Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Anesthesiology and Intensive Care

Cerebral Venous Thrombosis: in Case of Failure of Heparin Therapy Associated with Thrombectomy, Rivaroxaban May Be a Suitable Alternative: Case Report and Review

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DOI: 10.36347/sjmcr.2023.v11i03.023 | **Received:** 17.02.2023 | **Accepted:** 14.03.2023 | **Published:** 19.03.2023

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Abstract **Case Report**

Cerebral venous thrombosis (CVT) is a rare pathology characterized by the diversity of its etiologies and clinical presentation, which are sometimes responsible for diagnostic delays. Basic treatment is curative anticoagulation, usually with heparin. However, direct oral anticoagulants are beginning to have a place in this condition. Prognosis is generally good, even in the presence of an important initial deficit. We report the case of a 20-year-old woman admitted in our intensive care unit for the management of a CVT who did not respond to the treatment associating heparin and thrombectomy and who was treated with rivaroxaban with a good outcome.

Keywords: Cerebral venous thrombosis, Direct oral anticoagulants, Heparin, Thrombectomy.

INTRODUCTION

Cerebral venous thrombosis (CVT) is rare and accounts for nearly 5% of strokes [1]. They are characterized by the great diversity of their clinical presentation and causes [2], making their diagnosis delayed. They may be presented as isolated intracranial hypertension syndrome (ICHT), focal deficit, or encephalopathy.

The management of CVT is multidisciplinary and imagery plays a crucial role in the diagnosis, particularly magnetic resonance imaging (MRI), which is the examination of choice for making the diagnosis, assessing the severity and determining the prognosis [3]. CVT treatment is threefold: symptomatic, etiological and antithrombotic. Prognosis is generally good even in the presence of an initial significant deficit [1].

CASE PRESENTATION

A 20-year-old female patient, with a 6-months history of oral contraception and a miscarriage one month ago, was admitted to emergency room for febrile consciousness disorder. A week before her admission, she had presented several generalized tonic-clonic convulsive seizures, complicated on her admission day to emergency by development of a consciousness disorder. On admission, she was unconscious with GCS of 10/15 (Y4, V1, M5) with equal and reactive pupils, tachycardic at 110 bpm, normotensive at 110/60 mmHg, polypneic at 30 cpm, saturated at 97% on room air, febrile at 38.7°C with a capillary blood glucose level at 1.36 g/l. Moreover, the patient did not present any motor deficit or meningeal stiffness. A brain contrast-enhanced CT scan was performed (Figure 1), showing superior sagittal sinus thrombosis, extended to lateral sinuses, great Galen's vein, and left jugular gulf, complicated by left fronto-parietal and right frontal venous infarction with hemorrhagic remodeling, responsible for subfalcoral involvement. After intubation for neurological criteria and monitoring (arterial, central venous and urinary catheters, repeated transcranial doppler and gasometries), the patient was treated with deep sedation, osmotherapy, noradrenaline to target arterial pressure, curative anticoagulation by low-molecular-weight heparin (LMWH) and antiepileptic drugs (sodium valproate, phenobarbital and clobazam). Biology revealed: hemoglobin at 10.2 g/dl; hyperleukocytosis at 17880 elements/mm³; platelets at 165000 elements/mm³ and CRP at 41 mg/l. A second brain imaging was performed, showing

extension of ischemic lesions, leading to decision to perform a sagittal sinus thrombectomy with in situ thrombolysis (Figure 2). On day 5, the patient presented an ICHT with pathological transcranial Doppler (IP at 2 and VD at 20cm/s), treated by deepening sedation and osmotherapy, followed by cerebral angioscanner showing extension of sagittal sinus thrombosis with diffuse cerebral edema. She was retaken for thrombectomy with unsatisfactory results, hence changing from LMWH to rivaroxaban due to suspected heparin resistance. On day 10, sedation was interrupted after repeated normal transcranial doppler and brain scan showing persistence of internal cerebral vein and right sinus thrombosis, partial repermeabilization of superior longitudinal and right lateral sinuses, persistence of left fronto-parietal and right frontal infarction foci responsible for sub-falcoral involvement. On day 14, the patient underwent weaning tracheotomy after failed extubation.

