

## CASE REPORT

# Anterior ischemic optic neuropathy comorbid with Factor V Leiden and PAI-1 4G/5G mutation

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**Abstract:** Acute anterior ischemic optic neuropathy (AION) is a disabling disease which impairs visual functions. AION is characterized by ischemic injury of the optic nerve caused by hypoperfusion in the short posterior ciliary arteries supplying the optic nerve head. AION is a complex multi-factorial disease and is difficult to diagnose based on clinical symptoms and signs alone. We describe the case of a 54-year-old patient affected by AION, with only known risk factors were PAI-1 4G/5G and Factor V Leiden mutation with hyperlipidaemia (Ref. 36). Full Text (Free, PDF) [www.bmj.sk](http://www.bmj.sk).

Key words: AION, Factor Leiden, G20210A, MTHFR, PAI-1 4G/5G, ACE.

Ischemic optic neuropathy is a common cause of visual loss in the elderly population. Anterior ischemic optic neuropathy (AION) is one of the most common causes of acute loss of vision in middle-aged and elderly persons. It occurs due to hypoperfusion in the short posterior ciliary arteries supplying the optic nerve head. AION presents with sudden painless loss of vision, pale edema of the optic disc, afferent papillary defect and visual field defects, typically in lower quadrants (1–5). The etiology of this disease is multi-factorial. The most important risk factors for developing AION include hypertension, nocturnal hypotension, diabetes mellitus, atherosclerosis and small cup in the optic disc (5, 7). In the described case, the patient had none of AION risk factors, wherefore we widened the scope of diagnostic examinations by testing the possible coagulation-enhancing defects in proteins of coagulation pathways.

## Case report

A 54-year-old man was hospitalized for sudden deterioration of sight in his right eye. The patient had no previous disease history and was taking no medicines. At admittance, his right eyesight was 0.5–0.6, and that of the left eye was 1.0. The eye pressure was bilaterally within normal limits, 18 mmHg. The right eye visual field was significantly narrowed, and that of the left eye was normal. The multislice computed tomography (MSCT) of brain and eye orbit was normal. The magnetic resonance imaging of brain showed no pathomorphological changes. The transcranial Doppler (TCD) and the

ultrasound of carotids showed normal age-adequate flows. Ophthalmologic examinations established this was a case of AION.

The basic biochemical laboratory tests were normal, except for elevated cholesterol and triglyceride values (cholesterol 8.5, triglycerides 2.85). All immunological blood tests were normal. Additional coagulation tests were done, as well. The induced thrombocyte aggregation was within its reference range values. Other coagulation tests with normal results included activated partial thromboplastin time (APTV), APTV ratio, thrombin time, d-dimers. Deviations from reference range values were found out in a number of coagulation tests, namely prothrombin time (PV), antithrombin III (AL III), ProCGlobal test, ProCGlobal/Factor V and fibrinogen.

Molecular gene analysis was done for Factor V Leiden (8), prothrombin G20210A mutation (9), plasminogen activator inhibitor (PAI-1) gene (10), and methylene-tetra-hydro-folate-reductase (MTHFR) gene (11).

Multiplication of a part of Factor V coagulation gene, by means of PCR, with specific tests for normal and modified types of FVQ gene506 established a heterozygotic type of Factor V gene.

Analysis of a part of coagulation factor II gene, by means of PCR and with specific restrictional endonucleases, for G20210A mutation, proved the factor II gene to be of normal type.

Multiplication of the promotoric part of PAI-1 gene by means of the referent PCR method, with specific tests, established the deletion-insertion 4G/5G polymorphism.

Multiplication of MTHFR part of the gene by means of PCR the method, with specific tests for C677T, established the type of gene was normal.

## Comments

AION is one of the most common causes of acute loss of vision in middle-aged and elderly persons. It occurs due to

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hypoperfusion in the short posterior ciliary arteries supplying the optic nerve head (3). It is a multi-factorial disease. Beside the already confirmed cardiovascular disease development risk factors, there are also a number of other possible causes of the disease, the therapeutic procedures and medications of which are still being subjected to research. The most commonly mentioned cause of AION is arteritis (12–18). However, among immunological causes of the disease mentioned are also uremic arteriopathy, Behcet's disease, Churg-Strauss syndrome and Wegener's granulomatosis (19–22). The etiology of AION following cardiac surgery with cardiopulmonary bypass is believed to be multi-factorial. Microembolisation and pump-related platelet dysfunction have been considered risk factors for the development of AION following cardiac surgery with cardiopulmonary bypass (23). Authors describe AION joined with a well-known risk factor, namely that of hypercholesterolemia (24). However, we question whether and to what extent AION occurrence is affected by primary thrombophilia (hereditary thrombotic tendency). Primary thrombophilia develops in cases of antithrombin III (AT III) deficit, protein C and/or S deficit, dysfibrinogenemia, activated protein C resistance due to mutations of Factor V Leiden (G1691A) and prothrombin gene G20210A, as well as those of PAI-1 and MTHFR genes. Activated protein C resistance (APCR) is a recently described mutation of Factor V (FV) gene that renders resistance to cleavage by activated protein C. APCR predisposes to thrombotic events (25, 26). Described is a case of AION with APCR (27) that raises a number of questions on primary thrombophilia and AION development. With our patient, a coagulation disorder was established: elevated fibrinogen level, PV, APTR was normal, and ProC Global test and ProC Global/FV values were lowered. The last two findings indicated a hypercoagulable disorder as a result of possible hereditary thrombophilia. Therefore, we have done additional gene tests, namely Factor V Leiden, prothrombin G20210A, PAI-1, MTHFR. We established the heterozygotic type of Factor V Leiden gene and deletion-insertion PAI-1 4G/5G polymorphism. Normal genotypes for prothrombin G20210A and MTHFR were established.

Numerous studies confirm the influence of genetic mutation responsible for coagulation and thrombotic processes: deep venous thrombosis, pulmonary embolia, myocardial infarction, ischemic cerebrovascular disease, cerebral sinus thrombosis (28–35).

Zotz et al in their study have not established any significant role of genetic risk factors (inclusive of Factor V Leiden and 4G/5G polymorphism of PAI-1) in AION occurrence (36).

This case report emphasizes the need for further researches of AION genotypes, especially in patients with no other thrombotic process risk factors, and especially in younger patients.

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