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SYSTEMIC EMBOLIC EVENTS ASSOCIATED WITH PERSISTENT FORAMEN OVALE – A CASE REPORT

SISTEMSKI EMBOLIJSKI DOGAĐAJI POVEZANI SA PERZISTENTNIM FORAMENOM OVALE – PRIKAZ SLUČAJA

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Summary

Introduction. Embolization into the systemic circulation through the persistent foramen ovale is known as paradoxical embolization. Coexistence of paradoxical embolism with pulmonary thromboembolism is rare and it requires detailed examination. The objective of this study was to present an unusual case of stroke that was complicated by the occurrence of pulmonary thromboembolism, with thrombosis of the superior mesenteric artery, and arterial infarction of numerous visceral organs, a few days after its onset. **Case Report.** A 60-year-old female patient was admitted to the Emergency Center with clinical symptoms of acute ischemic stroke, with sudden left hemiparesis. Computed tomography showed a fresh ischemia in the basin of the right anterior cerebral artery. The initial clinical course was favorable, with gradual regression of neurological symptoms. On the seventh day of hospitalization, the patient presented with a sudden worsening of symptoms. Computed tomography confirmed multiple infarctions of the liver, spleen and both kidneys, partial thrombosis of the superior mesenteric artery, as well as thrombosis of both pulmonary arteries and two fresh ischemic zones, namely right temporal and parieto-occipital, cortico-subcortical. A persistent foramen ovale was found by transesophageal echocardiography, which also confirmed the existence of an atrial septal aneurysm. In the further course, there was an improvement of symtoms. The patient was referred for further rehabilitation therapy. A surgical closure of persistent foramen ovale was indicated. **Conclusion.** Paradoxical embolism remains a pathology rarely mentioned by clinicians, although it can affect the functional and vital status and prognosis of the patient. Good cardiac evaluation and detection of persistent foramen ovale in every patient with embolic ischemia is of great importance.

Key words: Foramen Ovale, Patent; Embolism, Paradoxical; Tomography, X-Ray Computed; Heart Aneurysm; Infarction; Stroke; Pulmonary Embolism; Diagnosis; Signs and Symptoms

Sažetak

Uvod. Pojava embolizacije u sistemsku cirkulaciju kroz perzistentni foramen ovale naziva se paradoksalna embolizacija. Pojava paradoksalne embolizacije istovremeno sa plućnom tromboembolijom je retka i zahteva detaljan pregled. Cilj rada je prikaz neuobičajenog slučaja moždanog udara koji je nekoliko dana nakon početka bio komplikovan pojavom plućne tromboembolije, sa trombozom gornje mezenterične arterije i arterijskim infarktom brojnih visceralnih organa. **Prikaz slučaja.** Pacijentkinja stara 60 godina primljena je u Urgentni centar sa kliničkom slikom akutnog ishemijskog moždanog udara, sa iznenadnom levom hemiparezom. Kompjuterizovanom tomografijom je potvrđena sveža ishemija u slivu desne prednje moždane arterije. Inicijalni klinički tok je bio povoljan, uz postepenu regresiju neuroloških tegoba. Sedmog dana hospitalizacije došlo je do naglog pogoršanja simptoma. Kompjuterizovanom tomografijom su potvrđeni višestruki infarkti jetre, slezine i oba bubrega, uz prisustvo parcijalne tromboze gornje mezenterične arterije, kao i tromboza obe plućne arterije i dve sveže moždane ishemijske zone i to desno temporalno i parijetookcipitalno, kortiko-supkortikalno. Perzistentni foramen ovale je dokazan transezofagealnom ehokardiografijom, čime je potvrđeno i postojanje atrijalne septalne aneurizme. U daljem toku došlo je do poboljšanja tegoba. Pacijentkinja je upućena na dalji rehabilitacioni tretman. Postavljena je indikacija za operativno rešavanje perzistentnog foramena ovale. **Zaključak.** Paradoksalna embolija je patologija koja se retko pominje među kliničarima, iako može uticati na funkcionalno i vitalno stanje i prognozu pacijenta. Kod svakog pacijenta sa embolijskom ishemijom veoma je važna dobra kardiološka evaluacija i detekcija perzistentnog foramena ovale.

Ključne reči: perzistentni foramen ovale; sistemska embolizacija; CT; srčana aneurizma; moždani udar; pulmonarni tromboembolizam; dijagnoza; znaci i simptomi

Introduction

Simultaneous occurrence of stroke, pulmonary thromboembolism, arterial thrombosis and multiple infarctions of visceral organs is rare and requires detailed investigation [1].

