Unusual Presentation of Cerebral Venous Sinus Thrombosis Associated with Contraceptive Usage

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A 23-year-old woman was referred to our department complaining of intermittent double vision for 3 weeks. Best corrected visual acuity (BCVA) was 20/20 in both eyes (OU), the pupils were round and reactive to light with no relative afferent pupillary defect (RAPD), intraocular pressure (IOP) was 12mmHg OU; color vision by Ishihara pseudo-isochromatic plates and automated visual fields (Figure 1) were normal OU, as well. Orthoptic examination showed slight limitation of abduction and partial sixth nerve palsy in the left eye (OS). Dilated fundoscopy revealed bilateral optic disc edema (Figure 2). A high dose steroid (methylprednisolone) was initially administered with the clinical suspicion of an underlying neuro–inflammatory process.

Magnetic resonance imaging (MRI) excluded intracranial masses, hemorrhage, meningitis or other similar conditions causing optic disc edema. Lumbar puncture revealed elevated cerebrospinal fluid (CSF) opening pressure at 46 mmHg (normal up to 16 mmHg) with no abnormal constituents, therefore papilledema was verified. There was no history of weight gain, obesity, migraine headaches or tobacco use. The patient had been using an oral birth control pill, Yasmin 28 (drospirenone and ethinyl estradiol) over the past 5 months.

No abnormal findings were detected on an extensive hematology panel including erythrocyte sedimentation rate (ESR), complete blood count (CBC), kidney function, C-reactive protein (CRP) and partial thromboplastin time (PTT). Magnetic resonance venography (MRV) showed partial venous thrombosis of the right transverse and sigmoid sinuses (Figure 3).

Figure 1. Visual field testing (Octopus): no significant defects were detected in the right (upper image) and left (lower image) eyes.

Fraxiforte® (nadroparin calcium) injections 0.4 ml once daily, Sintrom® (acenocoumarol) and acetazolamide 250mg twice daily were administered as initial treatment and the steroid was tapered. One week later, BCVA and color vision were stable at 20/20 OU and 13/13 OU, respectively. Six months later the fundoscopic appearance improved, Sintrom® was discontinued and acetazolamide was reduced to 250mg daily for 1 month and 125mg daily for the next month. Ten months after the episode, the patient was clinically stable and optic disc edema had completely regressed (Figure 4).
DISCUSSION

The mechanism of increased intracranial pressure in cerebral venous sinus thrombosis (CVST) is compromised venous drainage. Subsequently, disruption of the blood brain barrier occurs resulting in vasogenic edema, which may be compounded by neuronal swelling from localized ischemia and damage to the intracellular ion channels.\(^1\) Large areas of the brain can be compromised, but not necessarily irreversibly damaged.

The association of anovulatory agents and venous thromboembolism (VTE) is well-defined in literature.\(^2,5\) Van Vlijmen et al\(^5\) reported the effects of combined oral contraceptives on the
absolute risk of VTE in women with single or multiple thrombophilic disorders such as protein S and C deficiencies. The annual incidence of VTE without the use of anovulatory agents was 1.64% in patients with such deficiencies as compared to 0.18% in normal women. The use of oral contraceptives almost triples the incidence of VTE in both populations. Mira et al reported 40 cases of VTE among women taking Yasmin 28 (drospirenone and ethinyl estradiol), including 2 fatal cases. Therefore, women with predisposing factors for VTE are strongly recommended to avoid using oral contraceptives.

In addition, patients with a history of smoking or migraine who use oral contraceptives may be at higher risk for CVST. The direct role of these risk factors on the development of CVST is not well-established yet; however a higher risk
of cardiovascular events and ischemic stroke has been reported.\textsuperscript{2,4} Migraine alone is a strong risk factor. When accompanied by smoking and oral contraceptive use, the risk of ischemic stroke increases considerably.\textsuperscript{2}

Our patient had no history of smoking, migraines, obesity or thrombophilic disorders. She was complaining of only one symptom: double vision. Diplopia, due to 6\textsuperscript{th} nerve palsy, could be explained by intracranial hypertension further manifesting as dilation of the optic nerves sheaths and concavity of the pituitary gland (Figure 5). Interestingly, our patient had no headache which is a common symptom in CVST.\textsuperscript{6} The patient was initially misdiagnosed as a case of optic neuritis, but further investigation with MRI, MRV and lumbar puncture established the correct diagnosis of CVST.

This case highlights that CVST may present with atypical symptoms such as diplopia. The history of oral contraceptive use is of high importance for diagnosing CVST among young women. Imaging techniques are crucial for prompt diagnosis and appropriate treatment as illustrated in this case report.

Conflicts of Interest

None.

REFERENCES

1. Biousse V, Ameri A, Bousser MG. Isolated intracranial hypertension as the only sign of cerebral venous thrombosis. Neurology 1999;53:1537-1542.
2. Allais G, Gabellari IC, Mana O, Schiapparelli P, Terzi MG, Benedetto C. Migraine and stroke: The role of oral contraceptives. Neurol Sci 2008;29 Suppl 1:S12-14.
3. Mira Y, Morata C, Vayá A, Ferrando F, Contreras T, Aznar J. Is Yasmin as safe as other contraceptive pills? Clin Appl Thromb Hemos 2006;12:378-379.
4. Trussell J, Guthrie KA, Schwarz EB. Much ado about little: Obesity, combined hormonal contraceptive use and venous thrombosis. Contraception 2008;77:143-146.
5. van Vlijmen EF, Brouwer JL, Veeger NJ, Eskes TK, de Graeff PA, van der Meer J. Oral contraceptives and the absolute risk of venous thromboembolism in women with single or multiple thrombophilic defects: results from a retrospective family cohort study. Arch Intern Med 2007;167:282-289.
6. Uzar E, Ekici F, Acar A, Yucel Y, Bakir S, Tekbas G, et al. Cerebral venous sinus thrombosis: an analyses of 47 patients. Eur Rev Med Pharmacol Sci 2012;16:1499-1505.