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A Case Report of Pediatric Cerebral Venous Thrombosis with Undiagnosed Complex Congenital Heart Disease: Tetralogy of Fallot with OS ASD: A Cataclysmic Ending

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Abstract

Cerebral Venous Sinus Thrombosis (CVST/CSVT) is occlusion of cerebral veins and venous sinuses of brain secondary to blood clot formation resulting in hindrance in the blood drainage system in brain, leading to disturbances the internal homeostasis of brain, raised intracranial pressure, cerebral edema, and 50% of cases will have venous infarction or venous hemorrhage (stroke). CVST although being a Rare disorder but may be more common in children than adults with greater risk in neonatal period *i.e.* first 28 days of life. Here we are discussing a case of Pediatric CVST in a 7-month-old baby boy who presented to Emergency Room (ER) with recurrent discrete episodes of vomiting, fever, seizures, drowsiness and respiratory distress. The fatal outcome in our child was attributed to delayed presentation in a tertiary care center, hence missed early diagnosis and treatment. In this child the CVST could be result of amalgamation of complex underlying ongoing multiple pathological processes: an acute systemic illness like sepsis, severe dehydration, undiagnosed and untreated complex congenital heart disease, tetralogy of fallot with osteum secondum atrial septal defect, worsening the coagulopathy. It takes this case even more unique. This discussion is to bring focus on the importance of knowledge about CVST amongst emergency physicians and primary care physicians, specially managing this rare disorder with flummox presentation mimicking other more common disorders, especially in pediatric and neonatal population where definitive history and chief complaints are often vague and difficult to obtain, making it more difficult to diagnose. We the authors hence reporting this case with intent to spread awareness of CVST, how to doubt it, detect it and then manage it, especially in places like

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Chhattisgarh, India, where CVST is not so uncommon. We believe early diagnosis, early presentation to tertiary care center with aggressive early treatment can significantly reduce the mortality. Should the parents brought the baby early to any tertiary care center owing to his complex deteriorating symptoms like high grade fever progressed to drowsiness and seizure episodes, could there be a different outcome for this child as well as his parents.

Keywords

Cerebral Venous Sinus Thrombosis (CVST), Pediatric CVST, Tetralogy of Fallot (TOF), Osteum Secondum Atrial Septal Defect (OS ASD)

1. Introduction

Cerebral Venus Sinus Thrombosis (CVST) is a presence of blood clot in the dural venous sinuses which drains blood from the brain, the cerebral veins or both. The clot keeps the blood from draining out of the brain and as a result of which pressure builds up inside the blood vessels and this can lead to disruption of internal homeostasis of brain, resulting in raised intracranial pressure, cerebral edema, and in almost 50% of cases it ultimately advances to venous infarction or venous hemorrhage (stroke). A stroke is characterized as a disruption of cerebral vessels, and classified into two major categories: 1) hemorrhage, and 2) ischemic. Ischemic strokes are far more common, and caused by an obstruction within the blood vessels preventing blood flow to the brain. What differentiates a perinatal stroke from other types of stoke is timing. Perinatal strokes can occur while the baby is in the uterus, during delivery, or within weeks after birth. Cerebral venous thrombosis is a rare stroke presentation in general population affecting all individuals including pediatrics and neonates [1]. Cerebral venous sinus thrombosis is more common in pediatric age group than in adults and neonates are at highest risk [2].

One can often wonder can babies have stroke? General assumption is stroke can only happened in adults. Unfortunately, stroke is quite common among babies, occurring in 1 in every 4000 babies. This rate is similar to one seen for large artery stroke in adults even though the symptoms and causes are markedly different.

The incidence of CVST in neonates is 0.6 - 15 per 100,000 newborns per year, which is higher than the incidence in the childhood period (0.67 per 10,000 children per year) [3]. Although data are limited the incidence is considerably higher in preterm than term infants, highest during neonatal period accounting to 30% - 50% of cases, more common in males accounting for 60% of cases [4] [5].

Causes are diverse and are highly age dependent so as the presenting features. Acute systemic illness is the dominant risk factor among newborns. In childhood CVST, acute infections of the head and neck such as mastoiditis are most common, followed by chronic underlying diseases like nephrotic syndrome, can-

cer, and inflammatory bowel disease. Presentation of CVST in a child is has a vary variable. Signs/symptoms of depressed mental status: drowsiness/lethargy/irritability, raised intracranial pressure *i.e.* headache, recurrent/projectile vomiting, seizures etc. can be present. Seizures and altered mental status are the commonest manifestations in newborns. Headache, vomiting, and lethargy, sometimes with 6th nerve palsy, are the most common symptoms in children and adolescents [6].