The mechanism of venous and arterial thrombosis is different. In the literature, their simultaneous occurrence is described in patients with persistent foramen ovale (PFO), atrial septal defect, pulmonary arteriovenous fistulas, and some other arteriovenous shunts [2].

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Abbreviations

PFO – persistent foramen ovale
PDE – paradoxical embolism
SMA – superior mesenteric artery
CT – computed tomography
ACA – anterior cerebral artery
CDUS – color duplex ultrasound

Foramen ovale is an inter-atrial communication in the fetal period. The PFO occurs in about 25% of the population, and the prevalence is significantly higher in patients with stroke of unclear cause [3].

Embolization into the systemic circulation through a PFO is known as paradoxical embolism (PDE). The occurrence of PDE simultaneously with pulmonary thromboembolism is rare and it is mainly part of a paraneoplastic syndrome, or it is found in patients with thrombophilia [2].

Patients with combined venous and arterial thrombosis require combined anticoagulant and antiplatelet therapy. Studies have shown that closing a PFO significantly reduces the risk of stroke [4, 5].

In this paper, we present an unusual case of stroke that was complicated by the occurrence of pulmonary thromboembolism, thrombosis of the superior mesenteric artery (SMA) and arterial infarction of numerous visceral organs a few days after its onset.

Case Report

A 60-year-old female patient was admitted to the Emergency Center with clinical symptoms of an acute ischemic stroke, with sudden left hemiparesis. The complaints started on the same day and were not accompanied by other symptoms. The patient denied comorbidities and risk factors for cerebrovascular diseases. At the time of admission, the patient was conscious, oriented and communicative, hemodynamically stable, and the neurological findings showed a left sided crural hemiparesis, National Institutes of Health stroke scale score 8. Computed tomography (CT) of the brain confirmed fresh ischemia in the basin of the right anterior cerebral artery (ACA) **(Figure 1).** A color duplex ultrasound (CDUS) of the carotid and vertebral arteries was performed, as well as a transcranial Doppler of the circle of Willis, where no stenotic lesions were detected. Routine laboratory findings were within normal limits.

Upon admission to the Neurology Clinic, sphenopalatine ganglion stimulation was initiated and it lasted for 5 days. The initial clinical course was favorable, with gradual regression of neurological symptoms. A control CT of the brain performed on the fifth day showed a clearly demarcated cortico-subcortical infarction in the basin of the right ACA, with signs of hemorrhagic transformation **(Figure 2).** The patient was hemodynamically and rhythmically stable. The lipid status was normal.

On the seventh day of hospitalization, the patient presented with a sudden worsening of symptoms, with abdominal pain, nausea and vomiting, and on the following day, hemianopsia appeared on the left. The patient was examined by an internist and a gastroenterologist and an ultrasound of the abdomen and an X-ray of the lungs and heart were performed, where no pathological changes were found.

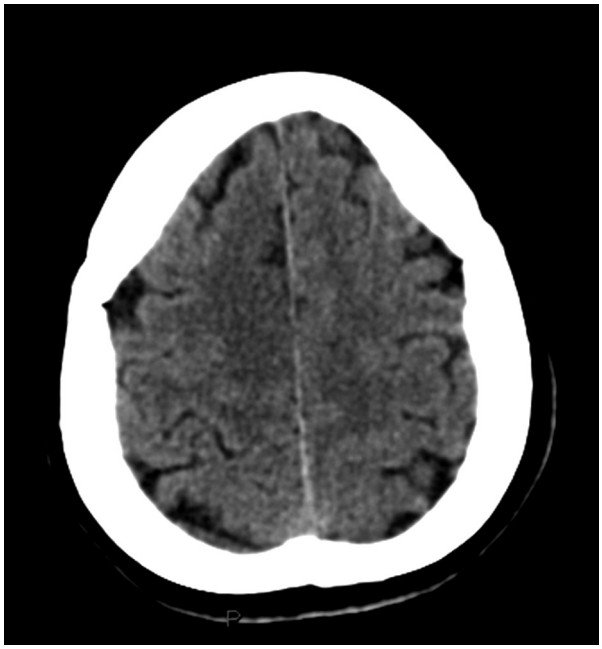

Figure 1. CT of the brain, fresh ischemia in the basin of the right anterior cerebral artery
Slika 1. *Snimak mozga kompjuterizovanom tomografijom – sveža ishemija u slivu desne prednje cerebralne arterije*

