Cerebral venous thrombosis in Kuwait

Clinical presentation, risk factors, and management

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ABSTRACT

الأهداف: التحقق من المظاهر السريرية، وعوامل الخطر، والجيوب الوريدية المصابة بالتخثر الوريدي الدماغي وذلك لدى مرضى أحد المراكز العصبية التي تقدم الرعاية من الدرجة الثالثة في دولة الكويت.

الطريقة: أُجريت هذه الدراسة الاسترجاعية في مستشفى ابن سيناء، الكويت وذلك خلال الفترة من يناير 2000م إلى أكتوبر 2010م، حيث قمنا باسترجاع الحالات المصابة بتخثر الأوردة الدماغية والتي كان عددها 71 حالة، ومن ثم قمنا بإدخال السجلات اللازمة في قاعدة البيانات. لقد قمنا بتقييم فرط التخثر لدى المرضى، كما أننا قمنا بعمل مجموعة من فحوصات التصوير الدماغي.

النتائج: شملت هذه الدراسة 71 مريضاً، وقد كانت نسبة الذكور إلى الإناث 1:1.5. وتمثلت المظاهر السريرية في كل من: الصداع (93%)، والتشنجات الصرعية (31%)، والعلامات العصبية البؤرية (37%). لقد كان لدى أكثر من ثلثي الإناث (العدد=30) تاريخ سابق بتناول أقراص منع الحمل، وقد وُجد ارتشاح في العصب البصري مع زيادة الضغط داخل القحف في 20 مريضاً (28%)، ومتلازمة فرط استجابة المبيض مع تخثر الأوردة المخية في مريضة واحدة، ومتلازمة بهجت في 10% من المرضى (العدد=7). ولقد كان أكثر الجيوب الوريدية المصابة بالتخثر كالتالي: جيوب سهمية علوية في 59% من المرضى (العدد=42)، وجيوب معترضة ومستقيمة (خيمية) في 54% (العدد=38)، فيما تم تسجيل احتشاء الأوردة النزفي في 18% من المرضى (العدد=13). لقد تعافى 50% من المرضى في غضون 2–4 أسابيع، وتعافى 15 مريضاً (21%) خلال 4–12 أسبوعاً، فيما أُدخل 15 مريضاً (21%) إلى وحدة العناية المركزة مع تزويدهم بجهاز الدعم التنفسي لمدة أسبوع إلى أسبوعين.

خاتمة: أثبتت الدراسة أن تناول أقراص منع الحمل عن طريق الفم يعد من العوامل الأولية التي تزيد من خطر الإصابة بتخثر الأوردة المخية بين المرضى الإناث، ويساعد الفحص المبكر مع التدخل العلاجي المباشر بمضادات التخثر في تقليل مضاعفات المرض ونسبة الوفيات. ولقد اتضحت أهمية عمل اختبار تخثر الدم (D–dimer) في سرعة الوصول إلى التشخيص الصحيح وذلك بدرجة حساسية تصل إلى 58%.

Objective: To explore the pattern of clinical presentations, risk factors, and the sinuses involved in cases of cerebral venous thrombosis (CVT) treated in a tertiary neurological center in Kuwait.

Methods: A retrospective analysis of cases of CVT treated at Ibn Sina Hospital, Kuwait, from January 2000 to October 2010. The records of 71 patients were retrieved and entered in a database. All patients were evaluated with hypercoagulable work up and relevant neuro-imaging studies.

Results: Seventy-one patients were included in our study, with a male to female ratio of 1:1.5. The clinical presentations were: headache (93%), seizures (31%), and focal neurological signs (37%). Over two-thirds (n=30) of female patients had a history of oral contraceptive use. Papilledema with raised intracranial pressure was recorded in 20 patients (28%), ovarian hyper-stimulation syndrome with CVT in one patient, and possible Neuro-Behçet's in 10% (n=7). The venous sinuses involved were superior sagittal sinus in 59% (n=42), and transverse and straight sinuses in 54% (n=38). Hemorrhagic venous infarctions were seen in 18% (n=13). Fifty percent of patients recovered within 2-4 weeks, 15 patients (21%) recovered within 4-12 weeks, and 15 patients (21%) required intensive care unit care with ventilator support for 1-2 weeks.