There is no large scale research for the treatment of CVST, its risk and benefits, in pediatric population. The guideline to treat CVST in children is based on adult studies. Treatment with anticoagulation, unfractionated heparin or low molecular weight heparin (LMWH) is safe and may be beneficial for reducing mortality and long-term morbidity, even in the presence of intracranial hemorrhage (ICH).

2. Case Presentation

2.1. Presentation in Emergency Department

Seven month old baby boy presentation to Emergency Room (ER) with complaints of multiple episode of vomiting since last 7 days on his presentation to ER along with high grade fever intermittent nature with abnormal body movements and up rolling of his eyeballs suggestive of seizures and progressive drowsiness since last 4 day and severe respiratory distress since 2 last days. The child had an uncomplicated prenatal, antenatal and birth history followed by normal growth and development.

He has been taken to community primary care physicians and then to various other local hospitals over past 1 week, since he noticed to be not doing well, by his parents. He has been treated with antipyretic, multiple antibiotics, antiepileptic and oxygen therapy. Unfortunately none of the primary care physicians treated the child in his initial presentation could thought about CVST. It leads to further delay in diagnosing the conditions until he presented to our hospital.

2.2. Clinical Examination & Initial Management

On presentation his vital signs were: Blood pressure (Bp): 80/40mmHg, Heart Rate (HR) 103/min, Respiratory Rate (RR): 36/min, Oxygen saturation (spo2) 70% on high concentration mask Temperature: 97.6 degree F, capillary Blood Glucose: 70 mg/dl, delayed capillary refill time with central and peripheral cyanosis noted.

Central Nervous System: He was irritable and lethargic, pupils were bilaterally (B/L) reactive to light.

Cardiovascular System: S1 and S2 audible with a murmur noted.

Respiratory system: B/L air entry in chest was diminished with significant intercostal, subcostal in drawing of chest, nasal flaring noted.

Per abdomen: Soft, non-tender, bowel sound present and no organomegaly noted.

12 lead ECG showed heart rate of 116 /min with ventricular bigeminy and ar-

terial blood gas suggested type one respiratory failure, metabolic acidosis.

In view of poor respiratory effort, patients was intubated and ventilated immediately with a target to maintain $SpO_2 > 94\%$, oxygen/FiO_2 was titrated accordingly. He required inotropic support after invasive positive pressure ventilation. Even after all supportive measures he failed to maintain saturation above 70% and remained haemodynamically unstable.

2.3. Further Investigation and Clinical Course

Blood investigations showed: hemoglobin (Hb): 10.45 gm/dl, total leukocyte count: 16,130/cumm, platelet count: 3.15 lakh/cumm, peripheral smear showing anisocytosis, poikilocytosis, macrocytes, microcytes and presence of sickled red cells.

Ferritin 76.9 micrograms/L, serum iron 26.1 mcg/dl, serum total iron binding capacity 246.2 mcg/dl. Sodium: 142 mEq/L, potassium: 5.6 mEq/L, renal function test was within normal limits. Prothrombin time: 108 seconds, INR: 8, APTT: 120 seconds.

One unit of fresh frozen plasma transfusion was done in view of deranged coagulation profile. He was treated with other supportive measures: broad spectrum antibiotic, antiepileptic, throughout the stay in PICU our child remained unstable, hypoxic, hypotensive and drowsy.

Being a tertiary care center we were privileged to do a MRI Brain with Venogram which concluded: Severe dural venous with deep venous system thrombosis with intracerebral hemorrhage. Extensive dural venous sinus thrombosis involving entire superior sagittal sinus, straight sinus, vein of Galen, internal cerebral veins, possibly inferior sagittal sinus and left transverse sinus and cortical veins, with resultant multiple large hemorrhagic venous infarct in bilateral basal ganglia and thalami and bilateral cerebral hemisphere. In **Figure 1** (from patient's MR Venogram Brain) showing abset flow in B/L veins of Trolard, entire sagittal sinus, left transverse sinus s/o venous sinus thrombosis. As shown in **Figure 2**, gross hemorrhagic extension, intraventricular breakthrough in entire ventricular system with mild hydrocephalas. Restricted diffusion involving bilateral basal ganglia and thalami, bilateral cerebral parenchyma (grey and white matter, both), with edematous gyri and multifocal small areas of restricted diffusion in brain stem and bilateral cerebral hemispheres s/o hypoxic brain injury. Absence flow signal in entire cervical and intracranial portion of left internal carotid artery s/o thrombosis, as shown in **Figure 3**.

