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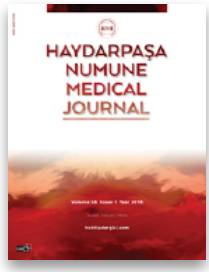

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CASE REPORT

Cerebral Venous Sinus Thrombosis Following IVF Treatment Presenting with Migraine-like Headache: A Case Report

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Abstract

Cerebral venous sinus thrombosis (CVST) is a relatively rare subtype of stroke that occurs as a result of hypercoagulability. It is more common in women than men, with a ratio of three to one. Gender-specific risk factors for women include oral contraceptives, pregnancy, puerperium, and assisted reproductive methods such as hormone therapy. We report a 38-year-old female patient with a history of migraine attacks, presenting with a migraine-like headache following in-vitro fertilization (IVF) treatment and diagnosed with CVST. The thrombophilia panel showed a homozygous methylenetetrahydrofolate reductase (MTHFR) A1298C mutation. Hereby, we aim to highlight the importance of evaluating thrombotic risk factors in women before initiating IVF treatment and the assessment of proper dosage for thromboprophylaxis. Especially those with a mechanical heart valve, antiphospholipid antibody syndrome (APS), antithrombin-3 deficiency, MTHFR, and factor V Leiden mutation are at high risk. Thromboprophylaxis should be started right after the initiation of IVF treatment and should be continued during pregnancy.

Keywords: Cerebral venous sinus thrombosis (CVST); in-vitro fertilization; thromboprophylaxis.

Infertility affects 10-15% of couples planning pregnancy [1]. IVF is one of the treatment options for infertility. Nevertheless, there are complications with high mortality and morbidity following IVF treatment, such as Ovarian Hyperstimulation Syndrome (OHSS) [2,3]. Hypercoagulability as a result of OHSS causes severe disability secondary to arterial and venous thromboembolism (VTE).

CVST is one of the rare but serious complications secondary to hypercoagulability. It involves thrombosis of dural sinuses or veins. It is an uncommon form of stroke, usually affecting young individuals and represents 1% of all strokes. Pregnancy, puerperium, oral contraceptives (OCS), infections, inflammatory diseases, and thrombophilia are risk factors for CVST; and it is more common in women than men [4,5]. Most of the affected women (60%) are 20-35 years old [4-7]. In several studies, it is shown that the risk is significantly increased during the third trimester in pregnancy and the peripartum period [8]. Clinical presentations vary from headache to seizure and coma. Patients usually complain of thunderclap headache.

We present a case of a patient (4-weeks pregnant following an IVF treatment), with a history of primary migraine headache, complaining of a headache just like her other migraine attacks but only longer in duration, which can be easily overlooked.

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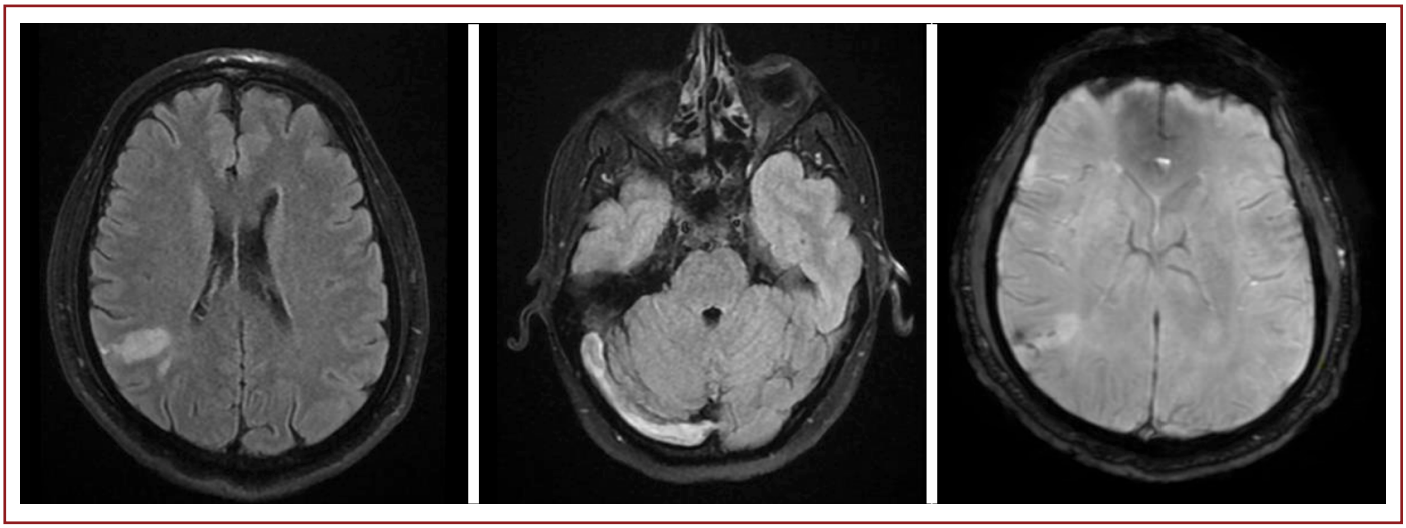

Figure 1. Fluid-attenuated inversion recovery (FLAIR) sequence shows a hyperintense, edematous lesion in the right parieto-occipital lobe with slow flow phenomenon in the right transverse sinus; susceptibility-weighted imaging (SWI) shows hypointense hemorrhagic components in the infarct area.

