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Cerebral venous thrombosis and Covid 19: Literature review

Abstract

Introduction: Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV-2) was first detected in December 2019 in the city of Wuhan, China, and has since taken on worldwide proportions. It is known that individuals with Coronavirus disease-19 (COVID-19) have systemic clinical manifestations. Among the multisystemic effects, cerebral venous thrombosis (CVT) is responsible for high mortality rates. In this sense, understanding the association between CVT and SARS-CoV-2 infection directly impacts the disease's morbidity and mortality.

Methodology: Literature review in the PubMed and Embase databases, with the following search terms: "COVID-19", "SARS-CoV-2", "Venous thromboembolism", "Thrombosis", "Cerebral Venous Thrombosis", "Intracranial Sinus Thrombosis" and "Cranial Sinus Thrombosis". The selected articles were written in English, which addressed the various aspects of COVID-19.

Results and discussion: CVT are a rare complication of COVID-19, with an incidence between 0.02 to 1% of hospitalized patients. However, it can reach about 75% of mortality in affected individuals. Pathophysiology seems to be associated with the state of hypercoagulability and the systemic inflammatory process resulting from viral infection. Thus, recent studies show a consensus on the early anticoagulation of patients affected by the virus, to reduce mortality in these cases. However, the differences between the types of anticoagulation, Low Molecular Weight Heparin (LMWH), Unfractionated Heparin (UFH), Dabigatran have not yet been well established, although there is a predilection for the use of LMWH. Also, thrombectomy is a therapeutic intervention option that should be evaluated, due to the risk of additional endothelial injury from the use of stent retrievers.

Conclusion: Although it has a relatively low incidence, CVT aggravates the condition and increases the risk of death for patients with COVID-19. Because of this, early diagnosis and evaluation of therapeutic options for CVT are essential for the development of clinical management.

Keywords: COVID-19, coronavirus, thrombosis, venous thrombosis, central nervous system, intracranial thrombosis

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Abbreviations: SARS-CoV-2, severe acute respiratory syndrome Coronavirus 2; RNA, ribonucleic acid; COVID-19, Coronavirus Disease-19; IL-1, Interleukin-1 beta; IL-8, interleukin-8; IL-6, interleukin-6; ICU, intensive care unit; CVT, cerebral venous thrombosis; VTE, venous thromboembolism; ACE2, angiotensin-converting enzyme; vWF, von Willebrand factor; INF I, I interferon; TF, tissue factor; NETs, neutrophil extracellular traps; HIF 1, hypoxia-inducible factor 1; CNS, central nervous system; Angio-CT, angio-computed tomography; MRI, magnetic resonance imaging; LMWH, low molecular weight heparin; UFH, unfractionated heparin; aPTT, activated partial thromboplastin time'; rt-PA, recombinant tissue plasminogen activator; EVD, external ventricular drainage; TICI 3–FPE, thrombolysis in cerebral infarction with first pass effect; MRI, Magnetic resonance imaging; RMv, magnetic resonance imaging with venography; N/R, not reported; OB, obesity; DM2, diabetis melitus type 2; HBP, high blood pressure; W/A, without antecedents; BCa, breast cancer; Hach, headache; CTv, computer tomography with venography; BV, blurred vision

Introduction

Coronavirus disease-19 (COVID-19) was first observed in December 2019, in the Chinese city of Wuhan.[1] Since that time, the infection caused by Severe Acute Respiratory Syndrome - Coronavirus 2 (SARS-CoV-2) has taken on global proportions and generated over 135 million cases worldwide.[2] The SARS-CoV-2 is a single-stranded ribonucleic acid (RNA) virus with the largest RNA genome already defined and presents three viral proteins in the virion envelope: envelope protein (E), membrane protein (M) and spike protein (S), the latter being responsible for determining cell tropism and the pathogenesis of the disease.[3,4] Despite being well-established that patients suffering from COVID-19 present with symptoms such as dry cough, fever, lack of air, throat pain, headache, fatigue and diarrhea,[5] there have been reports of multisystemic manifestations including thromboembolic and neurological complications.[6] In these cases, the predisposition to developing venous and/or arterial thrombosis after infection by the virus, seems to be related to the inflammatory picture, endothelial dysfunction, plaque activation and blood stasis.[7] A number of studies have suggested that the infection might promote the process known as pyroptosis (pro-inflammatory programmed cell death), resulting in severe endothelial dysfunction, concomitant with an increase in interleukin-1 beta (IL-1) and interleukin-8 (IL-8), resulting in a state of hypercoagulability.[7]

According to study by Matteo Nicolas,[8] in a sample of 5,487 patients with severe symptoms and 9,670 with moderate symptoms,

an extension of the prothrombin time, increase in D-dimers and high levels of fibrinogen were identified, simultaneously with platelet reduction, corroborating the thrombotic changes associated with the infection.[8] Moreover, it was found that the high levels of D-dimer are linked to an increase in the rate of vascular complications.[9]

In one Italian university hospital, thrombotic events occurred in 7.7% of closed cases,[10] while other studies found that, even with prophylaxis, the incidence of thrombotic complications with COVID-19 patients in ICU, was 31%.[11] Given this scenario, cerebral venous thrombosis (CVT) was reportedly associated with COVID-19.[12–16] In view of the copious articles published about changes caused by SARS-CoV-2 and by the growing prevalence of thrombotic events simultaneously with the viral condition, it has become extremely important to evaluate the elements which constitute CVT in this scenario.[10–16]

The aim of this study was to assess the impact of infection by SARS-CoV-2 on Cerebral Venous Thrombosis, investigating the topics: epidemiology, physiopathology, clinical picture, diagnosis, treatment and the outcome of the disease.

Material and methods

For the review of the literature, a search of the PubMed and Embase databases was carried out using the search terms "COVID-19", "SARS-CoV-2", "Venous thromboembolism","Thrombosis","Cerebral Venous Thrombosis", "Intracranial Sinus Thrombosis" and "Cranial Sinus Thrombosis". Only articles in the English language were selected. Inclusion criteria comprised studies relating to the physiopathology of the venous thromboembolism, epidemiology, clinical picture, diagnosis, treatment and outcome of cerebral venous thrombosis in patients with COVID-19.

Moreover, in order to gather various clinical data concerning cerebral venous thrombosis and infection with SARS-CoV-2, the patient data were summarized into tables based on articles containing cases reported in literature from articles in the PubMed database, using the search terms "COVID-19" and "Cerebral Venous Thrombosis".