2D ECHO was performed to evaluate persistent hypoxia in spite of invasive ventilation which diagnosed Tetralogy of Fallot (TOF)/osteum secondum atrial septal defect (ASD).

His high performance liquid chromatography (HPLC) result came back which was s/o hemolytic anemia, reduced platelet with sickled RBCs.

Urgent Neurosurgery opinion was taken who suggested grave prognosis and no surgical intervention. He was eventually developed cardiac arrest on 4th day of his hospitalization. Despite of all resuscitative measures our baby could not be revived and died.

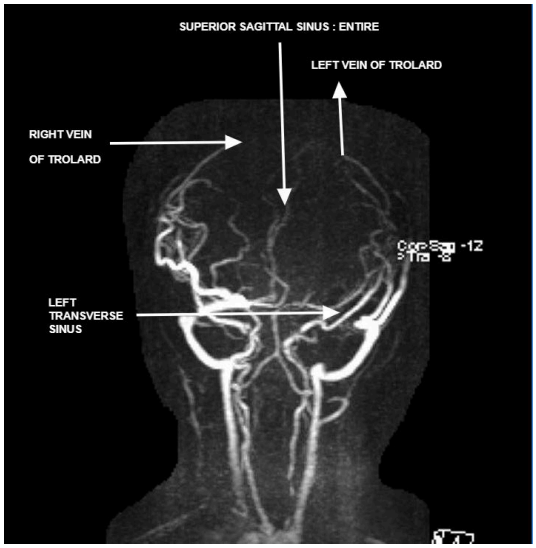

Figure 1. Mr venogram showing absent flow in B/L veins of trolard, entire sagittal sinus, left transverse sinus S/O venous sinus thrombosis.

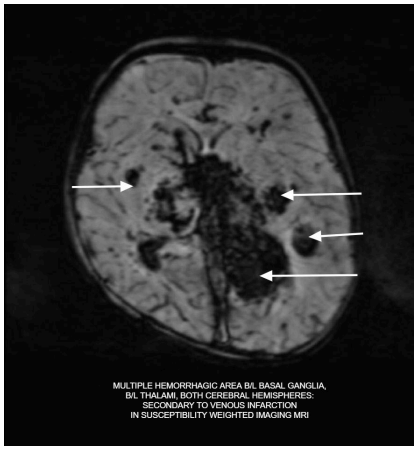

Figure 2. Multiple large hemorrhagic venous infarct in B/L basal ganglia, B/L thalami, B/L cerebral hemisphere.

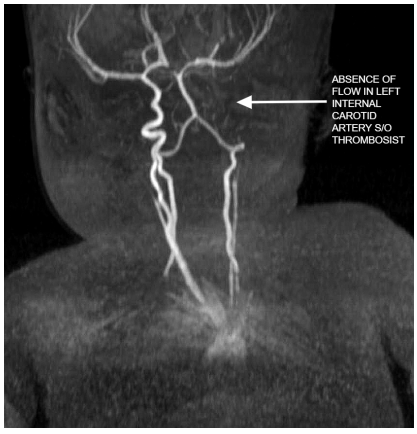

Figure 3. Absent flow signal in left internal carotid artery S/O thrombosis.

3. Discussion

A cerebral venous sinus thrombosis is the presence of blood clot in cerebral venous system or in small cortical vein, causing cortical vein thrombosis. It leads to complete or partial occlusion of the drainage of blood from brain and cerebral veins to jugular veins in neck. Cerebral Venus sinus thrombosis is a rare disorder of childhood, often under diagnosed owing to its indistinct etiologies and nonspecific presentations, widely diversified over different age groups. Neurological squeal reaching up to 40% of survivors and mortality approaching 10%. DeVeber G et al in his study concluded that CVST in children affects primarily neonates and results in neurological impairment or death in approximately half the cases [5].

3.1. Anatomy and Pathophysiology

Cerebral venous system is composed of a network of cortical, medullary, and deep veins which drain into dural venous sinuses. These comprise the superficial dural sinuses (sagittal, transverse, and sigmoid) and the deep venous system (straight sinus, vein of Galen) (see **Figure 4**).

The drainage systems of cerebral venous sinuses is depicted in **Figure 5**: Intracranial veins, unlike systemic veins do not follow their arterial counterparts, thus differ in their drainage territory from the arteries. The intracranial venous system has two major components, the dural venous sinuses and the cerebral veins.

