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Case report

Fatal consequences of climbing a ladder under apixaban and drunken

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ABSTRACT

Background: Apixaban, a factor-Xa-inhibitor, is one of the non-vitamin-K-antagonist oral anticoagulants (NOACs) which are increasingly used in atrial fibrillation (AF). In real life even patients with contraindications to vitamin K antagonists (VKAs) receive NOAC because NOAC are considered as ''safer'' than VKAs.

Case description: In a 61-years-old man with hypertension, heart failure and paroxysmal AF apixaban was started. Despite advices from his physicians, he continued alcohol abuse and suffered from recurrent falls. After 9 months he fell from a ladder and suffered from extensive subarachnoidal and intraparenchymal hemorrhages, subdural hematoma, brain edema with midline shift and a left-sided skull fracture. Because of the inability to reverse the anticoagulant therapy, no neurosurgical intervention was carried out and the patient died without regaining consciousness.

Conclusions: Patients with recurrent falls or chronic alcohol abuse should not be considered as candidates for NOACs. If anticoagulation is deemed necessary, VKA with its potential for prompt reversibility should be favored.

1. Introduction

Apixaban, a factor-Xa-inhibitor, is one of the non-vitamin-K-antagonist oral anticoagulants (NOACs) which are increasingly used in atrial fibrillation (AF). Apixaban was compared with vitamin-K-antagonists (VKAs) in the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) trial, and the rates of ischemic strokes and intracranial hemorrhages were lower with apixaban than with warfarin [1,2]. Patients with chronic alcohol abuse and hepatopathy were excluded [1]. In real life, however, these patients nonetheless receive NOACs because NOACs are considered as ''safer'' than VKAs.

2. Case report

The patient is a 61-years-old man with alcohol abuse since 40 years, hypertension since 10 years, heart failure due to dilated cardiomyopathy since 4 years, bleeding duodenal ulcer at age 59 years, pacemaker implantation at age 60 years because of bradycardia-tachycardia syndrome and paroxysmal AF. Apixaban (10 mg/d) was started in October 2013 because of a

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CHA_2DS_2VASc score of 2. Despite advices from his physicians, he continued alcohol abuse and suffered from recurrent falls. His medication comprised bisoprolol, digitoxin, furosemide, spironolactone, pantoprazole and valsartan.

In July 2014 he fell from the first step of a ladder without prodromal symptoms, 5 h after he had taken 5 mg apixaban. His wife witnessed the fall and phoned for the emergency service, which arrived 10 min later and found him pulseless due to electromechanical dissociation. Spontaneous circulation returned after 22 min resuscitation. At hospital admission, computed tomography (CCT) showed extensive subarachnoidal and intraparenchymal hemorrhages, subdural hematoma, brain edema with midline shift and a left-sided skull fracture. Interrogation of the pacemaker showed no dysfunction. The blood tests (Table 1) indicated alcohol intake. The patient was comatose with a Glasgow Coma Scale of 3. Because of the inability to reverse the anticoagulant therapy, no neurosurgical intervention was carried out. Follow-up CCTs showed deterioration with an increased midline shift, herniation of the temporal lobe and compression of the brainstem (Fig. 1). The patient died after 10 days without regaining consciousness.

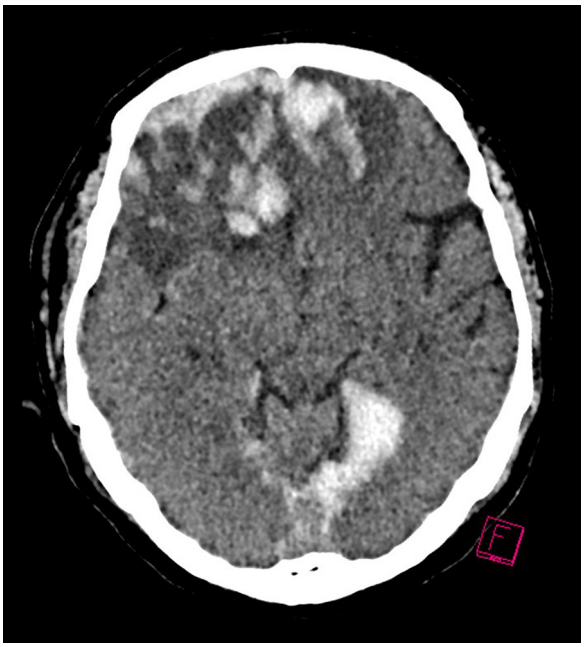

Fig. 1 – Cranial computed tomography showing extensive subarachnoidal and intraparenchymal hemorrhages, subdural hematoma, brain edema with midline shift and a left-sided skull fracture.