Epidemiology

Previous meta-analyses have reported an association between COVID-19 and high rates of venous thromboembolic complications.[17,18] Generally speaking, CVT is a rare form of venous thromboembolism (VTE) with an annual incidence of between 3 and 4 million adults and approximately seven per million children.[19] Precise data concerning the impact of the SARS-CoV-2 pandemic on the incidence of the pathology are not available, however, Favas et al.[20] estimate that the incidence of CVT in patients with COVID-19 is approximately 0.3%, indicating that recent epidemiological studies may demonstrate a real growth in the incidence of CVT.[20]

In agreement with the study of Favas et al. (2020), Tommaso Baldini et al. (2021) report that rates of CVT associated with SARS-CoV-2 have varied. In hospitalized patients it was around 0.02 to 1%, and 0.06% for those COVID-19 patients referred for neurological assessment.[21]

Both of these conditions, CVT and infection with COVID-19, occur independently in the young population, however, CVT is also related to additional risk factors such as trauma, use of oral contraceptives, malignant neoplasms, dehydration and a state of hypercoagulability.[22] Of the patients who presented with CVT while suffering from infection with the Coronavirus, it is suggested that there is a higher prevalence when there is a history of prior hypertension, diabetes and prior cerebrovascular disease.[23] The incidence of CVT associated with COVID-19 seems to be no different from CVT on its own, primarily affecting the female sex.[24] However, some studies have shown that the rate of mortality is significantly higher for patients infected with the virus than for patients suffering from CVT resulting from other etiologies.[25,26]

Physiopathology

Infection with SARS-CoV-2 and the correlation with thromboembolic events has not yet been fully explained. However, certain biological factors are associated with the development of thromboembolic events, including CVT.[17,18,21,27]

SARS-CoV-2 is a single-stranded RNA virus that binds to the target cell by way of the S-protein, which is responsible for the binding to the angiotensin-converting enzyme (ACE2) receptor and for the fusion of the virus in the host cell membrane.[28,29] The interaction between this protein and ACE2 produces a deregulation in the receptor, with hyperproduction of angiotensin II, which can cause generalized endothelial damage.[30–32] In addition, it has been reported that, with endothelial damage caused by the virus, there is more than three times the increased expression of the active von Willebrand factor (vWF), which is also a predisposing factor for thromboembolic events.[33]

Moreover, infection with SARS-Cov-2 may cause a state of excessive inflammation which, consequently, produces a prothrombotic condition.[7,15,34] Hyperactivation of the immune system occurs due to the viral expression of proteins that inhibit the synthesis of type I interferon (INF I), which causes a delayed antiviral immune response and facilitates replication of the SARS-Cov-2.[35] This causes the activation of monocytes and neutrophils that produce high rates of proinflammatory cytokines (e.g. IL-1, IL-6 and IL-8), culminating in hyperinflammation and in a "cytokine storm".[21] These proinflammatory cytokines suppress the anticoagulating pathways through the reduction of the tissue factor pathway inhibitor, release of ultra-large vWF and the induction of tissue factor (TF) expression.[36] Subsequently, vWF promotes the adhesion of monocytes, neutrophils, platelets and microparticles in the activated endothelium. This causes the release of Neutrophil Extracellular Traps (NETs), the activation of the coagulation pathway via TF/FVIIa and platelet activation.[30,34,36–38] Lastly, several studies have suggested that infection with SARS-CoV-2 contributes to an increase in the levels of D-dimer, fibrinogen, anticardiolipin antibodies and fibrinogen degradation product.[30,37,38] All of these processes create an imbalance between the procoagulant and anticoagulant systems, leading to a state of hypercoagulability.[36]

In addition to the physiopathological factors, the clinical condition and the hospitalization of patients with COVID-19 in critical condition could promote the formation of thrombi.[36] Immobilization and prone positioning (used for diverse patients with the infection), reduce venous return, contributing to creating a condition of blood stasis.[32] Moreover, hyperthermia contributes to the activation of the platelets and the coagulation pathways, associated with the hypovolemic state, due to the loss of gastrointestinal liquid and, in addition, there is an increase in blood viscosity.[34,36] For patients with hypoxemia, there may be vasoconstriction, culminating in reduced blood flow and the induction of the expression of hypoxia-inducible factor 1 (HIF 1).[34,36]

It is known that SARS-CoV-2 has neurotropic potential. Its dissemination into the Central Nervous System (CNS) occurs by means of two pathways: hematogenic pathway- where the virus affects endothelial cells of the blood-brain barrier or afflicts the CNS by means of infected neutrophils; and/or the retrograde neuronal

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pathway – where the arrival of the virus occurs through the axonal transport of the peripheral nerves, such as the olfactory nerve. This neurotropism may provoke neurological disorders like meningitis/encephalitis.[39] It is suspected that this direct invasion of the CNS may contribute to the pathogenesis of CVT, although the mechanism of how this takes place is still unclear.[21]

Clinical and radiological features

Generally speaking, the principal clinical manifestations associated with CVT are: signs of intracranial hypertension, headache (95%), blurred vision (15%), papilledema (30%), reduced consciousness (19%), focal neurological deficits (30%) and convulsion (19%).[40]

By evaluating a group of eight patients who presented with CVT at the same time as being diagnosed with COVID-19, it was found that the majority of patients present with symptoms not specifically related to the virus, and neurological symptoms such as syncope and focal neurological deficit were identified on a smaller scale [24] . In this group, the onset of CVT-related symptoms (hemiparesis, weakness, aphasia, altered vision) occurred, on average, three days after the initial COVID-19 diagnosis, being radiologically diagnosed between six and 16 days after the onset of the condition.[24] Initial symptoms of CVT may include an increase in intracranial pressure, progressive headache, sight problems, papilledema, focal neurological deficit, loss of consciousness and convulsions. However, progressive headache appears to be the most common symptom in patients with CVT, concomitant with the coronavirus.[41]

With regard to the signs and symptoms developed by patients with COVID-19 who presented with CVT, the following conditions were reported: headache (31 to 49%), focal neurological deficit (31 to 32%), fever (29%), reduced level of consciousness (24 to 31%), gastrointestinal tract symptoms (21%), coughs (19%), dyspnea (12%). In addition, the average time between the start of COVID-19 symptoms and the CVT diagnosis was between seven and 11 days.[13,42] The study presented by Baldini et al (2021) demonstrates that changes in mental state occur in around 60% and epileptic convulsion in 28% of cases of CVT in patients with COVID-19.[21]

Lastly, common symptoms of viral infection with SARS-CoV-2, like headache, can delay the diagnosis of CVT to the extent that the neurological symptoms may be aggravated [15]. Several authors note that the difference between viral headache and CVT-associated headache is based on the progressive worsening of pain when associated with CVT.[42]

