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CASUISTIC PAPER

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Fibromuscular dysplasia – a case description

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ABSTRACT

Introduction. Fibromuscular dysplasia is an idiopathic, non-inflammatory and non-atherosclerotic disease that affects the walls of arteries (mostly renal and carotid arteries). Histological classification distinguishes three main types of the disease, depending on the structural changes occurring in one of the three layers of arterial vessel walls.

Objective. We present here a case of fibromuscular dysplasia affecting the internal carotid arteries.

Case description. This article describes the case of a 52-year-old female patient with hypertension, hyperlipidemia, and a cardiac pacemaker in whom computed tomography angiography revealed a narrowing of the internal carotid arteries without atherosclerotic symptoms. We describe the diagnostic methods and various types of treatment that the patient suffering from fibromuscular dysplasia was subjected to.

Conclusions. Due to a low detection rate of fibromuscular dysplasia, if the disease is suspected, all available diagnostic methods should be employed. Taking into account the unknown etiology of the disease, it is not possible to use a preventive therapy, or a therapy focused on stalling the progression of the disease.

Keywords. fibromuscular dysplasia, arteries, computed tomography

Introduction

Fibromuscular dysplasia (FMD), according to the definition, involves changes in the structure of one or all layers of the large and medium arterial vessel walls. These changes consist of an overgrowth of the fibrous connective as well as the smooth muscle tissues that do not result from inflammatory or atherosclerotic changes and cause the narrowing of the arterial lumen.[1] The main locations of FMD involve: renal arteries, vertebral carotid arteries, celiac trunk, upper mesenteric artery and coronary arteries.[2] The frequency of occurrence of FMD is estimated at 4-6% in renal arteries and 0.3-3% in carotid arteries.[3]

The frequency occurrence of FMD in Poland is equal to 0.05% and the changes more often concern women. The average age at FMD diagnosis is 55 years.[4] Clinical symptoms are usually identical with the symptoms of atherosclerotic narrowing of the internal carotid

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artery that cause the symptoms of acute ischemia of the brain as well as the retina.[4,5] FMD leads to severe consequences, especially in the cervical-cerebral area where it may lead to hypoperfusion, subarachnoid hemorrhage, artery dissection or occlusion.[6]

Diagnosis

FMD can be diagnosed by arteriography, in which the changes start a few centimeters along the middle section of the internal carotid artery resembling beads on a string, or aneurysmal dilatations separated by annular fibrous narrowings.[3] In 65% of cases, the changes are diagnosed on both sides. Additionally, they may cause the development of the internal carotid artery aneurysm.[7]

Classification

Histological classification of FMD:

Type 1 – the changes are associated with the intima tunica and characterized by a circular growth of mesenchymal cells as well as subendothelial connective tissue, which leads to significant hardening of the intima tunica, leading to a narrowing of the artery lumen – mainly in the renal arteries of children and youth.

Type 2 – the changes are associated with the tunica media and characterized by loosening of the smooth muscle cells and progressing fibrosis of the fibrous connective tissue, especially in the external section of tunica media – the most common dysplasia type including 60-70% of the cases.

Type 3 – the changes are associated with the tunica adventitia and characterized by the overgrowth of the fibrous connective tissue in the adventitia as well as in the external elastic lamina – often coexistent with the changes in the tunica media; most commonly occurring in women over the age of 50; associated with 10% of the cases.

The above classification is not significant when it comes to the selection of treatment, as all types may coexist simultaneously in one patient, or may be associated with the same artery.[1,3,8]

