Case report

Risk factors of ischemic stroke/transient ischemic attack in young women: A case report

Elmira Mamytova[1], Aliya Kadyrova[2], Dzhamalbek Turgumbaev[3], Emir Zholdoshev[1], Yethindra Vityala[4], Tugolbai Tagaev[5]

[1]A.N. Murzaliev Department of Neurology and Clinical Genetics, I.K.Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan

[2]Department of Radiology, I.K. Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan

[3]Department of Neurology, Neurosurgery and Psychiatry, S.B. Daniyarov Kyrgyz State Medical Institute for Retraining and Advanced Studies, Bishkek, Kyrgyzstan

[4]Department of Pathology, International Higher School of Medicine, International University of Kyrgyzstan, Bishkek, Kyrgyzstan

[5]Department of Hospital Internal Medicine, Occupational Pathology with a Course of Hematology, I.K. Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan

(Received: February 2021 Revised: February 2021 Accepted: March 2021)

Corresponding author: **Elmira Mamytova.** Email: e.mamytova17@gmail.com

ABSTRACT

This case report aims to demonstrate the clinical significance of the left internal carotid artery (ICA) hypoplasia in a young woman who received a combined oral contraceptive (COC) and its association with arterial occlusion and the development of a lacunar stroke/lacunar cerebral infarct (LACI). Brain magnetic resonance imaging (MRI) of the left frontal lobe revealed multiple subcortical and periventricular amplification/ischemia foci (49.0×17.0 mm), and lacunar infarct loci (2.0×4.0 mm). Brain magnetic resonance angiography revealed a markedly narrowed lumen of the left ICA (2.0–3.0 mm). MRI diffusion-weighted imaging-fluid attenuated inversion recovery revealed a moderate diffuse wall thickening and reinforcement of the left ICA. The patient was diagnosed with LACI and congenital hypoplasia of the left ICA and underwent antiplatelet drug therapy (aspirin - 100 mg) and a complete withdrawal of COC. A full amelioration of neurological symptoms was observed after one month of treatment.

Keywords: Lacunar stroke; ischemic stroke; oral contraceptive; circle of Willis; hypoplasia

INTRODUCTION

Ischemic stroke/transient ischemic attack (TIA) remains a concern in neurology due to its wide prevalence, and high disability and mortality rates. Moreover, the cause of 37% of TIA cases in young people remains unknown (even with thorough clinical-instrumental examination) (1, 2). However, TIA rates in women of reproductive age (18-44 years) are 8.9-11 per 100,000 cases (3, 4). Prothrombotic effects develop during a reproductive period, which is evidence of the procoagulant conditions associated with childbirth, particularly in pathological pregnancy, 2nd-3rd periods of fetal development, oral contraceptive (OCP) intake, frequent migraine, etc., Lacunar stroke/lacunar cerebral infarct (LACI) is a type of ischemic stroke, and developmental anomalies in internal carotid artery (ICA) can lead to the formation of an unclosed arterial circle: the circle of Willis (CW).

Congenital internal carotid artery hypoplasia (CICAH) is rare (0.01% incidence) and associated with aneurysms (3, 5). In CICAH, ICA is significantly narrowed throughout its length, compared to its contralateral ICA. Hypoplasia is confirmed when the narrowed carotid canal at the skull base remains underdeveloped following the embryonic period of fetal development (6). Usually, radiology helps verify the dysembryonic nature of the ICA lumen restriction from chronic artery dissection or fibromuscular dysplasia when the carotid channel is of a normal size. Clinically manifested variants of abnormal CW development appear when it is associated with risk factors associated with sexual-age characteristics. In addition, hormonal contraception increases blood viscosity, and the risk of TIA in smoking women over 30 years of age increases by 22-fold after OCP usage (7, 8).

This case report aims to demonstrate the clinical significance of the left ICA in a young woman who received a combined oral contraceptive (COC), and its association with arterial occlusion and the development of LACI.