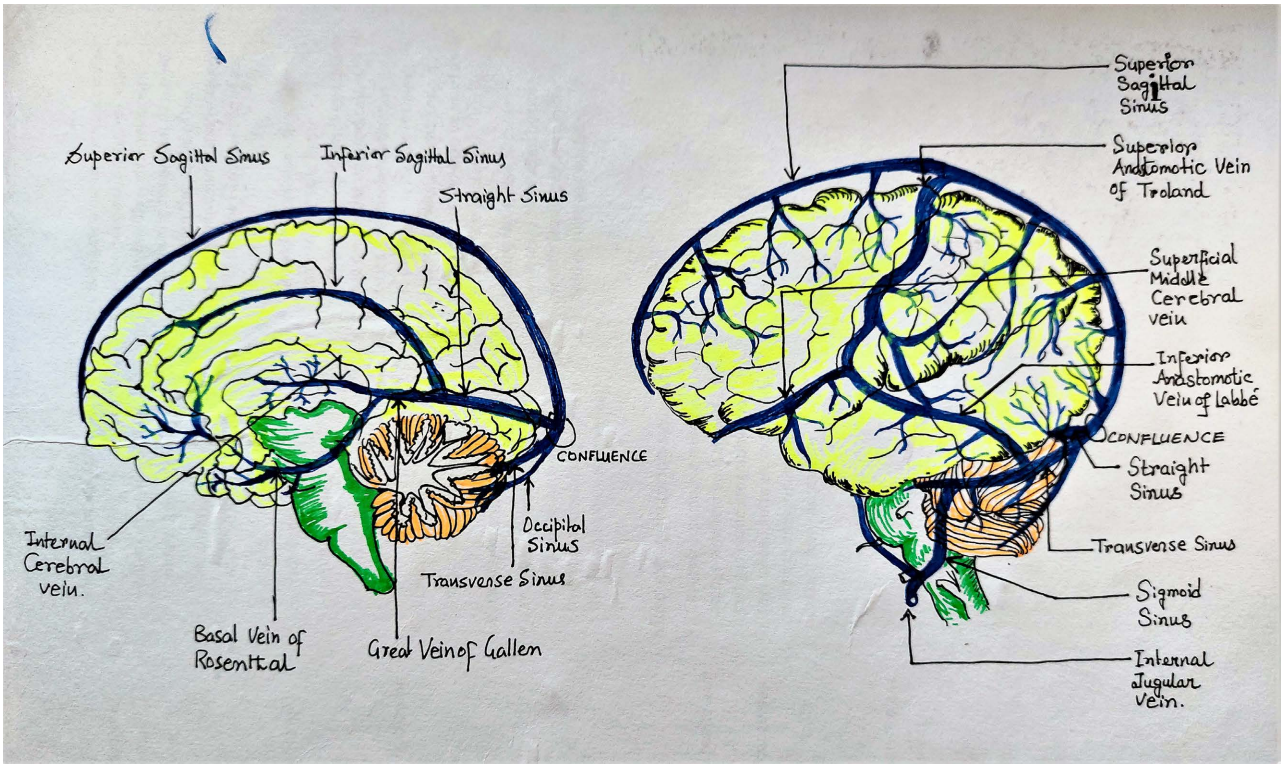

Figure 4. Anatomy of cerebral venous sinus drainage system © sayani banerjee 2022.

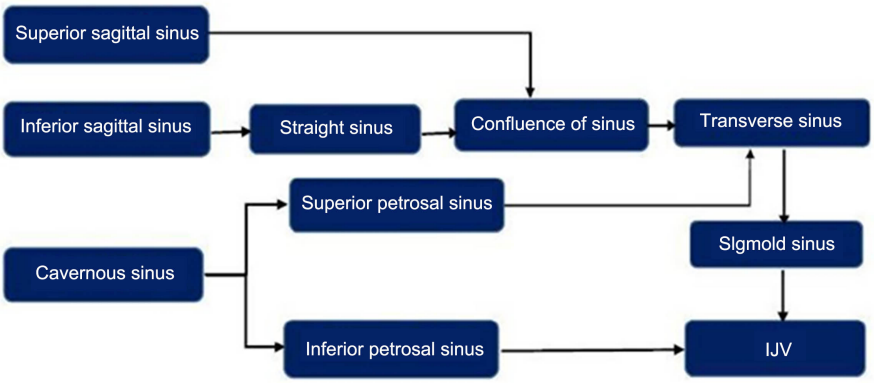

Figure 5. Flowchart depicting the venous drainage in the cerebral venous sinuses [7].

