CASE REPORT

Diagnosis and management of a young woman with acute isolated lateral sinus thrombosis

Dragoș Cătălin Jianu¹, Silviana Nina Jianu², Andrei Gheorghe Marius Motoc³, Mărioara Poenaru⁴, Ligia Petrica⁵, Adrian Vlad⁶, Sorin Ursoniu⁷, Anca Elena Gogu¹, Traian Flavius Dan³

¹Department of Neurology, "Victor Babeș" University of Medicine and Pharmacy, Timișoara, Romania
²Department of Ophthalmology, "Dr. Victor Popescu" Emergency Military Hospital, Timișoara, Romania
³Department of Anatomy and Embryology, "Victor Babeș" University of Medicine and Pharmacy, Timișoara, Romania
⁴Department of ENT, "Victor Babeș" University of Medicine and Pharmacy, Timișoara, Romania
⁵Department of Nephrology, "Victor Babeș" University of Medicine and Pharmacy, Timișoara, Romania
⁶Department of Diabetes and Metabolic Diseases, "Victor Babeș" University of Medicine and Pharmacy, Timișoara, Romania
⁷Department of Public Health Medicine, "Victor Babeș" University of Medicine and Pharmacy, Timișoara, Romania

Abstract
Isolated lateral sinus thrombosis (LST) was mentioned in the past as a complication of middle ear infection. In the recent years, it was not frequently studied. Our patient, a 23-year-old woman who was taking an oral contraceptive pill, displayed 24 hours of migraine, such as headache; her systemic examinations were normal. She underwent neuroimaging examinations in the first 36 hours of admission. Native head computed tomography (CT) revealed hyperdensities along the left tentorium, involving the left lateral sinus (LS). Cranial magnetic resonance imaging (MRI) showed hypointense signal on MRI T2*SW (susceptibility-weighted) in the region of the left LS. MR venography noted the absence of flow-related signal within the left LS. The clinical symptoms, signs and neuroimaging results formulated the diagnosis of left isolated LS thrombosis. Laboratory data demonstrated an elevated D-dimer and homozygosity for the factor V Leiden mutation. She was immediately started on anticoagulation in the form of low-molecular-weight Heparin; then, she was treated with Warfarin for an indefinite duration. The headaches resolved within two days and her neurological examination was also normal. A second MR venography achieved after two weeks demonstrated complete recanalization of the venous sinuses. We did not observe any LST recurrence, deep vein thrombosis or pulmonary embolism during one year of follow-up. The early initialization of anticoagulation produced a favorable evolution. An acute isolated left LST could be identified in her case on the head CT combined with MRI and MR venography.

Keywords: isolated lateral sinus thrombosis, head computed tomography, magnetic resonance imaging, MR venography.

Introduction
Cerebral vein and dural sinus thrombosis (CVT) represents a rare illness among the general population, less frequent than other types of strokes, with a higher frequency among young adults, females during pregnancy, the puerperium, or who take oral contraceptives, and patients with thrombophilia [1–3].

CVT manifests in a variable spectrum of symptoms and signs, which are often misleading, and can have different modes of onset [4–6]. Both aspects depend on various factors, especially on the site, extent, and rate of progression of thrombosis [7, 8].

The dural sinuses most commonly affected by thrombosis are the superior sagittal sinus (SSS), affected in 62% to 80% of cases, and the lateral sinus (LS), involved in 38% to 86% of cases [1–3]. In 3/4 of cases, several sinuses or veins are concomitantly thrombosed, the most frequent combination being SSS + LS [4–6]. It is rare for thrombosis to be confined to a single sinus or vein, with less than 30% for SSS and 10% for LS [7, 8].

Isolated LS thrombosis (LST) has frequently described in the past in ear or mastoid infections [9]. Symonds introduced the term “otitic hydrocephalus”, when LST manifested as isolated intracranial hypertension [10].

Recently, the clinical signs in patients with LST are likely to have changed, because of, first, LST caused by otological infections and mastoiditis have become less common due to the widespread use of antibiotics, and second, the early diagnosis of CVT using neuroimaging data [7].

