

# CEREBRAL VENOUS SINUS THROMBOSIS: STUDY OF FIFTEEN CASES AND LITERATURE REVIEW

PAULO PEREIRA CHRISTO<sup>1\*</sup>, GUSTAVO MARTINS DE CARVALHO<sup>2</sup>, ANTONIO PEREIRA GOMES NETO<sup>3</sup>

Research conducted in the Neurology division at Santa Casa de Belo Horizonte, Belo Horizonte, MG, Brazil

## ABSTRACT

**OBJECTIVE.** To analyze a series of 15 patients with cerebral venous thrombosis (CVT) and analyze the results were compared with data in literature.

**METHODS.** In a retrospective, cross-sectional and descriptive study, epidemiological features, clinical pictures, risk factors and prognosis were assessed in 15 patients with CVT admitted in the Neurology division of Santa Casa de Belo Horizonte during the period of April 2007 to December 2008.

**RESULTS** Diagnoses were reached through magnetic resonance imaging of the brain in 14 cases and through an angiography in one. The main risk factors identified were use of birth control pills (40%) and history of family member with deep venous thrombosis. Thrombophilia was found in two patients (13%). The veins more affected were the transverse sinus (73%) followed by the upper sagittal sinus (53%). Four patients had strokes and five had only isolated headache. Twelve patients were treated with heparin and oral anticoagulant.

**CONCLUSION** Treatment with heparin in the acute phase followed by an oral anticoagulant was shown as safe and efficient to prevent worsening of the disease, recurrence and for quick improvement of neurological symptoms of all treated patients. CVT is one of the possible diagnoses of secondary headache even in patients with no signs and symptoms.

**KEY WORDS:** Intracranial thrombosis. Venous thrombosis. Heparin. Thrombophilia. Signs and symptoms.

## \*Correspondence:

Av. Professor Alfredo  
Balena, 189, Sala 1708-  
Santa Efigênia  
Belo Horizonte- MG, Brazil  
CEP: 30130-100

## INTRODUCTION

Cerebral venous thrombosis (CVT), which is, the thrombosis affecting cerebral veins and sinus is a rare condition, responding for less than 1% of strokes. An epidemiological study on stroke in 164 young patients (15-49 years), in Brazil, identified CVT in only seven cases.<sup>1</sup> Incidence in adults is higher in the third decade of life with a ratio between male/female sex of 1.5-5.<sup>2</sup> The involvement of young women is important, which can be attributed to the use of oral contraceptives, main risk factor associated.<sup>3</sup> The use of oral contraceptives, as well as the prothrombin gene mutation (G20210A) are significant risk factors for CVT and should be routinely investigated.<sup>4,5</sup>

In 15% of cases, the cause might not be identified.<sup>6</sup> The diagnosis may be late or neglected due to the great clinical spectrum of symptoms, various forms of initial presentation and unspecific signs of neuroimaging.

This study intended to analyze 15 CVT patients seen in a neurology service, comparing them with data found in literature.

## METHODS

Epidemiological features, clinical picture, risk factors, and prognosis were assessed in all the 15 patients with cerebral venous sinus thrombosis seen consecutively in the Neurology service of Santa Casa de Belo Horizonte, in the period of April 2007 to December 2008, and results were compared with data found in literature.

## RESULTS

Of the 15 patients assessed (Table 1), 73% were women. Average and median of age were respectively 36.3 and 39 years. The most prevalent symptom was headache, found in all the patients, and in 5 of them (33.3%) it was the only one presented. The most affected sinus were superior sagittal and transverse. Four patients presented stroke, two of them had hemorrhage, one had ischemia, and another one had both (hemorrhage and ischemia). The most important risk factor found was the use of OAC (40%). Thrombophilia was found in only two patients (13%) in this series, particularly the anti-thrombin III deficiency.

