Dural Sinus Thrombosis Secondary to Protein C Deficiency in Infancy

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Abstract: Dural sinus thrombosis (DST) is an infrequent diagnosis that is not commonly thought of in the first instance especially when the clinical presentation is not specific. We describe the clinical presentation of a patient with infantile seizures which was promptly investigated and diagnosed as DST secondary to Protein C deficiency. He was successfully treated with unfractionated heparin and the patient had full clinical recovery with no focal neurological deficit. High index of suspicion helped us in diagnosing this rare presentation well in time before occurrence of any complications.

Key Words: Dural sinus thrombosis, Protein C deficiency, seizures

Introduction

Dural sinus thrombosis (DST) is a rare and under recognized cause of seizures and stroke in infants. The diagnosis can be difficult, because of its nonspecific clinical manifestations and radiological findings. Delay in diagnosis may lead to venous congestion, venous infarction, and even death. Early and accurate diagnosis of this condition is therefore important. Genetic and acquired Thrombophilias are frequently identified. So much so, that many experts have suggested thrombophilic evaluation in all children with DST independent of other established risk factors.[1]

Case

Our patient a 7 months old infant was brought in emergency department for an episode of sudden onset stiffening of body with upward deviation of eyes, non responsiveness, bluish discolouration of lips and fever. He was actively managed by oxygen inhalation and 1.5 mg IV midazolam after conforming normoglycemia. The baby was in mother's lap when the event happened and didn't follow any episode of vomiting.

He had acute gastroenteritis with fever 3 days back from which he was recovering. There was no history of poor feeding, lethargy, irritability, ear discharge, head injury or bleeding from any site.

Past history revealed an uneventful hospital delivery, by LSCS. He had a neonatal admission for pneumothorax, requiring chest tube intubation and was discharged at 13 days of age. He was the third issue of consanguineous parents. No family history of any bleeding disorder, epilepsy or recurrent abortions. However there was history of deaths of five children of elder brother between 1-2 years of age due to unexplained reasons. Like wise 4 children of a first cousin also died around 1-2 years of age for unknown reasons. Development, feeding and immunization history was unremarkable.

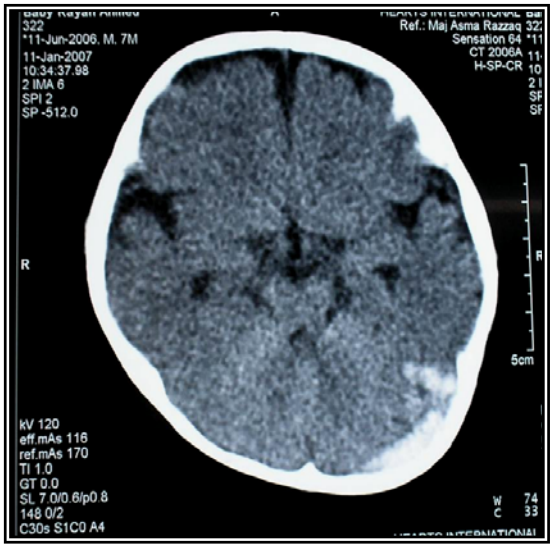

Figure I: Plain CT scan brain (axial view) showing linear areas of increased attenuation in Lt Transverse and sigmoid sinuses

On review examination in Intensive care unit he was found to be vitally stable, adequately hydrated, drowsy but arousable with normotensive anterior fontenalla and no pallor, jaundice, petechie, bruises or lymphadenopathy. GCS was 10/15, pupils were equal and reactive, deep tendon reflexes were elicitable and

planters were down going. Rest of the systemic examination was unremarkable.

Provisional diagnosis of Encephalitis was made and differential diagnosis included acute pyogenic meningitis, cerebrovascular accident, cerebral malaria, inborn errors of metabolism, infantile epileptic encephalopathy and Non accidental injury.

Empirical treatment with Inj Acyclovir, inj ceftriaxone and inj Quinine dihydrochloride were started. Loading dose of Inj phenytoin was given and IV fluids, electrolytes management and other supportive care were provided. Base line investigations revealed normal blood complete picture, urea, creatinine and electrolytes. Coagulation profile was normal, CRP was negative, D-dimers were less than 250 ng/ml and CSF examination was unremarkable.

