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Congestive Heart Failure and Cerebrovascular Accident in a Young Woman: A Case Report

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Abstract

Ischemic stroke is the most common type of cerebrovascular accident in older patients, but it is rare in younger adults. Here we present the case of a 27-year-old woman who presented with symptoms and signs of stroke and a medical history of nephrotic syndrome. Transthoracic echocardiogram revealed four chamber dilation, biventricular failure, global hypokinesis, concentric left ventricular hypertrophy, and severely depressed systolic function with an ejection fraction of 25%. The presence of nephrotic syndrome in conjunction with heart failure indicated need for further investigation and consideration due to the increased risk of thrombosis.

Keywords: Cerebrovascular accidents; Congestive heart failure; Obesity; Chronic kidney disease; Nephrotic syndrome

Introduction

Stroke is a major global health problem with a high incidence of mortality and severe morbidity in survivors. Ischemic stroke, which predominantly affects older adults with atherosclerosis, is the most common form of the disease, and it is characterized by disrupted cerebral blood flow and a lack of oxygen to the affected cerebral territory [1]. Only about 10% of cases of ischemic stroke occur in younger adults, this trend could change as new data emerges showing an increasing incidence of the disease in younger adults, especially those born after 1954 [2,3]. Kissela and colleagues [2] reported a decreasing incidence of ischemic stroke in patients aged >55 years but an increasing trend in those <55 years. Similarly, recent studies from the United States and Denmark detected an increase in stroke hospitalizations in the young [2,4].

The causes of stroke in young adults are more diverse than in the elderly and include premature atherosclerosis and hematological and immunological disorders [5,6]. Additionally, diabetes, hypertension, heart disease, smoking, migraine, and chronic alcohol consumption are risk factors for stroke in the young. Isolated central nervous system angiitis, heritable connective tissue disorders, and other genetic disorders (i.e. mitochondrial cytopathies, cerebral autosomal dominant arteriopathy with sub-cortical infarcts and leukoencephalopathy) account for a small portion of ischemic strokes in this population [6]. Despite improved diagnostic techniques and thorough workup, in one third of young patients the stroke is cryptogenic [7]. The management of stroke in this demographic, therefore, requires a modified approach that not only encompasses initial investigation and treatment but also counseling on the prognosis and its devastating psychological and physical consequences [8]. To highlight the etiologies and clinical imperatives of stroke occurring in the young, here we report a case of multiple ischemic strokes occurring in a young woman with multiple co-morbidities.

Case Report

In May 2014, a 27-year-old African American woman presented to the Emergency Department with a twelve-hour history of worsening right-sided weakness of the upper and lower extremities and slurred speech. Her past medical history was significant for two previous cerebrovascular accidents (CVAs) in 2011 and 2013 resulting in residual right-sided weakness, type I diabetes for 14 years, hypertension, and nephrotic syndrome (NS) diagnosed one year earlier. There were no complaints of chest pain, joint pain, fever, chills, blurry vision, headache, loss of consciousness, numbness and tingling in the extremities, urinary incontinence. No history of recent trauma, rashes, or travel. The patient's regular medications included aspirin, furosemide, lisinopril, gabapentin, insulin aspart, and insulin glargine. There were no reported drug or food allergies, and she did not smoke tobacco, drink alcohol, or use illicit drugs. Her family history was significant for diabetes and hypertension.

On presentation, she had a blood pressure of 130/80 mmHg, heart rate of 88 beats per minute, respiratory rate of 18 breaths per minute, temperature of 36.7°C, and oxygen saturation of 99% on room air. Physical examination revealed an alert and oriented patient; pupils equal, round, and reactive to light and accommodation; and intact extraocular movements. She reported mild dysarthria and mild right facial paralysis. The pulmonary and cardiovascular systems were positive for orthopnea, lung crackles bilaterally, and systolic and diastolic murmurs. Her abdomen was soft, non-tender, and non-distended with bowel sounds. Cranial nerves (CN) II-XII were intact except for CN XI on the right side (inability to shrug her shoulder), and she had normal sensation bilaterally in all dermatomes, 2 out of 5 muscle strength in the upper and lower limbs on the right and 5 out of 5 on the left. She had bilateral pitting edema of the lower legs, making the lower extremity pulses impalpable.