In relation to the location of the thrombi, imaging data suggest that thrombosis in multiple veins is more common than an event in a single vein. Moreover, the transverse sinus is the most affected location (65%), followed by the sigmoid sinus (47%), superior sagittal sinus (44%) and straight sinus (21%). Thrombosis could also occur in the deep venous system (37%) and in the cortical venous system (21%).[21]

Diagnosis

The diagnosis of CVT is made on the basis of clinical and laboratory suspicions, confirmed by way of imaging examinations.[21] According to the study by Baldini et al (2021), the laboratory data in patients with CVT and COVID-19 presented fibrinogen abnormalities, an increase in D-dimer and C-reactive Protein. In addition, the most frequently employed imaging method for the diagnosis was Angio-Computed Tomography (Angio-CT), although Magnetic Resonance Imaging (MRI) may also be used.[13]

In the context of CVT, rapid diagnosis and treatment is vital given the severity of the condition. In this regard, patients with high levels of D-dimer and fibrinogen, with headache, convulsion and/or focal symptoms, should be investigated to eliminate cerebral venous thrombosis.[43]

Treatment

Anticoagulants

The basis for the treatment of CVT is anticoagulant therapy, the aim of which is to recanalize the obstructed vessel, avoid the propagation of the clot, prevent pulmonary embolism and treat the prothrombotic condition.[43,44] Although there exist few studies concerning CVT therapy in connection with COVID-19, the thromboprophylaxis recommendations are general and the drug of choice may be either unfractionated heparin (UFH), or low molecular weight heparin (LMWH).[44] The use of anticoagulants produces a significant reduction in mortality, particularly in patients who present with high levels of D-dimer (>3.0 µg / mL).[45] LMWH seems to favor a reduction in thrombotic complications when compared to UFH, in that it is safer, more effective, and has a more predictable pharmacokinetic profile.[45]

For those patients with a diagnosis of acute CVT, in a randomized clinical trial comprising 66 individuals with CVT, a statistically significant reduction in hospital mortality was identified for patients using LMWH in comparison with patients using UFH (0% versus 19%). As well as the reduction in mortality, the group that used LMWH recovered better than the group using UFH, however there was no statistical evidence to support this comparison.[38]

The use of heparins is based on evidence that suggests the medication is capable of binding to the S-proteins of the viral envelope, helping to reduce IL-6, which has a negative impact on immune activation, reducing the systemic inflammatory process and, consequently, the physiopathological aspects that promote the development of CVT.[13]

In the study conducted by Tu et al. (2020), the survival rate using anticoagulation was 60%, suggesting that the treatment employed for CVT of different etiology, is also effective for COVID-19-related CVT.[13] This strengthens the possibility of early anticoagulation as a strategy for reducing CVT-associated mortality.[13] In a sample of 14 patients treated with anticoagulants, five died, of which three were deemed to be in critical condition and two in the moderate stage, which leads to the perception that the degree of viral infection may or may not impair the patient's neurological status, generating a worse prognosis regardless of the type of therapeutic approach.[21]

In a sample of 38 patients with CVT, where anticoagulants were being used on 37 adult patients and aspirin for one pediatric patient, Baldini et al.[21] observed a mortality rate of 40% (14/35).[21] Moreover, seven patients treated with anticoagulants needed surgery even while undergoing drug treatment. Six of these patients ended up dying.[21] In this study, the pediatric patient on whom the strategy of platelet anti-aggregation with aspirin was carried out, did not require subsequent surgery and achieved partial recovery from her condition.[45]

Several authors have suggested that, despite LMWH presenting statistical data favorable to the treatment of CVT, the use of UFH should be considered for patients in a critical condition, who may require subsequent surgery, due to the activated partial thromboplastin time (aPTT) returning to normal levels one hour after the completion of the drug infusion.[46]

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There is precious little data in the literature concerning CVT and the use of the new oral anticoagulants. Pang et al.[46] demonstrated satisfactory results with the use of dabigatran in just one patient, in whom the number of platelets, D-dimer, thromboplastin time (aPTT) remained unaltered and with no evidence of elevated inflammatory markers.[46] This patient recovered fully from the CVT condition.[27,47] Two other studies demonstrated safety with the use of dabigatran but, due to the sample size, there was no consensus about the superiority of this drug in patients infected with SARS-CoV-2.[48,49]

Studies have shown a significant reduction in mortality in patients treated with anticoagulation, irrespective of the choice between UFH and HBPM, mainly in individuals with very high levels of D-dimer.[48] Preventive anticoagulation continues to be recommended for patients with severe infection.[48] The use of other medication, such as recombinant tissue plasminogen activator (rt-PA) was associated with a temporary clinical improvement, but did not interfere with the mortality of patients with COVID-19-related CVT.[12]

Surgery

The use of thrombectomy is advocated to treat patients with severe CVT.[12] The study by Cavalcanti et al. (2020) showed one patient, with a positive result for SARS-CoV-2 and CVT, subjected to thrombectomy following complications.[21] Despite the fact that the patient ended up dying due to a worsening of the respiratory condition, it was reported that the superficial venous system showed significant improvement.[50]

In some cases, surgery has been employed ancillary to treatment with medication. In the study by Baldini et al. (2021), mortality resulting from thrombectomy was approximately 85% (6/7).[50]

Kananeh et al. (2020), in a sequence of four cases subjected to surgery, three of which were arterial ischemic stroke and one was CVT, three patients ended up dying, including the patient with the diagnosis of CVT. In this case, thrombectomy was not carried out on the patient with CVT, opting instead for external ventricular drainage (EVD), hypertonic therapy and anticoagulation with heparin [7]. On the other hand, a better evolution was found in the individual who underwent the thrombectomy, in combination with rt-PA and aspirin as secondary prevention.[51]

Although the physiopathology has not been well defined, it is known that VTE in patients with COVID-19 occurs via endothelial damage resulting from the inflammatory process.[52] In this regard, it is suggested that thrombectomy using stent retrievers is associated with a risk of repeat thrombosis due to the exacerbated endothelial inflammatory response.[53] So, in addition to the choice of surgery, COVID-19-related CVT requires an evaluation of the different forms of thrombectomy, due to differences in the efficacy of each technique.[54] The total reopening of the vessel, according to the scale known as Thrombolysis In Cerebral Infarction with First Pass Effect (TICI 3 - FPE), is the standard thrombectomy protocol, associated with low mortality (16.3%) and significant beneficial results have been observed in patient evolution.[54] In a study conducted on patients infected with coronavirus, and with large-vessel CVT, none of the evaluated patients underwent complete reopening of the vessel after the first pass (TICI 3 FPE), suggesting that removal via thrombectomy in patients infected with the virus is more difficult than in patients with CVT but without COVID-19.[21,55,56]