During her ICU stay, the patient presented two septic shocks. The first on the 20th day following acinitobacter baumanii ventilator-associated pneumonia treated by intravenous tigecycline and nebulized colistin. The second on the 38th day following bacteremia with carbapenemase-secreting enterobacteria treated by ceftazidime + avibactam (zavicefta), amikacin and colistin. Respiratory weaning was made difficult by occurrence of resuscitation neuromyopathy prolonging the ICU stay. She was decanulated on the 60th day with failed decanulation because of persistent laryngeal dyspnea requiring recanulation. Two days later, she was referred to neurology department for further management with a good outcome after 12 months.

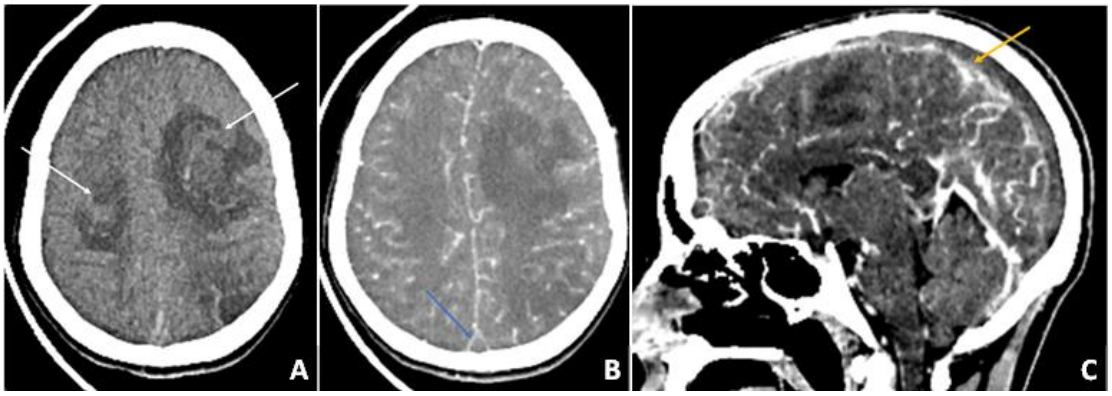

Figure 1: Brain contrast-enhanced CT scan: A) Hypodense cortico-subcortical folds (white arrow), mostly subcortical, left fronto-parietal and right frontal, without arterial systematization, containing spontaneously hyperdense petechiae, related to hemorrhagic changes. B) DELTA sign (blue arrow). C) Extensive superior longitudinal sinus thrombosis (yellow arrow), extended to the left transverse sinus and the right lateral sinus, as well as to the right sinus and the great vein of Galen and the internal cerebral veins

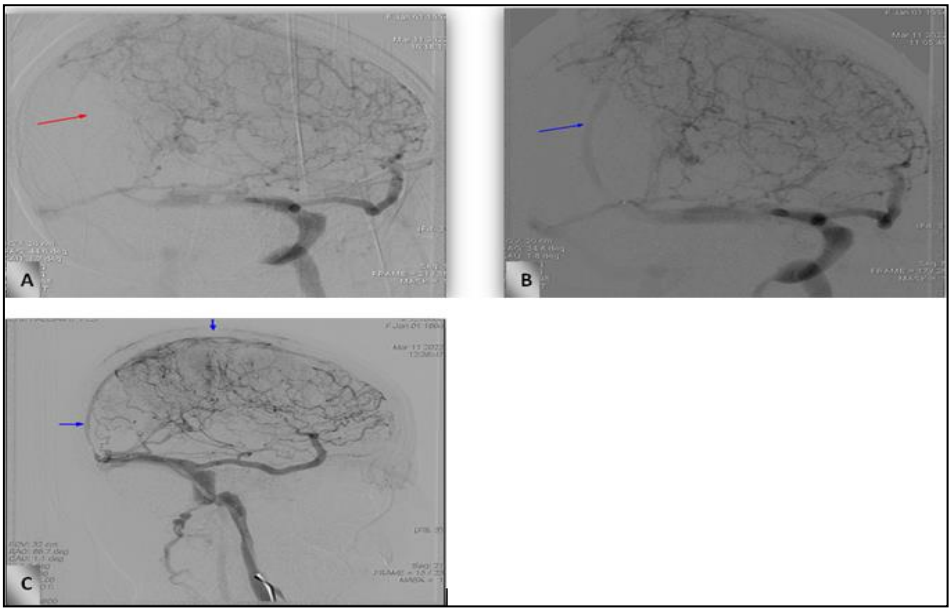

Figure 2: Angiography: A) Superior longitudinal sinus opacification defect (red arrow). B) Opacification of the superior longitudinal sinus after stenting (blue arrow). C) Final result after thromboaspiration and fibrinolysis: Superior longitudinal sinus repermeabilization

DISCUSSION

Cerebral venous thrombosis is defined as cerebral venous sinuses occlusion, often associated with cortical veins thrombosis [4]. It occurs at any age but specific factors such as oral contraceptives, pregnancy and childbirth are responsible for the predominance in young women [1]. The etiologies and risk factors for CVT are very varied.

