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A clinical dilemma about a new oral anticoagulant treatment

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Introduction

Atrial fibrillation (AF) is the most common chronic cardiac arrhythmia (1, 2). Major mortality and morbidity are associated with stroke and systemic embolism in patients with AF (3). The CHA_2DS_2-VASc is a clinical score for estimating the risk of stroke in patients with non-valvular AF and is used to determine whether anticoagulation therapy treatment is required or not (2-4). The numerous limitations of the clinical usage of warfarin have led clinicians to search for alternative agents. New oral anticoagulants (NOACs), such as dabigatran, appear to be preferable in these patients (5, 6). Herein, we present a patient with acute ischemic stroke (AIS) occurring under dabigatran treatment, causing fainting, which resulted in a traumatic large lower leg hematoma.

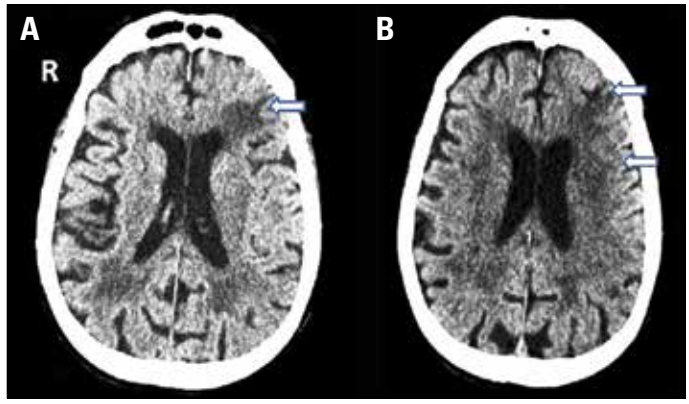

Figure 1. A, B. Axial NECT (non-enhanced computerized tomography) images show hypoattenuation and sulcal effacement in the left middle cerebral artery distribution (arrows)

Figure 2. A photograph of the large hematoma after linear incision for drainage

Case Report

An 82-year-old lethargic female patient was admitted to our emergency department with complaint of sudden loss of consciousness. On physical examination, a traumatic large hematoma (21x16 cm) was noticed on her right lower leg. On neurological examination, motor aphasia and right hemiplegia were observed. Ten months ago, she had been diagnosed with a transient ischemic attack, persistent AF, and hypertension. Based on the European Society of Cardiology (ESC) Committee Guidelines (2), she had been considered to be in a high-risk group (CHA_2DS_2-VASc score: 6 points), and 110 mg oral dabigatran (b.i.d.) had been initiated as an anticoagulant. Brain computerized tomography showed hypoattenuation in the left frontoparietal subcortical deep white matter and sulcal effacement in the left frontal lobe,

which are compatible with acute middle cerebral artery infarction (Fig. 1). Her creatinine clearance was within normal limits. Her activated partial thromboplastin time (aPTT) and international normalized ratio (INR) levels were 61.7 sec and 1.3, respectively. On follow-up, she became stable gradually and regained consciousness within 2-3 hours. Dabigatran was stopped. A linear incision was made to drain the large hematoma on her right lower leg (Fig. 2). Homeostasis was ensured 36 hours after administration, and subcutaneous enoxaparin was initiated. The patient was referred to another hospital for reconstruction surgery. At that facility, a diagnosis of ischemic stroke was confirmed by cerebral magnetic resonance imaging (MRI) and diffusion MRI. After a successful operation, dabigatran 150 mg (b.i.d.) was initiated on the 15th day, and since then she has had no complaints.

Discussion

Unlike warfarin, dabigatran has a predictable pharmacokinetic profile with minimal adverse interactions and allows a fixed-dose regimen, so that monitorization of its activity by standard blood tests is not required. Although there is no specific antidote in the case of major bleeding, discontinuation of dabigatran is generally sufficient to reverse its activity because of its short half-life (6). General clinical recommendations on this NOAC are well defined. Nevertheless, a lack of long-term follow-ups and real world experience is its main handicap (5). Thrombin clotting time (TT) and aPTT are accessible qualitative methods for determining the anticoagulant effects of dabigatran; however, they have low sensitivity at supratherapeutic levels (6, 7). Due to the lack of a facility, TT could not be measured in our patient, and despite mildly elevated aPTT levels, a serious extracranial hemorrhagic complication occurred.

Concomitance of these two different complications (hemorrhagic and ischemic), the managements of which are completely different, makes our case more complicated and significant. Clinical trials have shown that dabigatran (110 mg b.i.d.), rivaroxaban, and apixaban provide similar protection from AIS in AF patients compared to well-controlled warfarin (7-9). Only dabigatran (150 mg b.id.) showed superiority in this efficacy endpoint (7). The 2012 ESC guidelines suggest that clinicians may consider the use of dabigatran 150 mg b.i.d. in patients with AIS occurring while taking an NOAC (2). However, clinicians should assess patients' bleeding risks before increasing the dosage of dabigatran. Because there are no clinical research data available about AIS under 150-mg dabigatran treatments, physicians may choose different treatment pathways that they tailor for each patient's needs. Switching the treatment with warfarin or another NOAC, like rivoraxaban or apixaban, the action mechanisms of which are different, or continuing to use 150 mg dabigatran (b.i.d.) are possible treatment options. Combination of an NOAC with an antiplatelet agent is another alternative. However, it was shown that combination therapy increases the bleeding risk but does not change the AIS rate (6, 10).

In our case, although the dosage of dabigatran needed to be increased to 150 mg, it was stopped initially due to the presence of a large hematoma. This dilemma is not rare, and current guidelines are insufficient. There is no certainty about which anticoagulant should be preferred in these cases. Despite having a short half-life and low risk of hemorrhage, NOACs are not generally preferred in the acute management of such cases due to lack of experiences.

Conclusion

Despite the rapidly increasing the usage of NOACs, the lack of standard monitorization or specific antidote in emergency situations, as well as many reports about their hemorrhagic side effects, indicates that the clinicians should not be comfortable while using these drugs, especially in high-risk patients. The management of some certain clinical situations, such as serious hemorrhagic and ischemic complications in patients who are on NOAC, and the optimal timing of the initiation of NOACs following AIS are still controversial.

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