1. Doutor em Neurologia - Assistente da clínica neurológica da Santa Casa de Belo Horizonte e Hospital das Clínicas da Universidade Federal de Minas Gerais – UFMG, Belo Horizonte, MG
2. Clínica Médica - Residente de neurologia pela Santa Casa de Misericórdia de Belo Horizonte, Belo Horizonte, MG
3. Neurologista - Professor da Faculdade de Medicina de Ciências Médicas de Belo Horizonte, Belo Horizonte, MG

**Table 1 - Epidemiological and clinical features of 15 patients assessed with CVT**

Patients	Age (years)/ Sex	Clinical Picture	Affected Venous Sinus	Risk Factors	Associated Stroke	Treatment	Outcome
1	17 – F	IH	LTS + SSE + RIJV	OC	-	Oral Anticoagulant	Asymptomatic
2	47 – M	Mental confusion and seizure	SSS+ RTS + RSS	HF of TVP	IS and HS	Clopidogrel	Asymptomatic
3	21a – F	Isolated Headache	LTS	OC	-	Oral anticoagulant	Asymptomatic
4	47a – F	IH	RTS + LTS + SSS	OC	-	Oral anticoagulant	Asymptomatic
5	45a – M	IH	RTS + RSS	Previous TVP/Anti-thrombin III Def.	-	Oral anticoagulant	Asymptomatic
6	22a – F	Isolated Headache	SSS	OC	-	Oral anticoagulant	Asymptomatic
7	39a – F	Isolated Headache	LTS + SSS	Puerperium	-	Oral anticoagulant	Asymptomatic
8	19a – F	Isolated Headache	LTS	OC	-	Oral anticoagulant	Asymptomatic
9	36a – F	Headache/ seizure/ focal deficit	LTS	HF de TVP	HS	-	Asymptomatic
10	47a – M	IH	RTS	HF de TVP	HS	-	Asymptomatic
11	43a - F	Headache/ seizure/ focal deficit	SSS	OC + HF de TVP	IS	Oral anticoagulant	URL Paresthesias
12	61a – M	IH/ seizure/ focal deficit	SSS + LTS	Previous TVP		Oral anticoagulant	Loss of visual acuity
13	17a – F	Headache/ focal deficit	SSS + SSE	Puerperium/ TVP HF	-	Oral anticoagulant	Asymptomatic
14	61a – F	Isolated headache	SSS + RSS	Hormon replacement/ tooth abscess	-	Oral anticoagulant	Asymptomatic
15	22a – F	Headache/ seizure/	LTS	Pregnancy / TVP HF	-	Oral anticoagulant	Asymptomatic

LTS: left transverse sinus; RTS: right transverse sinus; USS: superior sagittal sinus; RSS: right sigmoid sinus; RIJV: right internal jugular vein; deep venous thrombosis; OC: oral contraceptive; IH: intracranial hypertension; HS: hemorrhagic stroke; IS: ischemic stroke; URL: upper right limb.

The CVT diagnosis was confirmed by a magnetic nuclear resonance (MNR) of encephalon in 14 cases, by means of a demonstration of the thrombosed sinus by the alteration of the signal in the images pondered in T1 and T2 by cerebral angiography in one case.

The follow up time of patients varied from 2 to 20 months and none of the cases presented new thrombotic events. Thirteen patients (87%) presented a good evolution with total recovery of signs and symptoms in the early phase of the treatment (attack phase). Only two remained with neurological deficits in the follow up: in one patient there was permanent visual loss due to intracranial hypertension, and in another one, paresthesia in upper right member, consequence of an ischemic cerebral infarction associated to CVT.

## DISCUSSION

In this series of cases, we have identified two main risk factors: the use of oral contraceptive in six patients and the presence of deep venous thrombosis in lower limbs preceding the picture in two patients or a history of the disease in first degree relatives in other six. Azin et al.<sup>3</sup> observed that the oral contraceptive was the main risk factor associated in a study with 61 patients. Other important risk factors associated are: pregnancy and puerperium, primary antiphospholipid syndrome, hereditary thrombophilias (C and S protein deficiency, antithrombin III deficiency, Leiden V factor, prothrombin gene mutation) and pre-meningeal infections.<sup>7</sup>

Indeed various disturbances may cause or predispose CVT patients as all the gynecologic-obstetric, surgical causes that lead to thrombosis in lower limbs, cancer, hematologic diseases, vasculites, and cranioencephalic trauma.<sup>8</sup> However, CVT is typically multifactorial, which means that the identification of a risk factor or cause should not interrupt the propaedeutics. Sometimes idiopathic cases are elucidated months later.