Dural Venous Sinuses: Endothelium-lined channels, contained between the outer (periosteal) and inner (meningeal) dural layers. It is subdivided into an antero-inferior group and a postero-superior group. The postero-superior group is the more prominent, consisting of the superior sagittal sinus (SSS), inferior sagittal sinus (ISS), straight sinus (SS), sinus confluence (torcula herophili), transverse sinuses (TSs), sigmoid sinuses, and jugular bulbs. The antero-inferior group consists of the cavernous sinus (CS), superior and inferior petrosal sinuses (SPSs, IPSs), clival venous plexus (CVP), and sphenoparietal sinus (SphPS). Bilateral cerebral hemispheres are drained via multiple cortical veins, few of them being prominent and named. The vein of Trolard, vein of Labbé, and superficial middle cerebral veins vary in size, maintaining a reciprocal relationship with each other. If one or two are dominant, the third anastomotic vein is usually hypoplastic or absent.

A venous clot leads to occlusion and impairment of drainage of cerebral veins. The result is, increased venous pressure, diminished capillary blood flow, vasogenic edema, and infarction, usually hemorrhagic in nature. Thrombosis can be diagnosed by imaging with or without parenchymal involvement.

3.2. Risk Factors

1) Maternal/Child factors: Primiparity, Multiple births, Gestational diabetes, Pre-eclampsia, Preterm birth, Chorioamnionitis, Complicated delivery (vacuums, forceps), meconium aspiration, intubation at birth, hypoxia, acidosis, and asphyxia, Acute systemic illness: sepsis and dehydration, acute respiratory failure, hypoxia, Acute head and neck infections like meningitis, mastoiditis, sinusitis, Congenital heart disease, ECMO: infants who require ECMO are at risk of CSVT due to retrograde thrombosis following and occlusion of right jugular flow.

2) Prothrombotic factors: Abnormal levels of prothrombotic factors are found in 10% - 20% of infants with CSVT but the abnormalities are usually minor and occur in the context of other risk factors, recent studies investigating thrombophilia in neonatal CSVT do not predict recurrence [8] [9].

3) Other Factors: Male sex [10].

Risk factors vary in different age groups, they are multifactorial and high re-

currence rate of CSVT noted in children than adults [3]. We, the authors, called attention to our case, a 7 month of infant presented to us with life threatening, complicated CVST, which could have be a rare squeal of complex congenital cyanotic heart disease along with systemic serious illness, pneumonia, sepsis and severe dehydration. Though exact cause could not be found as the child remained critically ill and died before a detailed work up could be performed.

3.3. Diagnosis of CVST

Diagnosing CVST/secondary stroke in pediatric population remains challenging like any other illness, as children usually unable to articulate, presentations are mostly nonspecific, conspicuous, masked with the symptoms/signs of underlying causative etiologies. Signs/symptoms of depressed mental status: drowsiness/lethargy/irritability, raised intracranial pressure *i.e.* headache, recurrent/projectile vomiting, seizures etc. can be present. Additional features are of underlying ongoing pathologies, like meningism in meningitis, reduced urine output, delayed capillary refill time, shrunken eyes, lost skin turgor in case of severe dehydration/shocked child etc.

In our case report, the child was brought to us at a very late stage of the disease. Parents wasted golden hours wondering in multiple primary care centers and primary care physicians lacking expertise to suspect CVST in this child owing to its rarity and atypical presentations, shortage of tertiary care hospitals in peripheries of state like one in this case. Only after development of grave complications and when child's advanced to impending respiratory arrest, was ultimately referred to a tertiary care hospital, *i.e.* to us, after 7 days. It is hence appropriately said that time is brain, which we lost in this child. Hence this case report is of great significance, to make primary & emergency care physicians aware of CVST and pediatric stroke.

In this child multiple risk factors could lead to CVST as we the authors concluded in the background of our findings including his underdiagnosed TOF with os ASD. Tetralogy of Fallot (TOF) is a cardiac anomaly that refers to a combination of four related heart defects that commonly occur together. The four defects are:

1) Ventricular septal defect (VSD)—a hole between the right and left pumping chambers of the heart.

2) Overriding aorta—the aortic valve is enlarged and appears to arise from both the left and right ventricles instead of the left ventricle as in normal hearts.

3) Pulmonary stenosis—narrowing of the pulmonary valve and outflow tract or area below the valve that creates an obstruction (blockage) of blood flow from the right ventricle to the pulmonary artery.

4) Right ventricular hypertrophy—thickening of the muscular walls of the right ventricle, which occurs because the right ventricle is pumping at high pressure.