Laboratory tests revealed a prothrombin time of 10.9 seconds, international normalized ratio (INR) 1.03, PTT 26.9 seconds, potassium 4.3 mmol/L, sodium 141 mmol/L, blood sugar (BS) 95 mg/dl, blood urea nitrogen (BUN) 50 mEq/dl, creatinine 3.1 mg/dl, B-type natriuretic peptide 856 pg/ml, white blood cell count (WBC) 6740/mm3, red blood cell count (RBC) 2.64 million/mm3, hemoglobin (Hb) 7.4 g/dl, hematocrit (Hct) 22 g%, platelets (PLT) 348,000/mm3, and anti-thrombin III 58% of normal (normal 75-125%). Her HbA1c was 5.8%.

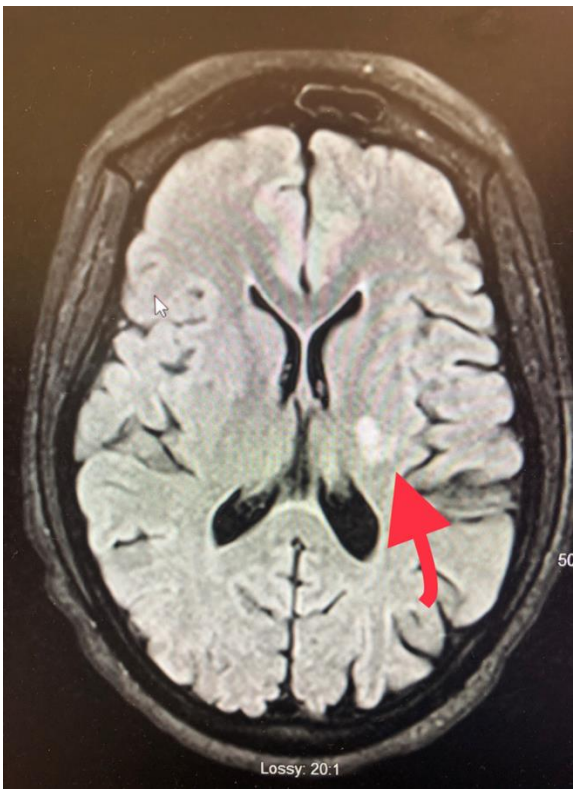

Figure 1: MRI brain showing small acute infarct in the posterior limb of the left internal capsule.

Initial head CT showed a tiny lacunar infarct at the lateral aspect of the genu of the left internal capsule of indeterminate age. There was no evidence of recent hemorrhage or mass effect. Brain MRI showed chronic microvascular white matter and brainstem ischemic changes and a small acute infarct in the posterior limb of the left internal capsule. Electrocardiography showed sinus tachycardia of 106 bpm and probable left ventricular hypertrophy with secondary repolarization changes. A carotid Doppler was normal. Coagulopathy screens (protein C and S antigen, plasma homocysteine, antiphospholipid antibody panel, D-dimers, anticardiolipin antibodies, lupus anticoagulant, thyroid stimulating hormone, Leiden V factor, prothrombin gene mutations, fibrinogen, C3, C4, CH50, anti-nuclear antibodies, and partial thromboplastin time) were normal. Iron studies revealed decreased total iron and total iron binding capacity (TIBC) but normal ferritin and elevated reticulocyte count.

The patient had a transesophageal echocardiogram three years earlier after the first CVA in 2011, which showed no chamber dilation and adequate wall motion. There was no hypertrophy and no regurgitation nor stenosis in any valve. The estimated left ventricular ejection fraction (LVEF) at that time was 55% to 65%. By contrast, at the present admission, a transthoracic echocardiogram revealed four chamber dilation, biventricular failure, global hypokinesis, concentric LVH, severely depressed LV systolic function with an ejection fraction of 25%, moderate mitral and tricuspid regurgitation, moderate pulmonary hypertension, pulmonary artery pressure 64 mmHg, and no shunt on bubble study. No LV thrombus was seen.

The patient was consulted by cardiology and started on carvedilol, hydralazine, isosorbide, furosemide and rosuvastatin with outpatient follow up for evaluation of ICD placement. Neurology recommended to continue aspirin/dipyramidole. Nephrology recommended to start patient on sodium bicarbonate, sevelamer, metolazone and lisinopril with careful potassium monitoring. Renal biopsy was planned as outpatient. Diabetes Mellitus treated with insulin and the patient was discharged to an inpatient rehabilitation facility.

