

Oral Contraceptive Consumption and Cerebral Venous sinuses Thrombosis

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Abstract

Introduction: Cerebral venous sinus thrombosis (CVST) is a rare cause of stroke and the clinical presentation is variable. One of the more common acquired risk factors of venous sinus thrombosis is oral contraceptive medications. While the prognosis for CVST is favorable, it is important to identify and treat early to prevent neurologic deficits. CVST accounts for 0.5% of strokes and most commonly presents with headaches and in many cases focal neurologic deficits. Diagnosis is confirmed with neuroimaging including CT angiography or MR angiography. Treatment consists of anticoagulation and in some cases, thrombolytic therapy is beneficial. The overall prognosis of CVST is favorable.

The objective of the study is to describe the features of a series of patient with CVST due to consumption of OCPs, treated in the department of Neurosurgery, Bir hospital and OM hospital, and to discuss the risk factors associated with consumption of OCPs, its presentation, and outcome.

Methods: This is a retrospective case series carried out in the department of Neurosurgery, Bir hospital and OM hospital during the year September 2012 to September 2014. Demographic features like age, presenting symptoms, clinical findings and outcome were analyzed. All cases received heparin or LMWH followed by Warfarin.

Results: Nine patients were identified over a period of 2 years. The presenting symptoms included headache, vomiting, loss of consciousness, focal neurological deficit, seizure and neck pain. Signs found included papilloedema, fever, slurring of speech and focal neurological signs.

Conclusion: Dural sinus thrombosis is a rare and under-recognized cause of headache that should be considered in women with recent introduction of hormonal contraception. The absence of papilledema and a negative CT brain should not halt further workup. MRI/venogram is mandatory to confirm the diagnosis.

Key Words: Cerebral Venous sinus Thrombosis (CVST), Heparin, OCP (Oral Contraceptive pills)

Introduction

Cerebral venous sinus thrombosis (CVST) is a rare and potentially deadly condition. Known conditions that increase the risk of CVST include hypercoagulable states, dehydration, adjacent infectious processes,

low cerebral blood flow, oral contraceptives, hormone replacement therapy, pregnancy, and puerperium.^{1,2} As the thrombus enlarges, it causes venous congestion and leads to cerebral edema with mass effect and a resultant

increase of intracranial pressure. If the thrombus is untreated, the intracranial pressure continues to rise and the vascular supply is compromised, leading to ischemia. This contributes to worsening of neurological status, frequently at an unpredictable and accelerated rate. Complete obstruction of the venous system can occur with exacerbation of cerebral edema, vascular compression, and brain herniation, leading to death.

Monitoring in an intensive care unit (ICU) may be indicated depending on the person’s neurological status and diagnostic results.¹ Medical management begins with systemic anticoagulation therapy with heparin and intravenous (IV) hydration.² Direct clot lysis or clot retrieval for rapid recanalization of the affected sinus can now be considered, as a result of recent advancements in interventional neuroradiology.

The objective of this study is to describe the features of a series of patient with CVST due to consumption of OCPs and to discuss the risk factors associated with consumption of OCPs, its presentation, and early outcome.

Methods

This was a retrospective case series carried out in the department of Neurosurgery, Bir hospital and OM hospital during the year September 2012 to September 2014 (2 years). All patients diagnosed as dural venous and sinuses thrombosis with consumption of oral contraceptives were included. The diagnosis was based on CT scan and MRI/MRV of the brain. Hypercoagulable states due to other factors were excluded by history and hematological investigations. Demographic features like age, presenting symptoms, clinical findings, and outcome were also analyzed and complications associated with anticoagulation such as thrombocytopenia, hemorrhages etc were looked for. Follow up was made at three months.

Results

Nine Patients were identified over the period of two years fulfilling the criteria of radiological evidence of dural venous and sinus thrombosis with the concurrent use of oral contraceptive pills. Majority of the patients were from 3rd and 4th decade of their life. Headache was the commonest presenting symptom followed by vomiting. (Table 1) Most of the patients had papilloedema. (Table 2)

Table 1: Presenting symptoms (No of Patients)

| Presenting symptoms | No of Patients |
|--------------------------------------|----------------|
| headache | 9 |
| vomiting | 5 |
| loss of consciousness | 1 |
| seizure | 1 |
| focal neurological deficit (paresis) | 1 |
| fever | 1 |
| neck pain | 1 |

Table 2: Objective findings (No of Patients)

| Papilloedema | 6 |
|--------------------|---|
| paresis | 1 |
| neck rigidity | 1 |
| hemianopia | 1 |
| slurring of speech | 2 |

As observed in CT scan and MRI/MRV of the brain, transverse sinus was the most frequently involved sinus (4 patients) followed by superior saggital sinus (2 patients) (Fig. 1). One patient had Straight sinus involvement and two had multiple sinus involvement. All cases received heparin or LMWH followed by Warfarin. There were no anticoagulants related complications. All the patients were managed conservatively and recovery was uneventful. There was no mortality or major morbidity over three month’s follow up.