Conclusion: Oral contraceptive use was the primary risk factor in female patients. Early diagnosis and immediate treatment with anticoagulants reduce the morbidity and mortality. Serum D-dimer level is more helpful for early diagnosis with sensitivity of 58%.

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Cerebral venous thrombosis (CVT) results from thrombosis of cortical or deep veins, or intracranial venous sinuses. It is a rare disorder with an incidence of approximately 5 people per million and accounts for 0.5% of all strokes, occurring more frequently in females. Cerebral venous thrombosis is associated with a variety of conditions including infection, coagulation disorders, chronic inflammatory diseases, venous stasis, and trauma. The signs and symptoms associated with CVT may be broad. If the disease is unrecognized, a delay in treatment may result in cerebral edema, intracranial hypertension, cerebral ischemia, and hemorrhagic infarction, resulting in rapid neurological worsening, coma, and even death. The mortality ranges from 5-30%. The CVT often remains a diagnostic and therapeutic challenge to the physicians or specialists owing to the nonspecific symptoms and the broad spectrum of presentation. Radiological studies are crucial in establishing the diagnosis.[1] The development and availability of more sophisticated diagnostic tools, such as MRI, MR angiography, and MR venography, have facilitated prompt diagnosis and treatment of CVT, and resulted in improved outcome (80-90%).[2,3] In this study, we retrospectively analyzed 71 patients, reviewing the clinical data, pattern of clinical presentations, associated risk factors, the pattern of sinuses involved, and the treatment; we also reviewed various clinical studies.

Methods. In this retrospective analysis, the records of all the patients with a diagnosis of CVT who were evaluated and treated between January 2000 and October 2010 in Ibn Sina Hospital, a center for tertiary neurological care in Kuwait, were retrieved and entered in a database. The patient's files were collected, and the data were abstracted anonymously for this review, which was given "exemption" status by the ISH Institutional Medical Ethical Committee, not requiring consent from the patients. The diagnosis of CVT was made based on clinical presentation and by imaging studies. The CT, MRI, and MR-venography using 1.5 Tesla GE sigma machine were the important imaging procedures. Patients were admitted within 3 days to 3 months after the onset of symptoms and were evaluated clinically with relevant blood investigations, including serum D-dimer level, antiphospholipid antibodies, vasculitis, and hypercoagulable work up such as Protein C or S deficiency, anti-thrombin-III, lupus anticoagulant antibodies, Factor V Leiden mutation, and anticardiolipin antibodies on admission. D-dimers are fragments of cross-linked fibrin, digested by plasmin that have been shown to be sensitive for the diagnosis of deep vein thrombosis and pulmonary embolism. The measurements of D-dimer levels were performed in the laboratory, both by a rapid (30 minute) procedure (Biomeyrieux, Craponne, France) and a conventional enzyme-linked immunosorbent assay method (Asserachrom Ddi, Stago, France). The sensitivity, specificity, and positive predictive values of conventional D-dimer levels are >500 ng/ml, or 0.05 µg/ml, for the diagnosis of CVT. All patients were treated with systemic anticoagulants, heparin, and low molecular weight heparin (LMWH), antibiotics, antiedema measures, and anticonvulsants, on an individual basis and need. The demographic details of incidence of age, gender, nationality, and the associated risk factors were analyzed. The common presenting symptoms, neurological deficits, the type, extent, size, and distribution of sinuses involved were studied. Based on the data, frequencies of various parameters were calculated without detailed statistical analysis.

Results. In this period, the records of 71 patients who presented with signs and symptoms of CVT were retrieved. Their ages ranged between 20-60 years, with a median age of 30, and a male to female ratio of 1:1.5. The numbers of patients according to age, gender, and ethnicity are summarized in **Table 1**. The maximum number of patients were in the age group of 20-29 years, with young females predominantly affected. Ethnically the number of Arabs was more than non-Arabs. In women, the main risk factor was the use of oral contraceptives, for variable periods of time. The next risk factor was in the post-partum period with a history of recurrent abortion. Other risk factors were early pregnancy, in the first trimester with hematological causes, like antiphospholipid syndrome or Protein C or S deficiency. One patient, developed CVT after induction of ovulation by hormones, ovarian hyper stimulation syndrome (OHSS).[4] Other factors noticed were anabolic steroid use, hormonal therapy (n=6), smoking, chronic alcohol use, and Hubble bubble users. Infectious causes were seen in 5 patients, the most common source of infections were from the para-nasal sinuses after tooth extraction or meningitis. There were a few cases with symptoms of oral and genital ulcerations with arthralgia, suggestive of Behçet's disease, presenting with CVT, (n=7, 10%). Three cases developed CVT in the postoperative period following lumbar disc surgery,

Table 1 - The incidence of age, gender, and racial distribution of patients with cerebral venous thrombosis.

