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Oral contraceptives and cerebral venous thrombosis: case report and a brief review of literature

Mughis Sheerani
Aga Khan University

Mian Zainul Sajadeen Urfy
Aga Khan University

Case Report

Oral Contraceptives and Cerebral Venous Thrombosis: case report and a brief review of literature

Mughis Sheerani, Mian Zainul Sajadeen Urfy
Department of Medicine, The Aga Khan University Hospital, Karachi.

Abstract

Cerebral venous thrombosis remains an important and sometimes an elusive cause of strokes. Oral contraceptives seem to have a strong causative association with this entity. We describe a case that highlights the importance of asking specific questions about oral contraceptive use in patients with strokes due to cerebral venous sinus thrombosis, especially, where the cause remains cryptic.

Introduction

The role of oral contraceptives in deep vein thrombosis has been well documented and proven in the contemporary literature. The risk of deep leg thrombosis in women with Factor V leiden mutation who use oral contraceptives compared with a control has been estimated to be more than 30-fold.[1] Cerebral Venous sinus thrombosis represents a rare disorder usually in middle age group. Independent trials and retrospective data analysis in several countries in the world show markedly increased predisposition in women who are taking oral contraceptives especially with genetic hypercoagulable disorder.[2] A recent Italian case-control study in patients with sinus thrombosis found an odds ratio of 4.2 for oral contraceptive use, after exclusion of pregnant and puerperial women.[3] Another study by Cerebral Venous Sinus Study Group, Academic Medical Centre Netherlands reported 30 fold increased risk in women who use oral contraceptives along with hereditary prothrombotic conditions as compared to women who have neither.[4]

We present a case of a middle aged lady, who visited The Aga Khan University Hospital emergency department with acute neurological deficits and was later on found to have Transverse Sinus Thrombosis. A brief review of literature is added.

Case Report

A 42 year old house wife was admitted to the stroke unit with sudden onset of left sided numbness and mild weakness. She was otherwise healthy with no history of any previous medical problems.

On examination her weight was 64 kg, blood pressure was 130/79 mmHg, pulse 80 per minute and she was afebrile. General examination was unremarkable. Cardiac and respiratory examination was also normal.

Neurological examination showed normal cranial nerves except for mild flattening of the left naso-labial fold. There was mild weakness on the left side which was graded as 4 on MRC scale. Left side also showed decreased sensation as compared to the right side.

Magnetic Resonance Imaging (MRI) of the brain showed small right parietal stroke. Magnetic Resonance Angiogram (MRA) was normal.

A workup for hypercoagulable state was performed including anti-phospholipid antibodies, protein C & S activity, antithrombin III, Factor V leiden deficiency and homocystein levels were within normal range.

As no definite cause of stroke was found, the history was re-assessed. Patient was asked several directed questions about medications. It was revealed by the husband that she had been on oral contraceptives for several days prior to this episode. She took oral contraceptives to cease her menstrual cycle temporarily as she was going for 'Hajj'. This information was not disclosed by the patient.

Magnetic Resonance Venogram (MRV) was performed after this information and a thrombus was seen in the right transverse sinus.

Patient was started on anticoagulation and she recovered completely.

Discussion

Cerebral venous sinus thrombosis is a relatively rare condition which over the past two decades has been diagnosed more frequently due to greater availability of non invasive diagnostic methods like MRI and MRV. It presents usually in a relatively younger age group than other vascular neurological conditions and can result in a significant morbidity and mortality which ranges from 5 to 30 percent. Though relatively uncommon, CVST is a complex disease due to multitude of etiologies that cause it. The etiologies vary from complex hypercoaguable states to simple physiological states like dehydration, pregnancy and peurperium.[5] Only a few iatrogenic factors can lead to this condition. The oral contraceptives, androgen therapy and C-Asparaginase therapy have been implicated as a causative factor for CVST.

The role of oral contraceptives in the development of deep venous sinus thrombosis is clearly established. CVST being a rare disease, relatively scarce amount of data is present in literature as compared to other vascular neurological abnormalities. But even with the information we have, there is ample evidence to prove that there is a clear causal relationship between oral contraceptives and the development of CVST. Increased incidence of CVST in oral contraceptive using women was reported for first time in 1970 by Buchanan et al.[6] Thereafter, little importance was given to oral contraceptives as being a significant risk factor because of lack of biological plausibility until the start of last decade, when several retrospective studies showed a strong causal relationship between the two. A survey from 1993-94 on health care cost and utilization in United States revealed oral contraceptive usage as an independent risk factor for intra-cerebral venous thrombosis.[7] Since then many studies have been published particularly from Central Europe, establishing oral contraceptives usage as a risk factor for CVST.[8] To our knowledge, no case series or clinical trial has been published from any center in Pakistan concerning risk factors for CVST in our population.

In our Case Study, a complete hypercoaguable workup was carried out and was unremarkable. The only major risk was found to be oral contraceptives use prior to the event. In literature, however, the use of oral contraceptives seems to be associated with CVST, more strongly in presence of hereditary hypercoaguable disorders, like Factor V leiden deficiency, Protein C or S and anti thrombin deficiency and more recently prothrombin gene mutation at position 20210 (guanine to adenine).[9] This mutation was not checked in our case as it is not available in Pakistan.

A case control study by a Dutch group on CVST revealed that odds ratio increased from 13 to 34 in women using oral contraceptives along with hypercoagulable disorders.[4] Similar findings have been reported by 3 different Italian Studies showing oral contraceptives alone as well in combination with hypercoagulable disorders to be a significant risk factor for the development of CVST.[8] This led to the argument whether women should be screened for hypercoaguablity before prescribing oral contraceptives. The next question was whether oral contraceptives should be withheld in women with hereditary thrombotic disorders. Considering the prevalence of CVST which is estimated to be around 1 per 1000[10], it will not be a cost effective modality and such screening is not recommended any where in the world. As far as question of withholding oral contraceptives in carriers of hypercoagulable genes, no clear cut guidelines are available. It is, however, recommended that other methods of contraception should be used in women with previous episodes of thrombosis.[10]

As far as management of CVST is concerned, it does not change with the attributed risk factor and includes anticoagulation with recommended guidelines. Our patient recovered completely with anticoagulation using heparin and then switching to warfarin as oral therapy. The prevalence of oral contraceptives use in Pakistan is relatively low as compared to western world due to various socio-religious reasons. Women also tend not to share this information with their physicians, as in our case. This case also highlights the importance of complete documentation of medication history, which may lead to diagnosis of these rare diseases and prevent unnecessary investigations.

Conclusion

Though infrequent, CVST remains an important cause of strokes in young individuals, with oral contraceptives as one of the iatrogenic causes. Oral contraceptives should be prescribed with caution in women with history of hypercoaguabilty. A detailed medications history might lead to the diagnosis of "cryptogenic strokes" where no obvious causes are apparent.

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