A small percentage of children with tetralogy of Fallot may also have addi-

tional ventricular septal defects, an atrial septal defect (ASD) or abnormalities in the branching pattern of their coronary arteries. Some patients with tetralogy of Fallot have complete obstruction to flow from the right ventricle, or pulmonary atresia. Tetralogy of Fallot may be associated with chromosomal abnormalities, such as 22q11 deletion syndrome. An ostium secundum atrial septal defect is a type of congenital heart defect called an atrial septal defect (ASD). An ASD is a hole in the wall (septum) between the two upper chambers of the heart (the atria). ASDs can be classified by location. An ostium secundum ASD is a hole in the center of the atrial septum. Normally, the right side of the heart pumps oxygen-poor blood to the lungs, while the left side pumps oxygen-rich blood to the body. An ASD allows blood from both sides to mix, causing the heart to work less efficiently. A patient with tetralogy of fallout (TOF) is susceptible to serious complications and for this reason most children undergoes complete repair in 1st few months of life making it rare to present with complications, like CVST and others rare ones. Cerebral thrombosis in TOF occurs due to extreme polycythemia and dehydration. Our patients may had iron deficiency anemia with hemoglobin and hematocrit level in normal range but too low in the presence of a cyanotic heart disease. Congenital cardiac disease can lead to the formation of a thrombus inside the heart, which can later throw clots as emboli into the peripheral circulation; one study even suggested that congenital heart disease has a role in increasing thrombogenicity [11] which we also suspected in this patient. Ammash *et al.* reported two cases of cerebrovascular embolism among eight patients diagnosed with TOF over a seven-year period. There are several factors that increase risk of pathogenesis of thrombosis in patients with congenital heart disease (CHD). For example, chronic acidosis increases fibrin deposition, secondary erythrocytosis, and hypoxia/hypoxemia-induced activation of the procoagulant pathways, increasing tissue factor expression and impaired fibrinolysis [12]. Adults with cyanotic CHD also have an increased red blood cell (RBC) mass. This secondary erythrocytosis may increase blood viscosity, and it may thereby reduce cerebral blood flow, which can predispose the patient to chronic hypoxia, clot formations. Chronic hypoxemia will also activate neutrophils and mononuclear cells that release vasoactive and chemotactic factors, resulting in endothelial injury. Platelets and endothelial cells interact and activate platelets and enhance intravascular thrombus formation by thrombin, which activates the coagulation cascade. In addition, an impaired fibrinolytic system due to increased plasminogen activator-1 levels can contribute to thrombogenicity and not just blood turbulence; thus, all these factors should also be taken under consideration for CVST and stroke in TOF patients [12].

Other reasons could be hot and humid climate, genetic predisposition to hypercoagulable congenital disorders of the state, Chhattisgarh which makes CVST more common than any other part of the country or globally. Here, in Chhattisgarh CVST is not so rare after all.

He had h/o seizure which was an alarming sign in our patient with h/o mul-

tiple visits to smaller clinic where early recognition and aggressive treatment could have improved the outcome. Recognition of CVST would need high index of suspicion as its symptom is easily confused with underlying disease. An early visit to a tertiary care setup could have changed the outcome.

Identifying or suspecting the potentiality of CVST is the utmost important step in diagnosis. It requires very high index of suspicion and awareness regarding CVST among emergency physicians and primary care clinicians, and it can only come with good knowledge regarding the diverse presentation, early signs and symptoms of CVST. Time is brain. Delay in diagnosis is often fatal to the child or causing lifelong debilitation. Primary/emergency physicians in a state like Chhattisgarh should suspect CVST if neonates or children present triad of with altered or depressed mental status, headache and vomiting, or seizures, mainly in neonates with underlying chronic illness carrying risk for CVST, like: nephrotic syndrome, hereditary hypercoagulable state, immunological disorders, anemia, leukemia and congenital heart disease, like TOF as in our case of our child. Primary care physician, would have suspect CVST in the first visit for this child, it could have led to a favorable outcome for this child. Non contrast enhanced CT scan of brain (cord sign) is not very insensitive in identifying CVST, contrast enhanced CT brain (empty delta sign) with CT and MR venography is necessary in demonstrating filling defects in cerebral venous system and lastly CT/MR brain angiography (corscrew appearance of veins) are mainstay diagnostics. Magnetic resonance imaging (MRI) and MR venography offer the most detailed and sensitive means to assess the clot burden and extent of parenchymal injury. CT offers the advantage of greater accessibility and speed of imaging. Roland *et al.* found that non-enhanced CT has a 73% sensitivity for correctly identifying CSVT, with a very low rate of false positives, but involves exposure to ionizing radiation and contrast, which is of particular concern in the pediatric population. Once CVST diagnosis is established, or even in cases of high index of suspicion clinically/radiological appearance, neurologist must be consulted at the earliest possible and pediatrician or primary care physician needs to investigate for underlying risk factors. In neonates with an open anterior fontanelle Doppler imaging is also an alternative mode to diagnose and monitor of the neonatal Sino Venus thrombosis. When the above studies do not clarify the diagnosis to, the gold standard would be intravenous Digital subtraction angiography [3] [13] [14].