Age group in years	Male	Female	Arab	Non-Arabs	Total
20-29	6	22	25	3	28
30-39	10	12	15	7	22
40-49	9	7	13	3	16
50-60	3	2	4	1	5

lumbar myelography, and after cesarean section surgery. Six patients presented with features of cavernous sinus thrombosis. The presenting symptoms were headache, fever, visual impairment, and pain in the affected eye, with drooping of the upper eyelids. Clinically, all the cases of cavernous sinus thrombosis had neck stiffness, proptosis, variable degrees of gaze palsies to total ophthalmoplegia and multiple cranial nerve palsies. The CT scan or MRI/MRV revealed evidence of cavernous sinus thrombosis in the ipsilateral cavernous sinus. These cases were associated with systemic infection or focal soft tissue infection in the paranasal sinuses. In one patient, a maxillary sinus mass, probably carcinoma, extending to the left temporal lobe compressing the lateral wall of the cavernous sinus, with thrombosis, was seen.

Out of the 71 cases with CVT, 40 patients, (56%) presented with bilateral papilledema, with signs and symptoms of raised intracranial hypertension. In 20 patients, the CSF monitoring showed high CSF pressure, between 250-600 mm of H_2O. In the remaining 20 patients, the CSF pressure was normal. Another risk factor was found in a 30-year-old female patient who after normal delivery under epidural anesthesia had post-dural headache. She developed severe venous thrombosis and detailed investigations did not reveal any other risk factor.

Table 2 - The pattern and distribution of venous sinuses in patients with cerebral venous thrombosis.

Pattern of sinuses involved in the patients	No. of patients	Male	Female	Frequency (%)
Superior sagittal sinus	42	10	32	(59)
Transverse + straight sinuses	38	11	27	(54)
Sigmoid + jugular veins	18	6	12	(25)
Deep venous system	3	2	1	(4)
Cavernous sinus thrombosis	5	4	1	(7)
Hemorrhagic infarction/ subarachnoid hemorrhage	13	4	9	(18)

Table 3 - Signs and symptoms in patients with cerebral venous thrombosis and their frequency.

Presenting signs and symptoms	No. of patients	Frequency (%)
Headache	66	(93)
Seizures/focal or generalized	22	(31)
Coma/decerebrate sign	10	(14)
Cranial nerve palsies	17	(24)
Hemi-paresis/monoparesis	20	(28)
Monoplegia or paraplegia	4	(6)
Papilledema ↑ CSF pressure	20	(28)
Papilledema alone	20	(28)
Fever, neck stiffness, and CSF reaction	21	(30)
Behçet's disease symptoms	7	(10)
Cavernous sinus thrombosis	5	(7)
Meningitis/CSF reaction	5	(7)

The pattern and distribution of venous sinus involvement is shown in **Table 2**, and the presenting signs and symptoms are shown in **Table 3**. Among 40 patients who had papilledema, 12 patients had focal neurological deficits and bilateral papilledema. Multiple venous sinus involvement was seen in 5 out of these 12 patients. The remaining 28 patients had only papilledema mimicking the clinical presentation of pseudotumor cerebri. Among these 28 patients, 18 patients had involvement of multiple venous sinuses. Seizures (focal or generalized) with focal neurological deficits were seen in 10 female and 5 male patients. The focal deficits were hemiparesis, monoparesis, or paraparesis with cranial nerve involvement. The brain lesions were mostly venous infarctions in the occipital, parietal, or multiple sites in 15 patients, correlating well with clinical deficits. Rarely, the brain lesions were intra-cerebral hemorrhages, sub-arachnoid hemorrhage, or hemorrhagic venous infarctions.