Headache was reported by all the patients of the series, datum verified in the literature,<sup>2</sup> and it appeared in each five of them as the only symptom. Five patients presented with intracranial hypertension syndrome. There was a cerebral infarction in four cases and convulsive crises in five. Seizure is more frequent in CVT, comparing arterial strokes, possibly present in up to 40% of the cases.<sup>2</sup>

CVT might manifest itself with an ample spectrum of signs and symptoms, possibly simulating various other neurological diseases; nevertheless, four patterns develop more usually: isolated intracranial hypertension, focal syndrome, cavernous sinus syndrome, and sub-acute encephalopathy.<sup>8,9</sup> The possibility of headache as single symptom has been described recently and made, therefore, the suspicion and diagnosis in such patients difficult.<sup>10</sup>

Initial exam for assessing patients with CVT may be both a cranial tomography (CT) with technical refinement (other cutting-planes, bony window, and study with emphasis on venous circulation) and, when available, encephalic MNR that may show a higher number of alterations resulting from venous congestion and perform the diagnosis. Around 30% of CVT patients present normal cranial CT in the beginning of the clinical picture.<sup>11</sup> Angioresonance has the advantage of being a non-invasive exam capable of confirming suspect or inconclusive cases, indicated by MNR images.<sup>12</sup> (Figure 1)

Most patients with CVT present a seric increase in the D dimer. Its elevation intensity is related to the time of installation and extension of cerebral disease. Normal levels make the diagnosis little probable, but not impossible, so it should not replace, yet, the clinical suspicion and imaging exams at diagnosis.<sup>13</sup> Dimer D may in the future become part of CVT propaedeutics, helping in the exclusion of this diagnosis

The most affected sinus was the transverse, in 73% of cases, followed by the upper sagittal, in 53%. In more than half the cases, thrombosis was found in two or more sinus. Wysokinska et al.,<sup>6</sup> in a study with 163 patients, showed that transverse sinus was affected in 79%, sigmoid in 50%, upper sagittal in 49%, and in 66% of cases two or more sinus were involved.

Twelve patients received heparin in the acute phase and warfarin for maintenance. In three patients anticoagulant therapy was discouraged by the assistant doctor due to the presence of associated cerebral hemorrhage. Nevertheless, despite the little evidence based on randomized tests, it is a current consensus that CVT patients receive anticoagulant treatment with low molecular weight heparin or unfractionated heparin; and the presence of spontaneous cerebral hemorrhage does not contraindicate its use.<sup>2</sup> In the 19th Century, CVT was commonly diagnosed by autopsy and generally showed hemorrhagic lesions, which,

**Figure 1- Partially recanalized left transverse and left sigmoid sinus in the cerebral angioresonance image**



by analogy with arterial stroke, lead physicians to think about contraindicating the use of heparin.<sup>8</sup>

According to the guide of the European Federation of Neurology and CVT Treatment, in cases secondary to transitory risk factors, the use of oral anticoagulant must be kept for 3 months. In these idiopathic with less severe thrombophilia, as C and S protein deficiency, heterozygosis for V Leiden factor or prothrombin gene mutation for up to 12 months. In the presence of relapsing disease and severe thrombophilic factors, such as antithrombin III deficiency, homozygosis of the mutant V Leiden factor or two or more associated factors, therapy should be kept indefinitely.<sup>2</sup>

The objectives of antithrombotic treatment in CVT are recanalization of the sinus or occluded vein, prevention of the propagation of the thrombus and treatment of the underlying prothrombotic state, preventing venous thrombosis in other part of the body, such as pulmonary embolia, and the recurrence of CVT.

