CLINICAL PROFILE AND RISK FACTORS FOR CEREBRAL SINUS VENOUS THROMBOSIS IN A PAEDIATRIC COHORT FROM A TERTIARY CARE CENTRE

C. Justin[1], M. R. Manivannan[2], S. Ramu[3]

[1]Senior Assistant Professor, Department of Neurology, Madurai Medical College.
[2]Professor, Department of Neurology, Madurai Medical College.
[3]Resident, Department of Neurology, Madurai Medical College.

ABSTRACT

BACKGROUND

Cerebral sinus venous thrombosis in children is a rare disease accounting for <1% of all strokes[1]. The risk factors are varied and differ from adults.[1] Here, we present the clinical profile, risk factors and outcome of cerebral sinus venous thrombosis in a paediatric cohort.

OBJECTIVES

To determine the clinical features, risk factors, imaging findings and outcome of children with cerebral sinus venous thrombosis in a tertiary care centre from 2013 to 2014.

MATERIALS AND METHODS

Prospective observational study totally 10 children presented during this period.

RESULTS

Males predominated the study (70%), septic CVT was the commonest (70%), majority of the patients had multiple venous sinuses involvement (70%). Majority of the patients had complete recovery (60%).

CONCLUSION

Local and systemic infections are the common cause of cerebral sinus venous thrombosis in children. Majority of them have multiple sinuses involvement. Deep venous system involvement is not seen in this cohort. Two thirds have a complete recovery.

KEYWORDS

Cerebral Sinus Venous Thrombosis, Risk Factors.

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INTRODUCTION: Cerebral sinus venous thrombosis in children is a rare disease accounting for <1% of all strokes. The risk factors are varied and differ from adults.[1] Cerebral venous thrombosis (CVT) in children is multifactorial in which both genetic and acquired risk factors play a role. In the first year of life, thrombosis usually occurs either in association with indwelling catheters or as renal vein thrombosis. In older children, catheterisation remains some of the most frequent risk factors for development of thrombosis. Additionally, surgery, malignancy, infections, autoimmune disorders, homocystinuria and trauma have been described as the other contributory risk factors. Although trauma has been shown to be one of the major risk factors for thrombosis in the adult population, only a few publications exist in children.

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Corresponding Author:
Dr. C. Justin,
#6, Lourdhu Nagar, 7th Street, 2nd Cross,
K. Pudur, Madurai-625007.
E-mail: drjustin2001@yahoo.com
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The factor V Leiden (FVL) mutation is the most widely recognised cause of hereditary thrombophilia.[1] The diagnosis now is in increasing phenomenon due to more sensitive diagnostic procedures and increasing clinical awareness. Both genetic and acquired risk factors play a role. CVT can occur in various clinical situations starting from infection, dehydration, renal failure, trauma, cancer and haematological disorder. Clinical manifestations of CSVT are nonspecific and may be subtle. Most of the clinical scenarios occur at all ages and the clinician should consider this diagnosis in a wide range of acute neurological presentations in childhood. CVTs often have variable clinical presentation, variable mode of onset, imaging appearance and outcome. Hence, its prognosis is largely unpredictable. MRI may play a role in detecting venous congestion and MR venography is the method of choice for investigation of cerebral venous thrombosis. Here, we present the clinical profile, risk factors and outcome of cerebral sinus venous thrombosis in a paediatric cohort.

AIMS AND OBJECTIVES: To assess the various clinical profile, risk factors and outcome of cerebral sinus venous thrombosis in a paediatric cohort in our case profiles of tertiary care centre.

MATERIALS AND METHODS: Prospective cohort study.

Inclusion Criteria: Children of age group between 2 to 12 years of age attending our Department of Neurology, Madurai presenting with fever, headache, vomiting, seizures, altered sensorium, weakness of limbs, cranial nerve palsies or any one of the above.

Exclusion Criteria: Children of group< 2 yrs. and > 12 years of age.

RESULTS: There were 10 children who presented with CSVT during this period. Males (70%) predominated the study.[2] 60% belonged to more than five years age group. Fever (80%), headache (70%), vomiting (50%), drowsiness (40%), irritability (40%), seizures (30%) were the common presenting symptoms. The common clinical signs were altered sensorium (40%), bilateral papilledema (40%), cranial nerve palsies (40%), hemiparesis (20%) and monoparesis in one.

