Case report

A rare case of central post-stroke pain in a patient with migraine and lacunar infarcts in the medulla oblongata

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ABSTRACT

Studies about headaches associated with acute ischemic stroke in patients suffering from migraine were limited, and therefore we present a clinical case of central post-stroke pain (CPSP) in a 47-year-old woman with migraine and lacunar infarcts in the medulla oblongata and also possible mechanisms of CPSP in patients with migraine. Magnetic resonance imaging of the brain revealed lacunar infarction in the medulla oblongata on the right (vertebral artery basin) and a single focus of gliosis in the parietal lobe on the right. Magnetic resonance angiography of cerebral vessels showed the fetal type of structure of both posterior cerebral arteries. This clinical case is a complex clinical situation of a combination of secondary headaches (post-stroke) in a patient with a primary headache (migraine), which was successfully treated by the combined administration of first-line drugs for the treatment of neuropathic pain in a patient with lacunar infarcts in the medulla oblongata. The treatment of CPSP is a difficult task due to the insufficiently unexplored mechanisms of development, the most effective approaches are those aimed at reducing the increased excitability of neurons.

Keywords: Migraine; acute ischemic stroke; central post-stroke pain; lacunar infarcts; medulla oblongata.

INTRODUCTION

Migraine is a common and chronic disease characterized by episodes of moderate-to-severe headache, affecting up to 20% of the population (1). In turn, acute ischemic stroke (AIS), is characterized by the sudden appearance of a neurological deficit of vascular origin, usually occurring after the age of 50 years (2, 3). AIS is a type of stroke that remains a concern in neurology due to its wide prevalence, high disability, and mortality rates (4-7).

Migraine has been studied as a risk factor in thromboembolic cerebrovascular diseases (CVDs), especially in young women under 45 years of age (8–10). The absolute annual risk of stroke is 17 per 100,000 in migraineurs and 52 per 100,000 in patients with classic migraine (migraine with aura) (11, 12). Migrainous infarction as a complication of migraine is part of the etiological group of ischemic cerebral infarcts of unusual causes according to the CVD classification (13).

Migraine and stroke differ greatly by gender, age of onset, clinical picture, outcome, and treatment; however, migraine can be one of the risk factors for stroke. Although, Migraine and stroke are two common and heterogeneous neurovascular disorders the mechanism of the association between migraine and stroke is unknown.

Studies about headaches associated with AIS in patients suffering from migraine are limited, and therefore we present a clinical case of central post-stroke pain (CPSP) in a 47-year-old woman with migraine and lacunar infarcts in the medulla oblongata and also possible mechanisms of CPSP in patients with migraine.

CASE PRESENTATION

A 47-year-old woman was admitted to our department of the hospital on August 24, 2021, with complaints of dizziness, difficulty in walking, double vision, numbness of the face (right-sided), severe pain in the right ear, neck, jaw, the frontal-orbital region with the burning and pulsating sensation, which were accompanied by nausea, vomiting and jaw movements during sleep.

On August 22, 2021, after climbing into a high-altitude area (Semenov Gorge located on the northern shore of Lake Issyk-Kul, Kyrgyzstan at an

altitude of 2200–2500 meters (m) above sea level), the patient experienced dizziness, fatigue, and weakness, which regressed after descending from the mountain but she did not seek medical support and blood pressure was not measured.

On August 23, 2021, during the shower, the patient felt an acute shooting pain in the right ear, followed by a change in the pain to a burning sensation and acute weakness in the right leg with dizziness; further right upper limb weakness is observed with difficulty in walking. In the patient, blood pressure was 200/100 mm Hg and later patient got hospitalized.

For the past six years, the patient was suffering from migraine without aura and there was a history of hormone replacement therapy with Femoston 2/10 mg for three months before hospitalization. She experienced migraine attacks frequently and had a tobacco addiction. In June 2021, the patient suffered from thrombocytopenia after getting affected by COVID-19.

During the time of admission, the following findings were reported: blood pressure, 185/95 mmHg; heart rate, 64 beats/min; temperature, 38.6°C; O_2 saturation, 96%; respiratory rate, 66 breaths/min; body mass index, 24.7. On pulmonary auscultation, there was no wheezing. Other physical examination results were normal.

Neurological status of the patient during admission, she was in a minimally conscious state and delayed verbal reactions. Hypoesthesia in the area of innervation of the I branch of the V pair of right primary motor neurons, the right nasolabial fold is smooth, fissured tongue, reduced pharyngeal reflexes, muscle strength reduced by 4 points on the right, and the Romberg test was positive as per observation.