The laboratory findings showed an increase in pro-inflammatory parameters (C-reactive protein and procalcitonin), as well as high D-dimer values. Gastroscopy showed hyperemia of the duodenum, probably of vascular ischemic etiology. A CT of the abdomen and pelvis was performed and it showed multiple infarctions of the liver, spleen and both kidneys, with the presence of partial thrombosis of the

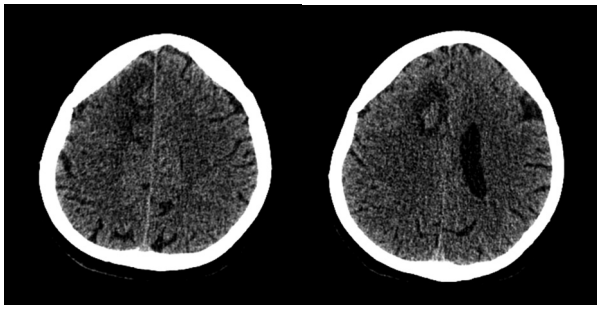

Figure 2. Control CT of the brain performed on the fifth day, cortico-subcortical infarction in the basin of the right anterior cerebral artery with signs of hemorrhagic transformation
Slika 2. *Kontrolni snimak mozga kompjuterizovanom tomografijom petog dana, kortiko-supkortikalni infarkt u slivu desne prednje cerebralne arterije sa hemoragičnom transformacijom*

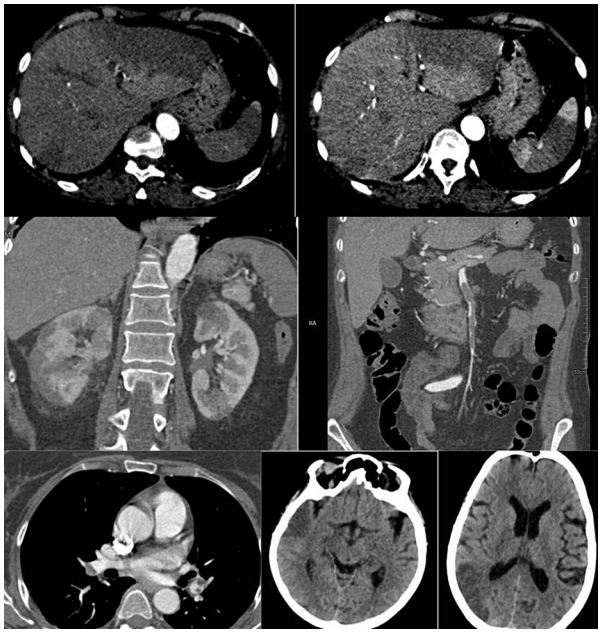

Figure 3. Multiple infarctions of the liver, spleen and both kidneys, partial thrombosis of the superior mesenteric artery, thrombosis of both pulmonary arteries, fresh ischemic zones – right temporal and parieto-occipital, cortico-subcortical

Slika 3. *Multipli infakti jetre, slezine i oba bubrega, parcijalna tromboza gornje mezenterične arterije, tromboza obe pulmonalne arterije, sveže ishemijske zone – desno temporalno i parijeto-okcipitalno, kortiko-supkortikalno*

SMA, as well as thrombosis of both pulmonary arteries **(Figure 3).** In the same act, a CT of the brain was performed, where two fresh ischemic zones were found, right temporal and parieto-occipital, cortico-subcortical **(Figure 3).** An urgent echocardiography of the heart was performed, which was without thrombotic masses in the heart cavities.

Anticoagulant therapy with high doses of low molecular weight heparin was initiated, with gradual transfer to oral anticoagulant therapy. Laboratory tests were performed in the direction of thrombophilia and immune disorders. Immunological tests indicated the presence of antinuclear antibodies on HeP-2 cells, positive nucleoplasm, while other findings were negative. During the entire hospitalization, the patient was hemodynamically stable, conscious, oriented and communicative.

The existence of PFO was suspected by transcranial Doppler bubble ultrasonography and it was also confirmed by transesophageal echocardiography, as well as an atrial septal aneurysm. Deep and superficial vein thrombosis was ruled out by CDUS of the veins of the lower extremities.