We present here the case of a young female with an acute left LST induced by homozygosity for the factor V Leiden mutation, and oral contraceptive therapy. The main purpose of our paper is to discuss the clinical and neuroimaging features, the treatment and outcome of our patient, and compare them with those described by other authors.

Case presentation
A 23-year-old female developed severe (8/10) left-sided headache associated with nausea, and photophobia for 12 hours. No other symptoms or signs were present.
She used oral contraceptives. Neurological, ophthalmological (intraocular pressure, direct ophthalmoscopy, color fundus photography), ear-nose-throat (ENT), and systemic examination findings in the Emergency Department were unremarkable; her blood pressure was 122/62 mmHg. Her diagnosis was established as migraine. Because treatment with rectal suppositories of Indomethacin (50 mg) had improved her symptoms, she was discharged, and was guided to her physician. She returned six hours later with severe cephalalgia (8/10), and normal physical examination: modified Rankin Scale (mRS) score 1, so she was admitted in our Hospital.

She underwent neuroimaging examinations, including head computed tomography (CT) and magnetic resonance imaging (MRI) combined with MR venography in the first 36 hours of admission. MRI sequences were performed with a 1.5-T MR unit (Siemens Medical Systems), including T1- and T2-weighted sequences, fluid-attenuated inversion recovery (FLAIR) imaging sequence, diffusion-weighted imaging (DWI) sequences with apparent diffusion coefficient (ADC) calculations, and susceptibility-weighted imaging (SWI). MR-angiography [three-dimensional time-of-flight (3D-TOF) sequences], and MR venography (2D-TOF) were obtained during the same imaging session.

The diagnosis of acute left LST was obtained on the association of positive signs [definite spontaneous left LS hyperdensity on non-enhanced CT (Figure 1A) and hypointense signal on MRI T2*SW imaging (Figure 1B)] and negative signs [non-visualization – absence of flow-related signal within the entire left LS at MR venography (Figure 1C)].

Unenhanced head CT revealed hyperdensities along the left tentorium. The absence of parenchymal lesions was assessed on both non-enhanced CT scan and MRI (T1, T2, FLAIR, DWI sequences with ADC calculations, and T2*SW imaging). We did not observe any mastoid air sinus abnormalities.

The neurological symptoms and neuroimaging results revealed the diagnosis of acute left isolated LS thrombosis, because it was not associated with SSS, deep venous system, or straight sinus thrombosis; we did not identify any cortical vein thrombosis, including any vein afferent to the thrombosed left LS; on the other hand, the onset was ≤2 days.

Laboratory tests showed an elevated D-dimer and homozygosity for the factor V Leiden mutation. The other laboratory data were normal. She was rapidly treated with low-molecular-weight Heparin (Nadroparin) within the first 24 hours of hospitalization. After a few days, Nadroparin was gradually discontinued, and she began transitioned treatment with Warfarin with an international normalized ratio (INR) target range of 2.0 to 3.0. The headaches resolved within two days and her neurological examination was also normal. At discharge (after six days), she presented complete recovery (mRS score 0).

A second MR venography achieved after two weeks demonstrated complete recanalization of the venous sinuses. Also, the follow-up blood tests after the same period revealed normal D-dimer level. Because she presented risk factors for CVT (oral contraceptives associated with thrombophilia with factor V Leiden mutation), she was advised to avoid oral contraceptives. She was treated with Warfarin for 12 months of follow-up (INR 2–3), and was instructed for permanent oral antiocoagulation. We did not observe any recurrence, deep vein thrombosis, or pulmonary embolism, during all this period. The disability at one year was classified as complete recovery (mRS score 0).

Discussion

Ferro et al. [4] and Piazza [5] noted that at least one risk factor can be identified in 85% of patients with CVT. Damak et al. [7] asserted that in previous studies, which were elaborated in ENT departments, LST was a complication of otitis media or mastoiditis, which we did not observe in our case; on the other hand, local infections (ear) should be systematically examined by an ENT specialist in patients with LST.