3.4. Treatment of CVST

There is no large scale research for the treatment of CVST, its risk and benefits, in pediatric population. The guideline to treat CVST in children is based on adult studies. Treatment with anticoagulation, unfractionated heparin or low molecular weight heparin (LMWH) is safe and may be beneficial for reducing mortality and long-term morbidity, even in the presence of intracranial hemorrhage (ICH). Duration of anticoagulation 3 - 6 months is a reasonable dura-

tion of treatment for patients with provoked CSVT; 6 - 12 months for patients with spontaneous unprovoked CSVT in the absence of a strong permanent thrombophilia; lifelong for patients with a severe thrombophilia (severe genetic deficiency of protein C or S or antithrombin III, homozygous prothrombin or factor V Leiden mutation, antiphospholipid antibody syndrome).The use of fibrinolytic therapy or endovascular therapy may be life-saving in critically ill patients experiencing clinical deterioration despite treatment with anticoagulation therapy. Addition of aspirin or steroids is not recommended due to an association with higher rates of mortality and poor outcome [15]-[21]. Supportive treatment with neuroprotection strategy: Control seizures, normalization of blood sugar, BP, optimize ventilation and oxygenation, correct and prevent dehydration, treat sepsis and meningitis, avoid hypo and hyperthermia, early rehabilitation.

4. Conclusion

This discussion is to bring focus on the importance of knowledge about CVST amongst emergency physicians and primary care physicians, specially managing this rare disorder with flummox presentation mimicking other more common disorders, especially in pediatric and neonatal population where definitive history and chief complaints are often vague and difficult to obtain, making it more difficult to diagnose. We the authors hence reporting this case with intent to spread awareness of CSVT, how to doubt it, detect it and then manage it, especially in places like Chhattisgarh, India, where CSVT is not so uncommon. We believe early diagnosis, early presentation to tertiary care center with aggressive early treatment can significantly reduce the mortality.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Bousser, M.G. and Ferro, J.M. (2007) Cerebral Venous Throm-Bosis: An Update. *The Lancet Neurology*, **6**, 162-170. https://doi.org/10.1016/S1474-4422(07)70029-7

[2] Ichord, R. (2017) Cerebral Sinovenous Thrombosis. *Frontiers in Pediatrics*, **5**, Article 163. https://doi.org/10.3389/fped.2017.00163

[3] Ramenghi, L.A., Govaert, P., Fumagalli, M., Bassi, L. and Mosca, F. (2009) Neonatal Cerebral Sinovenous Thrombosis. *Seminars in Fetal and Neonatal Medicine*, **14**, 278-283. https://doi.org/10.1016/j.siny.2009.07.010

[4] de Veber, G., Andrew, M., Adams, C., *et al.* (2001) Cerebral Sinovenous Thrombosis in Children. *The New England Journal of Medicine*, **345**, 417-423. https://doi.org/10.1056/NEJM200108093450604

[5] Grunt, S., Wingeier, K., Wehrli, E., Bolthauser, E., Capone, A., Fluss, J., *et al.* (2010) Cerebral Sinus Venous Thrombosis in Swiss Children. *Developmental Medicine and Child Neurology*, **52**, 1145-1150.

https://doi.org/10.1111/j.1469-8749.2010.03722.x

[6] Mallick, A.A., Sharples, P.M., Calvert, S.E., Jones, R.W., Leary, M., Lux, A.L., *et al.* (2009) Cerebral Venous Sinus Thrombosis: A Case Series Including Thrombolysis. *Archives of Disease in Childhood*, **94**, 790-794. https://doi.org/10.1136/adc.2008.154708

[7] Carducci, C., Colafati, G.S., Figa-Talamanca, L., Longo, D., Lunardi, T., Randisi, F., Bernardi, B. (2016) Cerebral Sinovenous Thrombosis (CVST) in Children: What the Pediatric Radiologists Need to Know. *La Radiologia Medica*, **121**, 329-341. https://doi.org/10.1007/s11547-016-0630-9

