

# Lateral sinus thrombosis in a young patient with sudden neurosensorial hearing loss and genetic thrombophilia: A case report

ZINA CUZMICI-BARABAȘ<sup>1,2</sup>, ANDREEA CĂȚANĂ<sup>1,2</sup>, MARIELA SANDA MILITARU<sup>1,2</sup>,  
OANA GARBEA<sup>1</sup>, IULIU VLAD CĂȚANĂ<sup>3</sup> and IOAN VICTOR POP<sup>1</sup>

<sup>1</sup>Department of Molecular Sciences, University of Medicine and Pharmacy, 400012 Cluj-Napoca;

<sup>2</sup>Department of Oncogenetics, 'I. Chiricuță' Institute of Oncology, 400015 Cluj-Napoca;

<sup>3</sup>Department of Otorhynolaryngology, 'Venart' Clinic, 400486 Cluj Napoca, Romania

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**Abstract.** Sensorineural hearing loss (SSHL) with a sudden onset is frequently encountered as a medical emergency in the ear, nose and throat (ENT) practice. The exact pathophysiology of the disease remains unknown, with the most likely etiologies being viral infection, inflammation, drug toxicity, trauma, or autoimmune response. Even though thrombophilia and cerebrovascular complications may lead, among others, to sudden neurosensorial hearing loss, its diagnosis is most often made following the onset of thrombotic complications. A case of a young female patient with unknown congenital hypercoagulation status complicated with lateral sinus thrombosis and unilateral drug-induced reversible hearing loss is presented. Molecular testing confirmed the diagnosis of genetic thrombophilia, due to the homozygous V Leiden, homozygous *MTHFR* A1298C, and heterozygous *MTHFR* C677T mutations. Although hereditary thrombophilia is a well-known topic in medical practice, current guidelines require continuous improvement, especially among patients treated in departments where this pathology is more difficult to recognize and manage.

## Introduction

It is already well known that genetic thrombophilia risk factors such as mutations in the Factor V Leiden and the prothrombin genes have contributed to the understanding of the environment-gene interaction in the development of thrombosis (1). Data emerging from the extensive studies

from the past two decades identify abnormal Factor V Leiden activity as the most common coagulation abnormality in patients with cerebral venous thrombosis, with a prevalence of 20 to 25% (2-4). Otogenic lateral sinus thrombosis is an intracranial, potentially life-threatening complication frequently associated with acute and chronic otitis media (5), but also observed in other ear-associated pathologies such as cholesteatoma (6). Thrombotic manifestations are extremely heterogeneous, with the diagnosis often being made in acute and complicated clinical circumstances.

The case of a young patient with lateral sinus thrombosis is presented, complicated with unilateral sudden sensorineural hearing loss (SSHL) and facial palsy, caused by genetically-inherited thrombophilia.

## Case report

A 27-year-old female was admitted, August 2018, to the Department of Otorhinolaryngology ('Venart' Clinic, Cluj-Napoca, Romania) for unilateral hearing loss in the left ear, facial asymmetry of sudden onset, tinnitus, and dizziness associated with progressive left hemi-cranial pain which appeared in the 24 h preceding her admission, having increasing intensity. Prior to admission, she presented subfebrile and febrile states, with temperature values ranging from 37.5 to 39°C.

Anamnesis revealed a history of recurrent left otitis. The patient had undergone surgical treatment for left ear cholesteatoma two years prior to the current admission. It is important to note that the patient also had a history of two spontaneous abortions in the first trimester of pregnancy, but their etiology had not been thoroughly investigated at the time. Her family history revealed the presence of three family members (mother, maternal aunt, maternal grandfather) diagnosed with life-threatening cerebral ischemic thrombotic vascular events.