In the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) cohort, a thrombophilia was identified in 34% of cases with CVT and an inherited thrombophilia was observed in 22% of them [4]. Inherited thrombophilia include increased resistance to activated protein C with factor V Leiden mutation (10–20% of cases with CVT) [5, 11]; our patient had homozygosity for the factor V Leiden mutation. For this reason, screening for thrombophilia should be performed in such cases [5, 11]. Other risk factors for patients with CVT and thrombophilia are pregnancy, puerperium or oral contraceptives [5]; just as in our case.

Two pathophysiological mechanisms are noted in patients with CVT, including LST; first, the thrombosis...
of the cerebral veins or dural sinus, leading to cerebral lesions (with ischemic injury and cytotoxic edema, disruption of the blood–brain barrier with vasogenic edema, break of capillaries and arterioles, and occurrence of brain hemorrhage); and, second, the occlusion of the dural sinus, resulting in disturbance of cerebrospinal fluid absorption and increased intracranial pressure (contributing to parenchymal hemorrhage and vasogenic and cytotoxic edema) [1–3].

LST has a varied clinical spectrum [4–6]. The patients with LST due to ear infections are with fever, headache, nausea, vomiting, retroauricular swelling, and otorrhea [7–10]; we did not come across in our case.

On the other hand, four major clinical syndromes can occur in CVT patients, including LST cases: isolated intracranial hypertension, focal cerebral signs (deficits, and/or seizures), and subacute encephalopathy [7, 8].

Our patient presented an isolated headache. According to Damak et al. [7], when comparing the clinical presentation of isolated LST (just as in our case) with other CVT, the main difference consists in the fact that the first presents more isolated headache and less encephalographic signs [7]. Headache can be acute in onset 20% of the time [4, 8, 12–15], and, sometimes, is initially diagnosed as a migraine [12]; just as in our case. Damak et al. [7] asserted that focal cerebral signs (the main focal sign in left LST is fluent Wernicke’s aphasia) and encephalopathy (with disorders of consciousness) are less frequent (one third) in isolated LST than in other CVT (two thirds). They noted that these distinctions in clinical aspects are related to a major difference of brain lesions: 31% in isolated LST versus 51% in other CVT [7]. Our patient did not present any encephalographic signs or brain lesions either.

Even though an elevated D-dimer has proven helpful in diagnosis of CVT (just as in our case), a normal D-dimer level does not exclude the diagnosis of CVT in cases with similar clinical aspects [5, 12, 16, 17].

Neuroimaging has dramatically improved in recent years the ability to confirm the clinical suspicion of CVT [1–3, 11].

Head CT with and without injection of contrast material can identify different abnormalities within the bony structures of the skull (erosion of the middle ear structures, mastoiditis, or paranasal sinus infection); it may also detect other alternative diagnoses (tumors, etc.) [4–6, 11]; we did not come across in our case. On the other hand, head CT can show direct and indirect signs of CVT [7, 8, 11]. The direct signs on unenhanced CT are represented by hyperdensity in the area of a thrombosed dural sinus – the dense triangle sign; just as in our patient (Figure 1A) or a thrombosed cortical vein (cord sign), respectively filling defects, especially in the SSS (empty delta sign), in contrast-enhanced CT studies [1–3, 11]; we did not come across in our case. Indirect signs of CVT are represented by dilated transcerebral veins, small ventricles, intense contrast enhancement of the falk and tentorium, and parenchymal abnormalities (cerebral edema or venous infarcts or hemorrhages) [4–6, 11]; we did not come across in our case.

According to different authors, MRI combined with MR venography is the most sensitive examination technique for the diagnosis of CVT in different evolution phases, because the combination of an abnormal signal in a sinus and a corresponding absence of flow on MR venography supports the diagnosis of CVT [4–8, 18, 19]. Direct visualization of the thrombus confirms the diagnosis of CVT; the features of the signal depend on the age of the thrombus [4–8, 18, 19]. In the first five days, the thrombus is isointense on T1-weighted images and hypointense on FLAIR and T2-weighted images; just as in our case, due to increased deoxyhemoglobin [4–8, 18, 19]. Non-thrombosed hypoplastic sinuses will not have an abnormal low signal in the sinus on gradient echo (GRE) and/or SW imaging [4–8, 18, 19]; our case presented such an abnormal signal on T2*SW imaging (Figure 1B). Different parenchymal abnormalities associated with CVT such as focal edema, venous infarction or intracerebral hematomas are better diagnosed by MRI [4–8, 18, 19]; we did not come across these in our case. Damak et al. [7] noted that in patients with LST we can find ipsilateral mastoid abnormalities with increased T2-weighted signal in the mastoid air spaces; they represent mucosal edema and effusion, due to venous congestion produced by LST; they should not be mistaken for mastoiditis; we did not come across in our case. The contrast-enhanced MR venography differentiates LST from LS hypoplasia [7] (Figure 1B); just as in our case.