CASE PRESENTATION

A 27-year-old woman reported at our hospital with increasing weakness in her right limbs and numbness in her right-leg. Two months prior, she reported weakness and decrease of exteroceptive sensation in the right-hand, which increased a month prior. One year prior, she took COCs (drospirenone 3 mg, ethinylestradiol 0.02 mg) to prevent an unwanted pregnancy. She reported no history of smoking, diabetes, hypertension, or hypercholesterolemia. Her systemic examination yielded normal results. Neurological examination revealed central facial palsy of facial nerve, dysarthria, and pyramidal signs in the right-leg and right-hand (Right-hand hemihypesthesia) with level 4 muscle strength. Neurologic examination was otherwise non-

contributory. Blood pressure was 148/96 mm Hg. Complete blood cell count, biochemistry panel and electrocardiogram were normal. Coagulation tests revealed hyperbilirubinemia and increased antistreptolysin titers (625 U). Brain magnetic resonance imaging (MRI) of the left frontal lobe revealed multiple subcortical and periventricular amplification foci/ischemia foci (49.0×17.0 mm) and lacunar infarct loci (2.0–4.0 mm). Brain magnetic resonance angiography revealed a markedly narrowed lumen of the left ICA (2.0–3.0 mm). MRI diffusion weighted imaging–fluid attenuated inversion recovery (DWI-FLAIR) revealed multiple subcortical and periventricular amplification foci in the left frontal lobe, without diffusion restriction and with E2-lumen effect on the DWI, corresponding to the ischemia foci in the substage, and moderate diffuse wall thickening and reinforcement of the left ICA (Fig.1a) and (Fig.1b). The patient was diagnosed with LACI and congenital hypoplasia of the left ICA and underwent an antiplatelet drug therapy (aspirin - 100 mg) and a complete withdrawal of COC. A full amelioration of neurological symptoms was observed after one month of treatment.

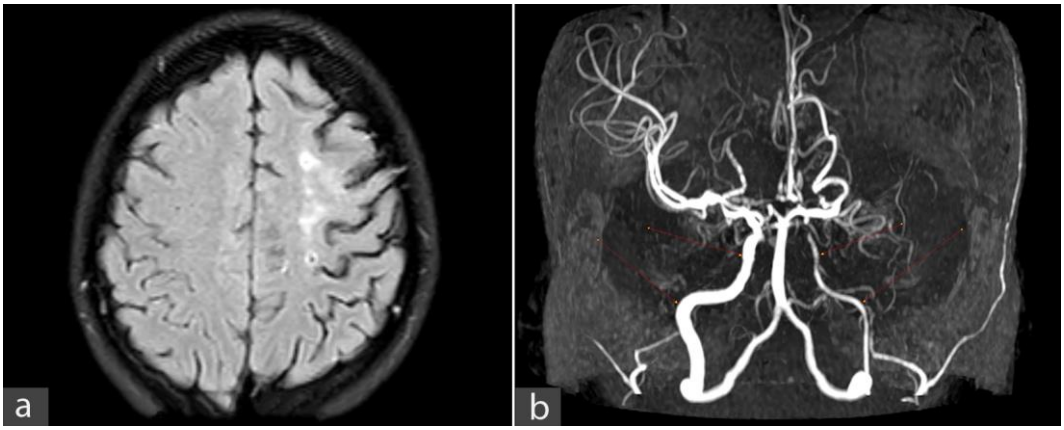

Fig. 1: Magnetic Resonance Imaging diffusion weighted imaging–fluid attenuated inversion recovery reveals (a) lacunar infarct in the left frontal lobe and (b) moderate diffuse wall thickening and reinforcement of the left internal carotid artery.

DISCUSSION

This clinical case demonstrates the increased risk of developing LACI in young women taking COCs against a history of anomalies in the arterial development of the WC. The causes of the ICA's developmental anomalies and mechanism of CICAH are mostly unknown. CICAH is associated with other anomalies, such as intracranial aneurysm and WC; therefore, it is important to check these deviations in its presence.

Studies regarding CICAH are limited. The recommended pharmacotherapy after TIA and lacunar strokes includes antiplatelet, statins, and anti-hypertensive drugs (9). In this clinical case, antiplatelet therapy was administered for one month and COCs were completely withdrawn, resulting in complete recovery of the motor deficit.

Estrogen can have both positive and negative effects on the cardiovascular system (10). Estrogen shows positive effect on lipids, reduces low-density lipoproteins, and increases high-density lipoproteins. It also allows vasodilation by nitrogen oxide and prevents atherosclerotic vascular damage. On the other hand, estrogen increases the level of triglycerides and C-reactive protein (11, 12). In addition, estrogen has many prothrombotic effects; it increases prothrombin level and decreases antithrombin level III, which increases the risk of venous thromboembolism (10, 12).

Young women who take long-term OCPs with high estrogen levels have an increased risk of TIA, depending on the dose, and on the venous thromboembolism case. A decrease in estrogen level is followed by a partial reduction in TIA risk (11, 13). This is associated with increased blood clotting as a result of stimulation by estrogen synthesis of coagulation factors in the liver and the effect on intracerebral vessels, similar to this case (2, 3, 13). The risk of taking large doses of estrogen (>50 µg) is five times higher compared to those who take low doses, and not affected by the type of progesterone and the duration of OCP use (7).

