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SAGITTAL SINUS THROMBOSIS IN ANTIPHOSPHOLIPID SYNDROME: A VERY UNUSUAL CAUSE OF SECONDARY HEADACHE.

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Abstract: Background: Antiphospholipid syndrome (APS) is characterized by venous and/or arterial thrombosis. APS may be a primary condition or it may occur secondary to an underlying disease, usually systemic lupus erythematosus (SLE). An uncommon manifestation of APS is Cerebral vein thrombosis (CVT) which is a rare form of cerebrovascular accident. We present a case of 13 year old female child presented with headache because of cerebral sagittal sinus thrombosis associated with APS.
Case Report: A13 year old female child admitted with the complaint of progressively increasing diffuse, severe headache and nausea not relived by medications since one month. No family history of migraine. On examinations vitals and CNS examination were normal except there was bilateral papilledema. Other systems normal.MRI with venography showed sagittal sinus thrombosis. Coagulation profile showed normal PT with prolonged APTT. Anti cardiolipin IgG and IgM were 2 times above cut off level and lupus anticoagulant test was positive. SLE screening tests were negative. Child was diagnosed as a probable case of antiphospholipid syndrome as per Sapporo (Sydney) criteria and started on Low molecular weight heparin therapy. Patient responded well to treatment, papilledema resolved and was discharged on warfarin. Repeat MRI venography shows resolution of sagittal sinus thrombosis. Follow up Anti cardiolipin antibodies and lupus coagulant were positive even after 12 weeks. Diagnosis of APS is confirmed and child is currently on warfarin maintenance therapy and under follow up.
Conclusion: Cerebral venous thrombosis is an unusual cause of secondary headache and is an important differential diagnosis of headache presented with papillodema. MRI venography brain is an investigation of choice for cerebral deep vein thrombosis. In a case of cerebral sinus thrombosis, along with prolonged APTT, anti phospholipid syndrome should be ruled out.

Keywords: Antiphospholipid antibodies, Cerebral vein thrombosis, Intracranial sinus thrombosis.

Introduction: Cerebral venous thrombosis (CVT) is a rare cause for severe headache[1]. Its pathophysiology is characterized by loss of equilibrium between endogenous thrombogenic and fibrinolytic factors. In addition, the presence or absence of efficient venous collaterals alters the time course of CVT. The etiology of cerebral venous sinus thrombosis (CVST) includes contraceptive use, pregnancy, puerperium, infectious diseases, prothrombotic states, malignancy, and autoimmune inflammatory diseases. However, CVST is a relatively rare phenomenon of APS (Anti phospholipid syndrome). The main pathologic mechanism of venous thrombosis is hypercoagulable state. Antiphospholipid syndrome (APS), which is also known as “Hughes Syndrome,” is a systemic non-inflammatory autoimmune disease. The characteristic features of APS are recurrent arterial and/or venous thrombosis, thrombocytopenia, recurrent foetal losses and miscarriages, [2, 3] accompanied by the presence of antiphospholipid antibodies (aPLs). This syndrome can occur alone (primary APS) or may be associated with other connective tissue disorders, such as systemic lupus erythematosus (SLE), Sjogren’s syndrome, and certain infections.[4, 5] The estimated incidence of APS is around 5 new cases per100000 individuals per year and the prevalence around 40-50cases per 100,000 population.[6] Most prominent clinical features of APS, are thrombotic events which may occur virtually in any blood vessel. The most common manifestation of APS, is Venous thrombo embolism (VTE), particularly deep vein thrombosis (usually in the legs), with a prevalence of 31.7%-38.9% of VTE.[7, 8]

CVT cannot be diagnosed on clinical grounds, as it has no single pattern of presentation, therefore requires neuroimaging for diagnosis.

Because of varying clinical presentations, it is difficult to make an early confirmed diagnose which is potentially fatal to the APS patients. To improve diagnosis and prognosis of the disease more insights are essential in CVST and APS. Till now, the pathogenic mechanisms of CVST in APS are complex and not fully elucidated, but could be related to the presence of aPLs which may interfere different pathways, and cause immune-mediated damage, and complement activation. Recurrent thrombosis despite adequate anticoagulation is an important feature of APS. Current treatment guidelines for APS emphasize the importance of early diagnosis and aggressive therapy to prevent recurrence of thrombosis.[9,10] However, optimal duration and the intensity of anticoagulation therapy of CVST in patients with APS remains controversial.[11,12] Besides, further clarification required in the diagnosis and treatment of recurrent thrombosis in APS patients. Currently, the available data on clinical characteristics, imaging manifestations, treatment and prognosis of CVST in APS patients are limited due to the low incidence; few detailed studies conducted in APS patients with CVST.