Involvement of superior longitudinal (70%) and lateral sinuses (70%) are the most frequent, followed by right (15%) and cavernous sinuses (3%) [5]. Two main CVT forms can be distinguished:

- Form without parenchymal lesion mainly includes headache, nausea, vomiting, visual disturbances, integrated in ICHT syndrome.
- Form with cerebral parenchymal involvement (hematoma, edema or venous ischemia) are noisy: convulsions, deficit signs, encephalopathy [4]. Our patient had presented a parenchymal form with venous ischemia showing convulsive seizures followed by consciousness disorder and secondary complicated by ICHT.

The clinical diversity, the unpredictable evolution, the poor prognosis of neglected forms and the existence of effective treatment make reliable and accessible diagnostic imaging necessary. The best examination at present is MRI. In fact, brain contrast-enhanced CT-scan is the most commonly used imaging method to confirm or eliminate CVT, because of greater accessibility [4]. However, it remains normal in 4% to 25% of patients with confirmed CVT, especially in cases of isolated ICHT [5]. MRI, complemented by magnetic resonance venous angiography and gadolinium injection, provides direct visualization of the thrombus and its possible parenchymal consequences, demonstrates a possible underlying cause, and eliminates differential diagnoses [4]. Conventional angiography, because of its invasiveness and MRI / CT performance, is no longer performed for positive diagnosis of CVT [6]. Lack of diagnostic certitude after conventional imaging and search for isolated cortical or deep system vein thrombosis seem to be the only remaining indications [7].

The CVT treatment includes: etiological treatment of predisposing conditions and precipitating factors, anticoagulant treatment and symptomatic therapies (ICHT, seizures, headache). There are few controlled clinical trials to make recommendations for CVT treatment [8]. Curative anticoagulation, particularly to prevent the thrombosis extension [9], is the cornerstone of treatment, including when there are hemorrhagic brain lesions [10]. Traditionally, treatment with unfractionated heparin (UFH) is started with an activated partial thromboplastin time (APTT) target of between 2 and 3, followed by anti-vitamin K (AVK) therapy [1] with an international normalized ratio (INR) target of between 2 and 3. However, LMWH has also proven its efficacy, as demonstrated by recent study [11], with an efficacy and safety rate comparable to UFH.

Today, the question of direct oral anticoagulants (DOAs) is being raised, as their efficacy is increasingly proven and their indications are expanding. There are several studies comparing DOAs with conventional anticoagulants in lower limb venous thrombosis and pulmonary embolism, but there are fewer studies evaluating the indication of DOAs for other locations because of the low statistical power related to the rarity of these locations [1]. A recent study, including a group of 63 atypical venous thrombosis (cerebral, splanchnic, ovarian and renal) compared to a group of typical venous thrombosis (lower limb venous thrombosis and pulmonary embolism), evaluated in both groups the treatment with DOAs (rivaroxaban and apixaban) versus enoxaparin and warfarin. No difference was found between the two therapeutic classes regarding efficacy and bleeding risk [12]. More specifically, two retrospective studies evaluating the efficacy and safety of these drugs attempt to answer this question. The first included 16 patients who, after short treatment with heparin, were treated with rivaroxaban (n=7) or AVKs (n=9) according to the treating physician's choice. Overall, the outcome was excellent in 94% of cases, and all patients had at least partial repermeabilization. One patient in the AVKs arm and two in the rivaroxaban group, respectively, had minor bleeding during median follow-up of 8 months (range 5-26 months). No statistically significant differences were found between the groups. The authors conclude that rivaroxaban has a similar clinical benefit to AVKs in the CVT treatment [13]. The same scheme was used in the second study with dabigatran (11 patients) versus AVKs (7 patients) with 19 months follow-up concluding that they were equally effective as AVKs [14]. We can deduce that DOAs could have their place in the treatment of choice for CVT, but we do not have, to date, powerful studies to confirm this.