Septic cerebral sinus venous thrombosis was the commonest (70%) cause noted among this cohort. Otitis media and mastoiditis topped the list (30%), followed by pyogenic meningitis (20%), local infection in the face in one, systemic infection with increased antiphospholipid antibody IgG in one. Protein C and S deficiency was the risk factor in one child each and another child due to chemotherapeutic agents.

Multiple sinuses were involved in the majority (70%). Transverse and sigmoid sinuses in four, superior sagittal, transverse and sigmoid in three, sigmoid sinus and jugular vein in one, cavernous sinus in one and superior sagittal sinus with superficial cortical veins in one. One child had peripheral deep vein thrombosis in addition to cerebral venous thrombosis.

Neuroimaging revealed haemorrhagic infarct in two, intraventricular haemorrhage in two, abscesses in three and hydrocephalus in one. Repeat imaging after 3 months showed complete recanalisation in 50%, partial recanalisation in 20% and persistent thrombosis with collaterals in 30%.

Five children received anticoagulants in addition to antibiotics, three antibiotics alone and two anticoagulants alone. 60% had a complete recovery and the remaining had residual deficits in the form of hemiparesis, delayed development and speech delay.

DISCUSSION: Cerebral venous thrombosis in children is a serious but uncommon diagnosis that can be associated with several underlying systemic conditions. Deficiencies of various anticoagulants such as antithrombin, protein C or protein S have been associated with childhood venous thrombosis. The frequency of protein C and protein S deficiency is 3.8% and 3%, respectively in selected patients with venous thrombosis.

CSVT occurs in various clinical settings which includes the following situations such as infection, dehydration, renal failure, trauma, cancer and haematological disorders. Many children have multiple risk factors. Although the frequency of septic thrombosis is decreasing, due to antibiotic development, recent studies have shown that it was still responsible for a substantial proportion of thrombosis in older children. Infection appears to be a particularly common trigger in previously well children, as is microcytosis suggestive of iron deficiency. Before the widespread use of early corrective surgery, CSVT used to be a common complication of congenital cyanotic heart disease, in which it occurred predominantly in patients over 2-3 years of age, usually with iron deficiency.

Most of the clinical manifestations of CSVT are nonspecific and subtle. It presents at all ages and hence the clinician should consider this diagnosis in any acute neurological presentations in childhood starting from stroke, headache, seizures, coma, and raised intracranial pressure. Any illness starting from ear infections, meningitis, anaemia, diabetes and head injury can be complicated by CSVT. CSVT also determines the outcome of nontraumatic coma. Clinical presentation with pseudotumour cerebri has also been documented. There are few data on the prevalence of CSVT in otherwise unexplained hydrocephalus or in convulsive and non-convulsive seizures and status epilepticus.

Depending up on the location of thrombus, the clinical manifestation varies.[3] When the thrombus is localised to superior sagittal sinus, they manifest mainly as an isolated increased intracranial hypertension. Thrombus localised to lateral sinuses can present with isolated intracranial hypertension. Thrombosis of cortical veins, alone or in association with a sinus thrombus causes venous infarction. Depending up on the site of venous infarction, patient may present with hemiparesis, seizures, coma, etc., The manifestations of deep cerebral venous thrombosis are typically characterised by altered consciousness, decerebrate posturing, changes in extrapyramidal tone and psychiatric symptoms such as confusion as a result of infarction in the thalami and basal ganglia and white matter structures. With early diagnosis and prompt treatment, partial or complete recanalisation is possible. With regard to clinical features. It has been observed that toddlers often present with seizures and focal signs, mainly hemiparesis, whereas older children often present with headache, altered mental status and headache. Seizures are less common in older children.

CT scan is done as the first investigation as it is easily available and less time consuming. It can show hyperdense thrombus sign, cord sign, dense triangle sign and it can also show venous infarcts. Contrast CT can show empty delta sign and thrombus occluding the sinuses.

MRI has a sensitivity of 90% and MRI and magnetic resonance venography (MRV) together provide diagnosis in all cases.[4]

In our series of cases, we identified that septic cerebral sinus venous thrombosis was the commonest (70%) cause noted among this cohort. Among the septic CVT, otitis media and mastoiditis topped the list (30%) as the cause, followed by pyogenic meningitis (20%).With regard to clinical manifestations, CVT manifest in several ways starting from isolated clinical hypertension, focal syndrome, cavernous sinus syndrome and subacute encephalopathy.[3,5] In our case series, 70% of the cases had headache. With regard to clinical presentation, majority of the patients presented as altered sensorium, bilateral papilledema and cranial nerve palsies. Motor weakness presented only in 20 % cases.