The clinical criteria for the diagnosis of APS were established in 1998, in Sapporo, Japan, and are known as the Sapporo criteria.[13] This criteria have good sensitivity and specificity, although systemic lupus and systemic lupus-like conditions may overlap when using the Sapporo criteria and may cause misdiagnosis of APS 1to 3% of cases.[13] A variety of immune-mediated vascular and inflammatory effects may cause neurological manifestations and most of the time, the signs and symptoms are related to ischemia and/or thrombosis.13 Antiphospholipid antibodies may activate endothelial cells, platelets and coagulation cascades, leading to ischemic stroke and/or thrombosis in patients of all ages.[14,15]

A wide range of investigations should be carried out once diagnosis is established and treatment should be started as soon as possible [16, 17].An association between oral contraceptives use and the development of cerebrovascular diseases such as CVT, is suggested by Lorentz et al In 1962. [18] Since then, many studies have been conducted in women taking oral contraceptives and many cases of cerebral venous thrombosis have been reported in the literature.[19- 21]

We present a case of 13 year old female child presented with headache because of cerebral sagittal sinus thrombosis associated with APS.

Case report: A 13 year old female child admitted with the complaint of progressively increasing headache and nausea since one month. The head ache was diffuse, severe, no diurnal variation, or associated sleep disturbances and it is not relived by medications .There were no precipitating or relieving factors for the head ache. There is no family history of migraine. On examinations vitals were normal; there were no neuro-cutaneous markers. CNS examination was normal except there was bilateral advanced papilleodema on fundus examination (Figure-1) .Other systemic examination was normal. MRI with venography was done in view of papilleodema which showed sagittal sinus thrombosis (Figure-2). Patient was investigated for thrombophilia. Coagulation profile showed normal PT with prolonged APTT. Anti cardiolipin IgG and IgM were 2 times above cut off level and lupus anticoagulant test was positive. SLE screening tests were negative for this child. Child was diagnosed as a probable case of antiphospholipid syndrome as per Sapporo (Sydney) criteria and started on Low molecular weight heparin therapy. Patient's headache responded to treatment, papilloedema gradually resolved and child was discharged on warfarin. Repeat MRI venography shows resolution of sagittal sinus thrombosis. Follow up Anti cardiolipin antibodies and lupus coagulant were positive even after 12 weeks. Diagnosis of APS is confirmed and child is currently on warfarin maintenance therapy and under follow up.

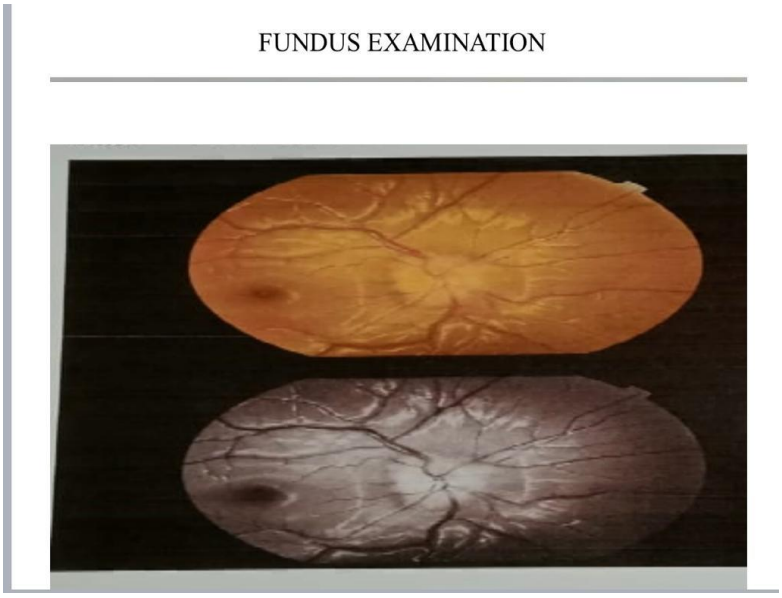

Figure-1: Fundus examination showing Papilloedema in our case.