Case description

The patient (B.P.CH) (52) was diagnosed with hypertension, hyperlipidemia, and had been implanted with a single chamber pacemaker due to bradyarrhythmia in the course of a permanent atrial fibrillation; the patient is currently undergoing therapy with oral anticoagulants that are not vitamin K antagonists (dabigatran). She was initially hospitalized in the Neurology Department due to a double episode of right-hemisphere transient ischemic attack. The computed tomography (CT) scan of the head was performed at that time, and revealed multifocal angiogenic brain damage. Computed tomography angiography revealed a significant narrowing of the internal carotid arteries and did not reveal the presence of atheromatous plaques nor any vascular malformation. The neurological examination performed on the day of discharge showed a trace left-sided deficit. The patient underwent cardiologic consultation to arrange the planned closure of the left cardiac auricle. A month later the patient was hospitalized again in the Neurology Department with symptoms of ischemic stroke of the right hemisphere. The neurological examination revealed a central paresis of nerve VII on the left side, as well as a moderate paresis of the left limbs. A CT scan of the head revealed a wide hypodense area with features of right hemisphere edema; additionally, the examination showed scattered malacic foci in the left hemisphere. During hospitalization, fluctuating heterochronous intensification of the paresis and speech disorder was observed together with a significant increase in the National Institutes of Health Stroke Scale (NIHSS) score. The patient was discharged for the planned left cardiac auricle closure procedure with a recommendation for treatment with a 2×150mg dose of dabigatran. Neurological symptoms on the day of discharge: upper left limb monoplegia and moderate lower left limb paresis. Moreover, the date for the planned admission to the Neurological Rehabilitation Department was established. After the procedure of surgery-free closure of the left cardiac auricle with the Amulet 25mm occluder, an antiplatelet treatment therapy with acetylsalicylic acid and clopidogrel was recommended. After the procedure, the patient was transferred again to the Neurological Department in a neurological state similar to that on the day of discharge. A head CT scan revealed a presence of heterochronous angiogenic changes in the external capsules, the subcortical nuclei, and in the right frontal lobe with the possibility of hemorrhagic conversion at the border between the frontal and temporal lobes. During the 6th day of hospitalization, a degradation of the neurological state (intensification of left limb paresis with the paresis of the lower right limb – 21 points in the NIHSS scale) as well as a deterioration of the patient's mental condition with the presence of productive symptoms was observed. A control head CT scan did not show any new ischemic changes. Generalized tonic-clonic cluster epileptic seizures were observed. A neuroleptic agent as well as anticonvulsant drugs were introduced into the treatment. In accordance with the cardiologist's recommendations, antiplatelet drugs were also included (low-molecular-weight heparin at the therapeutic dose). The patient was transferred to the Neurological Rehabilitation Department for further rehabilitation in the following neurological state: triparesis, plegia of the left limbs as well as of the lower right limb. Due to the neurological state at the time of admission to the Rehabilitation Department (no verbal contact, psychomotor retardation, dozing off, selective instruction fulfillment, central paresis of nerve VII on the left side, weakened palatal and pharyngeal reflexes, quadriparesis with increased muscle tone in the left limbs, monoplegia of the lower right limb, severe paresis of the

upper right limb, no defense in the Baniewicz test, bilateral Babiński reflex, right foot clonus, lying) and based on a CT image of the head showing intracerebral hematoma of the right hemisphere, a decision was made to admit the patient to the Neurological Department. Magnetic resonance imaging of the head was performed in cooperation with the cardiologist (pacemaker reprogramming) – the examination revealed changes that did not correspond with the expected widespread damage – ischemic stroke within the limit of the frontal and parietal lobes of the right hemisphere as well as the left frontal lobe with the presence of small hematomas (petechiae) in the cortical layer (subacute phase), hematoma in the area of subcortical nuclei of the right hemisphere (subacute phase). A lumbar puncture was carried out – the examined cerebrospinal fluid did not demonstrate inflammatory features. Due to the fact that the ultrasound of the internal carotid and vertebral arteries confirmed a decrease of the flow velocity in both internal arteries to 30-35cm/s, an angio-CT examination from the aortic arch was performed to reveal a significant/critical narrowing of the lumen in the internal carotid arteries throughout their whole length, and significant limitation of the flow in the arterial circle arteries accompanied by a lack of atherosclerotic features. During the previous hospitalizations, the patient had undergone a wide range of "stroke in young people" examinations where no deviations had surfaced. The patient was examined by a rheumatologist and the antinuclear antibodies were collected (the results were correct), as well as by a vascular surgeon – she did not qualify for any intervention. Due to patient's deteriorating mood, sertraline was introduced in the treatment. The patient was rehabilitated with clinical improvement. A neurological examination on the day of discharge: logical contact, speech with features of dysarthria, slow, understandable, patient follows instructions, fed using a spoon, seated in a wheelchair, put in an upright position, residual triparesis of the left limbs and the lower right limb, increase of physical strength in the upper right limb. Subsequent image examinations showed a correct evolution of the hematoma. A new oral anticoagulant was introduced into the treatment. The patient was transferred to the Rehabilitation Department for further rehabilitation.