COCs with estradiol <0.03 mg are the safest form of combined oral hormonal contraception. In our patient, the level of estradiol did not exceed >0.03 mg. In this report, the patient had hyperbilirubinemia with a history of the COC intake, and the narrowing of the ICA and MCA developed a small perforating artery occlusion and LACI.

CONCLUSION

CICAH is not considered as an independent risk factor for TIA. However, ultrasound studies show a pathology of ipsilateral blood flow in association with CICAH, which can lead to local hypoperfusion and subsequent focal neurological deficits. Existing studies also confirm the risk of TIA, which is closely related to both atherosclerotic and prothrombotic (Reproductive age women are more susceptible) condition in both young and old patients. In this

report, the combination of CICAH, increased risk of thrombosis (OCPs), and CW anomalies were risk factors which caused small perforating artery occlusion followed by the development of LACI.

ACKNOWLEDGEMENT

The authors acknowledge their patient for kind cooperation and for providing consent. No financial support was received for the study.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. Ahmed, S. B., Hovind, P., Parving, H-H., Rossing, P., Price, D. A., Laffel, L. M., *et al.,* Oral contraceptives, angiotensin-dependent renal vasoconstriction, and risk of diabetic nephropathy. Diabetes Care. 2005; 28(8): 1988-1994.
2. Chan, W. S., Ray, J., Wai, E. K., Ginsburg, S., Hannah, M. E., Corey, P. N., *et al.,* Risk of stroke in women exposed to low-dose oral contraceptives: a critical evaluation of the evidence. Arch Intern Med. 2004; 164(7): 741-747.
3. Ciccone, A., Melis, M. Ischemic stroke risk in oral contraceptive users. Stroke. 2003; 34(12): e231.
4. Gillum, L. A., Mamidipudi, S. K., Johnston, S. C. Ischemic stroke risk with oral contraceptives: A meta-analysis. JAMA. 2000; 284(1): 72-78.
5. Chen, C. J., Chen, S. T., Hsieh, F. Y., Wang, L. J., Wong, Y. C. Hypoplasia of the internal carotid artery with intercavernous anastomosis. Neuroradiology. 1998; 40(4): 252-254.
6. Gunawansa, N. Hypoplastic Ipsilateral Internal Carotid Artery as a Cause of Acute Ischemic Stroke: A Case Report. World J Surg Surgical Res. 2018; 1: 1060.
7. Roach, R. E., Helmerhorst, F. M., Lijfering, W. M., Stijnen, T., Algra, A., Dekkers, O. M. Combined oral contraceptives: the risk of myocardial infarction and ischemic stroke. Cochrane Database Syst Rev. 2015; 2015(8): CD011054.
8. Staikov, I., Stoyanov, I., Staneva, M., Neykov, N., Kirova, G., Polomski, P., *et al.* Diagnostic value of color-coded duplex sonography in patients with ischemic stroke and congenital changes in the circle of Willis. Cor et Vasa. 2016; 58(6): e591-e599.
9. Mujagić, S., Kozić, D., Huseinagić, H., Smajlović, D. Symmetry, asymmetry and hypoplasia of the intracranial internal carotid artery on magnetic resonance angiography. Acta Med Acad. 2016; 45(1): 1-9.
10. Wassertheil-Smoller, S., Hendrix, S. L., Limacher, M., Heiss, G., Kooperberg, C., Baird, A., *et al.* Effect of estrogen plus progestin on stroke in postmenopausal women: The Women's Health Initiative: a randomized trial. JAMA. 2003; 289(20): 2673-2684.
11. Kemmeren, J. M., Tanis, B. C., van den Bosch, M. A., Bollen, E. L., Helmerhorst, F. M., van der Graaf, Y., *et al*. Risk of Arterial Thrombosis in Relation to Oral Contraceptives (RATIO) study: oral contraceptives and the risk of ischemic stroke. Stroke. 2002; 33(5): 1202-1208.
12. Lidegaard, O., Kreiner, S. Contraceptives and cerebral thrombosis: a five-year national case-control study. Contraception. 2002; 65(3): 197-205.
13. Lidegaard, O. Smoking and use of oral contraceptives: impact on thrombotic diseases. Am J Obstet Gynecol. 1999; 180(6 Pt 2): S357-S363.