Outcome

In the literature, there are reports of high mortality associated with CVT, ranging from 40 to 75% of cases.[56,57] Studies still need to be conducted to help define risk and prognosis, however immediate treatment of the patient can contribute towards a positive outcome, while elevated levels of D-dimer indicate a more critical prognosis.[55] In addition, there seems to be no direct connection between the severity of respiratory symptoms and CVT-related mortality.[13,38,48,56,58]

There is a consensus over the prescription of anticoagulants and their effect on the rates of patient mortality and recovery.[7,21,23,46,53] Moreover, the difference in the patient's evolution appears to be subtle when compared to surgery and the use of anticoagulants, such that the outcome of death and worse prognoses are linked to high systemic inflammation indices.[20]

Summary of the data in Table 1

In our review were include 28 articles, including a total of 39 cases of patients infected with CVT associated with COVID 19. This analysis contains the following data: age, gender, previous comorbidities / relevant factors, time between symptoms of COVID-19 and CVT, NIHSS, clinical manifestations, MRI findings, computed tomography / magnetic resonance findings with venography, treatment and prognosis. The mean age was 41,64 (the exact age of two pacientes has not been report, so they were not considered in the calculation), however was a wide age variation among the patients (σ=18,67). The gender distribution was 59% men (23/39). The time between symptons of COVID-19 and the appearance of CVT varied. But, in 43,6% of the cases (17/39), the symptoms of COVID-19 and CVT appeared at the same time, while in one other case CVT appeared 37 days after COVID 19 symptoms. There was also a case which CVT manifested four months after infection with SARS-CoV-2, she was a womam who already had history of previous bleeding, in addition to other thrombocytic diseases.

The NIHSS (National Institute of Health Stroke Scale score) has been reported seven times. The mean result was 6,4 and three patients had NIHSS greater than 4. The neurological and systemic symptoms were: headache 59% (23/39), fever 28,2% (11/39), weakness 20,5% (8/39), convulsion 15,4% (6/39), loss of consciousness 15,4% (6/39), aphasia 12,8% (5/39), blurred vision 10,2% (4/39), confusion 10,2% (4/39), dysarthria 7,7% (3/39), hemiparesis 7,7% (3/39), vomit 7,7% (3/39), lethargy 5,1% (2/39), numbness 5,1% (2/39), hemiplegia 5,1% (2/39), imbalance 5,1% (2/39), astenia 5,1% (2/39), epileptic attack 5,1% (2/39), tingling 5,1% (2/39), agitation 5,1% (2/39), body pain 2,56% (1/39), change in mental status 2,56% (1/39), executive dysfunction 2,56% (1/39), dyspraxia 2,56% (1/39), anosmia 2,56% (1/39), absence of stimulus to pain 2,56% (1/39), chills 2,56% (1/39), fatigue 2,56% (1/39), delirium 2,56% (1/39), bone pain 2,56% (1/39), diarrhea 2,56% (1/39), papilledema 2,56% (1/39), dysphasia 2,56% (1/39), disorientation 2,56% (1/39) and drowsiness 2,56% (1/39). It is important to note that many studies did not report systemic symptoms of COVID 19, which made it difficult to analyze these data.

The most altered laboratory exam was the D-dimer. In the 39 cases the d-dimer was reported in 71,8% (28/39) of the patients and was elevated in 85,7% (24/28) of reported cases. Fibrinogen was abnormally elevated in 50% (10/19) of the 19 cases that reported.

The mostly used anticoagulant therapy was the heparins: enoxaparin 36% (13/36), low molecular weight heparin 28% (10/36), heparin 19% (7/36; undifferentiated in the case report if was used LMWH or UFH), and unfractionated heparin 14% (5/36). Other medications used were: dabigatran 8% (3/36), apixaban 6% (2/36), rivaroxaban 6% (2/36), warfarin 3% (1/36), edoxaban 3% (1/36) and tPA 3% (1/36). Surgical treatment was utilized in eight patients: decompressive craniectomy 8% (3/36), thrombectomy 3% (1/36), and external ventricular drain insertion 3% (1/36). Three cases had no reported the treatment.

Table 1 Literature review of case reports and case series of Cerebral Venous Thrombosis in patients with COVID 19