In our study, more than 50% of patients recovered within 2-4 weeks of treatment. Twenty patients (28%) recovered within 1-2 weeks time, and 15 patients, (21%) recovered within 4-12 weeks time. Intensive care unit care was required for another 15 patients (21%) with ventilator support for 1-2 weeks. The overall outcome, in our study group was good with independent survival of four-fifths of the patients with no mortality in those patients with cortical or deep venous thrombosis. The patients were treated with systemic anticoagulants followed by oral anticoagulants for 6 to 9 months. Follow up imaging were carried out in most of the cases, and clear recanalization of affected sinuses were seen. Patients with genetic factor deficiencies or hematological causes were advised lifelong prophylactic anticoagulation.

Discussion. Cerebral venous thrombosis has been a well-known disorder since the early 19th century; however, it was usually diagnosed at autopsy. With modern radiological imaging techniques, visualization of the cerebral venous sinuses and venous circulation is improving, making early diagnosis and initiation of treatments much easier.[3] In cerebral venous sinus thrombosis (CVST), symptoms are caused by obstruction of the cortical veins or superior longitudinal sinus (superior sagittal sinus [SSS]). Impairment of CSF absorption, causing raised intracranial tension, or obstruction of the draining veins, results in regional infarction, with focal signs or seizures and headache. Disorders of consciousness alone, might be due to deep cerebral vein thrombosis. Extensive CVT, prolonged unconsciousness, or status epilepticus with dense neurological deficit, indicates a poor prognosis. The main cause of death is hemorrhagic infarction, sepsis, pulmonary embolism, brain edema, and herniation, or

with underlying systemic disorder like malignancy.[1,2] In antiphospholipid syndrome the phospholipids-associated protein-β2-GP1, anticardiolipin, and lupus anticoagulants, by their interactions, cause venous thrombosis. The anticardiolipin antibodies could represent an important risk factor for CVT.[4] Bugnicourt et al[5] reported that elevation of plasma factor VIII level and Von Willebrand factor is the most common prothrombotic risk factors for cerebral sinus venous thrombosis. In our study, Protein C or S deficiency, and antithrombin-III deficiency were seen only in 5 patients (7%).

Headache was the most frequent symptom and presenting complaint (93%) in patients with CVT in our study. It often antedates any obvious symptoms or signs of increased intracranial pressure, mimicking idiopathic intracranial hypertension. Mild intracranial hypertension was found with symptoms of headache and vomiting, but without associated ocular sign of papilledema in 30 patients (42%) out of 71 patients. Cumurciuc et al,[6] reported that headache may be the only symptom of CVT. Stavrinou et al[7] reported a case of acute headache with hydrocephalus in a young lady proved to be cerebellar venous infarct, caused by unilateral transverse sinus thrombosis.

Papilledema, an alarming clinical sign was found in 56% (n=40) of our patients who presented with headache, and among these 40 patients, 20 (28%) patients had elevated CSF pressure. It is not clear why the remaining 20 patients did not develop raised CSF pressure. Subash and Parmar[8] reported that papilledema can be the sole manifestation of postpartum CVST. Lockhart and Baysinger[9] in a review article discussed in detail the incidence of intracranial venous thrombosis in the parturient. They described the incidence of intracranial venous thrombosis in patients with postpartum headache that had undergone regional epidural anesthesia. Jungmann et al[10] reported a case of CVST in a young woman in the post-partum period after epidural anesthesia during delivery. We had a similar patient: a young woman developed extensive venous thrombosis after normal delivery under epidural anesthesia, with severe visual loss due to raised intracranial pressure. With increasing use of regional anesthesia in obstetrics, venous sinus thrombosis should be considered as a differential diagnosis of post-dural puncture headache.[10] Another young lady, after hormonal therapy for sterility, in her early pregnancy, developed OHSS and CVT, with recurrent focal and generalized convulsions, as reported earlier.[11] In our study 20 patients (28%) developed CVT in the postpartum period.