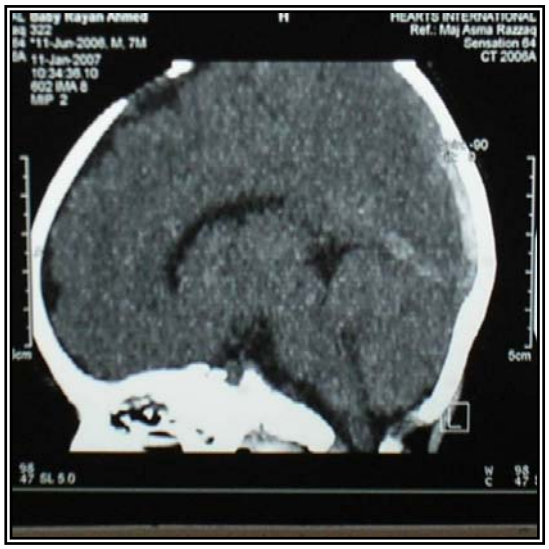

Figure 2: Plain CT scan brain (saggital view) showing involvement of superior saggital and straight sinuses with normal brain parenchyma

The infant improved remarkably in ensuing 24 hours with full recovery to GCS of 15/15, with no focal neurological deficit or seizure activity and started tolerating feeds. Samples for Protein C and S levels were sent to specialized labs, considering infants deaths in closed relatives and CT scan brain was asked to rule out any intracranial pathology.

Plain CT scan brain revealed linear areas of increased attenuation in Left Transverse and sigmoid sinuses (Figure I) and saggital view showed involvement of superior saggital and straight sinuses with normal brain parenchyma (Figure II). Thrombophilia workup showed, Protein C levels of 30 %(70-140%) and Protein S levels of 68% (55-130%). So final diagnosis of, Hetrozygous Protein C Deficiency leading to Dural Sinus Thrombosis was made.

As a result treatment was revised. Antiviral, antibiotics and antimalarial therapy was stopped. Phenytoin was switched to oral preparation in maintenance doses. Low Molecular Weight (LMW) heparin, 6mg subcutaneously 12 hourly along with Tab warfarin 1.5mg once daily (OD) were started, with daily INR monitoring. Dose of warfarin was titrated and patient was discharged on Tab warfarin 5 mg od with INR of 3.0 which was monitored weekly for first month, and then monthly for next three months of treatment. Phenytoin was tapered over next 3 months. The infant was followed up for 6 months, with normal development without any neurological deficit. Repeat MRI/CT scan was refused by parents due to financial constraints.

Discussion

Baily and Hass2 and Byers and Hass3 were the first to describe Dural sinus thrombosis (DST) in infancy, in the early 1930s. According to a Canadian DST registry, the estimated incidence is 0.67 per 100,000 children per year.[4] It is not uncommon to incidentally diagnose DST in children with pseudo tumor and in neonates with lethargy and seizures.[5] The incidence of childhood DST varies according to age and neonates are most commonly affected. 4,6 Almost 23% to 65% of children prior to the diagnosis of DST are reported as being healthy.[4,5,7] Most common associations of DST in infancy are dehydration, hypercoagulable states due to polycythemia8 or protein C deficiency.[9]

Seizures as the initial presentation are reported in 71% to 80% of neonates with DST.[4,7] However, older children are more likely to present with headache, vomiting, or altered consciousness. Focal neurologic signs like hemi-paresis, and cranial nerve palsies are also commonly seen in older children. In a Canadian stroke study, 48% of children older than 30 days of age had seizures around the time of initial presentation of DST.[4] Coma may be seen as a presenting symptom in around 28% of children in DST.[7]

With advancement in neuroimaging techniques DST is now diagnosed with increased speed and accuracy. Currently available diagnostic tools include non contrast head CT, CT venogram, MRI, MR venogram (MRV), conventional angiogram, and transcranial Doppler ultrasound (TCD).[1] Non contrast head CT remains the most commonly used screening tool. A dense cord sign (hyper dense fresh blood clot) is seen by non contrast head CT in 1% to 5% of cases. Indirect evidence includes hemorrhagic/multifocal infarcts and diffuse cerebral edema. One of the classic stigmata of DST, the empty delta sign, is present in 10% to 30% of cases on post-contrast CT. The combination of MRI with MRV gives the greatest visualization of the cerebral sinuses and veins. Venous TCD is an emerging non invasive diagnostic tool in DST.[10]

Current treatment strategies for children with DST are based on the best evidence available, adult studies, and expert opinion. The mainstay of DST treatment is with anticoagulation and supportive care. Acute anticoagulation has proved to be safe in children with DST.[5] Indefinite anticoagulation is recommended for recurrent DST or DST with a "severe" hereditary thrombophilia.[1] Various studies suggest anticoagulation may be a reasonably safe therapy in children.[4,5] The true benefit of anticoagulation will ultimately have to be answered by a larger, prospective interventional trial in children. Other proposed treatment strategies have included steroids, diuretics, osmotherapy, antiplatelet agents, surgical interventions and thrombolysis.[1]

Conclusion

We believe that DST represents a distinct under recognized clinical entity in infants, who present with neurologic symptoms like seizures, altered sensorium or stroke. Known risk factors should be excluded especially thrombophilia and similar conditions. MRI should be performed promptly if CT has been the initial investigation and is not diagnostic. In acute cases early anticoagulation should be started as it will improve the outcome. Oral anti-coagulation is then continued, but the duration of treatment and efficacy remains to be evaluated.

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