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Ischemic stroke in a young adult patient: Excess of Factor VIII

8 **ABSTRACT**

Aims: Ischemic stroke in young adult patients is an increasing public health problem. Hypercoagulability states and thrombophilia are both rare conditions behind ischemic strokes in young patients. We report a case of ischemic stroke in a young patient due to an excess of factor VIII.

Presentation of Case: A 38-year-old woman with a medical history of depression treated with Clomipramine was admitted to the emergency room for coma. The initial brain CT-Scan showed an image of a spontaneously hyperdense basilar artery, and brain MRI found a right occipital and left capsule-thalamic ischemic stroke with total occlusion of the basilar arterial trunk. A standard biological assessment has been performed showing an isolated elevation of factor VIII level at 200%.

Discussion: Approximately 80% of all strokes are ischemic strokes. Thrombophilic disorders and their contribution to the stroke risk are uncommon and factor V Leiden mutation accounts for almost half of the thrombophilic states. Case-control studies have suggested an association between elevated levels of FVIII and cryptogenic stroke in particular, which was nearly four times higher in people with elevated FVIII.

Conclusion: Factor VIII excess is a recently described, apparently common, and under-recognized cause of hypercoagulability. This case should make consider the fact that ischemic stroke is not only a pathology of the old subject. Also, it highlights the implication of excess in factor VIII in the states of hypercoagulability as a cause of young patient's ischemic stroke.

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Keywords: [Ischemic stroke , Factor VIII excess , young patient, thrombophilia]

22 **1. INTRODUCTION**

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24 Risk factors for ischemic stroke in younger adults are not unique to younger adults and overlap considerably with those of
25 older adults but do vary in terms of the percent contribution to ischemic stroke subtypes[1]. Of the more traditional risk
26 factors, that are highly prevalent among older adults (hypertension, dyslipidemia, and diabetes mellitus)[2], clinical case
27 studies and administrative studies have found that these risk factors are also highly prevalent among younger adult stroke
28 patients, although smoking is even more prevalent among younger stroke patients compared with older adults [1]. An
29 ischemic stroke occurs, due to a decreased blood flow in a certain area of the brain. This can be the consequence of an
30 obstruction of one of the blood vessels that irrigate the brain, or it can occur due to low systemic blood pressure. The most
31 common causes of blood vessel obstruction, are thrombosis and embolization. Thrombosis usually develops
32 atherosclerotic plaques[3].

2. PRESENTATION OF CASE

A 38-year-old woman, with a medical history of depression, treated with Clomipramine was admitted to the emergency room for coma. On admission, the patient was unconscious, with a Glasgow Coma Scale at 8/15, and left anisocoria. Blood pressure was normal at 130/60 mmHg, a heart rate of 95 beats/min, a normal glucose level of 1,05g/l, moreover, the patient presented an initial oxygen saturation of 92%, associated with abnormal auscultation with bilateral basal crepitant rales, otherwise cardiac auscultation was normal, the rest of the somatic examination was without particularity. Orotracheal intubation was immediately performed, with the placement of a central venous line, as well as a gastric tube and a urinary catheter.

After stabilizing the patient, we performed a cerebral scanner and thoracic imaging:

- The initial brain CT-Scan (Figure 1), showed an image of a spontaneously hyperdense basilar artery, with no image of constituted ischemia, or hemorrhage.
- The thoracic scanner showed the presence of bilateral basal pneumonia that may be related to inhalation pneumonia.
- A brain MRI (Figure 2) , was performed later, finding a right occipital and left capsulo-thalamic ischemic stroke with total occlusion of the basilar arterial trunk.