The next most common presenting symptom was seizure, partial or generalized. Early partial epileptic seizures, which were mostly the first symptom and associated with motor or sensory deficits and neurologic dysfunctions fluctuated in almost all patients. There were clinical correlations with focal seizures and parenchymal lesions such as venous infarction associated with hemorrhagic changes.[1,2] Masuhr et al[12] reported the predictors of early epileptic seizures in acute cerebral venous and sinus thrombosis. Patients with focal motor deficits due to cortical vein thrombosis and intracerebral hemorrhage carried the highest risk for early seizures. In addition, early symptomatic seizures were found in 86 (44%) of his patients, and status epilepticus was an important cause of morbidity and early mortality. Ferro et al[13] reported early seizures in cerebral vein and dural sinus thrombosis. He concluded that patients with CVT with supra-tentorial lesions had a higher risk for both presenting and early seizures, whereas patients presenting with seizures as the first symptom had a higher risk of recurrent seizures within 2 weeks. In our study, 22 patients (31%) presented with focal or generalized seizures and anticonvulsant treatment was given for one year. The EEG in these patients were abnormal showing either focal or generalized paroxysmal, epileptiform activities. Patients with dural sinus thrombosis or deep venous stroke may present with some degree of impaired consciousness. The transient altered consciousness may be related to seizure generalization and severe consciousness impairment could be due to the involvement of deep structures in the brainstem, as noticed in some of our patients with CVT. The etiologic mechanisms in patients with CVT, dural sinus thrombosis, or deep cerebral vein thrombosis is more or less similar. Saadatnia et al[14] reviewed all the etiological risk factors associated with CVST. Previously it was related to otomastoid, orbital, and central face cutaneous infection, now it is more often related to neoplasm, pregnancy, puerperium, systemic disease, intracranial tumors, oral contraceptives, and coagulopathies, as the most common causes. The CVT has also been found in association with fibrous thyroiditis, hyperthyroidism, and jugular vein thrombosis after catheterization or idiopathic jugular vein stenosis. Maes et al[15] reported a case of CVT in a patient with hyperthyroidism, with increased factor-VIII procoagulant protein as a predisposing factor for CVT. Fatehi et al,[16] reported a case of CVT associated with oligodendroglioma and pregnancy. The CVST associated with iron deficiency anemia was reported by Ogata et al,[17] and the pathological mechanism was found to be iron deficiency anemia associated with an elevation of D-dimer and thrombin-antithrombin–III complex (TAT). After the anemia was corrected with the treatment of peptic ulcer and iron supplementation, the TAT and D-dimer levels were normalized and the

occluded veins recanalized well. In our case series, we found a few patients with iron deficiency anemia as the etiological factor.

Oral contraceptives usage is a frequent and important risk factor in young women, with hereditary prothrombotic conditions.[1,2,14] Kajtazi et al[18] published a case series on the variables of clinical and etiological risk factors in venous thrombosis. In our study, CVT was found to be more common in women of child-bearing age, and the combined risk factors of pregnancy, puerperium, and oral contraceptives use were the potential predisposing conditions in more than 50% of this study group, similar to previous case series.[14,18] The other possible etiologic factors were infective causes, accounting for 32% of reported cases. In our series, 5 patients had infectious causes like bacterial meningitis, chronic bacterial cranial infections, paranasal sinuses infections, meningitic processes, and infection after tooth extraction; all responded very well to systemic antibiotics. Behçet's disease is a relatively rare cause of CVT. However, in our study it was a potential cause of CVT in 7 patients (10%), which included 5 females and 2 males. Saadoun et al[19] analyzed the clinical findings, treatment outcome, and prevalence of CVT in a large cohort of patients with Behçet's disease from a single center. They reported the incidence of CVT in Behçet's disease was 7.8% of 820 patients. Another observation among Behçet's disease patients who developed CVT earlier, was 5 times lower incidence of CNS parenchymal involvement. In the concise report by Tunc et al,[20] it was explained that CVT in Behçet's disease was strongly associated with peripheral major vessel disease and occurred earlier in the disease course than the parenchymal type of neuro-Behçet's disease.[20]

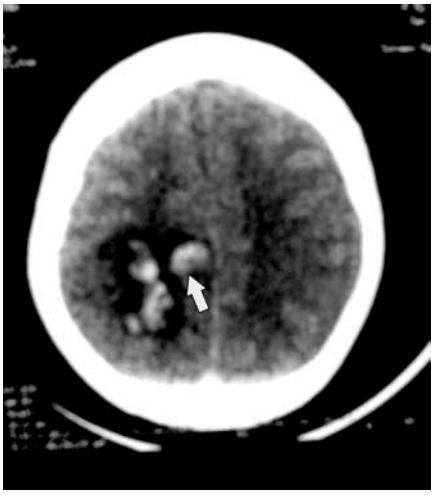

Figure 1 - Non-contrast axial CT scan showing right parieto-occipital venous hemorrhagic infarction secondary to right transverse sinus thrombosis.

