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Dabigatran in the Treatment of Extensive Cerebral Venous Thrombosis: A Case Report

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Abstract

Background: Cerebral venous thrombosis (CVT) is a rare type of cerebrovascular disease associated with a 15% rate of death or function dependence. The mainstay of treatment for CVT is systemic anticoagulation, despite venous hemorrhagic infarction. Vitamin K antagonists have long been the only available option for anticoagulation; however, the past few years have brought the development of many new target-specific drugs, collectively called non-vitamin K antagonist oral anticoagulants (NOACs). Although emerging evidence suggests NOACs have an acceptable safety and tolerability profile in CVT, there are limited data available and no randomized controlled trials have been performed to date. **Case Presentation:** This describes the case of a patient with CVT occurring during an infection who was successfully treated with a NOAC, dabigatran, after a difficult time on warfarin. **Conclusions:** A case of extensive and deep CVT was identified. Dabigatran 150 mg treatment twice daily in this patient resulted in no additional damage to the brain. This case study illustrates that the use of NOACs such as dabigatran can be safe and effective in patients with CVT.

Keywords

Cerebral Venous Thrombosis, Dabigatran, Non-Vitamin K Antagonist Oral Anticoagulant, Safety

1. Introduction

Cerebral venous thrombosis (CVT) is a rare type of cerebrovascular disease as-

sociated with a 15% rate of death or function dependence. CVT accounts for ~0.5% of all strokes, and has an estimated annual incidence of 3 - 4 cases per million people. It can occur at any age but most often affects young adults [1] [2].

Pathophysiological mechanisms involved in CVT are due to the occlusion of the cerebral veins and major sinuses that leads to cerebral edema associated with venous infarction, and impaired absorption of cerebral fluid from the development of intracranial hypertension. CVT has a varied clinical presentation and course [3]. The most common symptom is headache, however, other signs such as focal neurological deficits, seizures, and coma, as well as other non-specific symptoms, can be present early on. This wide spectrum of symptoms at presentation mimics those seen with other conditions, making accurate diagnosis a challenge. Magnetic resonance imaging (MRI) with venography is the most common method used to confirm a diagnosis of CVT and to investigate the underlying etiology [1] [2] [3].

Acute-phase treatment with low-molecular-weight heparin or unfractionated heparin is recommended, even in patients with intracranial hemorrhage [4]. Oral anticoagulation therapy is used after the acute phase although there are currently no controlled data on the benefits and optimal duration of anticoagulant therapy [4]. Another option for the treatment of CVT is vitamin K antagonists (VKA) but the shortcomings associated with the use of VKAs such as the need for frequent monitoring, and drug and food interactions, mean that non-vitamin K antagonist oral anticoagulants (NOACs) present a possible treatment alternative.

Here, we present a case of extensive and deep CVT of infectious etiology that was treated with the NOAC dabigatran after failed warfarin therapy, without recurrence or complications within 6 months of follow-up.

2. Case Presentation

A 56-year-old previously healthy woman from south of Brazil was admitted to our emergency room with a 2-week history of progressive headache. On the day of admission, she had displayed left-hand motor dyspraxia and, later, she experienced a seizure. Her concerned relatives brought her to the hospital. The woman's medical history revealed hypertension, glaucoma, and neurosurgery for a benign tumor 5 years previously. She was also taking treatment for sinusitis that started when she first experienced the headache.

During the initial evaluation, the patient was alert but confused; she had no motor deficits. There were no other abnormalities on physical examination. Laboratory findings revealed a mild thrombocytosis with a platelet count of 650,000/μL and a white blood cell count of 12.7 thousand per mm, and no other alterations. A computed tomography scan of the head showed a hypodense lesion in the right parietal lobe and a post-surgical gliosis in the left frontal lobe. The next day, the patient developed a right-side hemiparesis and dysarthria

along with fever; therefore she underwent an urgent MRI. The brain MRI showed an acute intraparenchymal hemorrhage in the right parietal lobe accompanied by extensive cerebral venous sinus thrombosis involving the right transverse and sigmoid sinuses, and deep cerebral veins (Figure 1). There was also some inflammation in the right mastoid air cells, consistent with mastoiditis. Further investigations for thrombophilia, autoimmune disease, and malignancy revealed no abnormalities.

The patient was started on anticoagulation with subcutaneous enoxaparin 1 mg/kg twice daily followed by oral warfarin. Because of an episode of fever and evidence of sinusitis and mastoiditis, she also received ceftriaxone 2 g/day for 21 days. During this period of hospitalization, the international normalized ratio (INR) was monitored frequently, but it was not possible to achieve an INR between 2.0 and 3.0. Even after increasing the warfarin dose to 12.5 mg/day, the maximum INR reached was 1.5. Therefore, the decision was made to prescribe dabigatran 150 mg twice daily in an attempt to produce the desired anticoagulation effect. The patient was informed that CVT is a deep vein thrombosis and so