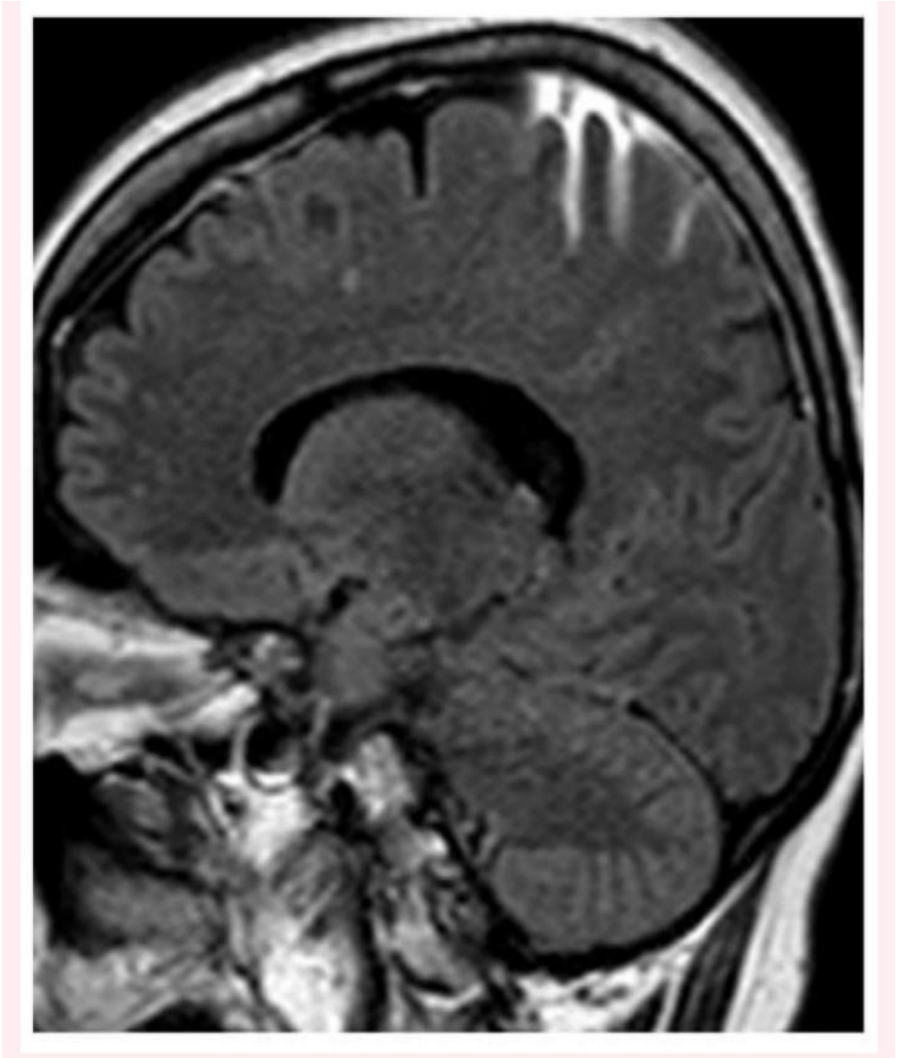

Figure -2: MRI Brain sagittal section Cerebral sagittal sinus thrombosis in our case.

Discussion: As reported by Bousser [22], the mode of onset of CVT is variable and it presents with different symptoms. Its onset is sub acute in 50% of cases, acute in 30% and chronic in 20%. The wide range of clinical symptoms that occur in CVT may be grouped into at least four main patterns (a) focal neurological deficits or partial seizures; (b) the pseudo tumour cerebri syndrome; (c) sub acute encephalopathy with depressed consciousness and sometimes seizures without recognizable features of intracranial hypertension; and (d) a slowly progressive cavernous sinus thrombosis with a moderately painful third or sixth nerve palsy[22]. However unusual patterns of headache cannot be classified into the previously mentioned groups. The presence of headache as the only symptom may simulate other conditions such as sub-arachnoid haemorrhage or migraine, and may be misleading. As per previous studies, headache is the common synptom found in 70%–91% of patients with CVT, while the most frequent sign is papilledema, occurring in 27%–80% of patients [22–24]. When the headache, described by the patient as the first or the worst experienced, the physician should suspect a secondary headache, such as headache in cerebral venous thrombosis. As intracerebral venous thrombosis goes unrecognized in many patients its real incidence is unknown. Its incidence is likely to be lower than the incidence of deep-vein thrombosis which is approximately 1 per1000 persons per year. Our case is a 13 year old female child presented with progressively increasing headache with nausea which is not relieved by medication. On examinations her vitals and CNS examination were normal except there was bilateral papilledema.