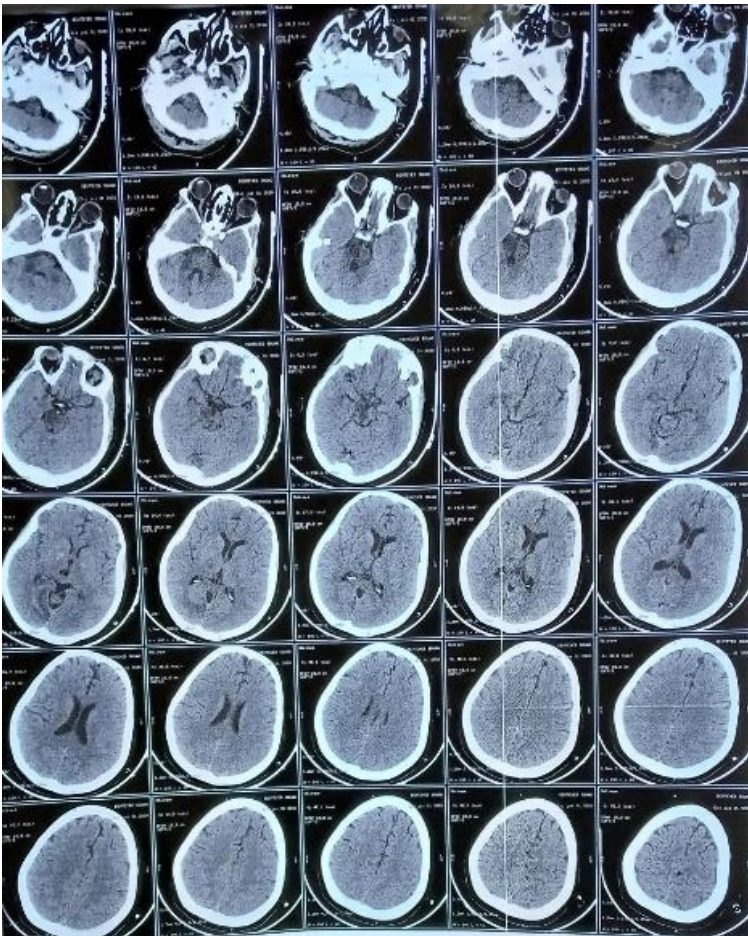
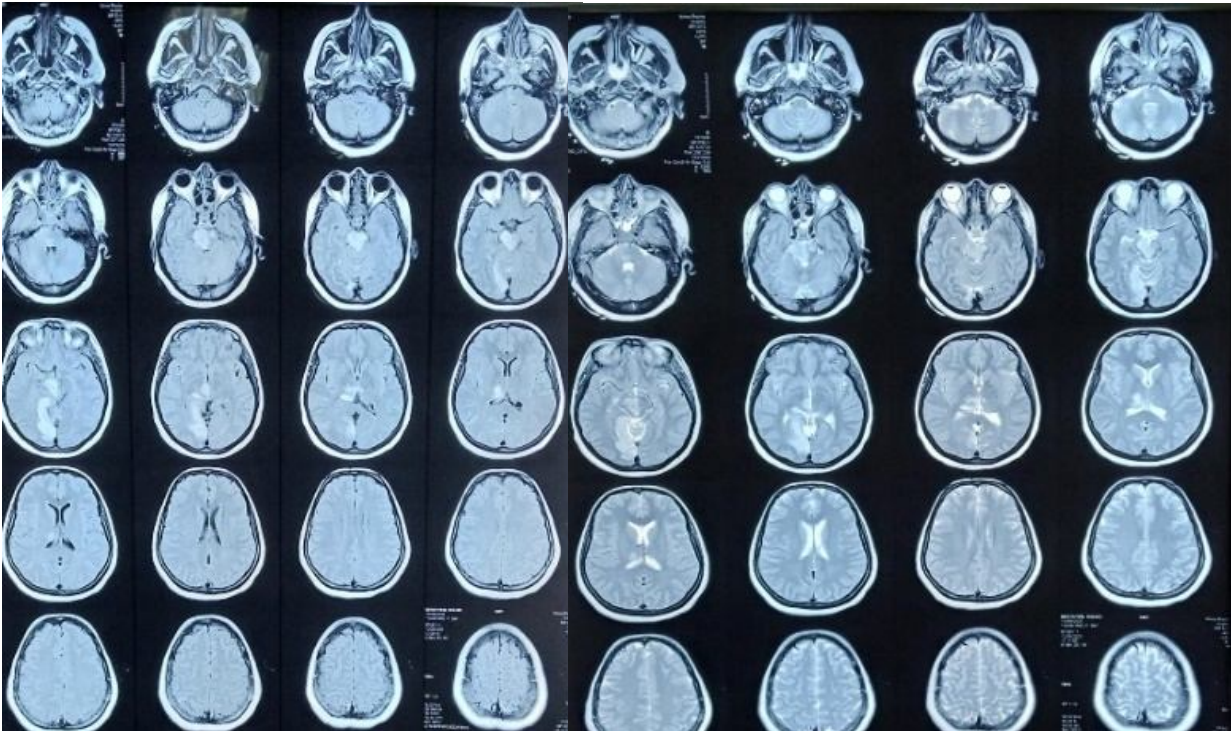


Figure 1 : Spontaneously hyperdense aspect of the basilar artery, on the initial brain scan

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84 *Figure 2 : Total occlusion of basilar trunk associated with hypodense lesions on brain MRI*

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86 The electrocardiogram (ECG) performed did not find any arrhythmias or conduction disorders. We also performed a trans
87 thoracic echocardiogram which showed the absence of intracavitary thrombosis or other malformations that could explain
88 the ischemic stroke in our patient.