Blood and biochemical studies were normal, except for increased triglyceride levels of 2.5 mmol/L (High –2.3 to 5.6 mmol/L), antibodies to beta (2)-glyco- protein, and positive serologically for hepatitis C.

Computed tomography (CT) of the chest organs, ultrasound of the vessels of the lower extremities and neck, and electrocardiogram showed no deviations. CT of the vessels of the neck and brain showed an anterior third of the common carotid artery on both sides, aplasia of the left transverse sinus, closed circle of Willis, and stenosis of the V4 segment of the right vertebral artery.

Magnetic resonance imaging of the brain revealed lacunar infarction in the medulla oblongata on the right (vertebral artery basin) and a single focus of gliosis in the parietal lobe on the right (Fig. 1a). Magnetic resonance angiography of cerebral vessels showed the fetal type of structure of both posterior cerebral arteries (Fig. 1b).

Ultrasound of internal organs suggested cholecystitis and angiomyolipoma of the left kidney. Echocardio- graphy showed aortic atherosclerosis, degenerative changes in the aortic valve (atherogenesis) without expansion of the cavities, and contractility violations of the ventricles. The patient was obese and hypertensive with nicotine dependence. The patient had comorbidities such as chronic viral hepatitis C (remission phase), varicose veins of the lower extremities with a minimal degree of activity, and neurotic otalgia.

After the patient was transferred from the intensive care unit to the general ward, the intensity of the headache began to increase and was poorly treated with painkillers, which increased the frequency of the need for painkillers (3–5 times/day).

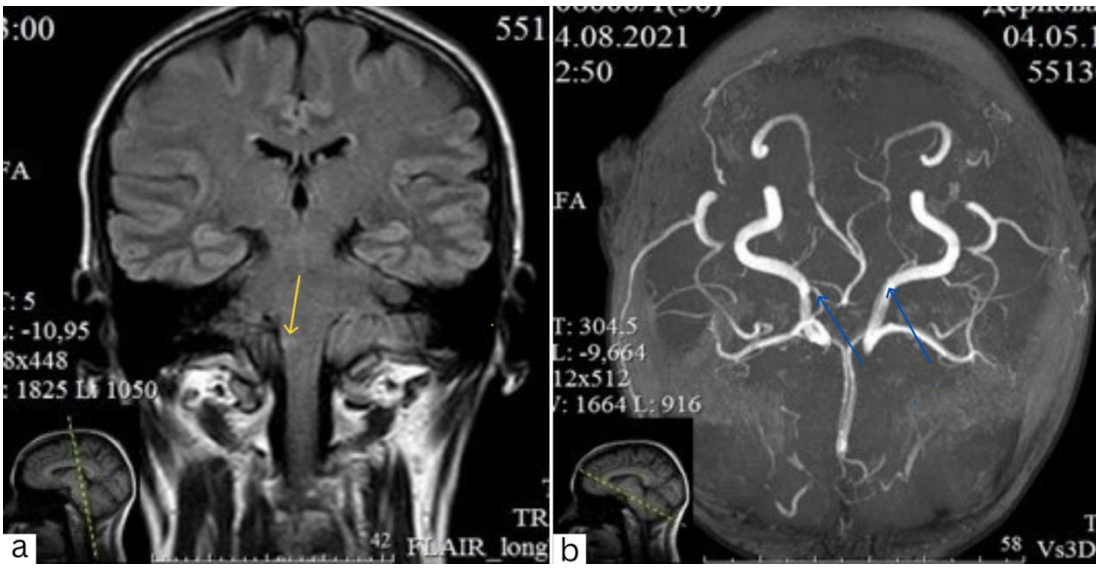

Fig.1: (a) Magnetic resonance imaging of the brain showing the focus of infarction in the medulla oblongata on the right (yellow arrow). **(b)** Magnetic resonance angiography blue arrow shows the fetal type of structure of both posterior cerebral arteries (blue arrow).

Due to the lack of effect from taking carbamazepine, and indomethacin and the frequent need for NSAIDs, after a neurologist consultation, the patient started undertaking pregabalin 150 mg (2 times /day), which reduced the intensity of pain. A tricyclic antidepressant, amitriptyline at an average therapeutic dose of 25 mg (3 times/day) was included in the treatment, where the headache significantly regressed after the 3–7 days of administration. For the treatment of the AIS, hypolipidemic, hypotensive, and anti-platelet therapy was performed**.**

After discharge, the patient was recommended to reduce the dose of pregabalin with its gradual abolition, as a maintenance therapy, it was recommended to continue taking amitriptyline at a dose that was left as a prophylactic for the prevention of migraine attacks with the observation by a neurologist every 3–6 months. The patient was counseled about quitting smoking, abstinence from hormonal contraception, and compliance with the recommendations of specialists.