Based on its aetiology CVT can be classified into infective and non infective. Septic CVT incidence has been reduced in developed countries because of availability of antibiotics. Congenital thrombophilia is the most frequent noninfective medical causes of CVT, particularly the increased resistance to activated protein C with factor V Leiden mutation and the 20210 G to A mutation of the prothrombin gene. Thrombosis secondary to severe local head injury is well known. Rheumatologic diseases which are associated with CVT are Systemic lupus erythematosus, Behçet's disease and periarteritis nodosa. Nephrotic syndrome, antithrombin III deficiency, cancer and pregnancy are the other hyper coagulable states which may cause CVT. Cardiac diseases that may associated with CVT are congestive heart failure, cardiac insufficiency and pace maker use. CVT can also be caused by Crohn's disease, ulcerative colitis and cirrhosis of liver[1, 22]. In our case systemic examination and fundus examination revealed papilloedema. Our patient was investigated for thrombophilia. Coagulation profile showed normal PT with prolonged APTT. Anti cardiolipin IgG and IgM were 2 times above cut off level and lupus anticoagulant test was positive. SLE screening tests were negative for this child.

The CVT can be diagnosed with computed tomography or MRI. The CT shows direct signs of CVT in one-third of cases, while MRI allows the thrombus to be dated, since its signal features change with progression of the disease. In the hyper acute phase (0–24 hours), the thrombus is hypo intense on T1-weighted images and hyper intense onT2-weighted images. In the acute phase (1–5 days), MRI shows hypo intense images on both sequences. Later, the thrombus is hyper intense on both T1 and T2-weighted images in the sub acute phase (5–14 days) and dis homogeneous after day 16. These changes depend on haemoglobin metabolism. But, MRI does not correlate with disease prognosis, because signal anomalies can be also observed months after thrombosis, without correlation to clinical findings [25].In our case MRI with venography was done in view of papilleodema which showed sagittal sinus thrombosis. (Figure -2)

Treatment of CVT depends upon the clinical progression of the disease. Some physician's prefer conservative treatment and they reserve interventions only in patients with clinical deterioration. In 1942, Stansfield, first used heparin in a puerperal woman with focal neurological deficits secondary to venous thrombosis [26]. After that two randomized studies conducted in patients with cerebral venous thrombosis, who were on anti-coagulant therapies by Einhaupl et al. [27] and De Brujin and Stam et al.[28] which stated that heparin treatment is not only safe but also beneficial in these patients, even in cases with associated intracranial haemorrhage. Fibrinolytic therapy is advocated by some other physicians, with the goal of rapid clearance of the thrombus from the venous system. Selective catheterization via trans femoral venous catheter and direct instillation of thrombolytics (e.g. urokinase, streptokinase,

rt-PA) allowed the successful treatment of many patients. However, risk of minor haemorrhage or systemic coagulopathy seems to be correlated with the use of rt-PA. Even in individuals with haemorrhage and non hemorrhagic venous infarcts selective fibrinolytic therapy is reported to be safe. However, fibrinolytic therapy should be reserved to patients with fast clinical deterioration after the failure of systemic therapy with heparin [29].Our case was diagnosed as a case of antiphospholipid syndrome and started on Low molecular weight heparin therapy. Patient's headache responded well to treatment, papilledema gradually resolved and child was discharged on warfarin. Repeat MRI venography shows resolution of sagittal sinus thrombosis. Follow up Anti cardiolipin antibodies and lupus coagulant were positive even after 12 weeks. Diagnosis of APS is confirmed and child is currently on warfarin maintenance therapy and under follow up.

Conclusion: Cerebral venous thrombosis is an important differential diagnosis of headache presented with papillodema and is an unusual cause of secondary headache. Investigation of choice for cerebral deep vein thrombosis is MRI venography of the brain. Anti phospholipid syndrome should be ruled out in a case of cerebral sinus thrombosis, along with prolonged APTT. The Physicians, Neuro physicians and Paediatricians should be aware of the rare clinical presentations of Anti phospholipid syndrome so as to handle them in time for good results.

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