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90 As part of the biological assessment we carried out a complete biological assessment :

- 91 - Toxicological screening performed was normal.
- 92 - Normal platelets count at 258 000/mm³
- 93 - Normal prothrombin time at 98%
- 94 - Normal activated Partial Thromboplastin Time at 23 seconds

- Normal liver function : enzymes aspartate transaminase (AST) and alanine transaminase (ALT) respectively 10 and 18 UI/l and Albumin level at 34 g/l
- Moderately Elevated C reactive protein (CRP) at 26 mg/l
- Normal Procalcitonin level at 0.04 ng/ml
- Negative coombs test
- Normal anti-nuclear antibodies (ANA) , Rheumatoid factor (RF) and anti-DNA antibodies limits

We completed with an assessment of thrombophilia showing:

- A normal level of antithrombin 3, protein C and S at 109%, 115% and 140% respectively
- Elevated factor VIII level at 200%
- Absence of anti-phospholipid antibodies including:
 - Search for 'Lupus'-Type Circulating Anticoagulant by chromometric technique
 - Search for anti-cardiolipin and anti-beta2 glycoprotein1 antibodies by ELISA technique.
 - Absence of resistance to activated protein C, with RPCa at 0.68 seconds (0.86 - 1.10).
 - Absence of hyperhomocysteinemia
 - Absence of Prothrombin gene G20210A mutation
 - Absence of factor V Leiden mutation

Based on the results of this workup, clinical examination and in the absence of signs for a secondary cause, ischemic stroke has been linked to increased factor VIII levels.

The patient was put on mechanical ventilation, with continuous sedation for 48 hours. Antiplatelet therapy was started with the association clopidogrel/aspirin.

Weaning from sedation was performed for neurological assessment, the patient could open her eyes spontaneously, with noninteraction, and with persistent anisocoria, and tetraparesis.

The evolution was marked by a failure of ventilation weaning, the patient underwent a tracheostomy after 12 days of mechanical ventilation and was discharged from the ICU after 49 days of hospitalization.

3. DISCUSSION

Stroke is a devastating disease that affects 15 million patients worldwide each year, resulting in death in about one-third of patients and severe disability in two-thirds of the survivors[4]. Approximately 80% of all strokes are ischemic strokes. Although the incidence of ischemic stroke increases with age, an estimated 10% to 20% of these events occur in young people aged 18 to 50 years. Compared with stroke in older adults, stroke in the young has a disproportionately large economic impact by leaving victims disabled before their most productive years[5]. In addition to traditional causes of strokes as vascular risk factors, including hypertension, hypercholesterolemia, diabetes mellitus, and obesity that they share with elderly subjects, young people present other etiologies with a predominance of cryptogenic strokes[6]. thrombophilic disorders and their contribution to the stroke risk are uncommon and factor V Leiden mutation accounts for almost half of the thrombophilic states[7].

Factor VIII was significantly associated in men with coronary heart disease events (RR=1.5) and mortality (RR=1.8), and in women with stroke/transient ischemic attack (RR=1.4)[8]. Case-control studies have also suggested an association between elevated levels of FVIII and cryptogenic stroke in particular, which was nearly four times higher in people with elevated FVIII, regardless of hypertension, smoking, and low high-density lipoprotein cholesterol, and FVIII was the only clotting abnormality positively associated with the disease among several others thrombophilic conditions, as in the case with our patient[9]–[11].

The relationship between factor VIII and arterial thrombosis may be based on the combination of increased thrombin formation and increased platelet adhesion/aggregation, induced by vWF (von Willebrand factor), at sites of arterial wall damage[12].

4. CONCLUSION

Factor VIII excess is a recently described, apparently common, and under-recognized cause of hypercoagulability. This case should make consider the fact that ischemic stroke is not only a pathology of the old subject. Also, it highlights the implication of excess in factor VIII in the states of hypercoagulability as a cause of young patient's ischemic stroke.

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152 **COMPETING INTERESTS**

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154 Authors have declared that no competing interests exist.
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156 **AUTHORS' CONTRIBUTIONS**

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158 Machrouhwalid and houdakouam wrote the first draft of the manuscript. 'mohamedanassfehdimanaged the literature
159 searches, YassineHafiani and HanaaBencharef and afaknsiri made the critical revision, RachidAlharrar made the final
160 approval. All authors read and approved the final version of the manuscript.

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162 **CONSENT (WHEREEVER APPLICABLE)**

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164 All authors declare that written informed consent was obtained from the patient for publication of this case report and
165 accompanying images
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