DISCUSSION

The presented clinical case is an example of a combination of secondary (central post-stroke) headache in a woman suffering from primary (migraine) headache. CPSP is a neuropathic pain syndrome that develops after an acute cerebrovascular accident (14). Loss of sensitivity and the presence of signs of hyper- or hypesthesia in the pain zone in patients with CPSP indicates a combination of deafferentation with the subsequent development of increased excitability of neurons. The most common cause of CPSP is vascular damage to the thalamus (ventroposteriomedial and ventroposteriolateral nuclei). However, central pains can also occur with extrathalamic lesions. The lesion of the bridge and lateral parts of the medulla oblongata (Lateral medullary syndrome or Wallenberg syndrome) is more often accompanied by algic manifestations than other structures, similar to this case.

The criteria for persistent headache after stroke are (15):

1. Exclusion of other potential causes of pain.
2. The pain has a clear and anatomically justified localization (unilaterally of the focus in the central nervous system on the body and/or face, or unilaterally on the body with contralateral involvement of the face).
3. Having a past history of stroke (sudden development of neurological symptoms, the pain appeared simultaneously with the stroke or later).
4. Identification of clear and anatomically justified disorders during clinical neurological examination (sensitivity disorder with a positive or negative sign in the painful area, pain is localized in the zone of sensitive disorders, and the location of the zone of sensitive disorders corresponds to the localization of the lesion in the central nervous system).
5. Identification of the corresponding vascular focus using neuroimaging methods (CT or magnetic resonance imaging visualizes a focus that can explain the localization of sensitivity disorders).

CPSP in the posterior arterial pool observed in this case (posterior cerebral arteries, branches of the main and vertebral arteries) is more common than in the anterior. There are several possible explanations such as

- The posterior circulation may have special cerebral autoregulation (16), which is characterized by being more susceptible to fluctuations in vasomotor tone and permeability of the vessels. After an AIS, there may be an increase in pressure in the posterior cranial fossa compared with an anterior stroke.
- Finally, the association with migraine acts as an aggravating factor. Migraines, especially with aura, have a particularly increased risk of ischemic stroke (17).

A study of residents of high-altitude areas has shown that altitude causes an aggravation of migraines and this manifests itself in an increase in the frequency, duration, and intensity of attacks. Altitude headache is a consequence of climbing high-altitude above 2500 m, whereas the relationship between altitude and migraine was strongest below 2500 m (18) and occurs more often in people who are regularly exposed to high-altitude terrain. In this case, the patient from another neighboring country visited Kyrgyzstan as a tourist and visited the high-altitude area for the first time.

In the development of migraine and altitude headache, there are similar mechanisms of hypoxia that occurred similar to our case. This can be described as a breakdown of the cerebral autoregulation of maintaining cerebral blood flow and a violation of adequate oxygenation of brain tissue, which was associated with a rapid ascent to altitude in a person whose body has not yet developed adaptive mechanisms. It should be noted that high-altitude residents are fully adapted to maintain adequate tissue oxygenation in conditions

of chronic hypoxia against a background of low atmospheric pressure. According to many studies, hypoxia or even normobaric hypoxia can cause migraine attacks in patients with a history of migraine (19, 20). A study on the association between altitude and migraine concluded that the prevalence of migraines increased with altitude from 27.9% at an altitude of fewer than 500 m to 45.5% at an altitude of 2000-2499 m. Interestingly, the prevalence of migraine decreased to 37.9% above 2500 m (21). In this case, the patient ascended to a height of 2200 m.

Therefore, altitude may aggravate migraine leading to an increase in the frequency, duration, and intensity of headaches. The prevalence of migraine and its severity indicators are closely related to height, but the mechanisms are unknown and require further studies.

CONCLUSION

The presented clinical case is a complex clinical situation of a combination of secondary headaches (post-stroke) in a patient with a primary headache (migraine), which was successfully treated by the combined administration of first-line drugs for the treatment of neuropathic pain in a patient with lacunar infarcts in the medulla oblongata. The treatment of CPSP is a difficult task due to the insufficiently unexplored mechanisms of development, the most effective approaches are those aimed at reducing the increased excitability of neurons.