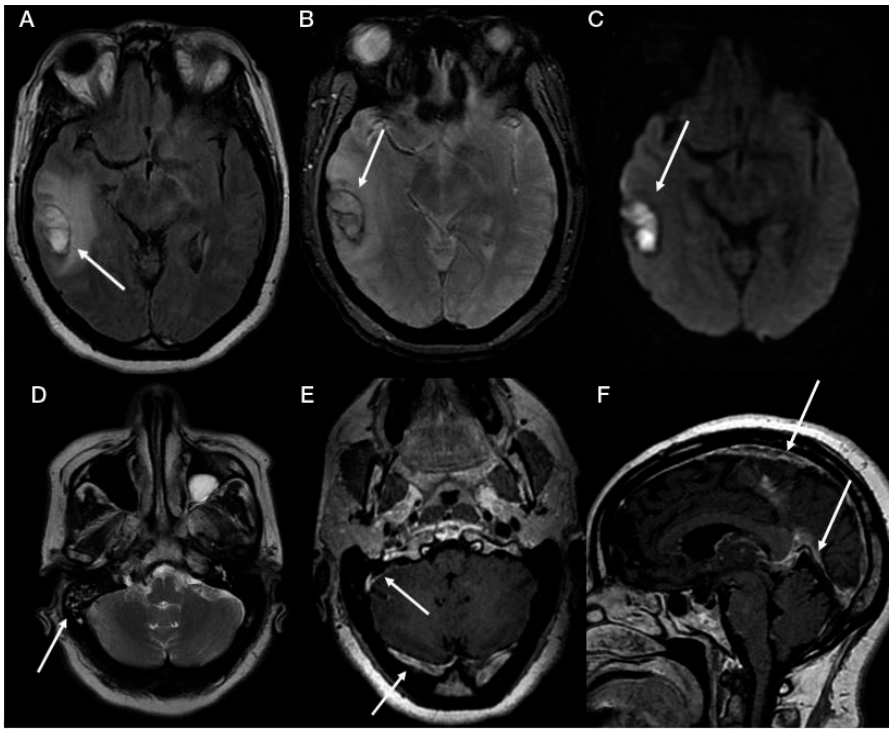

Figure 1. Magnetic resonance imaging results of a 56-year-old woman from Brazil after she developed a right-side hemiparesis, dysarthria, and fever. (A) Axial fluid-attenuated inversion recovery reveals an ovoid hemorrhagic lesion surrounded by an area of vasogenic edema in the temporal lobe (arrow); (B) Axial gradient-echo confirms the presence of peripheral hemosiderin surrounding the temporal hematoma (arrow); (C) Axial diffusion-weighted imaging shows central hyperintensity related to blood susceptibility artifact (arrow); (D) Axial T2W image shows fluid in the mastoid cells related to mastoiditis (arrow); (E) Post-contrast axial T1W reveals thrombosis of the transverse and sigmoid sinuses (arrows); (F) Post-contrast sagittal T1 shows thrombosis of the straight and superior sagittal sinuses (arrows).

was covered by the label claim of dabigatran, but that there is a lack of evidence to support the use of dabigatran in CVT and that dabigatran is contraindicated in intracranial bleeding. She was also told about the risk of intracranial bleeding and other side-effects. She gave her written informed consent to receive the treatment.

During her hospitalization, the patient's headache improved and she did not report any other symptoms. Three months later, a new brain MRI showed no additional damage. The anticoagulation treatment was stopped and she had no further recurrences of headache.

3. Conclusions

In the present report, we describe a case of extensive and deep CVT treated with dabigatran. Dabigatran is a NOAC that is indicated for the prevention of stroke in adults with non-valvular atrial fibrillation, and for treatment and secondary prevention of venous thromboembolism. In the Randomized Evaluation of Long-term anticoagulant therapY (RE-LY®) trial in patients with acute thromboembolism, dabigatran was shown to be as effective as warfarin in preventing systemic embolism and future stroke, while providing a lower risk of major hemorrhage [5].

A review about potential new uses of NOACs beyond treatment and prevention of strokes has been published recently [6]. The outcomes of treatment with NOACs have been shown to be similar to those achieved with VKAs, albeit with a lower bleeding risk in patients with atrial fibrillation and venous thromboembolism. Therefore, NOAC use has been discussed for other scenarios where the neurologist would normally prescribe VKA therapy, such as for CVT, although there is currently a lack of data to support the use of the NOAC group in CVT. One reason for this is the difficulty in performing a randomized controlled trial comparing NOAC and VKA therapy due to the low overall prevalence of the disease [6].

We found only two retrospective studies that describe patients receiving NOACs for CVT in the literature. The most recent study evaluated 15 cases of CVT treated with dabigatran after the acute phase; no cases of recurrence or of hemorrhagic complications were reported. In about 20% of cases patients did not achieve reperfusion; however, in all instances, this was deemed related to old age or non-modifiable risk factors such as cancer and lupus [7]. The second study evaluated the use of rivaroxaban in the acute treatment of CVT and found no significant recurrences or complications during 8 months of follow-up [8]. Two major limitations of these studies were their retrospective design and small sample size. Another CVT case report has been presented previously [9]; however, to our knowledge, the current case is the first one involving dabigatran in the treatment of extensive and deep CVT due to infectious etiology.

We believe that until new clinical trials evaluating the role of NOACs in the treatment of CVT are carried out, it will be important to report cases like these,

in order to share experiences on the use of these therapies in different clinical scenarios that challenge clinicians' usual therapeutic choices.

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Competing Interests

The authors declare that they have no competing interest.

Author's Contributions

VV, LM, NM, WM, CS, LF, RS, and AM: Preparation of manuscript; VV, LM, NM, WM, CS, LF, RS, and AM: Diagnosis of patient; VV: Design of case study; VV, LM, NM, WM, CS, LF, RS, and AM: Review of manuscript. All authors read and approved the final manuscript.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Declarations

Ethical Approval and Consent to Participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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