Livedo Reticularis as a clue to Diagnosis of Recurrent Stroke and Epilepsy

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Abstract

Introduction: Homocysteimemia has been associated with increased risk for cerebralvasuclar disease and recurrent stroke. Homocysteinmia has primary atherogenic and prothrombotic properties. It can lead to both venous and arterial thrombosis by several mechanisms. We present a 45 years old female patient with hyperhomocysteinemia and past medical history of epilepsy, two strokes like attacks, livedo reticularis and a new ischemic stroke. Risk factors such as hypertension, diabetes, ischemic heart disease and hyperlipidemia were all absent. Hypercoagulation and vasculities tests were normal. Livedoretiularis was the clue in this patient that led us to consider homocysteinemia as the most probable diagnosis. This suggests that considering skin lesions in juvenile stroke may help to limit the differential diagnosis and treat the etiologic factor more rapidly.

Key words: homocysteinemia, recurrent stroke, epilepsy, livedo reticularis

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Introduction

Homocysteinemia has been associated with increased risk for recurrent stroke.[5] Modest elevation in homocysteine is now recognized as an independent factor for atherosclerosis and ischemic stroke.[2,6] Histopathologic hallmarks of homocysteine-induced vascular injury include several pathogenesis such as intimal thickening, elastic lamina disruption, smooth muscle hypertrophy, marked platelet accumulation and the formation of platelet-enriched occlusive thrombi.[1] Homocysteinemia occurs due to genetic defects such as reduction of cystathione β synthase activity, decreased level of methionine synthase and mutation of methylentetrahydrofolatereduclase (MTHFR), or due to acquired factors including Vitamin B_{12}, folic Acid deficiency, renal insufficiency and age more than 70.[13] Here we present a 45 years old female patient with a history of epilepsy, two strokes like attacks and livedo reticularis who has referred with a new ischemic stroke. She was diagnosed as homocysteinemia due to mutation in methylen tetra hydro fulute reductase gene.

Case Report

A45 years old, right handed, married female had referred to Iranian Center of Neurological Research with acute onset of left limbs weakness and fever. The patient had one stroke like attack (hemiparesia and dysartheria) and visual loss in her left eye ten and six months ago respectively. She had no hypertension, diabetes, ischemic heart disease and hyperlipidemia. She was on carbamazepin for many years. In her systemic examination she had a systolic murmur in apex and livedo reticularis in distal of calfs and feet. Her neurological examination revealed left hemi paresis and hypotonia. Brain MRI was performed and showed multiple ischemic changes in right parietal lobe and the left posterior parietal and both occipital lobes. Echocardiogram revealed MVP and trivial TR, with normal left ventricular ejection fraction. Cervical Doppler sonography was normal. Primary hypercoagulate state tests such as protein c, protein s, anti thrombin III and factor V Leiden were normal, as were vasculitis tests. CSF analysis showed no abnormality. Plasma homocysteine level was high (20.5n/mol) and there was urine homocysteine. Genetic test for MTHFR mutation (C677T) with PCR method was heterozygote. Plasma level of Vit B_{12} was slightly decreased and plasma level of folate was normal. Abdominal sonography was also normal. Electroencephalogram showed some abnormality. Thus homocysteinemia was stablished and treated with folic acid, vitamin B_6 and vitamin B_{12}.

Discussion

Stroke in young adults is a surprising event. Ischemic stroke is much more common than hemorrhagic one.[10] The

potential etiologic factors for ischemic stroke in young adults are broader than that for older ones (Table1). [7]