In our study group, 13 patients had either hemorrhagic venous infarction or small areas of subarachnoid hemorrhages (**Figure 1**). All patients with CVT, with evidence of intracerebral hemorrhage or venous hemorrhagic infarction, received a full course of anticoagulants. A few patients (n=10, 14%) with high hemorrhagic risk were treated with LMWH followed by oral anticoagulants for 6-9 months. Fink and McAuley[21] reported a small case series of patients treated with heparin followed by oral anticoagulants, and highlighted the safety of anticoagulation for CVT associated with intracerebral hematoma. In our current practice of treating venous thrombosis with heparin, there was no evidence of increased risk, or poor outcome due to new hemorrhages in the brain, even in those with hemorrhagic venous infarct. The other causative factors that were seen are drugs, and substance abuse in 5 patients (7%), hormonal therapy in 6 patients (9%), and 3 patients developed CVT following surgical treatment.

Early diagnosis of CVT is a crucial point to initiate early treatment. Agid et al[3] described that when available, MR supplemented with the technique of Gadolinium enhanced MRV, was the method of choice for the diagnosis of dural sinus thrombosis, as well as most other pathologic entities affecting the intracranial venous system. The MRI is now the imaging technique of choice in the diagnosis of CVT.[3] The hallmark of thrombus is the lack of signal void on SE sequences, and the absence of signal on MRV. The development of a collateral circulation affects the epicranial, superficial, and transcortical medullary veins. The MRV is the technique of choice, to assess, and identify a collateral pathway of veins. Fellner et al[22] highlighted the importance of T2-weighted gradient-echo MRI for diagnosis of cortical vein thrombosis. They reported that the venous thromboses were best detectable in T2-weighted conventional GRE sequences in all patients. The use of Echo-Planar T2-weighted MRI was described earlier by Selim et al.[23] This report highlights the usefulness of the T2-weighted MR sequence in the rapid detection of CVT and enables the diagnosis prior to MR venography. The MR venography is almost always required to confirm the diagnosis of CVT. Absence of flow signal on MRV suggests intraluminal thrombus.

The outcome of patients with cortical venous stroke is generally good, but not in those with deep venous system involvement. Although cerebral dural and venous thrombosis are increasingly recognized, thrombosis of the cerebral deep venous system is very rare. Thrombotic occlusion of the internal cerebral veins is a dangerous form of CVT, as it causes venous infarction of the thalami. Because both thalami drain into the vein of Galen and straight sinus, bilateral thalamic involvement

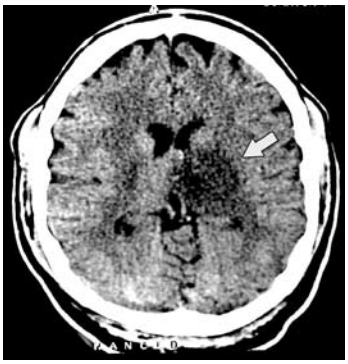

Figure 2 - Axial non-contrast CT scan showing hypo-dense lesion in the left thalamus representing venous infarct, mimicking a tumor.

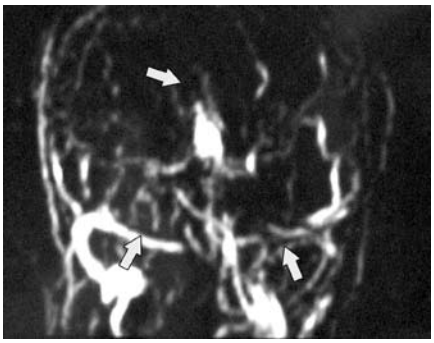

Figure 3 - Magnetic resonance venography in a 42-year-old lady who developed cerebral venous thrombosis showing extensive thrombosis of cerebral venous sinuses, as shown by arrow heads.

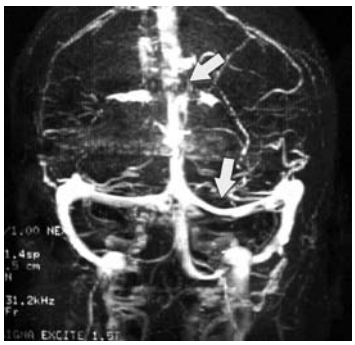

Figure 4 - Three weeks later, with treatment, the patients MRV showing partial recanalization of the occluded venous sinuses.