Following physical examination at the Department of Otorhinolaryngology, the patient was diagnosed with left peripheral facial palsy. The otoscopic examination revealed a small post-surgical scar in the left ear with no signs of infection and inflammation. Audiometry revealed unilateral

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*Correspondence to:* Dr Andreea Cătană, Department of Oncogenetics, 'I. Chiricuță' Institute of Oncology, 34-36 Republicii Street, 400015 Cluj-Napoca, Romania  
E-mail: catanaandreea@gmail.com

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severe neuro-sensorial hypoacusis in the left ear. The neurological consult described the patient as alert and oriented with no signs of confusion or lethargy. Kernig's and Brudzinski's signs were negative and there were no signs of meningeal syndrome. Other than the minor facial asymmetry, the patient exhibited no motor deficits in the upper and lower limbs or incoordination. The fundoscopic eye exam revealed mild papilledema (Fig. 1).

Laboratory investigations included complete blood count, erythrocyte sedimentation rate, blood chemistry, electrolytes, lipid profile, C-reactive protein, fibrinogen protein C, protein S, antiphospholipid panel including lupus anticoagulant, cardiolipin and beta-2 glycoprotein I. Results were all within the normal range.

The computed tomography (CT) angiography highlighted lateral sinus thrombosis, affecting the internal auditory meatus and nerve.

Corroborating the clinical findings, the audiometry and CT angiography results with the personal and family history of thrombotic events, the hypothesis of genetic thrombophilia was formulated, and genetic testing was recommended. The Multiplex PCR Strip Assay, which allows the simultaneous detection of 13 different DNA targets in a single PCR reaction, followed by strip hybridization for the further described gene variants linked to thrombosis, (Screening trombofilico kit; Nuclear Laser Medicine srl.) included the analysis of the following variants: Factor V Leiden, V 4070 A>G (Hr2), prothrombin G202210A, *MTHFR* C677T, *MTHFR* A1298C, *CBS* 844ins68, *PAI-1* 4G/5G, glycoprotein IIIa T156C (HPA01a/b), *ACE-DEL/INS*, ApoE<AGT M235T, *ATR-1* A1166C, fibrinogen-455 G>A and Factor XIII Val34Leu (7).

Three mutant genotypes were identified: homozygous V Leiden, homozygous *MTHFR* A1298C, and heterozygous *MTHFR* C677T. These results confirmed the diagnosis of genetic thrombophilia.

Intensive anti-inflammatory, antithrombotic and antibiotic treatment was initiated (low-molecular weight heparin 7.5 mg daily, dexamethasone 4 mg every 8 h, and ceftriaxone 2 g daily), and under this course of therapy, the evolution of the patient was favourable. The hearing significantly improved, and according to the statement of the patient, within 14 days following admission, normal bilateral hearing had been regained. A control CT angiography on the 7th day during therapy did not reveal any detectable signs of cerebral vascular thrombosis.

The patient provided written informed consent for the publication of this case report.

## Discussion

SSHL is defined as rapid onset of hearing impairment developing in one or both ears over 72 h (8). It is considered an otorhinolaryngological emergency since it requires prompt management to rapidly detect a potentially life-threatening condition, although the majority of cases remain of idiopathic nature (9,10).

SSHL is usually unilateral, with most cases being idiopathic, and patients usually regain hearing spontaneously. In a minority of cases, the etiology lies within the broad group of autoimmune, vascular, metabolic, infectious,



Figure 1. Magnetic resonance imaging showing left lateral sinus thrombosis involving the auditory meatus and acoustic nerve.

neoplastic, traumatic, or inflammatory conditions, and in these circumstances, recovery is usually incomplete or even unachievable (11,12).

Cerebral venous thrombosis (CVT) is extremely heterogeneous and its wide spectrum of clinical presentations includes headache, dizziness, seizures, various focal neurological deficits including cranial nerve involvement causing ipsilateral facial palsy, blepharoptosis, blurry vision or diplopia, vertigo, and hearing loss (2-4). In our case, the patient only presented with sudden onset unilateral hearing loss associated with headache and ipsilateral peripheral facial palsy.