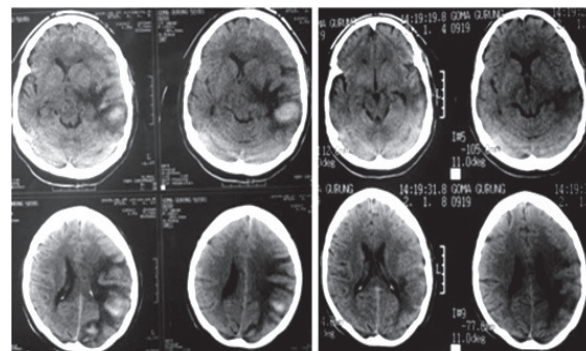


Figure 1: Pre- and post treatment CT Scan

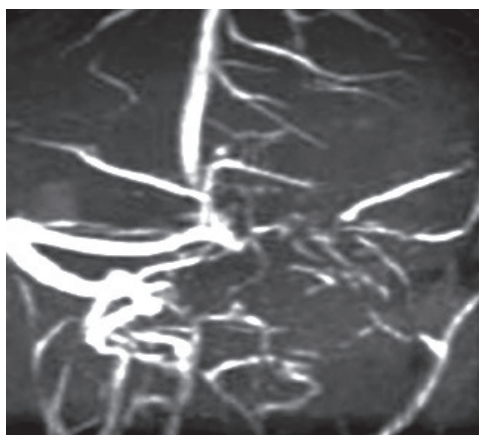


Figure 2: MR Venogram Showing obliteration of left Transverse and Sigmoid sinus

Discussion

Dural sinus thrombosis is an uncommon condition with varied clinical presentation usually affecting middle-aged women. It has acquired attention recently because of improved imaging techniques and better awareness among physicians, particularly neurologists. Although more than 100 causes have been described in the literature, pregnancy and puerperium are the most frequent risk factors.^{3,4} A study in the USA, based on the data from the 1993–1994 healthcare cost and utilization project, estimated that dural sinus thrombosis complicated 11.6 in every 100 000 deliveries, and that increased maternal age was a major risk factor.⁵ Prothrombotic states are another important cause for dural sinus thrombosis. Since the introduction of hormonal contraception in the early 1960s, case reports emerged describing its association with increased risk of thrombosis.⁶ This has been presumed to be because of the estrogenic component irrespective of the route of administration. More recent data showed a higher incidence of venous thrombosis with third-generation (desogestrel and gestodene) rather than second-generation progestins (e.g. levonorgestrel and norgestrel), with an estimated risk of 1.4–4 times as high as that associated with second-generation preparations.^{7,8} The procoagulant effect of oral contraceptive pills (OCPs) is due to the resultant increase in the levels of coagulation factors and decreases in the levels of the anticoagulant proteins: antithrombin and protein S.⁹

Despite a low absolute risk (15 cases per 100 000 cardiovascular events per year), women who are taking OCP have a 3–6 times greater risk of venous thromboembolism than women who do not.¹⁰ The risk is highest during the

first year and increases with age (> 35 years), obesity, recent surgery, and some forms of thrombophilia, especially factor V Leiden mutation.¹¹ For this reason, some experts believe that all first-time OCP users should be screened for factor V Leiden mutation.¹⁰ Women with prothrombotic defects and concomitant oral contraceptive use had an increased odds ratio of 30 to develop cerebral sinus thrombosis, relative to women that did not carry this defect.¹³

The most common sites of thrombosis associated with OCP are the deep veins, which may be complicated by pulmonary embolism. Arterial thrombosis is less frequent and is usually predisposed by other concomitant risk factors, such as smoking.¹⁴ It is generally accepted by medical authorities that the health risks of OCP are lower than those from pregnancy and birth. However, complications are still possible in a certain category of high-risk patients. For this reason the WHO has created a graded scheme of precautions when considering which patients should not use hormonal contraception. Women identified with WHO category 4 diagnoses should not be given OCP.¹³ Category 4 includes patients with a history of venous thromboembolism, cerebrovascular or coronary artery disease, patients whose age is greater than 35 years and smoke 20 or more cigarettes per day, patients with history of headache with focal neurological symptoms, prior history of diabetes mellitus with complications, hypertension (blood pressure of >160/100 mmHg or with concomitant vascular disease), patients with liver disease, patients with breast cancer, and patients undergoing major surgery with expected prolonged immobilization. In an attempt to reduce the risk of thrombosis, products with lower dosage of estrogen should be utilized (e.g. Alesse, Loestrin 1/20, Levlite, and Mircette). Headache resistant to treatment in middle-aged women taking OCP should not be taken lightly, especially when the more common causes of headache are excluded. Two serious conditions must be promptly ruled out: benign intracranial hypertension and dural sinus thrombosis. Fundoscopic examination should be performed looking for signs of increased intracranial pressure. Papilledema can be a latent sign of increased intracranial tension and its absence does not rule out intracranial hypertension. Benign intracranial hypertension is characterized by the presence of slit-like ventricles on the CT brain and increased cerebrospinal fluid pressure greater than 25 mmHg. Dural sinus thrombosis, which has a worse prognosis, is not evident on non-contrast brain CT, and MRI/venogram with and without contrast is necessary to confirm the diagnosis. Although CT contrast venography remains popular in some centers and may be a superior technique in certain cases, the classic empty delta sign is present in only 20% of the cases.^{15, 16}

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