Table 1. Patient's laboratory examination results

		Referential norms
CRP	0.19 [mg/dl]	0-0.5 [mg/dl]
ESR	5 [mm/h]	0-15 [mm/h]

Discussion

What draws attention in the abovementioned case description is the significant, rapidly progressing and recurring character of the symptoms similar to the case described by Langis et al.[9] The key examination turned out to be the most common and readily available one – the USG Doppler examination of the internal carotid and vertebral arteries, which revealed a decreased blood flow in the internal carotid arteries.[10] Owing to this result, a decision was made to expand the diagnostics with the angio-CT examination of the vessels from the aortic arch, which confirmed the diagnosis. Given the magnitude of the changes, the patient was not qualified for further surgical intervention. Artery atherosclerosis was considered during differential diagnosis, however, the factor that distinguished atherosclerosis from dysplasia the most was the location of the vessel disease – in atherosclerosis the initial sections of the arteries are affected, whereas it's their middle and final sections in FMD.[11] Due to the non-inflammatory character of FMD, another disease unit considered in the diagnosis was vasculitis.

Cases where the already heightened inflammation indexes remain within the norms have been reported[12-16] Similarly as in the FMD case described by Altun et al. as well as Sarinen and Palomäki, the patient's ESR and C-reactive protein concentration remained within the referential norms.[15,16] (Table 1). Currently, due to the unknown pathogenesis of the disease, it is not possible to develop any therapy that would prevent or stall the progress of the disease.[3] It is difficult to determine the risk factors - the only one that is established is cigarette smoking.[17,18] Most of the decisions made in relation to the treatment must be based on the analysis of the particular case, as the literature examples are associated with individual reports based on small retrospective patient groups (the incidence is not known exactly, and is associated mainly with renal arteries). The analysis of literature data performed by Mettinger, which encompassed 1197 patients, has shown that 58% of FMD cases are associated with renal arteries, 32% with carotid arteries, and approximately 10% with other arteries (including the mesenteric artery and the intracranial arteries).[19] The low detectability of the disease still remains the main diagnostic problem. The incidence associated with carotid, vertebral, and intracranial arteries is still underestimated, and is related with the fact that its occurrence in these locations is rare and does not have the characteristic symptoms (frequent and common vertigo, tinnitus, headache), and sometimes its course is asymptomatic for a prolonged period of time.[20,21] Currently there is no known cure for FMD, and the pharmacological treatment focuses on alleviating the symptoms associated with the disease. Moreover, the treatment is hindered and limited due to the lack of randomized clinical studies. The antiplatelet and antithrombotic treatment – the antiplatelet therapy – is applied in patients with ischemic episodes, as in all cases of non-cardiogenic ischemic brain stroke (aspirin in the 75-325 mg/d dose). [22,23] However, the antiplatelet drugs only act

as factors diminishing the risk and do not treat the disease. The patients after stenting or after angioplasty are treated in the same way as the ones that experienced these procedures due to atherosclerosis.[24] The patients suffering from artery dissection in the extracranial section are treated with heparin and warfarin, or with antiplatelet drugs (aspirin or clopidogrel) for 3-6 months.[25]

Conclusions

Due to the unknown pathogenesis of FMP, it is not possible to develop a therapy that would prevent or stall the progress of this disease.

Due to the non-atherosclerotic character of pathological changes, the effectiveness of statins has not been proven.

It is difficult to determine the risk factors of FMP - the only one that is well established is cigarette smoking.

Given the significant dominance of women and the possibility of the hormonal influence on the disease, one should consider discontinuation of hormonal contraceptive drugs or, if a substitutive hormonal therapy is necessary, a decrease of dosage to the lowest effective level. If the patient is symptomatic (transient ischemic attach or brain stroke), the therapy should not be used.

Vessel dissection or anticoagulation treatment contraindications constitute an indication to the procedure associated with the carotid arteries in patients with recurring brain symptoms.

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