

Cryptogenic embolic stroke in a girl with a trisomy 21 mosaic

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Abstract Stroke in trisomy 21 may be due to cardioembolism, atherosclerosis, vasculitis, moyamoya disease, sinus venous thrombosis, internal carotid hypoplasia or infections like endocarditis with septic emboli, meningitis or brain abscess. In rare cases, however, stroke etiology remains unexplained. We present a 19 year old Caucasian girl with trisomy 21 with a 47XX+21 karyotype who suffered at age 11 years from a transient ischemic attack with left hemiparesis, and at age 17 years from an ischemic stroke in the territory of the right cerebral medial artery. She suffered from arterial hypertension, obesity and hypercholesterolemia. Since blood coagulation studies, immunologic parameters, blood cultures, 24-h Holter monitoring, transthoracic and transesophageal echocardiography, magnetic resonance angiography of the extra- and intracranial vessels, thoracic and abdominal aorta and renal arteries did not provide any explanation for the stroke, implantation of a loop recorder is considered in order to detect episodes of clinically silent atrial fibrillation.

Keywords Down syndrome · Stroke · Immunology · Atrial fibrillation

Stroke in trisomy 21 may be due to cardioembolism, atherosclerosis, vasculitis, moyamoya disease, sinus venous thrombosis, internal carotid hypoplasia or infections [1, 2]. In rare cases, however, stroke etiology remains unexplained.

A 19 year old Caucasian girl was diagnosed with trisomy 21 with a 47XX+21 karyotype. Clinical neurologic investigation showed facial dysmorphism typical for Down syndrome, intellectual decline, and reduced speech without other abnormalities. At age 11 years, a transient ischemic attack with left hemiparesis occurred. Severe obesity and arterial hypertension were diagnosed. At age 17 years an ischemic stroke in the territory of the right cerebral medial artery occurred. Blood tests were normal except for cholesterol 209 mg/dl, HDL cholesterol 38 mg/dl, LDL cholesterol 139 mg/dl, lipoprotein A 71 mg/dl (normal: <30), antistreptolysin-O-test 577 U/ml (normal: <200) and heterozygous factor V Leiden mutation. Blood cultures were negative. 24-h Holter monitoring showed only sinus arrhythmia. Transthoracic and transesophageal echocardiography disclosed slight aortic and tricuspid regurgitation and neither right-to-left shunting nor endocarditis. Magnetic resonance angiography showed normal extra- and intracranial vessels, normal findings of the thoracic and abdominal aorta and renal arteries. She was discharged without any neurologic deficit on a medication with acetylsalicylic acid 100 mg/day, enalapril 2.5 mg/day and simvastatin 20 mg/day. No stroke recurred since then. She never received any kind of hormonal contraception.

Follow-up transesophageal echocardiograms, 24-h Holter monitoring and cerebral magnetic resonance imaging were unchanged (Fig. 1). Blood sedimentation rate and

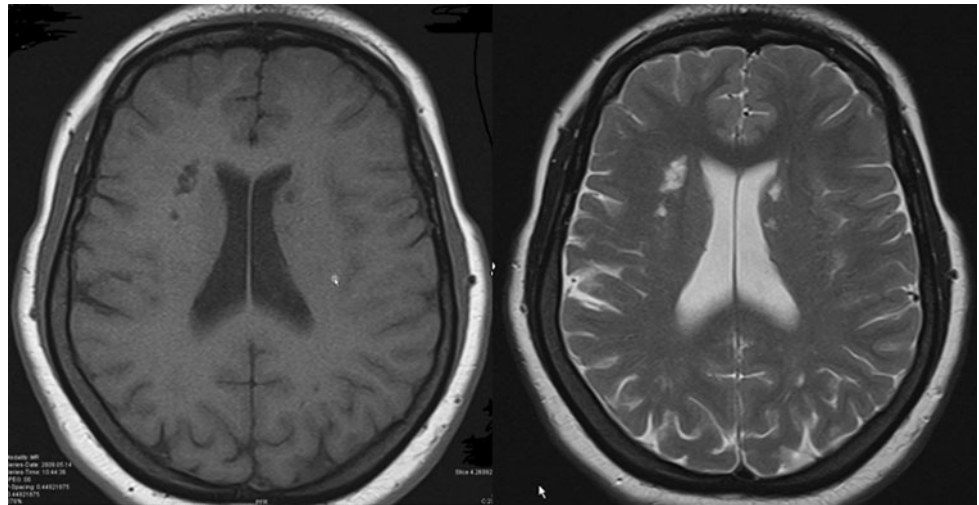
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Fig. 1 T1 and T2 weighted cerebral MRI images showing old white matter lesions more on the *right* than on the *left* side of which only the right-sided lesions manifested clinically as stroke



C-reactive protein levels remained elevated without clinical signs of infection.

Immunologic investigations disclosed citrulline antibodies 21.2 U/ml (normal: <20), antistreptolysin-O-test 802 U/ml (normal: <408), C-reactive protein 3.34 mg/dl (normal: <0.3), positive findings for collagen type I–IV (normal: negative), immunoglobulinG₁ 1,161 mg/dl (normal: 490–1,140), immunoglobulinG₂ 84 mg/dl (normal: 150–640), immunoglobulinG₃ 135 mg/dl (normal: 20–110), no immunoglobulinG₄ (normal: 8–140 mg/dl) and C1 binding immune complexes 1.1 U (normal: negative). Echocardiography and 24-h Holter monitoring were unchanged.

The cause of stroke remained cryptogenic [3]. Immunologic findings were typical for Down syndrome but not for vasculitis [1]. The most likely cause was embolism from clinically silent atrial fibrillation (AF). Due to the patient's intellectual situation, episodes of AF might have been unreported. Arterial hypertension might favor AF, although AF is rare in healthy adolescents [4]. It is unknown if adolescents with trisomy 21 are more prone to AF than adolescents with a normal karyotype. AF can be detected by implantable loop recorders [5]. Detection of AF would lead

to effective secondary stroke prophylaxis by oral anticoagulation. Thus, implantation of a loop recorder to detect silent AF is considered. Another option would be oral anticoagulation without documented AF. Because of side effects and bleeding risks of oral anticoagulation, we consider that option ethically not correct.

Conflict of interest None.

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