Recently, a retrospective study, including 109 patients with CVT, attempted to determine predictive factors for poor clinical response to curative anticoagulation. The factors found were: age >65 or <10 years, GCS ≤12 and focal motor deficits on admission, clinical deterioration after admission, clinical seizures during hospitalization, radiological evidence of ischemia or hemorrhage on admission, superior sagittal sinus thrombosis, and bilateral transverse sinus involvement. These factors were combined to create the PRACT-CVT (Poor Response to Anticoagulation Therapy in CVT) score (Table 1). A PRACT-CVT score ≥ 7 points showed 71% sensitivity and 95% specificity for predicting poor response to anticoagulation alone [15]. But this study had several

limitations (retrospective nature, small sample size...) hence the need for validation of the PRACT-CVT score in larger prospective cohorts. In addition, all patients were treated with heparin (LMWH or UFH) and therefore, perhaps this score will be predictive of a poor response to heparin therapy without DOAs being concerned. Our patient had a PRACT-CVT score of 20 points with a poor response to heparin therapy and even thrombectomy, but responded very successfully to rivaroxaban.

The duration of anticoagulant treatment is between 3 and 6 months in patients with secondary CVT, between 6 and 12 months in patients with CVT without known cause, and indefinitely in patients with recurrent CVT, or associated with lower limb deep vein thrombosis, pulmonary embolism or other atypical site, and finally a first CVT in severe thrombophilia [16].

Thrombectomy or in situ thrombolysis cannot replace a well-conducted anticoagulant treatment, and is used as a complement in case of worsening clinical status. Endovascular treatment allows rapid repermeabilization of venous sinuses. Intravenous fibrinolysis has only been described in isolated cases. It is currently not recommended.

Hydration is an essential component of treatment. By reducing blood viscosity, it prevents the thrombosis spreading. It should be used carefully in ICHT cases. In case of epileptic seizure, antiepileptic treatment should be introduced and maintained for 6 to 12 months and then gradually stopped (the risk of late epilepsy being minimal). The prophylactic use of antiepileptic drugs is disputed, one argument for their use being the high risk of epileptic seizures during the acute phase. In ICHT, deep sedation, hyperosmolar solutions and control of secondary systemic brain damage may be effective, whereas corticosteroids have not been shown to be useful. If these measures are insufficient, decompressive craniectomy may be discussed in case of threatened involvement [1].

Etiological treatment is adapted to the underlying cause whenever possible. This is particularly important in septic forms, which require antibiotic therapy adapted to the entry point, sometimes combined with surgical treatment. Similarly, specific treatment is necessary in some general diseases such as cancer, hematological diseases and connectivities, before deciding to stop antithrombotic treatment [17].

The prognosis of CVT is significantly better and neurological recovery is faster than in arterial stroke. Despite a mortality of 5-15% during the acute phase, only 13% remain with significant sequelae (modified Rankin score >1). Acute phase mortality is dominated by transtentorial engagement secondary to mass effect of infarct or diffuse cerebral edema. Remote mortality is often the consequence of the underlying pathology (infection, cancer). The poor prognostic factors are summarized in Table 2 [1].

Table 1: The PRACT-CVT score (Poor Response to Anticoagulation Therapy in CVT)

Prognostic factor	Point
Age > 65 or < 10 years	1
Focal motor deficit on admission	2
Papilledema	1
Clinical deterioration after admission	9
Seizure during hospitalization	2
Radiological evidence of ischemia or hemorrhage on admission	1
Superior sagittal sinus thrombosis	1
Bilateral transverse sinus thrombosis	1
GCS ≤ 12 on admission	6

Table 2: Poor prognostic factors for cerebral venous thrombosis

Older age
Male gender
Epilepsy
Coma on admission
Cerebral hemorrhage
Posterior fossa involvement
Deep venous system involvement
Cancer
Central nervous system infection
Aggravation or appearance of a new focal sign after admission

CONCLUSION

Cerebral venous thromboses are relatively rare cerebral strokes affecting particularly young women. Clinical symptoms are very varied and positive diagnosis is based on cerebral angioscan and cerebral MRI. Treatment is symptomatic, etiological and

antithrombotic. Heparin therapy is the first-line antithrombotic, even in cases of hemorrhagic brain injury. Given their efficacy and safety, which are identical to those of heparins and warfarin, DOAs could have a place in the treatment of choice for stroke, but to date we have no powerful study to confirm this.

Conflict of Interest: No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGMENTS

The authors would like to thank Dr. Zineb Soulaimani for their invaluable help in the preparation of this article.