Author	Dakay et al. - Patient 1[15]	Dakay et al. - Patient 2[15]	Cavalcanti et al. - Case 1[12]	Cavalcanti et al. - Case 2[12]	Cavalcanti et al. - Case 3[12]	Hughes et al.[16]	Garaci et al.[63]	Klein et al.[38]	Sugiyama et al.[41]	Hemasian and Ansari[60]
Age	17	72	38	41	23	59	44	29	56	65
Sex	M	F	M	F	M	M	F	F	M	M
Previous comorbidities / relevant factors	OB	BCa	Autistic spectrum	Use of estrogen-based oral contraceptives	W/A	DM2 and HBP	W/A	W/A	W/A	W/A
Time between symptoms of COVID-19 and symptoms of CVT	At the same time	Three days	At the same time	Short period of time	One week	At the same time	Two weeks	One week	Twelve days	At the same time
NIHSS	0	1	14	16	N/R	10	N/R	N/R	N/R	N/R
Clinical condition	Headache, BV	Dysarthria, weakness in the left hand and dyspnoea	Headache for 7 days and change in mental status in the last 2 days	Confusion and aphasia	Headache, body aches, fever, dry cough and lethargy.	Persistent high-intensity Headache, fever and hypertension	Progressive dyspnea, Headache, mental confusion, aphasia and hemiparesis on the right side.	Headache, agitation, aphasia, moderate paralysis of the right face and convulsion.	Severe Headache and vomiting.	Convulsion and, after hospital admission, drowsiness.
Laboratory findings **	APTT = 25.7s TP = 11.3s INR = 1.06 Fibrinogen = 355 mg / dL	APTT = 33.5s TP = 11.7s INR = 1.10 Fibrinogen = 509 mg / dL Prot. C react. = 2.8 mg / dL	N/R.	N/R.	D-dimer = 2032 ng / mL	TPTP = 19.7s TP = 11.2s Prot. C react. = 20 mg / L Fibrinogen = 4.9 g / L	D-dimer = 5975 ng / mL Platelets = 42,000 / µL CKMB = 6.9 ng / mL	APTT = 28.7s Prot. C react. = 37 mg / L Fibrinogen = 4.9 g / L D-dimer = 2876 ng / L	D-dimer = 10.3 µg / mL	N/R
MRI findings	Thrombosis of the dural venous sinus in the left transverse and sigmoid sinuses extending to the left internal jugular and straight sinuses; possible thrombus in the left Labbe's vein.	Without changes.	N/R.	N/R.	Pathologically reduced diffusion throughout the subcortical area of deep white matter.	N/R.	N/R.	Hemorrhagic infarction in the left temporoparietal area, with extinguishment of the left lateral ventricle and the third ventricle with a deviation of 4 mm to the right.	Results compatible with TEC at the confluences of the left transverse sinus.	RMR demonstrates thrombosis of the right and transverse sigmoid sinuses.
CT / RMv findings *	RMv - Elongated filling defect at the confluence of the left transverse and sigmoid sinuses and the proximal internal jugular vein. Partial extension of the right transverse and superior sagittal sinuses. Large thrombus in a straight sinus and in Labbe's left vein.	CT - Filling defects in the right sigmoid sinus and jugular bulb	CT - hyperdensity in the straight sinus, superior distal sagittal sinus and right transverse sinus. CTv - almost occlusive thrombus in the right internal cerebral vein.	CT - venous infarction of the left basal ganglia, thalamus and mesial temporal lobe, intraventricular hemorrhage and obstructive hydrocephalus. CTv - occlusion of the internal cerebral veins with significant enlargement of the Galen vein and distal straight sinus.	CT - irregular areas of low density in the two cerebral hemispheres, with a focus of subcortical hemorrhage in the left occipito-parietal region.	CT - hyperdensity in the superior sagittal sinus, right transverse, sigmoid sinus and right upper internal jugular vein. CTv - no changes. After 4 days, CTv revealed a filling defect in the right sigmoid sinus and transverse sinus.	CTv - filling failure in the Galen vein, straight sinus and torcular herophilus due to thrombosis in the dural sinus with poor representation of the left internal cerebral vein.	CT - Hemorrhagic venous infarction in the left temporoparietal area with edema and venous thrombosis in the left distal transverse sinus and sigmoid sinus.	CT - Results compatible with TEC at the confluences of the left transverse sinus.	CT - hemorrhagic infarction in the temporal lobe.
Treatment	Enoxaparin	Anticoagulants were not administered due to change in treatment strategy	Enoxaparin 70mg 2x / day, after worsening, thrombectomy and microcatheter incision were performed for tPA infusion at a rate of 2 mg / h. Lopinavir-ritonavir was inserted.	Insertion of an external ventricular drain and a bolus heparin infusion was started.	N/R	After the second exam treated with low molecular weight heparin and after high apixaban 10mg 2x / day for 7 days in the reference service.	Tocalizumab and low molecular weight heparin.	Correction of anemia with two units of red blood cells and ferrous sulfate 325mg / day, after stabilization started intravenous heparin and, subsequently, 50mg subcutaneous enoxaparin 12 / 12h.	Unfractionated heparin was administered and replaced by edoxaban (60mg / day) six days later.	Therapy with anticoagulant, levetiracetam, hydroxychloroquine and amoxicillin + acid. clavulanic.

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Table Continued...

Author	Dakay et al. - Patient 1[15]	Dakay et al. - Patient 2[15]	Cavalcanti et al. - Case 1[12]	Cavalcanti et al. - Case 2[12]	Cavalcanti et al. - Case 3[12]	Hughes et al.[16]	Garaci et al.[63]	Klein et al.[38]	Sugiyama et al.[41]	Hemasian and Ansari[60]
Prognosis	He was discharged, readmitted two weeks later with scotomas, stable neuroimaging	Due to the patient's critical condition and desire, there was a transition to palliative care and he died in the hospital.	Improvement in neurological symptoms, however worsening in respiratory function, leading to cardiac arrest and death 32 hours after admission.	The patient had loss of brainstem reflexes and died 4 days after hospital admission.	The patient was intubated due to acute fulminant respiratory distress syndrome in the days before death.	Discharge for home recovery.	N/R	After 7 days he showed improvement in alertness, however he still presented moderate aphasia and persistent bilateral paralysis of the 6th cranial nerve.	Significant improvement in thrombosis in the left transverse sinus with subsequent discharge from hospital.	High on the 10th day in good general condition.

Author	Asif and Mahony[61]	Logan et al.[62]	Guendouz et al. - Case 1[48]	Guendouz et al. - Case 2[48]	Kaur et al.[63]	Cardoso et al.[64]	Haroon et al. - Case 1[65]	Haroon et al. - Case 2[65]	Haroon et al. - Case 3[65]	Pang et al.[46]
Age	18	34	56	19	41	48	47	32	30	35
Sex	M	M	F	F	M	M	M	M	M	M
Previous comorbidities / relevant factors	W/A	W/A	DM2, hyperthyroidism, BCa in treatment	Migraine and OB grade II	W/A	N/R	W/A	OB	N/R	W/A
Time between symptoms of COVID-19 and symptoms of CVT	One week	One month	At the same time	At the same time	Positive IgG, without symptoms of COVID-19	Thirty-six days	Same time	thirteen days	At the same time	At the same time
NIHSS	N/R	0	N/R	N/R	N/R	4	N/R	N/R	N/R	N/R
Clinical condition	Severe Headache	Headache and BV, imbalance in walking and numbness with tingling in the lower and upper limbs.	Hemiplegia and fever	Tonic-clonic seizure, Headache, cough and severe asthenia.	Severe frontal Headache and aphasia	Left upper limb numbness, weakness and decreased balance sensitivity.	Weakness in the left side and lethargy.	Weakness of the facial muscles, dysarthria and weakness on the right side.	Headache in the occipital region for four days followed by weakness in the left arm.	Headache, fever and cough.
Laboratory findings **	Prot. C react. = 30 mg / L	D-dimer = 2.31 mg / L	Prot. C react. = 54 mg / L	D-dimer = 2150 g / L Prot. C react. = 11.5 mg / L	Erythrocyte sedimentation rate = 29 mm / hr Prot. C react. = 44.89 mg / L	TP = 12.8 s D-dimer = 0.77 µg / mL	D-dimer = 1.23 µg / mL Fibrinogen = 6.9 g / L HB_{A1C} = 13.1 mmol / L	Prot. C react. = 129 mg / L D-dimer = 0.72 µg / mL Fibrinogen = 4.8 g / L	Prot. C react. = 19 mg / L D-dimer = 1.02 µg / mL	No relevant changes
MRI findings	N/R	It confirms the presence of thrombosis in the dural venous sinus and signs of minor subarachnoid hemorrhage in the frontal lobe (posterior left) and then parietal.	It revealed thrombosis of the superior sagittal sinus and the right lateral sinus spreading to the right internal jugular vein, as well as signs of subarachnoid hemorrhage in the right region and parietal intraparenchymal hematoma.	N/R	Consistent with the presence of acute thrombosis of the superior sagittal sinus, extending to the left transverse sinus and sigmoid sinus.	Presence of a lesion in the right parietal vein.	N/R	Multiple infarctions in the left frontroparietal lobe, probable embolic etiology.	Venous infarction in the frontal lobe (upper right area), thrombus in the superior sagittal sinus, with no visualization of the superior sagittal sinus and transverse sinuses.	No relevant changes
CT / RMv findings *	CTv - filling defects in the sigmoid and transverse sinuses (bilaterally), extending to the rectum and superior sagittal sinuses. No signs of bleeding.	CT with angiography - filling defects in the upper sagittal sinuses, torus, left transverse and left sigmoid, as well as in the proximal part of the left internal jugular vein,	CT - extensive venous infarction with hemorrhagic transformation leading to subphalcin and transtentorial herniation	CT with angiography - thrombosis of the superior sagittal sinus, frontal cortical vein and right sigmoid sinus without repercussions in the parenchyma.	CT - consistent with the presence of acute thrombosis of the superior sagittal sinus, extending to the left transverse sinus and sigmoid sinus. No signs of bleeding or edema.	CT - small acute hemorrhage in the right parietal lobe.VMRI - confirmation of the diagnosis of cerebral venous thrombosis, showing blockage of the right parietal vein and a filling defect at the entrance of the vein in the superior sagittal sinus.	CT - infarction in the frontal lobe (right region) and basal ganglia.	CT - ischemic changes detected in the left posterior parietal lobe.	CT - hemorrhagic infarctions in the frontal lobe (upper right area), with suspected CVT.	RMv - filling defects in the left transverse and sigmoid sinuses suggestive of CVT.