[8] Mahal, S., Tiwari, S., Yadav, T., Khera, P.S., *et al.* (2020) Looking Deep into Cerebral Venous System: Is That a Pathology or Just a Normal Variant? *ECR*, C-07764. https://dx.doi.org/10.26044/ecr2020/C-07764

[9] Lehman, L.L., Beaute, J., Kapur, K., *et al.* (2017) Workup for Perinatal Stroke Does Not Predict Recurrence. *Stroke*, **48**, 2078-2083. https://doi.org/10.1161/STROKEAHA.117.017356

[10] Curtis, C., Mineyko, A., Massicotte, P., *et al.* (2017) Thrombophilia Risk Is Not Increased in Children after Perinatal Stroke. *Blood*, **129**, 2793-2800. https://doi.org/10.1182/blood-2016-11-750893

[11] Berfelo, F.J., Kersbergen, K.J., van Ommen, C.H., *et al.* (2010) Neonatal Cerebral Sinovenous Thrombosis from Symptom to Outcome. *Stroke*, **41**, 1382-1388. https://doi.org/10.1161/STROKEAHA.110.583542

[12] Gurgey, A., Ozyurek, E., Gümrük, F., *et al.* (2003) Thrombosis in Children with Cardiac Pathology: Frequency of Factor V Leiden and Prothrombin G20210A Mutations. *Pediatric Cardiology*, **24**, 244-248. https://doi.org/10.1007/s00246-002-0170-z

[13] Alioglu, B., Avci, Z., Tokel, K., Atac, F.B., Ozbek, N., (2008) Thrombosis in Children with Cardiac Pathology: Analysis of Acquired and Inherited Risk Factors. *Blood Coagulation and Fibrinolysis*, **19**, 294-302. https://doi.org/10.1097/MBC.0b013e3282fe73b1

[14] Celorrio, C.S.Y., Palma, B.L. and Rodríguez, P.L.R. (2018) Cerebral Venous Thrombosis. *Rev Cubana Neurol Neurocir*, **8**, 1-23.

[15] Monagle, P., Chan, A.K.C., Goldenberg, N.A., Ichord, R.N., Journeycake, J.M., Nowak-Göttl, U. and Vesely, S.K. (2012) Antithrombotic Therapy in Neonates and Children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*, **141**, 737S-801S. https://doi.org/10.1378/chest.11-2308

[16] Roach, E.S., Golomb, M.R., Adams, R., Biller, J., Daniels, S., Deveber, G., *et al.* (2008) Management of Stroke in Infants and Children: A Scientific Statement from a Special Writing Group of the American Heart Association Stroke Council and the Council on Cardiovascular Disease in the Young. *Stroke*, **39**, 2644-2691. https://doi.org/10.1161/STROKEAHA.108.189696

[17] Chalmers, E., Ganesen, V., Liesner, R., Maroo, S., Nokes, T., Saunders, D., Williams, M. (2011) Guideline on the Investigation, Management and Prevention of Venous Thrombosis in Children. *British Journal of Haematology*, **154**, 196-207. https://doi.org/10.1111/j.1365-2141.2010.08543.x

[18] Raffini, L. and Thornburg, C. (2009) Testing Children for Inherited Thrombophilia: More Questions than Answers. *British Journal of Haematology*, **147**, 277-288. https://doi.org/10.1111/j.1365-2141.2009.07820.x

[19] Kenet, G., Kirkham, F., Niederstadt, T., Heinecke, A., Saunders, D., Stoll, M., *et al.*

(2007) Risk Factors for Recurrent Venous Thromboembolism in the European Collaborative Paediatric Database on Cerebral Venous Thrombosis: A Multicentre Cohort Study. *The Lancet Neurology*, **6**, 595-603.
https://doi.org/10.1016/S1474-4422(07)70131-X

[20] Mortimer, A.M., Bradley, M.D., O'Leary, S. and Renowden, S.A. (2013) Endovascular Treatment of Children with Cerebral Venous Sinus Thrombosis: A Case Series. *Pediatric Neurology*, **49**, 305-312.
https://doi.org/10.1016/j.pediatrneurol.2013.07.008

[21] Waugh, J., Plumb, P., Rollins, N. and Dowling, M.M. (2012) Prolonged Direct Catheter Thrombolysis of Cerebral Venous Sinus Thrombosis in Children: A Case Series. *Journal of Child Neurology*, **27**, 337-345.
https://doi.org/10.1177/0883073811421827