In the further course, there was an improvement of the complaints, as well as a gradual normalization of the laboratory parameters. A control CT of the brain, thorax, abdomen and pelvis with native, arterial and venous phase was performed 10 days later. The previously described ischemias of the brain were in the chronification phase, without new fresh ischemias. Both pulmonary arteries and SMA were completely recanalized. The liver parenchyma was without signs of previously described ischemic zones. Ischemic lesions of the spleen were in the chronic phase. Ischemic lesions persisted on the right kidney also in the chronic phase. On the left kidney, the ischemic zones subsided. There were no infiltrative lesions on the control CT of the chest, abdomen and pelvis.

After the rehabilitation treatment started, there was a significant regression of the neurological deficit, with residual mild left-sided hemiparesis, dominantly expressed on the leg with the National Institutes of Health stroke score 2. Walking was performed with aid (Modified Rankin Score 3). The patient was referred for further rehabilitation treatment. A surgical closure of PFO was indicated.

Discussion

Ischemic strokes can be classified into two major categories: a) those with a known cause, such as large-artery atherosclerosis, intracardiac thrombus, small-artery occlusion, and b) those without a known cause, i.e. cryptogenic infarction.

The detection of a PFO in a patient with a confirmed stroke does not necessarily mean that the cause of the stroke has been identified [6].

A PDE is expected to cause brain infarcts that are similar on brain imaging to those of other (cardiac or arterial) embolic causes. At brain imaging, the occlusion of a superficial arterial branch or the presence of a large infarct involving more than one lobe is strongly suggestive of embolic infarction, which was identified in our patient [7].

Scattered lesions or cortical-subcortical territorial lesions are also indicative of embolic infarction. Multiple acute infarcts, especially those that are bilateral and affect various networks of cerebral circulation, are strong indicators of a proximal embolic source or a systemic cause [7, 8]. Our patient presented with scattered lesions, cortical-subcortical territorial lesions, and multiple acute infarcts.

Although the presence of hemorrhagic transformation is a strong indicator of embolic infarction, published data do not demonstrate an association between PFO and hemorrhagic infarcts [9].

The presence of one or more aberrant anatomic structures in association with a PFO can increase the probability of PDE. These abnormal structures include a Chiari network, an atrial septal aneurysm, and a persistent Eustachian valve. Cryptogenic stroke with an "embolic" pattern is more common when PFO and atrial septal aneurysm coexist [10], which was found in our patient by transesophageal echocardiography.

An atrial septal aneurysm is another important anatomic feature to consider when evaluating PFO. An atrial septal aneurysm is defined as a bulge that protrudes more than 15 mm beyond the plane of the atrial septum [11].

Atrial septal aneurysms are found in approximately 4.6 – 10% of cases by transesophageal

echocardiography. An atrial septal aneurysm associated with a PFO has a prevalence of 30 – 60% and is most likely associated with an increased rate of embolic events. Among patients with normal patency of the carotid arteries, which was the case in our patient, atrial septal aneurysm is more prevalent in those with cerebral ischemia (28%) than in those without cerebral ischemia (10%) [12, 13].

The PFO is implicated in the pathogenesis of many diseases [14, 15]. The precise incidence of PDE that complicates PFO is unknown. The PDE occurs in a minority of patients with venous thromboembolic disease who also have a PFO. In patients with a PFO, pulmonary embolism is thought to be associated with a small but definite risk for PDE [16].

Patients with a PFO and hemodynamically important pulmonary embolism are more likely to experience an ischemic stroke (13% vs 2.2%), peripheral arterial embolism (15% vs 0%), and arterial hypoxemia, possibly due to PDE [17, 18].

Although PDE is an uncommon cause of acute arterial occlusion, it can have catastrophic sequelae, and the possibility that it is present should be considered in all patients with an arterial embolus in the absence of a cardiac or proximal arterial source. It is frequently associated with cryptogenic stroke and peripheral embolism [19]. Uncommon complications include brain abscess, decompression sickness in scuba divers, myocardial infarction, and mesenteric infarction [20–23]. On the seventh day of our patient's hospitalization, a CT of the abdomen and pelvis showed multiple infarcts of the liver, spleen and both kidneys, with the presence of partial thrombosis of the SMA, as well as thrombosis of both pulmonary arteries, with subsequent chronification or regression - the pulmonary arteries were completely recanalized, as well as SMA. The liver parenchyma was without signs of ischemia and the ischemic lesions of the spleen were in the chronification phase. Ischemic lesions persisted on the right kidney also in the chronic phase. On the left kidney, the ischemic zones subsided.

Conclusion

Paradoxical embolism remains a pathology rarely mentioned by clinicians, although it may affect the functional and vital prognosis of the patient. Good cardiac evaluation and detection of persistent foramen ovale in every patient with embolic ischemia is important.

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