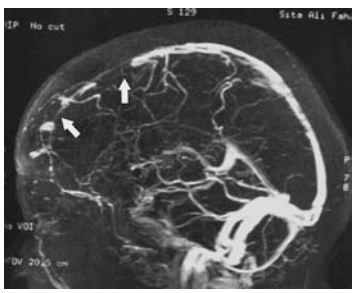

Figure 5 - Six weeks later follow-up MRV in sagittal view shows the filling defect in the anterior part of the superior sagittal sinus due to thrombosis.

is frequently encountered in internal CVT. Unilateral thalamic edema occurs when all internal cerebral veins are occluded.[24] This may mimic a thalamic tumor (**Figure 2**). Haug et al[25] reported a case of unilateral venous thalamic infarction in a child mimicking thalamic tumor. The authors concluded that unclear unilateral thalamic lesion might be symptomatic of cerebral deep venous thrombosis and might mimic a thalamic tumor. Sagduyu et al[26] in their case series, described in detail the occurrence of cerebral cortical and deep venous thrombosis without sinus thrombosis as well as their clinical and MRI correlates. They concluded that, in patients who present with partial or generalized seizures followed by focal neurologic signs, if CT, MRI, and diffusion-weighted imaging studies show an ischemic and/or hemorrhagic lesion that does not follow the boundary of classical arterial territories without signs of sinus thrombosis, this may predict cerebral deep venous thrombosis (**Figures 3-5**).

Angiography was considered as the definitive test for diagnosis of deep CVT. The CT venography showed persistent flow in the thrombosed veins.[23] Bergui et al[27] many years ago, described the clinical picture of patients with CVT and patterns of dural sinus involvement. He concluded that the isolated intracranial hypertension was more frequent in patients with more extensive thrombosis of the dural sinuses. In our study, thromboses of the SSS were more commonly involved, and the straight and transverse sinuses were involved next. In patients who presented with papilledema and focal neurological deficits, multiple venous sinuses were involved, and venous infarctions were found in 16 patients (22%). Tardy et al[28] reported that the measurement of D-dimer level in the blood of patients with acute headache with or without focal neurological deficit has potential utility in the diagnosis of CVT. The serum D-dimer test was underutilized as a diagnostic tool earlier in the last decade due to lack of availability, however, it is more commonly used now. The normal level is <500 ng/ml or 0-0.5µg/ml and in patients with CVT, the levels are increased 5 to 10 times.[28] D-dimer is useful in the diagnosis of cortical venous thrombosis. Misra et al[29] concluded that patients with positive D-dimer test results should be urgently sent for MR imaging. In our study, D-dimer levels were increased in 21 patients out of 36 patients tested, and the sensitivity and positivity found to be 58%.

Heparin remains the first line of treatment for CVT because of its efficacy, safety, and feasibility. This treatment is aimed at preventing thrombus extension, and to maintain venous pathways. It has been shown to be the most effective treatment modality, though its risk and benefits need to be evaluated on an individual basis. Wasay and Kamal[30] in their report, criticized the use

of anticoagulation in CVST. Independent predictors of death due to CVST include coma, age more than 37 years, deep CVST, right intracerebral hemorrhage, and posterior fossa lesion, worsening of previous focal deficits or de novo focal deficits, hemorrhages on the CT, CNS infection, or cancer. Canhão et al[31] reviewed the causes and predictors of death in CVT, and concluded that the main cause of acute death was neurologic, the most frequent mechanism being transtentorial herniation. They described the various modes of acute mortality reviewing the "VENOPORT" study.[31] Stam, in his report,[32] clearly described that venous thrombosis should be treated with anticoagulation. The treatment of CVST with heparin has been controversial for decades, but most experts now agree that patients with CVST should receive a rapid and full course of anticoagulation as soon as the diagnosis is made. This concern was based on the fact that 30-40% of all patients with CVST have some degree of cerebral hemorrhage, at the time of admission. He emphasized more clearly the use, or benefit of heparin is real and it will do more good than harm to most patients with CVST, even in the presence of cerebral hemorrhagic infarcts before treatment. Anticoagulation is the treatment in patients with significant and life threatening complications, requiring that the balance versus benefit be individually assessed in each patient. The European Federation of Neurological Societies' guidelines on the treatment of cerebral venous and sinus thrombosis were well highlighted by Einhäupl et al.[33] This article, describes the current therapeutic measures of different modes of anticoagulants therapy, the use of thrombolysis, and symptomatic therapy, including control of seizures and elevated intracranial pressure. All patients with CVST without contraindication for anticoagulation, should be treated either with body weight-adjusted subcutaneous LMWH or dose-adjusted intravenous heparin.[33] Concomitant intracranial hemorrhages related to CVST is not a contraindication for heparin therapy.[18] Oral anticoagulation should be given for 6-12 months in patients with idiopathic CVST and in those with mild hereditary thrombophilia.