Table Continued...

Author	Asif and Mahony[61]	Logan et al.[62]	Guendouz et al. - Case 1[48]	Guendouz et al. - Case 2[48]	Kaur et al.[63]	Cardoso et al.[64]	Haroon et al. - Case 1[65]	Haroon et al. - Case 2[65]	Haroon et al. - Case 3[65]	Pang et al.[46]
Treatment	Initially only analgesia, after reevaluation, low molecular weight heparin was inserted and monitored for 24 hours. After high therapy with enoxaparin for 3 months.	Intravenous heparin	Decompressive craniectomy and anticoagulant therapy	Anticoagulation therapy (low molecular weight heparin followed by vitamin K antagonist) and levetiracetam.	Enoxaparin	Labetalol 20mg for pressure control; subcutaneous exoparina 80mg 12 / 12h, total of two doses; levetiracetam 500mg IV two doses.	Aspirin and atorvastatin started, prophylactic dose of enoxaparin (40 mg). Low molecular weight heparin was used to treat DVT followed by 150 mg dabigatran.	Thrombolysis was not performed on the patient due to the stabilization of the infarcted areas, 100 mg aspirin, 75 mg clopidogrel and atorvastatin 40 mg / day were prescribed.	Low molecular weight heparin, followed by rivaroxaban 15 mg / day for three weeks and after 20 mg / day for three months.	Dabigatran 150mg orally twice a day for three months.
Prognosis	After 2 weeks the patient reported significant improvement in symptoms and almost complete resolution of the Headache.	The patient was discharged with an end to the symptoms of paresthesia and Headache, but he still had some visual disturbances and imbalance.	He had bi-thalamic infarction and persistent coma.	He was discharged with improvement in symptoms, with only minimal Headache.	The patient was discharged with a recommendation for multidisciplinary follow-up.	He was discharged, with satisfactory progression and slow improvement of symptoms and signs.	On the 10th day of hospitalization, DVT was detected in the right MI, after the end of treatment, transferred to rehabilitation.	The patient recovered well and was discharged with minimal weakness.	Patient classified as COVID-19 LRTI and treated according to local guidelines.	Headache improvement without new symptoms.

Author	Hussain et al.[66]	Tu et al. - case 1[13]	Tu et al. - case 2[13]	Malentacchi et al.[67]	Poillon et al. - case 1[68]	Poillon et al. - case 2[68]	Thompson et al. [69]	Bastidas et al.[70]	Ramesh et al.[71]
Age	30	Mid-thirtieth	30s	81	62	54	50	13	22
Sex	M	M	M	M	F	F	M	F	F
Previous comorbidities / relevant factors	W/A	W/A	W/A	Ocular myasthenia, transurethral resection of the prostate for adenocarcinoma, chronic B lymphatic leukemia and hemolytic anemia	Morbid OB	BCa and hormone therapy	N/R	Patent oval foramen	W/A
Time between symptoms of COVID-19 and symptoms of CVT	At the same time	Four days	At the same time	Some days. He fell into a coma 19 days later	Fifteen days	Two weeks	One week	At the same time	At the same time
NIHSS	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Clinical condition	Four generalized tonic seizure episodes.	Chest pain, fever, chills, Headache	Neck trauma due to epileptic seizure. In the emergency room: confusion and restlessness	Breathing difficulty and loss of consciousness. Neurological examination demonstrated absence of pain stimulus	Fever, cough and dyspnoea	Fever and asthenia. Thereafter cough and Headache	Delirium, executive dysfunction and dyspraxia	Intense Headache and impaired level of consciousness.	Fever, Headache, diplopia and recurrent episodes of loss of vision in both eyes.
Laboratory findings **	TP = 15.1s D-dimer = 0.75 mg / L FEU	Analysis of cerebrospinal fluid 3 cells nucleated per mm3, 1000 red blood cells per mm3 and protein 0.76g / L	D-dimer = 4.6mg / L; Prot. C React. = 7.3mg; Hemocysteine 119.2 umol / L	Prot. C Reat. 13.62mg / dL; Fibrinogen 539mg / dL; D-dimer 2017ng / mL; ATTP 26.6s; INR 1.20 s	D-dimer 14.2mg / L; leukocytosis 20.22 × 109 / L; Elevated AST and ALT	D-dimer 2.36mg / L; Prot. C Reat. 170.8 mg / L; leukocytosis 18.32 × 109 / L	Fibrinogen 3.8g / L;	D-dimer = 33.96 mg / dL Lactate dehydrogenase = 322 U / L Prot. C react. = 12.55 mg / dL Ferritin = 240 ng / Ml Fibrinogen = 0 mg / dL Platelets = 55000 / mm³ Lymphocytes = 1800 / mm³	D-dimer = 1.04 mg / L Erythrocyte sedimentation rate = 122 mm / h Prot. C react. = 43.3 mg / dL PT = 18.5 s INR = 1.54 s TPPa = 57.5 s
MRI findings	Hematoma with hypointense blood products in the area of the lesion and subarachnoid hemorrhage in the Silviana fissure.	N/R	N/R	N/R	MRI and CT demonstrated confluent intraparenchymal hemorrhage in the left temporal lobes	MRI and CT revealed hemorrhagic infarction in the left temporal lobe	Radiological findings according to the cognitive profile	MRI with angiogram - bilateral thrombosis of the transverse sinuses extending to the right sigmoid sinus and internal jugular vein.	Eminent subarachnoid space around the optic nerve and flattening of the posterior sclera bilaterally with diagnosis of papilledema.