Damak et al. [7] asserted that the outcome of patients with isolated LST was better at discharge than that of patients with other CVT, but, at one year, the outcome was similar for the two groups. The great majority of patients had a complete or partial recovery (mRS<3); just as in our patient, but the proportion of dependency (mRS≥3) was 10% by 12 months of follow-up [20].

Recanalization occurs within the first few months after CVT (40–90% of patients, mostly within the first 3–6 months) and is limited thereafter [20–24]. For this reason, in addition to clinical follow-up, the American Heart Association/American Stroke Association (AHA/ASA) 2011 Scientific Statement [11] recommends for the patient to undergo MRI/MR venography three to six months after CVT to document the extent of recanalization. We did not come across in our case, because a second MR venogram performed after two weeks demonstrated complete recanalization of all the venous sinuses. Recurrence of CVT is rare (2.8%) [20]; we did not come across in our case. However, patients with CVT have an increased incidence of venous thromboembolism, especially within the first year [22]; we did not come across in our case.

According to different authors [4, 5], the treatment of acute CVT includes: (a) antithrombotic treatment (anti-coagulation), (b) symptomatic treatment of intracranial hypertension, seizures, etc., and (c) etiological treatment of different risk factors.

The aims of anticoagulation in CVT are: (a) to combat the propagation of the thrombus to the associated cerebral veins, (b) to recanalize the occluded sinus or vein, (c) to prevent pulmonary embolism, and (d) to treat the eventual prothrombotic state for prevent venous thrombosis in other parts of the body and the recurrence of CVT [4, 5, 11, 23–25]. There is a large consensus on the use of heparins in acute CVT with or without intracranial hemorrhage [4, 5, 11, 23–26]. We can use either intravenous (i.v.) unfractionated Heparin or subcutaneous low-molecular-weight Heparin (LMWH) [4, 5, 11, 23–26]; just as in our case. Prolonged oral anticoagulation with an oral
vitamin K antagonist (Warfarin) and a target INR of 2.0 to 3.0 is recommended after the acute phase of CVT, to prevent further venous thrombotic events [4, 5, 11, 23–26]; just as in our case. The European Federation of Neurological Societies (EFNS) Guidelines [26] recommend that when CVT is due to a transient risk factor (e.g., infection, pregnancy), oral anticoagulants may be used for three months. In patients with idiopathic CVT or CVT associated with “mild” thrombophilia, the period of anticoagulation is six to 12 months [4, 5, 11, 26]. On the other hand, in patients with severe thrombophilia (including homozygosity for factor V Leiden, just as in our case), anticoagulation should be permanent [4, 5, 11, 26]. Piazza [5] asserted that women with CVT who take oral contraceptive pills; just as in our case, should use other methods for contraception.

Conclusions
The principal distinguishing points of our case from the previous reports were that the thrombosis was limited to the left LS (without involvement of tributary veins), the patient presented an atypical clinical picture (migraine-like acute isolated headache), and LST was not due to an ear infection. In consequence, we have to systematically look for LST (and other CVT) in patients with recent ear infection. In consequence, we have to systematically look for LST (and other CVT) in patients with recent ear infection. The authors declare no conflict of interests.

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References

Corresponding author
Andrei Gheorghe Marius Motoc, MD, PhD, Specialist in Obstetrics–Gynecology, Professor of Anatomy, Department of Anatomy and Embryology, “Victor Babeş” University of Medicine and Pharmacy, 2 Effimie Murgu Square, 300041 Timişoara, Romania; Phone/Fax +40256–220 482, Mobile +40722–277 806, e-mail: amotoc@umft.ro

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