Discussion

Strokes occurring during the first two decades of life are usually associated with infectious or inflammatory conditions. However, in patients aged 20-39, hypercoagulability and structural causes are more common [9]. CVAs are also associated with multiple co-morbidities. For instance, the incidence of CVAs in African Americans with type I diabetes was 3.3% over a period of six years, which is significantly higher than the 0.2-0.3% reported for the general population [10]. In addition, cardiovascular disease (CVD) presents earlier in patients with type 1 diabetes compared to those with type 2 diabetes. Women are at equal risk of CVD as men. Kidney disease and high blood pressure are consistently associated with a higher incidence of stroke, and anemia has also been shown to increase the incidence of stroke, especially in patients with chronic kidney disease [11].

Some risk factors associated with stroke recurrence are hypertension, alcohol abuse, and previous cerebral infarction, the latter reported as one of the strongest risk factors for recurrent embolism [12]. Therefore, this group of patients must be screened regularly with imaging modalities such as MRI or MRA.

Nephrotic syndrome (NS) is characterized by heavy proteinuria, hyperlipidemia, peripheral edema, and thrombotic disease. Infection and thromboembolism are the two most significant complications in adult patients with NS [13], occurring in almost 25% of NS patients [13]. An underlying renal pathology of membranous nephropathy confers the greatest risk of thromboembolism in these patients, and in both adults and children, thromboembolism is more prevalent earlier in the course of disease. Kerlin et al. reported a time lag of ~70 days between NS diagnosis and a thromboembolic event [14]. A subsequent study showed that the risk of thromboemboli forming in the arterial circulation was eight times higher in patients with NS than in the general population [15].

The causes of thromboembolism in patients with NS are multifactorial. A genetic predisposition, especially mutations and single nucleotide polymorphisms in the genes encoding protein C or S or factor V Leiden and prothrombin G20210A mutations are associated with thrombophilia. Another cause of hypercoagulability in NS patients stems from the loss of anticoagulant proteins such as antithrombin III and protein S. Due to a glomerular defect in patients with NS, the leakage of these proteins shifts the hemostatic balance in favor of a more pro-thrombotic and hypercoagulable state [16].

Therefore, deficiency of anticoagulant proteins antithrombin III and proteins C and S are possible causes of thrombophilia and miscarriages in women of reproductive age. The patient's miscarriage in 2009 could be attributed to low antithrombin III levels. Another study reported an association between worse pregnancy outcomes in women with type I diabetes compared to the general population [17].

Our patient also exhibited signs and symptoms of heart failure such as bilateral pitting edema and shortness of breath. Echocardiography showed an LVEF of 25% with biventricular failure and left ventricular hypertrophy, probably secondary to her longstanding

history of type 1 diabetes. Kidney disease and diabetes are two known independent risk factors for the development of heart failure [18]. Some studies have shown an association between low LVEF and mortality in patients that have had an ischemic stroke [19]. Therefore, the heart failure seen in this patient could be due to multiple etiologies including diabetic nephropathy, NS, and hypertension. The DIABHYCAR study reported that heart failure in the setting of high urinary albumin concentrations had a particularly poor prognosis, with a ten-fold higher mortality in these patients compared to patients with a high urinary albumin but without heart failure [18]. Agents that block the renin-angiotensin-aldosterone pathway, beta blockers, and diuretics are the main therapies for patients with heart failure and chronic kidney disease.

One of the most significant challenges faced by physicians managing patients with NS is to decide if or when to use anticoagulation, and there is a lack of randomized trials showing the effectiveness of this approach. Some studies [20] have shown that in patients with membranous nephropathy with very low serum albumin levels, prophylactic anticoagulation can be considered given the low bleeding risk. The choice of anticoagulation in many cases is determined by the serum albumin level, with patients with albumin levels of 2-3 g/dL given aspirin and those with levels <2 g/dL receiving low molecular weight heparin for three months before bridging to warfarin.

In case of a thromboembolic event, anticoagulation should consist of starting the patient on low molecular weight or unfractionated heparin followed by bridging to warfarin [20]. Most studies have shown that anticoagulation with warfarin should be continued for as long as the patient has signs and symptoms of NS, barring any hemorrhagic event [20].

Conclusion

It is essential to evaluate all the risk factors that could potentially contribute to CVAs in a young patient. A mixture of risk factors can have a cumulative effect contributing to the occurrence and recurrence of stroke. In patients with NS, the pros and cons of prophylactic anticoagulation need to be weighed and management should be on a case-by-case basis. Future studies on biomarkers of thromboembolism and prospective trials on the use of anticoagulation would help improve the management of patients with NS.

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