3. Discussion

To our knowledge, this is the second description of a traumatic cerebral hemorrhage under apixaban. The first case with a fatal outcome despite administration of 4-Factor Prothrombin Complex Concentrate as an antidote was described recently [3]. In ARISTOTLE, 37 patients during apixaban suffered from major hemorrhages, but information is lacking about cause, location, therapy or outcomes [2]. In ARISTOTLE, 52 patients under apixaban suffered from intracranial hemorrhages, but it is unknown how many of them were traumatic [2]. Traumatic intracranial bleeding occurred in 4 patients under rivaroxaban, another factor-Xa-inhibitor, but neither therapy nor outcomes were reported [4]. Data about traumatic brain-injury during edoxaban, a further factor-Xa-inhibitor, are unknown.

Hepatopathy was probably alcohol-induced and is a contraindication for apixaban [1]. The hyponatremia was most probably also alcohol-induced [5]. Unfortunately, no laboratory test for factor-Xa-activity was available to measure anticoagulant intensity [6]. Antidotes to reverse NOACs are only under investigation. Phase III clinical trials with a

Table 1 – Laboratory findings.

Parameter (normal range)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day10
BUN, mg/dl (8–23)	4	3	6	7	8	8	9
Creatinine, mg/dl (<1.1)	0.62	0.37	0.52	0.45	0.48	0.43	0.29
Cr clearance[a], ml/min (>90)	168	281	201	232	217	242	359
Potassium, mmol/l (3.5–5.5)	3.4	4.6	4.3	4.0	NM	3.7	4.6
Sodium, mmol/l (135–150)	121	131	134	137	NM	145	138
Hemoglobin, g/dl (14–17)	12.8	11.7	11.1	10.2	10.4	10.5	10.3
Thrombocytes/nl (150–450)	188	176	154	144	160	170	260
PT, % (70–130)	61	73	68	66	83	95	103
aPTT, s (<33)	31.2	30.8	31.6	32.4	30.8	29.0	29.3
TT, s (14–21)	NM	15.2	NM	NM	NM	NM	NM
Fibrinogen, g/dl (1.50–4.50)	NM	3.36	NM	NM	NM	NM	NM
ASAT, U/l (0–35)	384	197	127	126	148	140	52
ALAT, U/l (0–35)	131	100	70	59	74	81	47
Gamma GT, U/l (0–40)	515	408	322	289	302	302	189
Bilirubin, mg/dl (0.0–1.1)	0.62	1.47	2.33	2.69	1.92	1.46	0.5
Total protein, g/l (64–83)	54	52	NM	NM	NM	NM	NM
Aethanol, g/l (0.00–0.50)	2.15	NM	NM	NM	NM	NM	NM

ALAT, alanin-aminotransferase; aPTT, activated partial thromboplastin time; ASAT, aspartat-aminotransferase; BUN, blood urea nitrogen; NM, not measured; PT, prothrombin time; TT, thrombin time.

[a] According to the Cockcroft–Gault formula.

humanized antibody fragment directed against dabigatran (idarucizumab) and recombinant, modified factor Xa (andexanet alfa) are ongoing and the future will show if they are efficient in clinical practice [7,8]. But even in VKA-treated patients, reversal of anticoagulation may not always result in good clinical outcome, if the initial trauma is severe [9,10].

4. Conclusions

Patients with recurrent falls or chronic alcohol abuse should not be considered as candidates for NOACs. If anticoagulation is deemed necessary, VKAs with their potential for prompt reversibility should be favored.

Conflict of interest

None declared.

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None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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