REFERENCES

1. Seddik Sifaoui, L., & Hosseini, H. (2019). Thromboses veineuses cérébrales. EMC-Cardiologie, 14(1), 1-10 [Article 11-730-A-20].
2. Dagain, A., Haen, P., Sellier, A., Dulou, R., & Faivre, A. (2017). Thrombophlébites craniofaciales. EMC-Chirurgie orale et maxillo-faciale, 12(2), 1-14 [Article 22-043-A-10].
3. Alami, B., Boujraf, S., Quenum, L., Oudrhiri, A., Lamrani, M. A., Haloua, M., ... & Maâroufi, M. (2019). La thrombose veineuse cérébrale: aspects clinico-radiologiques, à propos d'une série de 62 cas. *JMV-Journal de Médecine Vasculaire*, *44*(6), 387-399.
4. Machet, A., Mellerio, C., Ladoux, A., Legrand, L., Rodriguez, C., & Meary, E. (2014). Thromboses veineuses cérébrales. EMC - Radiologie et imagerie médicale – musculosquelettique - neurologique – maxillofaciale, 9(3), 1-25 [Article 31-644-A-10].
5. Arquizan, C. (2001). Thrombophlébites cérébrales: aspects cliniques, diagnostic et traitement. *Réanimation*, *10*(4), 383-391.
6. Willinsky, R. A., Taylor, S. M., TerBrugge, K., Farb, R. I., Tomlinson, G., & Montanera, W. (2003). Neurologic complications of cerebral angiography: prospective analysis of 2,899 procedures and review of the literature. *Radiology*, *227*(2), 522-528.
7. Saposnik, G., Barinagarrementeria, F., Brown Jr, R. D., Bushnell, C. D., Cucchiara, B., Cushman, M., ... & Tsai, F. Y. (2011). Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*, *42*(4), 1158-1192.
8. Jacquens, A., Guidoux, C., Mathon, B., Clarencon, F., & Degos, V. (2020). Prise en charge des accidents vasculaires cérébraux à la phase aiguë. EMC-Anesthésie-Réanimation, 40(1), 1-20 [Article 36-911-A-10].
9. Stam, J. (2005). Thrombosis of the cerebral veins and sinuses. *New England Journal of Medicine*, *352*(17), 1791-1798.
10. Einhäupl, K., Stam, J., Bousser, M. G., De Bruijn, S. F. T. M., Ferro, J. M., Martinelli, I., & Masuhr, F. (2010). EFNS guideline on the treatment of cerebral venous and sinus thrombosis in adult patients. *European journal of neurology*, *17*(10), 1229-1235.
11. Korathanakhun, P., Petpichetchian, C., Petpichetchian, W., & Sathirapanya, P. (2017). Comparison of the efficacy of fixed-dose enoxaparin and adjusted-dose unfractionated heparin in patients with cerebral venous thrombosis. *Clinical Neurology and Neurosurgery*, *159*, 50-54.
12. Janczak, D. T., Mimier, M. K., McBane, R. D., Kamath, P. S., Simmons, B. S., Bott-Kitslaar, D. M., ... & Wysokinski, W. E. (2018, January). Rivaroxaban and apixaban for initial treatment of acute venous thromboembolism of atypical location. In *Mayo Clinic Proceedings* (Vol. 93, No. 1, pp. 40-47). Elsevier.
13. Mendonça, M. D., Barbosa, R., Cruz-e-Silva, V., Calado, S., & Viana-Baptista, M. (2015). Oral direct thrombin inhibitor as an alternative in the management of cerebral venous thrombosis: a series of 15 patients. *International Journal of Stroke*, *10*(7), 1115-1118.
14. Geisbüsch, C., Richter, D., Herweh, C., Ringleb, P. A., & Nagel, S. (2014). Novel factor xa inhibitor for the treatment of cerebral venous and sinus thrombosis: first experience in 7 patients. *Stroke*, *45*(8), 2469-2471.
15. Montalvan, V., Neves, G., Bueso, T., Ota, R., Bushnaq, S., Windisch, T., & Bushnaq, S. (2022). Predicting poor response to anti-coagulation therapy in cerebral venous thrombosis using a simple clinical-radiological score. *Journal of Clinical Neuroscience*, *105*, 26-30.
16. Behgam, B., & Baruffi, S. (2018). Cerebral venous thrombosis. Treasure Island (FL): StatPearls.
17. Triquenot-Bagan, A. (2007). Thromboses veineuses cérébrales. *La Presse Médicale*, *36*(1), 158-165.