Table Continued...

Author	Hussain et al.[66]	Tu et al. - case 1[13]	Tu et al. - case 2[13]	Malentacchi et al.[67]	Poillon et al. - case 1[68]	Poillon et al. - case 2[68]	Thompson et al. [69]	Bastidas et al.[70]	Ramesh et al.[71]
CT / RMv findings *	CT - hypodense lesion in the anterior right temporal lobe with mild surrounding edema and mass effect. MRv - non-occlusive thoracic thrombosis, left transverse sinus and sigmoid sinus, extending to occlude the proximal part of the left internal jugular vein.	RMv - left transverse sinus and sigmoid filling defect	CT - thrombosis in the left transverse and sigmoid sinuses, extending to the right internal jugular vein	CT - bilateral subacute infarctions in the middle cerebral artery territory; Angiotomography - bilateral occlusion of the middle cerebral arteries; Contrast CT - sigmoid sinus filling defect	CT venography - showed cerebral venous thrombosis of the left transverse sinus, internal cerebral veins and Galen vein	CT venography - cerebral venous thrombosis of the transverse sinus	CT - Dural venous sinus thrombosis involving superior sagittal sinus, left transverse sinus and left sigmoid sinus, in addition to thrombosis in the Labbe vein	CT - intracerebral hemorrhage in the area of the right occipital lobe	RMv - bilateral venous thrombosis of the transverse sinuses.
Treatment	Levetiracetam 500 mg 2x / day, subcutaneous low molecular weight heparin 1.5 mg / kg followed by rivaroxaban 15mg 2x / day for three weeks and after 20 mg / day for at least three months.	Started with dabigatrana	Anticoagulation with heparin IV, levetiracetam IV and cobalamin replacement	Anticoagulant treatment and respiratory support (not specified)	N/R	N/R	On admission prophylaxis with enoxaparin. After CT intravenous heparin therapy	Hypertonic saline solution in bolus and transfusion of fibrinogen, platelets and plasma. After diagnosis of CVT, unfractionated heparin (10 U / kg / h) was adjusted to maintain aTTPa between 1.5 and 2.5 s, increased to 20 U / kg / h after new events.	Subcutaneous heparin, intravenous metiprednisone and antibiotic therapy.
Prognosis	He was discharged for follow-up at a quarantine center.	Patient was discharged. With CT follow-up after 4 weeks, he had complete resolution	After a week in hospital, there was an increase in haemorrhaphy and edema. Decompression craniectomy was performed, but the patient died the following day.	Patient died 2 days after falling into a coma	N/R	N/R	Clinical improvement with recanalization of the Labbé vein, partial recanalization of the transverse and superior sagittal sinus. He was discharged from the hospital	The patient was discharged with a good prognosis, asymptomatic and without neurological sequelae 24 days after admission.	The patient improved her symptoms with the progression of treatment for CVT.

Author	Loos et al.[72]	Baretta et al.[73]	Rigamonti et al.[74]	Abouhashem et al. - Case 1[14]	Abouhashem et al. - Case 2[14]	Roy-Gash et al.[75]	Bolaji et al.[76]	Nwajei et al. - Case 1[77]	Nwajei et al. - Case 2[77]	Nwajei et al. - Case 3[77]
Age	44	62	54	22	28	63	63	68	79	25
Sex	F	F	M	M	M	F	M	F	F	F
Previous comorbidities / relevant factors	Migraine, familial hemochromatosis and inflammatory bone disease.	HBP	W/A	W/A	W/A	N/R	DM2 and asthma	W/A	HBP	Evans syndrome, idiopathic thrombocytopenic purpura (using avatrombopag), von Willebrand's disease and history of multiple intracerebral hemorrhages.
Time between symptoms of COVID-19 and symptoms of CVT	At the same time	Three weeks	At the same time	At the same time	At the same time	Twelve days	Not specified	Three weeks	Three days	Four months
NIHSS	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Clinical condition	Headache with gradual worsening for three days, decrease in the level of consciousness, left spastic hemiperasia and Babinski's signal present bilaterally.	Headache, confusion, dysarthria and weakness in right limbs.	Two weeks of fever, cough and fatigue; Headache on the day of hospitalization. Neurological examination showed right hemianopsia, right hemiparesis and non-fluent aphasia.	Deterioration of the level of consciousness after a convulsive attack and a fall from a height of 4m.	Febrile and generalized bone pain for three days, on the day he presented progressive Headache with disturbances in the level of consciousness.	History of fever, cough and anosmia. In the emergency room, he presented aphasia, right hemiplegia and epileptic condition	Weakness and left hemiplegia, dysphasia and focal seizures. Epileptic condition worsened and patient fell into a coma	Four days of nausea, vomiting, generalized weakness and Headache.	Disorientation and Headache without focal deficits. Three days earlier she was hospitalized with nausea, vomiting and diarrhea.	BV in the right eye, horizontal diplopia, bilateral papilledema and tingling in the right hand.

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Table Continued...