In the series presented, the three patients with associated cerebral hemorrhage did not use anticoagulant and had a good neurological evolution. This result might be explained partly by the small number of patients in the series.

As predicting factors for death or dependence in the cerebral sinus thrombotic disease are cited: age over 37, altered mental state, coma, cerebral hemorrhage at admission, deep veins thrombosis, among others.<sup>14,15</sup>

In a study with 624 adult patients, Ferro JM et al.<sup>14</sup> reported 13% of mortality and permanent dependence. Factors related to a poor prognosis were coma, hemorrhage, and malignities.

In our small series, the four patients who presented stroke at admission had a benign course of the disease. Even the three patients who did not use specified therapeutics presented a favorable outcome.

In a series of 24 patients treated with anticoagulation, they did not present new bleedings or worsening of previous hemorrhages. Patients with parenchymatous lesions or thrombophilias had an increased risk of neurological sequelae. In another series of 50 CVT cases, a worse outcome of the disease was observed in African-descendant patients in comparison to Caucasians.<sup>16</sup>

There is no consensus yet on the efficacy or security of chemical thrombolysis and thrombectomy in the treatment of the disease. Tsai FY et al.,<sup>17</sup> treating 25 patients, suggested the use of chemical or mechanical thrombolytic therapy in cases experiencing a clinical worsening, despite the use of heparin, or in those that present with evidence of hemorrhage or edema (venous congestion). Stam et al.,<sup>18</sup> in a prospective study with 20 patients, concluded that endovascular treatment may be beneficial in patients with severe disease, but it might increase the risk of cerebral hemorrhage.

The five patients who presented seizures, three of them associated with cerebral infarctions, remained under antiepileptic therapy, based on literature data that suggest its use, for a minimal period of one year, in the cases associated with focal neurological deficits, edema, and cerebral infarctions.<sup>2</sup> Supratentorial lesions and convulsive crises at presentation are predicting factors for crises in a short period of time.<sup>19</sup>

Various studies have demonstrated the increase of cerebral venous thrombosis risk in patients using oral contraceptives and thrombophilia, particularly in the presence of

hyper-homocysteinemia, mutation of the V Leiden factor and prothrombin gene mutation.<sup>20</sup> The suspension of oral contraceptives should be recommended, so, for the patients that presented CVT, highlighting alternative contraceptive methods. In the presence of thrombophilia suspension is mandatory.<sup>20</sup> Due to the rarity of thrombophilic factors, a screening for women who want contraception might be based on the previous history of extra-cerebral venous thrombosis or familial history of the disease.<sup>20</sup> Patients with venous thrombosis associated to Antiphospholipid Antibody Syndrome should be indefinitely anticoagulated, and the RNI kept between 2 and 3 and between 3 and 4 in recurrent cases.<sup>21</sup>

Thrombophilia was found in 2 patients (13%) of this series, an approximate value to the one found by Wysokinska et al.,<sup>6</sup> who have identified the presence of thrombophilia in 10% in a cohort of 163 patients.

## CONCLUSION

CVT, due to the broad spectrum of clinical presentation, might be confused with other pathologies and, so, frequently neglected. In this series of 15 cases, the clinical picture varied from a headache refractory to analgesic treatment to severe forms as intracranial hypertension syndrome, focal deficits and coma. CVT, therefore, is within the differential diagnosis for secondary headaches even in the absence of other signs and symptoms.

The main risk factors identified were the use of oral contraceptive and a previous or familial history of deep venous thrombosis.

Treatment with heparin in the acute phase followed by oral anticoagulant has shown to be safe and effective in the prevention of disease progression, its relapse and rapid recuperation of neurological picture in the big majority of patients.