Other treatment modalities include corticosteroids, osmotic diuretics to reduce cerebral edema, sedatives to reduce metabolic needs, and CSF drainage to decrease intracranial pressure. The use of antiepileptic drugs is necessary in the presence of intracerebral hemorrhage and recurrent seizures as the presenting symptom. In general, anticonvulsant therapy is continued only if the patient's initial presentation, including seizure activity, is recorded in the EEG. This is discontinued after one year if the patient remains seizure-free as the risk of residual epilepsy is very low.[10,11] Intra cerebral hemorrhage occurs in 25-50% of cases of CVT.[18] Although there is increasing evidence that treatment with heparin remains safe and is appropriate in patients with hemorrhagic venous infarction, still some controversy remains on the use of anticoagulation for CVT in the presence of large intracerebral hemorrhages or hemorrhages located in the temporal lobes. For anticoagulation in patients with CVT associated with antiphospholipid syndrome, the initial management of venous thromboembolism should be with LWMH followed by a period of warfarin. Recurrent venous thromboembolism events are managed using long-term warfarin. Patients who suffer thrombosis while anticoagulated with a target INR of 2.5 (2.0-3.0) are candidates for more intensive anticoagulation with targets of 3.5 (3.0-4.0).[4]

Chow et al[34] reported that a combination of rheolytic thrombectomy with intra-arterial thrombolysis is a treatment modality that allows accelerated recanalization of occluded dural sinuses and cerebral veins with lower doses of thrombolytic agents. This paper described that an invasive method of using the combination of the AngioJet rheolytic thrombectomy catheter with intra-arterial thrombolysis may offer a new option in patients with resultant progressive neurological deterioration.[34] Similarly, another surgical option is by using transvascular mechanical thrombectomy, which can be performed using a specialized catheter that provides a vacuum to pull or extract the clot or a micro-guide wire that can assist the clot extraction.[35] Surgical thrombectomy with local use of thrombolytic agents can be used, but it is considered high risk.[35] Anticoagulation does not treat the acute thrombus, therefore, if there is a severe compromise of venous outflow or occlusion, thrombolytic agents may be used for clot lysis using thrombolytic agents. Indicators of poor prognosis include deep venous system involvement, extension of thrombus into the cortical veins, coma as the presenting symptom, rapid rate of symptom progression, more than 10 days delay in diagnosis, hemorrhage on initial CT scan, and presence of papilledema. A better prognosis was demonstrated in patients who presented with headache and papilledema alone, and who had rapid venous sinus recanalization or development of collateral veins.

This study had certain limitations. Since it was a retrospective case analysis, the methodology was not uniformly applied in all patients. Serum D-dimer test was not available in the initial period of the study, so this test was performed in 36 patients only. Once acute management was over, most of the patients were not followed up regularly.

In conclusion, in our current practice, CVT was found to be more common in women of childbearing age, as reported in many previous studies, and the most common risk factors were pregnancy, puerperium, abortion, oral contraceptives use, and hormonal

therapy. Headache was the most frequent symptom and presenting complaint (93%). The diagnosis was confirmed by using imaging techniques and also by serum D-dimer test. The measurement of serum D-dimer levels in patients with acute headache with or without focal neurological deficit has a potential utility in the diagnosis of CVT. Treatment with systemic heparin was used regularly, and there was no evidence of increased risk, or poor outcome, due to new hemorrhages in the brain. In our study, no patients needed more aggressive treatment modalities like thrombolytic therapy or any surgical invasive management. There was no mortality and all patients had good recovery.

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