Author	Loos et al.[72]	Baretta et al.[73]	Rigamonti et al.[74]	Abouhashem et al. - Case 1[14]	Abouhashem et al. - Case 2[14]	Roy-Gash et al.[75]	Bolaji et al.[76]	Nwajei et al. - Case 1[77]	Nwajei et al. - Case 2[77]	Nwajei et al. - Case 3[77]
Laboratory findings **	D-dimer = 1.9 µg / mL Prot. C react. = 19 mg / dL Anticardiolipin IgG = 45 GPL U / mL	D-dimer = 2768 ng / mL Prot. C react. = 19.45 mg / dL	D-dimer = 3000 ng / mL Prot. C react. = 9.7 mg / dL Fibrinogen = 936 mg / dL	N/R	N/R	Fibrinogen 7.2 g / L; ferritin 1427 µg / L	D-dimer 4.77 mg / L FEU; Prot. C react. 60 mg / L; INR 1.1; Fibrinogen 5.68 g / L	D-dimer = 6714 ng / dL Ferritin = 516 ng / mL Fibrinogen = 507 mg / dL Prot. C react. = 121.5 mg / L Erythrocyte sedimentation rate = 60 mm / h Lactate dehydrogenase = 348 U / L	Platelets = 113 K / UL D-dimer = 8457 ng / dL Ferritin = 812 ng / mL Prot. C react. = 96.4 mg / L Lactate dehydrogenase = 434 U / L	White cell count = 11.8 K / UL D-dimer = 241 ng / dL
MRI findings	Progressive vasogenic edema in the basal ganglia and deep white matter, with the presence of CVT within the internal brain veins, the lower sagittal sinus and the Rosenthal vein	N/R	N/R	On the 3rd day after admission, MRI showed left cerebral ischemia with persistence of the small subdural hematoma.	It confirmed the diagnosis of extensive CVT in the transverse sinus.	MRI - left temporal cerebral hemorrhage	N/R	Signs suggestive of thrombosis of the cortical vein and hyperdensity suggestive of venous congestion.	N/R	
CT / RMv findings *	CT - multiple hypodense and hyperdense areas, involving the right thalamus, left caudate nucleus and left pale globe.	CT - hypodense lesion in the left parietal area and subarachnoidal sulcal hemorrhage over the left temporal lobe CTv - CVT involving the right transverse sinus, right jugular bulb, superior sagittal sinus, straight sinus, Galen vein and both internal cerebral veins.	CT - ischemic hypodensity involving the left basal ganglia and the thalamic capsular region associated with a small hemorrhagic hyperdensity close to the caudate nucleus, associated with a mass effect and change in the structure of the midline. CT with angiography - thrombosis involving deep veins in the left hemisphere.	Initial CT - small left subduralcerebral hematoma with mild edema, pneumocephalus and skull fracture. CT after 4 days - progressive ischemia in the left hemisphere with change in the midline.	CT - hyperdense area in the transverse sinus and positive delta signal, suspected CVT.	CT - Cerebral venous thrombosis confirmed	CT - venous sinus thrombosis with bilateral cortical infarctions, in addition to acute cortiac hemorrhage	CTv - filling defects in the superior posterior sagittal sinus, torcula, straight sinus, Galen's vein, inferior sagittal sinus, internal cerebral veins and bilateral transverse sinuses.	CTv - curvilinear thrombus in the right transverse sinus.	RMv - thrombosis of the upper sagittal sinus and transverse sinuses bilaterally.
Treatment	Low molecular weight heparin and mechanical ventilation.	Unfractionated heparin 5000 U in bolus, followed by 1000 U / h adjusted according to aPTT; followed by subcutaneous enoxaparin 1 mg / kg every 12 hours.	Supplementation of oxygen, hydroxychloroquine, azithromycin and lopinavir / ritonavir. Afterwards, enoxaparin 100 IU / kg was started twice a day and anti-edema therapy.	Decompression craniectomy, two days after the procedure started enoxaparin due to the diagnosis of CVT.	Enoxaparin and prophylaxis with levetiracetam infusion.	Treatment with heparin and, for epilepsy, lacosamide. Subsequently, surgical evacuation of the intracranial hematoma and decompressive craniectomy.	Treatment with HPBM and levetiracetam. After an epileptic attack, he received lorazepam and phenytoin.	Unfractionated intravenous heparin, then replaced by enoxaparin. Started on the 2nd day, levetiracetam and lacosamide after EEG confirmed focal seizure.	Low molecular weight heparin, replaced by enoxaparin.	Unfractionated heparin, replaced by apixaban and substitution of immunotherapy for phosphatamatin for lower risk of thrombotic event
Prognosis	On day 45, after neurological improvement, he was transferred to a primary referral hospital for rehabilitation. Six months later, he had minimal hemiparesis, dysphagia and multiple cognitive deficits.	Transfer three weeks later, with switch from anticoagulant therapy to warfarin and discharge three months later with functional independence.	The patient worsened his neurological status 4 days after admission, going into a coma. The patient was intubated and underwent decompression surgery. There was no improvement in symptoms and the patient died 10 days later.	Death due to cardiopulmonary arrest three days after decompression surgery.	Rapid and progressive deterioration in general and neurological status with death after 5 days of admission.	After 14 days of admission to the emergency room, he presented further bleeding and persistent left venous thrombosis. He died 8 days later.	Transferred to a rehabilitation center, where mobility improved. He was discharged from the training center 3 weeks after the initial presentation at the hospital.	Improvement of mental and discharge status.	Improvement of mental and discharge status.	Patient was discharged.

MRI, magnetic resonance imaging; RMv, magnetic resonance imaging with venography; N/R, not reported; OB, obesity; DM2, diabetes mellitus type 2; HBP, high blood pressure; W/A, without antecedents; BCa, breast cancer; CTv, computer tomography with Venography; BV, blurred Vision

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According to images exam results (computed tomography and magnetic resonance imaging) compiled in table 1, the most affected areas by CVT were: left transverse sinus 51% (20/39), superior sagittal sinus 36% (14/39), right transverse sinus 31% (12/39), left sigmoid sinus 26% (10/39), straight sinus 23% (9/39), right sigmoid sinus 18% (7/39), Galen vein 13% (5/39), right internal cerebral vein 13% (5/39), left internal jugular vein 13% (5/39), jugular bulb 8% (3/39), inferior sagittal sinus 5% (2/39), left Labbé vein 5% (2/39), frontal cortical vein 3% (1/39), right parietal vein 3% (1/39), and Rosenthal vein 3% (1/39).

About the outcome, major part of the patients was recovered (69%; 27/36), of these: 44% (16/36) showed partial improvement of symptoms and was discharged or transferred for a reference service and 25% (9/36) showed full recovery and was discharged of the hospital. In relation to mortality, in the sample happens ten deaths (28%), of these: seven (19%) had directly connection with the CVT, two (6%) with indirectly connection and one (3%) don't have any connection whit the CVT. Three (8%) patients went to coma and two (6%) died, three cases had no reported prognosis.

Conclusion

CVT is a rare and severe complication in COVID 19. Clinical signs such as headache, mental confusion, aphasia and hemiparesis should raise suspicion of CVT, seeing that the consequences of this condition are potentially fatal. Moreover, in cases where there is an increase in the levels of D-dimer, fibrinogen and C-reactive protein, associated with neurological symptoms, imaging examinations should be performed to confirm the diagnosis. In addition, with a high suspicious or CVT confirmed, the treatment must be started. The anticoagulant therapy is the treatment for some cases and thrombectomy may be useful for severe CVT. It should also be mentioned that data in the literature on the topic are still scant, requiring more studies into the investigation of CVT associated with COVID-19, evaluating the epidemiology, physiopathology, diagnosis, the management and the outcome of the condition.

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None.

Conflicts of interest

The authors declare that they have no conflicts of interests.

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