**No conflict of interest** declared concerning the publication of this article.

## REFERENCES

- Zétola VH, Nývák EM, Camargo CH, Carraro H Jr, Coral P, Muzzio JÁ, et al. Accidente vascular cerebral em pacientes jovens: análise de 164 casos. *Arq Neuropsiquiatr*. 2001;59(3B):740-5.
- Einhäupl K, Bousser MG, Bruijn SF, Ferro JM, Martinelli I, Masuhr F, et al. EFNS guideline on the treatment of cerebral venous and sinus thrombosis. *Eur J Neurol*. 2006;13(6):553-9.
- Azin H, Ashjazadeh N. Cerebral venous sinus thrombosis - clinical features, predisposing and prognostic factors. *Acta Neurol Taiwan*. 2008;17(2):82-7.
- Rodrigues CA, Rocha LK, Morelli VM, Franco RF, Lourenço DM. Prothrombin G20210A mutation, and not factor V Leiden mutation, is a risk factor for cerebral venous thrombosis in Brazilian patients. *J Thromb Haemost*. 2004;2(7):1211-2.
- Gadelha T, André C, Jucá AA, Nucci M. Prothrombin 20210A and oral contraceptive use as risk factors for cerebral venous thrombosis. *Cerebrovasc Dis*. 2005;19(1):49-52.
- Wysokinska EM, Wysokinski WE, Brown RD, Karnicki K, Gosk-Beirska I, Grill D. Thrombophilia differences in cerebral venous sinus and lower extremity deep venous thrombosis. *Neurology*. 2008;70:627-633.
- Camargo ECS, Bacheschi LA. Trombose venosa cerebral: como identificá-la?. *Rev Assoc Med Bras*. 2001;47(4):278.
- Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. *Lancet Neurol*. 2007;6(2):162-70.
- Stam J. Thrombosis of the cerebral veins and sinuses. *N Engl J Med*. 2005;352(17):1791-8.
- Cumurciuc R, Crassard I, Sarov M, Valade D, Bousser MG. Headache as the only neurological sign of cerebral venous thrombosis: a series of 17 cases. *J Neurol Neurosurg Psychiatry*. 2005;76(8):1084-7.
- Gasparetto EL. Trombose venosa cerebral. *Radiol Bras*. 2006;39(5):3.

12. Ferreira CS, Pellini M, BoasquevisqueE, Souza, LAM. Alterações parenquimatosas na trombose venosa cerebral: aspectos da ressonância magnética e da angiorressonância. *Radiol Bras.* 2006;39(5):315-21.
13. Haapaniemi E, Tattisumak T. Is D-dimer helpful in evaluating stroke patients? A systematic review. *Acta Neurol Scand.* 2009;119(3):141-50.
14. Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke.* 2004;35(3):664-70.
15. Canhão P, Ferro JM, Lindgren AG, Bousser MG, Stam J, Barinagarrementeria F. Causes and predictors of death in cerebral venous thrombosis. *Stroke.* 2006;37(2):331-2.
16. Appenzeller S, Zeller CB, Annichino-Bizzachi JM, Costallat LT, Deus-Silva L, Voetsch B, et al. Cerebral venous thrombosis: influence of risk factors and imaging findings on prognosis. *Clin Neurol Neurosurg.* 2005;107(5):371-8.
17. Tsai FY, Kostanian V, Rivera M, Lee KW, Chen CC, Nguyen TH. Cerebral venous congestion as indication for thrombolytic treatment. *Cardiovasc Intervent Radiol.* 2007;30(4):675-87.
18. Stam J, Majoie CBLM, Delden OMV, Lieden KPV, Reekers JA. Endovascular thrombectomy and thrombolysis for severe cerebral sinus thrombosis. A prospective study. *Stroke.* 2008;39(5):1487-90.
19. Ferro JM, Canhão P, Bousser MG, Stam J, Barinagarrementeria F. Early seizures in cerebral vein and dural sinus thrombosis: risk factors and role of antiepileptics. *Stroke.* 2008;39(4):1152-8.
20. Saadatnia M, Tajmirriahi M. Hormonal contraceptives as a risk factor for cerebral venous and sinus thrombosis. *Acta Neurol Scand.* 2007;115(5):295-300.
21. Tuthill JI, Khamashta MA. Management of antiphospholipid syndrome. *J Autoimmun.* 2009;33(2):92-8.

---

Artigo recebido: 09/04/09  
Aceito para publicação: 20/01/10

---