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Case Report

Elevated Factor VIII Levels and Arterial Stroke in a Young Patient

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Abstract

Factor VIII is a clotting factor that plays a crucial role in the coagulation cascade. Above normal levels are found in 11% of the general adult population. Various studies have established a causal association between elevated factor VIII and venous thrombosis; some studies also suggest a relation with arterial thrombosis, particularly myocardial infarction andstroke.

Ischemic strokes may be caused by cumulative or independent effects of a variety of risk factors. High factor VIII level is one of those important but less known risk factors for arterialand venous thrombosis. We hereby provide a comprehensive review of the role of high factorVIII levels as a risk factor of arterial thrombosis. Moreover, we illustrate a case of 40-year-oldMoroccan male patient with Ischemic stroke whose only identifiable risk factor was revealed to be an elevated factor VIII level.

Keywords: *Factor VIII; Stroke; Thrombophilia; Young; Decompressive Craniectomy*

Introduction

Ischemic cerebrovascular accidents are a major health problem, affecting more than15 million patients each year worldwide, more than 10% of whom are young peoplebetween 18 and 50 years old [1], responsible for the death of a third of between them and disabling sequelae in 2/3 of the survivors [7].

strokes in young subjects are distinguishedby their etiological as well as therapeutic aspects, which makes decompressive craniectomy one of the best therapeutic pillars which improves the vital and functional prognosis of patients.

We report a case of ischemic stroke with elevation of factor VIII; in a young patient who underwent a decompressive craniectomy; with a favorable outcome.

Case Report

This is a 40-year-old Caucasian patient, asthmatic for 20 years under treatment with a BMI of 23 kg/m2 without known toxic habits, admitted to medical intensive care for left sylvian malignant ischemic stroke.

His symptomatology goes back to a day before his admission by the sudden onset of headaches in helmets which was complicated the next day by the installation of a heaviness of the right hemi body and motor aphasia, on the clinical examination patient had a GSC at 12/15; having total right hemiplegia with ipsilateral facial paralysis and aphasia withNIHSS at 24/42 , afebrile, hemody namicallystable (BP at 120/80 and HR at 90 bpm) and respiratory (RR at 16 cpm; and SaO2 at 98% in open air), a cerebral CT scan wascarried out which objectified a subacute left parietotemporal ischemic stroke with the beginning of cerebral engagement.

The thrombolysis was not indicated because the symptomatology exceeded the 4h30 deadline.

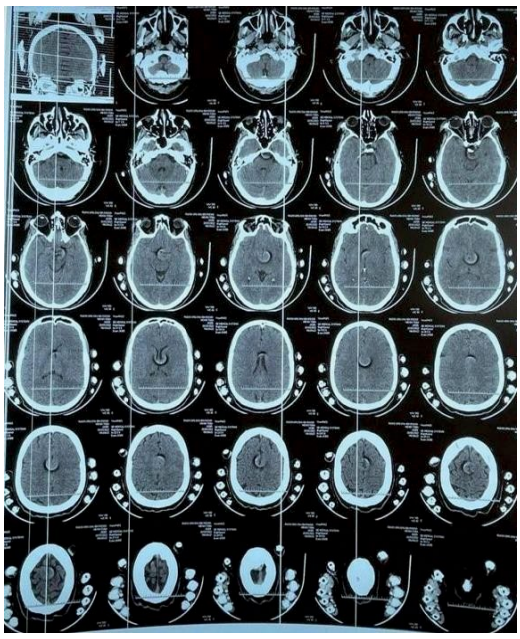

Figure 1: Axial section of a cerebral CT showing a patch of cortical hypodensity under the left parieto-temporal cortex

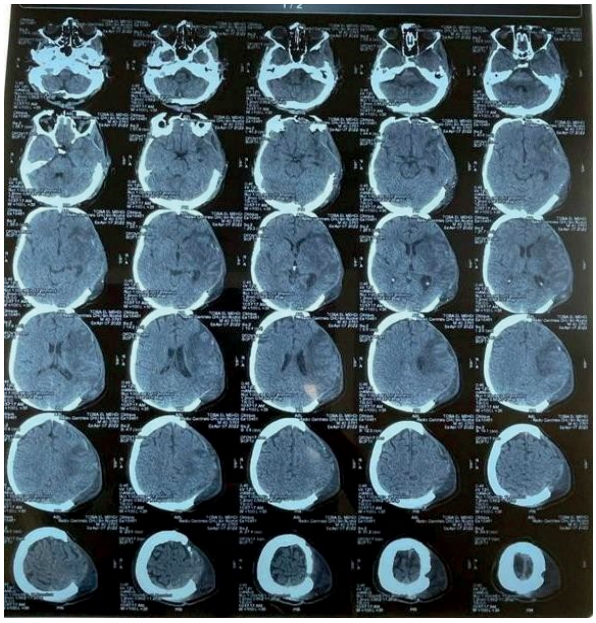

Figure 2: Axial section of a cerebral CT showing a decompressive flap next to a left parietotemporal ischemic stroke

Given the high NIHSS score of 24/42, the delay <48 h, young age < 60 years, the total Sylvian territory, a decompressive craniectomy was indicated, then the patient was sent to medical intensive care postoperatively for additional care.