CT angiography revealed left lateral sinus thrombosis; a complication most frequently associated with other intracranial and extracranial pathologies, especially middle and inner ear infections when thrombophlebitis can spread through the emissary veins without bony erosion. Our patient had a personal history of cholesteatoma, a cystic-like structure of keratinizing stratified squamous epithelium that is well known to have a high destructive and erosion potential of neighbouring structures (13). Cholesteatoma has also been revealed to be associated with lateral sinus thrombosis as a complication. The auricular exam did not reveal any signs of inflammation or infection that could suggest the diagnosis of recurrent cholesteatoma, and thus, the episode of thrombosis

was unlikely to be a consequence of ear pathology (14). However, thorough examination is recommended.

As far as molecular diagnosis is concerned, and despite clear guidelines (15), in Romania, testing for inherited thrombophilia remains deficient in numerous departments of different specialties in the national health system, and is not commonly suggested in clinical practice. Although in certain branches such as obstetrics and haematology, molecular testing for thrombophilia is frequently used (16); in others, such as otorhinolaryngology it is completely absent.

In our case, thrombophilia was diagnosed in a young patient with unilateral SSHL caused by lateral sinus thrombosis. Despite the patient's personal history of two spontaneous abortions in the first trimester of pregnancy, and despite a positive and significant family history of thrombotic events, both representing clear indications for thrombophilia testing according to current guidelines (17), the diagnosis of thrombophilia was only made following the occurrence of high-risk cerebral thrombotic complications.

Venous thromboembolism (VTE) represents a complex disease, the result of gene-gene and gene-environment interactions. It is well known that the clinical manifestations of hereditary thrombophilia are relatively heterogeneous, as far as severity and age of onset are concerned, due to the incomplete clinical penetrance of genotypes and to the additive and synergistic effect of multiple genotypes (2,4).

It may appear trivial but having a family history of VTE suggests that it is possible to find carrier relatives who may present higher risk for this condition. When there is also a positive history for thrombotic events in the proband, testing becomes mandatory. Although the etiology of miscarriage often remains idiopathic, it can be confidently affirmed that in the case of our patient, enough evidence exists to support hereditary thrombophilia as the cause of the two spontaneous abortions in her history.

The mutations found in our patient affect the Factor V Leiden and methylenetetrahydrofolate reductase. Mutations causing defects in Factor V Leiden are linked to resistance to activated protein C, leading to thrombophilia. Numerous studies have revealed an association between Factor V Leiden defects and CVT development (2,4,18). Although multiple studies were performed and some even show a higher prevalence of MTHFR pathological variants in patients with CVT, there is not enough conclusive data yet to clearly correlate the two conditions (2,19).

Current guidelines identify heterozygous and homozygous genotypes for several variants in the Factor V Leiden and prothrombin genes as significant etiological factors for spontaneous miscarriage in the first trimester of pregnancy. The American College of Obstetricians and Gynaecologists (ACOG) underlines the importance of targeted assessment for inherited thrombophilia in patients with personal history of VTE, with or without obvious risk factors, and no prior thrombophilia testing, and in patients with family history highly suggestive for inherited thrombophilia (20). Identification of thrombophilia risk in a patient, with or without thrombotic manifestations, could lead to the implementation of a specific prophylaxis which aims to lower the risk of occurrence of such potentially life-threatening events (21).

In conclusion, since management of patients with acute thrombotic events can be difficult in the context in which it represents a major medical emergency, rigorous, guideline-based identification of individuals at high risk for such manifestations remains mandatory.

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### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Authors' contributions

AC and MSM contributed to genetic consulting and counselling. ZCB and IVP interpreted the genetic testing. IVC completed the ENT exam and OG the imaging exam. All authors read and approved the final manuscript.

### Ethics approval and consent to participate

Not applicable.

### Patient consent for publication

The patient has provided written informed consent for this material to appear in *Experimental and Therapeutic Medicine*.

### Competing interests

The authors declare that they have no competing interests.

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