TABLE 1- DIFFERENTIAL DIAGNOSIS OF ISCHEMIC STROKE IN YOUNG ADULTS

1- Cardiac disease (including congenital, rheumatic valve disease. Mitral valve prolapse, patent foramen oval, endocarditis, atrial myxoma, arrhythmias, cardiac surgery)
2- Small vessel diseases:
- Premature atherosclerosis
- Dissection (spontaneous or traumatic)
- Inherited metabolic disease (heomocystinemia, fabry's, pseudoxanthoma elasticum, MELAS syndrome).
- Infection (bacterial, fungal, tuberculosis, syphilis, lyme)
- Vasculitis (collagen vascular disease, systemic lupus erythematosus. Rheumatoid arthritis, sjogren's syndrome, polyarteritis nodosa takayasu's disease. Wegner's syndrome, cryoglobulinemia, sarcoidosis, inflammatory bowel disease, isolated central nervous system angitis
- Moyamoya disease
- Radiation
- Toxic (illicit drugs, cocaine, heroin…)
- Fibromascular dysplasia
3- Hematologic disease
- Sickle-cell disease
- Leukemia
- Hypercoagulable state (antiphospholipid antibody syndrome, deficiency of antithrombin III or protein c or s, resistance to activated protein c, increased factor VIII)
- Disseminated intravascular coagulation
- Polycythemia vera
- Thrombotic thrombocytopenic purpura
- Cerebral venous occlusion

The clinical manifestations of stroke in young adults are the same as in older ages. Any sudden or acute onset of neurologic symptoms referable to the brain should suggest as a cerebrovascular event.[3]

Our patient presented with recurrent cerebrovascular accidents, epilepsy and

livedo reticularis. Regarding this clinical picture many illnesses could be considered as differential diagnosis such as systemic lupus erythmatous (SLE), antiphospholipids syndrome, Snedden syndrome and homocycteinemia.

Nearly 75% of patients with SLE have neurologic involvement among which episodic affective or psychotic disorder are the most common manifestations. Stroke, seizures and dyskinesia may also be presented. Absence of standard criteria for SLE such as positive ANA and anti ds DNA test ruled out this diagnosis.[12, 8]

Neurologic manifestations of antiphospholipids syndrome includes those of cerebral ischemia, cerebral vein thrombosis, seizure and migraine.[9] Laboratory tests such as antiphospholipid antibody, anticardiolipin antibody and prolonged prothrombin time were all normal in this case which was against recent diagnosis.

Elevated level of plasma homocysteine, positive urine homocysteine and positive genetic assessment for MTHFR mutation (C677T) with PCR along with clinical manifestations, made Homocysteinemia the most probable diagnosis in this case.

Sneddon syndrome is an uncommon disorder that is characterized by stroke and generalized livedo reticularis, headache, vertigo and seizure. There is not any known etiology for sneddon syndrome. Diagnosis of this disorder is only possible by exclusion of other causes of stroke and livedo reticularis.[11,4]

In conclusion, elevated total plasma homocystein is an independent risk factor for recurrent stroke and its measurement is becoming an integrated part in assessing patients with stroke. Considering this diagnosis among a numerous factors that cause a juvenile stroke is challenging. The fact that the presence of skin lesions such as livedo reticularis can direct us to restricted numbers of diagnosis, and looking for such lesions should always be considered in evaluation of every young patient with stroke.

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لویدورتیکولاریس ، راهنمای تشخیص درسکته مکرر مغزی و صرع

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چکیده

سابقه و هدف: افزایش همو سیستئین در خون با خطر افزایش بیماریهای عروق مغزی و سکته مکرر همراه است. هموسیستئین در خون خواص آتروژنیک و پروترومبوتیک دارد و با مکانیسمهای متعددی منجر به ترومبوز شریانی و وریدی میگردد.

روش بررسی: ما یک خانم ۴۵ ساله رامعرفی نموده ایم با سکته مغزی،هایپرهموسیستئینمی، لویدورتیکولاریس، سابقه قبلی صرع و دو حمله شبیه استروک. سابقه ای از هایپرتنشن،دیابت،بیماری قلبی وهایپرلیپیدمی وجود نداشت، تستهای انعقادی و واسکولیتی نیز نرمال بودند. لویدورتیکولاریس در این بیمار راهنمای تشخیص هایپرهموسیستئی نمی‌گردید. لذا در استروک جوانان توجه به ضایعات پوستی مهم است.

واژگان کلیدی: هایپرهمو سیستئینمی،سکته مکرر، لویدورتیکولاریس،صرع .