CONFLICTS OF INTEREST

Authors declare no conflicts of interest.

REFERENCES

1. Silberstein, S. D. Migraine. Lancet. 2004;363(9406):381-391.
2. Donnan, G. A., Fisher, M., Macleod, M., Davis, S. M. Stroke. Lancet. 2008;371(9624):1612-1623.
3. Schürks, M., Kurth, T. Is migraine a predictor for identifying patients at risk of stroke? Expert Rev Neurother. 2011;11(5):615-618.
4. Vityala, Y., Mamytova, E., Turgumbaev, D., Kadyrova, A., Toktomametova, A., Zholdoshev, E., *et al.,* Clinical features of acute ischemic stroke in moderately and severely ill patients with coronavirus disease 2019 (COVID-19). Biomedicine. 2021;41(2):397-400.
5. Mamytova, E., Kadyrova, A., Turgumbaev, D., Zholdoshev, E., Vityala, Y., Tagaev, T., *et al.,* Risk factors of ischemic stroke/transient ischemic attack in young women: A case report. Biomedicine. 2021;41(1):160-162.
6. GBD 2015 Neurological Disorders Collaborator Group. Global, regional, and national burden of neurological disorders during 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Neurol. 2017; 16(11):877-897.
7. Mamytov, M., Mamytova, E., Toktomametova, A., Miklukhin, D., Yethindra, V., Tagaev, T., *et al.,* Expression of autophagy and apoptosis biomarkers in patients with acute ischemic stroke. Biomedicine. 2022;42(5):988-991.
8. Granella, F., Sances, G., Pucci, E., Nappi, R. E., Ghiotto, N., Napp, G. Migraine with aura and reproductive life events: a case control study. Cephalalgia. 2000; 20(8):701-707.
9. Frigerio, R., Santoro, P., Ferrarese, C., Agostoni, E. Migrainous cerebral infarction: case reports. Neurol Sci. 2004;25 Suppl 3: SS300-SS301.
10. Chang, C. L., Donaghy, M., Poulter, N. Migraine and stroke in young women: case-control study. The World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. BMJ. 1999;318(7175):13-18.
11. Merikangas, K. R. Contributions of epidemiology to our understanding of migraine. Headache. 2013;53(2):230-246.
12. Kristensen, B., Malm, J., Carlberg, B., Stegmayr, B., Backman, C., Fagerlund, M., *et al.,* Epidemiology and etiology of ischemic stroke in young adults aged 18 to 44 years in northern Sweden. Stroke. 1997;28(9):1702-1709.
13. Díez-Tejedor, E., del Brutto, O., Alvarez Sabín, J., Muñoz, M., Abiusi, G. Classification of cerebrovascular diseases. Iberoamerican Cerebrovascular Diseases Society. Rev Neurol. 2001;33(5):455-464.
14. Mahmoud, A. N., Mentias, A., Elgendy, A. Y., Qazi, A., Barakat, A. F., Saad, M., *et al*., Migraine and the risk of cardiovascular and cerebrovascular events: a meta-analysis of 16 cohort studies including 1 152 407 subjects. BMJ Open. 2018;8(3): e020498
15. Lebedeva, E. R., Gurary, N. M., Olesen, J. New diagnostic criteria for headache attributed to transient ischemic attacks. J Headache Pain. 2019; 20(1):97.
16. Noseda, R., Melo-Carrillo, A., Nir, R. R., Strassman, A. M., Burstein, R. Non-trigeminal nociceptive innervation of the posterior dura: implications to occipital headache. 2019; 39(10):1867-1880.
17. Haubrich, C., Wendt, A., Diehl, R. R., Klotzsch, C. Dynamic autoregulation testing in the posterior cerebral artery. Stroke. 2004; 35(4):848-852.
18. Davis, C., Reno, E., Maa, E., Roach, R. History of migraine predicts headache at high altitude. High Alt Med Biol. 2016;17(4):300-304.
19. Burtscher, M., Mairer, K., Wille, M. Risk factors for high-altitude headache in mountaineers. Cephalalgia. 2011; 31:706-711.
20. Schoonman, G. G., Sandor, P. S., Agosti, R. M. Normobaric hypoxia and nitroglycerin as trigger factors for migraine. Cephalalgia. 2006; 26:816-819.
21. Linde, M., Edvinsson, L., Manandhar, K., Risal, A., Steiner, T. J. Migraine associated with altitude: results from a population-based study in Nepal. Eur J Neurol. 2017;24(8):1055-1061.