Case Report

A 39-year-old female patient, 4 weeks pregnant, with a history of migraine without aura, presented to our emergency department with a continuous headache for 3 days. The patient underwent IVF treatment after having 3 miscarriages. As an IVF treatment protocol, she was given, in addition to 12 days of follitropin-alpha and menotropin injections, a combined oral preparation of progesterone and estrogen. The oocyte was taken at the peak level of estrogen, and she was treated with 6 weeks of 4 mg estradiol before embryo implantation. She was also injected with progesterone before implantation and continued 5 days of oral estradiol treatment after the implantation process.

The patient was referred to the emergency service because of a headache lasting longer than 72 hours, accompanied by nausea, photophobia, and phonophobia. The Visual Analog Scale (VAS) score was 9. She described it as 'just like her other migraine attacks.' The possibility of a migraine headache worsening with pregnancy was one of the alternative diagnoses. After collecting data about her pregnancy, considering a resistant headache to migraine attack medication (10 mg of rizatriptan), CVST was considered as an alternative diagnosis. The patient underwent a direct and indirect ophthalmologic examination, and no papilledema was found. Neuroimaging with MR venography was positive for right transverse sinus thrombosis. Diffusion-weighted imaging (DWI) showed acute diffusion restriction in the right parietal lobe, which was diagnosed as a venous infarct (Fig. 1). The patient was admitted to the neurology clinic; her biochemistry, blood count, and urine work-up were clean. Homocysteine levels were within the normal range, and the vasculitis panel was negative. Cardiological examination revealed nothing. The thrombophilia panel showed a homozygous methylenetetrahydrofolate reductase (MTHFR) A1298C mutation. The patient was started on low molecular weight heparin (LMWH) in a therapeutic dosage of 6000 IU twice a day. She was discharged with a VAS score of 3 after 10 days and was prescribed LMWH.

Discussion

CVST occurs due to occlusion of the veins and dural sinuses which drain the brain parenchyma [9,10]. It is less frequent compared to arterial ischemia, but the mortality rates are around 3-8% when the diagnosis is delayed [9-12]. Whereas pregnancy is considered a common risk factor, sinus vein thrombosis following IVF treatment is only reported in several cases. Venous thromboembolism incidence ranges between 0.1-0.2% in patients with IVF treatment, 10 times higher compared to the normal population [13]; 2 times higher compared to pregnancy without induction [14].

In pregnancy without any ovarian stimulation, CVST risk is maximum in the third trimester and puerperium; for those receiving IVF, the risk is maximized in the first trimester. Older age, smoking, and obesity seem to be risk factors for IVF-induced CVST.

Ovarian stimulation with IVF treatment causes hyperestrogenism, which results in increased levels of von Willebrand Factor (vWF), factor 8, and factor 10; increased resistance to activated protein C; and decreased levels of fibrinolytic factors such as tissue plasminogen

activator, antithrombin-3, and protein S. Studies show that unsuccessful IVF treatment doesn't result in an increased risk of thromboembolism, so beta-human chorionic gonadotropin (beta-hCG) is held responsible for the initiation of thrombotic processes. Another study shows that venous thromboembolism (VTE) risk is 0.1-0.5%, whereas arterial thrombosis risk is less; 70% of all reported cases are venous thromboembolism; only 30% is arterial embolism; in 40% of women experiencing VTE, thrombophilia is present [15].

Patients with more than one risk factor are considered to have a high risk for VTE. In those patients, thromboprophylaxis should be continued during ovarian stimulation and also pregnancy.

Before the initiation of IVF treatment, every woman should be evaluated for risk factors and the appropriate thromboprophylaxis dosage and duration should be assessed after discussing with a hematologist. Patients with high and very high risk, such as those with a mechanical heart valve, antiphospholipid antibody syndrome (APS), recurrent thromboembolism (VTE), antithrombin-3 deficiency, MTHFR mutation, and factor V Leiden disease, should be followed closely during IVF treatment. Thromboprophylaxis should be started immediately after the initiation of IVF treatment. Sinus vein thrombosis should be considered in pregnant women receiving IVF treatment who present with acute isolated refractory headache.

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