Wysoniska et al[6] showed in his study that transverse sinus was affected in 79% cases followed by sigmoid sinus in 50% cases, upper sagittal in 49% cases and in 66% cases two or more sinuses are involved. In our series, majority of our patients showed more than one sinus involvement in 70% cases (transverse and sigmoid sinuses in four, superior sagittal, transverse and sigmoid in three, sigmoid sinus and jugular vein in one).[7]

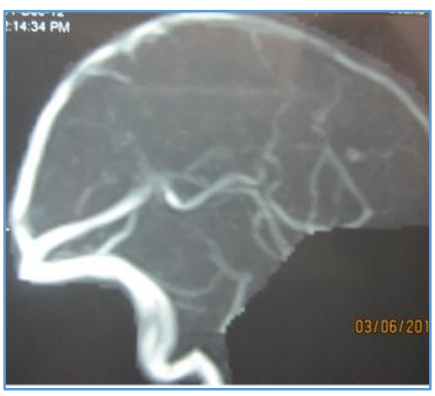
Prothrombotic disorders has also been found in between one third and half the cases in recent series of paediatric CSVT. Among the prothrombotic disorders, majority of these are acquired prothrombotic states, such as acute protein C and S and antithrombin deficiency secondary to infection or protein loss, e.g. in nephrotic syndrome, or antiphospholipid antibodies, and are often normal on repeated investigation. Genetic polymorphisms appear to be important as risk factors in adults but although there is evidence for an excess of prothrombotic risk factors in paediatric CSVT25, the relative importance of the factor V Leiden or prothrombin 20210 mutations is less clear. Hyperhomocysteinaemia and its genetic determinants may be worth excluding or treating with folic acid, B6 and B12 vitamin supplementation, as this has few risks, but further studies will be important. There are no data on whether longer-term treatment for any of the other prothrombotic disorders reduce the significant recurrence risk and international collaboration will be required to address that issue.

Treatment of CSVT includes general supportive or symptomatic measures, such as hydration, antibiotics for septic cases, control of seizure activity with anticonvulsants, and measures aimed at decreasing intracranial pressure.[8] Antithrombotic therapy of CSVT in childhood has been influenced by clinical trials in adults. De Veber and colleagues initiated a prospective cohort study of anticoagulant therapy in 30 children with CSVT from 1992 to 1996 and reported a mortality rate of 3/8 in untreated compared with 0/22 in treated children. Anticoagulant treatment was well tolerated, with no extensions of the CSVT. Johnson et al. have also reported encouraging data on the safety of anticoagulation in children with CSVT and data confirm these observations, with very similar results on safety and likely better cognitive outcome. The development of pseudotumour cerebri may not be influenced by anticoagulation but more data are needed for children.[9]

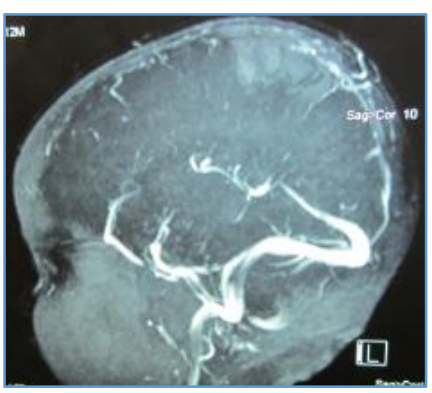
The options for treatment of infants and children include standard or low molecular weight heparin for 7-10 days followed by oral anticoagulants for 3-6 months.[10,11,12]

Thrombolytic therapy and mechanical thrombectomy are sometimes used for extensive thrombosis of superficial and deep venous structures.[13,14,9]

CONCLUSIONS: Cerebral sinus venous thrombosis is an underdiagnosed but important cause of stroke in childhood occurring most often in the neonatal period. Mortality and morbidity are significant, local and systemic infections are the common cause of cerebral sinus venous thrombosis in children. Majority of them have multiple sinuses involvement. Deep venous system involvement is not seen in this cohort. Two thirds have a complete recovery.



Partial Recanalisation after 3 Months



SSS Thrombosis in a Child with Pyogenic Meningitis

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