

## CLINICAL STUDY

# Amaurosis fugax caused by hereditary thrombophilia due to mutation of gene

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**Abstract:** We are presenting a 59-year old woman and 37-year old man with amaurosis fugax. They underwent a comprehensive ophthalmological and neurological examination. Standard diagnostic examination revealed no possible cause of this temporary condition, therefore additional genetic analysis for possible hereditary thrombophilia was performed. Examination established hereditary thrombophilia: the heterozygotic type gene for MTHFR (C677), deletion/insertion polymorphism for PAI-1 (4G/5G) in women and deletion/insertion polymorphism 4G/5G for PAI-1 and heterozygotic genotype DD (190 bp) for angiotensin converting enzyme (ACE) in man. In our patients, amaurosis fugax is probably caused by hereditary thrombophilia (*Ref. 16*). Full Text (Free, PDF) [www.bmj.sk](http://www.bmj.sk).

Key words: amaurosis fugax, thrombophilia, hereditary.

Most often, amaurosis fugax results from atherosclerotic changes in the brain blood vessels and/or the carotid arteries, but also from heart diseases, especially heart valves damage. Blood vessel atherosclerotic changes result in separation of microemboli that clog small blood vessels and cause temporary vision disturbances. The microemboli may also result from carotid artery surgeries (1–7). The heart is often source of microemboli that are being washed away. They occur in atrium fibrillation, damage of the heart valvular system, atrial septal defect, as consequence of endocarditis and/or creation of thrombotic masses in the heart cavity (8–9). Vasospasm and hyperproteinemia are being stated as possible causes of amaurosis fugax (10–12). Pathomorphological substrate for circulation disorders is diagnosed by Doppler examination (transcranial Doppler and carotid and vertebral blood vessel Doppler), as well as by magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA), but also by cardiological examination including electrocardiography, echocardiography, ergometry and Holter electrocardiography (8, 9, 13, 14). These are all reasons for the need of a comprehensive diagnostic examination to establish the cause of this phenomenon.

## Case report 1

A 59-year old woman, previously perfectly healthy, suddenly lost vision at her right eye. The disturbances lasted about ten minutes, followed by full recovery of the sight. A comprehensive diagnostic treatment was performed. Laboratory tests in-

cluded: basic blood count, biochemical tests including blood glucose, triglycerides, cholesterol, HDL, LDL, uric acid, protein electrophoresis, immunological tests including ANA, RF, ANCA, CIK, antiphospholipid and anticardiolipid antibodies, CRP. The neuroradiological examination included: transcranial Doppler, carotid and vertebral arteries Doppler, magnetic angiography (MRA) of the brain blood vessels, computerised tomography (CT) of the brain and magnetic resonance (MRI) of the brain. All the above tests had normal results. Therefore, additional genetic testing was performed for a possible hereditary thrombophilia. Performed were molecular analysis of genes for Factor V Leiden, prothrombin G20210A mutation, methylenetetrahydrofolate reductase (MTHFR), plasminogen activator inhibitor (PAI-1) gene and angiotensin converting enzyme (ACE).

Multiplication of a part of the coagulation Factor V, by the PCR method, with specific tests for normal and mutated type of the FVQ506 gene, established normal genotype for Factor V.

Analysis of a part of gene of the coagulation Factor II, by the PCR method and with specific restrictive endonucleases, for mutation of the G20210A, established normal gene for Factor II.

Multiplication of a part of the gene for MTHFR by the PCR method and with specific tests for the C677T, established heterozygotic type of the gene (CT) for MTHFR.

Multiplication of the promotion part of the gene for PAI-1 by the referral PCR method, with specific tests established deletion/insertion polymorphism (4G/5G).

Multiplication of a part of the gene for ACE by the PCR method, with specific tests, established homozygotic betotype II (490 bp).

## Case report 2

A 37-year old man suddenly noticed vision disturbances of his left eye. The disturbances lasted 10–15 minutes. Before that

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he had no health problems. He is obese, the body mass index (BMI) being 39 kg/m<sup>2</sup>. Established are marginal values of cholesterol and triglycerides, all other biochemical test results being normal.

The following immunological blood tests were done: ANA, RF, ANCA, CIK, C3, C4, antiphospholipid and anticardiolipin antibodies, all the results being normal. Subsequently, coagulation tests were done: antithrombin III, d-dimers, induced aggregation of thrombocytes, prothrombin time, activated partial thromboplastin time, thromb time, factor XIII and fibrinogen. All test results were normal except for raised fibrinogen, 3.99 g/l (reference values 1.80–3.50 g/l). Neurological diagnostic examination was done: transcranial Doppler sonography (TCD) of the brain blood vessels, carotid and vertebral blood vessel Doppler sonography, but also magnetic resonance angiography (MRA) of the brain blood vessels. All the above tests had normal results.

Cardiological examination was performed as well, heart ultrasound and Holter Electrocardiogram with normal parameters. Following this, molecular analysis of genes for plasminogen activator inhibitor (PAI-1), methylenetetrahydrofolate reductase (MTHFR), angiotensin converting enzyme (ACE), Factor V Leiden and prothrombin G20210A was performed. Established was a deletion/insertion polymorphism 4G/5G for PAI-1 and homozygotic genotype DD (190 bp) for ACE, whereas other molecular gene analyses showed normal genotype.

## Discussion

Amaurosis fugax presents with temporary vision disturbances, most often caused by atherosclerotic changes of blood vessels and cardiac diseases. Standard cerebrovascular disease risk factors are important factors for occurrence of amaurosis fugax. In the presented cases, except for adiposity, all standard risk factors were within normal limits, and common diagnostic treatment revealed no pathomorphological substrate. Therefore, additional laboratory tests were done – molecular genetics of genes for PAI-1, MTHFR, ACE, Factor V Leiden and prothrombin G20210A. Deletion/insertion polymorphism 4G/5G for PAI-1 and homozygotic genotype DD (190 bp) for ACE are causing significant inclination to thrombophilia.

Presence of genetic mutations for MTHFR and PAI-1 was established, which result in increased risk for thrombophilia.

So far, there have been only two presented researches on the role of hereditary thrombophilia in the development of amaurosis fugax. The researches were performed in smaller numbers of patients who had no other causal factors of thrombosis fugax (15, 16). Our patients test results support the assumption that hereditary thrombosis is an important factor for the occurrence of amaurosis fugax.

Presently it is not a standard approach to perform additional tests, molecular genetics for possible hereditary thrombophilia. The existing results indicate that the role of hereditary thrombophilia in the development of amaurosis fugax should be considered, especially in younger people with no other possible risk factors.

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