During his hospitalization the patient was put on Heparine preventive dose and antiplatelet agent 100mg / day, a first-line etiological assessment was carried out including a complete biological assessment, lipid assessment, EKG, echocardiography, ultrasound of the supra aortic trunks which turned out to be normal then a 2nd-line assessment was carried out including an autoimmune disease assessment looking for lupus or an antiphospholipid syndrome (anti AAN antibody ; anti DNA; anticardiolipidin; anti-beta 2 glycoprotein) which turned out to be normal and a thrombophilia assessment (protein C, S, antithrombin III and factor VIII) which objectified a significant increase in factor VIII to 408%.

Nom	Résultat	
HEMOSTASE		
Facteur VIII	408	%
Protéine C	130	%
Protéine S	86	%
AT	120	%
Conclusion	Augmentation du taux de facte	

Figure 3: Thrombophilia assessment

During his stays in intensive care, the evolution was marked by the extubation of the patient on Day 7 of hospitalization in front of the neurological improvement with a GSC at 15/15 and reflex of cough and swallowing present but he kept the right hemiplegia and aphasia, then the patient was transferred to the neurology department where he underwent cranioplasty as well as physical rehabilitation sessions.

Discussion

The incidence of ischemic stroke in young adults varies widely between countries, ranging from 7-8 per 100,000 person-years in Europe to over 100 per 100,000 person-years in sub-Saharan Africa. This variability can be explained by geographic differences in climate, genetics, ethnicity, prevalence of comorbid diseases, cardiovascular disease risk, and socioeconomic circumstances.

the new data suggest that this pathology is more and more frequent in young subjects In addition to the classic causes of strokes which they share with the elderly, young subjects present other etiologies with a predominance of "other determined causes" and "cryptogenic stroke", some vascular risk factors are more specific to young subjects: oral contraception, migraine, drug taking, pregnancy [5], as well as the high factor VIII level which is a common risk factor for venous thrombosis and may also be associated with increased risk of arterial thrombosis in coronary heart disease and stroke [15, 2, 6], in association with many stroke risk factors including, black race, diabetes, older age, index high body mass and non-O blood types.

This increase in the incidence of ischemic stroke in young adults is contemporary with an increased prevalence of classic cardiovascular risk factors in young subjects. The leading cause of ischemic stroke before the age of 45 is dissection of a cervical artery. The main causes between the ages of 45 and 50 are atherosclerosis of the great vessels (62%), lacunae and heart disease with a high embolic risk (20%) [14]. Nearly half of ischemic stroke in young adults remain without cause despite a balance sheet thorough. These cryptogenic strokes contain ischemic strokes for which no possible cause has been detected and those associated with a possible but uncertain cause, including thrombophilic diseases: protein S deficiency (5%) [14], protein C deficiency (2%) and others (2%).

These etiologies of cerebral ischemia in young subjects are multiple, their research must be rigorous in order to identify specific causes, assess the risk of recurrence and specify the therapeutic strategy [7]. Factor VIII is a glycoprotein synthesized almost entirely by the liver (very limited renal synthesis), present in many tissues (liver, kidney, spleen, lungs, etc.) [3, 4]. FVIII is the factor IX cofactor in the activation of factor X (FX); to exercise this role, he must break away from the Von Willebrand Factor. To do this, it is activated to FVIIIa under the action of thrombin or FXa. FVIIIa and thrombin form an amplifying loop for thrombin formation. Normal FVIII:C values are generally between 50 and 200%, defined relative to a pool of normal plasmas. These values should be interpreted according to the VWF level, which influences the FVIII level.

Several studies have shown that high levels of factor VIII can increase the risk of venous thrombosis via the formation of potentiated thrombin, as well as leading to an increase in platelet adhesion/aggregation, induced by vWF, at the sites of damage to the arterial wall which also increases the risk of arterial thrombosis.

The likely mechanisms for this increased thrombogenicity associated with elevated plasma FVIII are [8]:

a) Direct positive influence on thrombin generation (i.e., reduced lag time, increased peak thrombin formation, and

increased endogenous thrombin potential) [9].

b) Diminishing the influence of the anticoagulant pathway (e.g., a direct inverse relationship between plasma FVIII:C levels and activated protein C resistance) [10],

c) Acts as a potentiating risk factor in presence of other thrombophilic states (e.g., in women on oral contraceptive pills, pre-existing malignancy, factor V Leiden mutation) [11, 12 ,13].

Ischemic stroke in young subjects is a therapeutic emergency, and especially malignant cerebral infarction which is a potentially fatal condition with an 80% mortality rate in the event of conservative treatment. Hence the interest of decompressive craniectomy as a therapeutic approach that reduces functional sequelae and even mortality in this population [16].

In our case, we insisted on the interest of early decompressive craniectomy (within 48 hours of the ischemic stroke, without waiting for the signs of involvement) in improving the survival of selected patients (age less than 60 years, without serious comorbidities). The age and the precocity of the gesture are the two determining factors of the neurological prognosis [17].

Conclusion

high levels of FVIII are a possible cause of ischemic strokes. When looking for the causes of a stroke, it is better to take into account the coagulation balance, the concentration of FVIII, the anomaly of which can play an important role in cerebral ischemia.

However, more studies are needed to determine the relationship between FVIII abnormalities and stroke and to establish a treatment algorithm.

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