Stroke in young- due to Hyperhomocystinemia, with primary APLA and early Neurosyphilis

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Introduction: APLA associated with Hyperhomocystinemia is a known entity to cause stroke in young, but here co-associated neurosyphilis has been reported. Its known to get false positive VDRL in APLA, but CSF VDRL positivity is diagnostic of neurosyphilis. Stroke in young due to elevated homocysteine, positive antiphospholipid antibody and probable atypical neurosyphilis is been reported here.

Case report: Young male aged 24 years presented with right side hemiplegia having risk factors like, smoking, dyslipidemia and sexual exposure. Homocysteine levels were elevated, apl antibody titres remain elevated with four weeks gap and CSF VDRL was positive. He was treated with B12 and Folic acid supplementation, penicillin, anticoagulation and antiplatelet therapy.

Conclusion: Association of APLA with Hyperhomocystinemia is added factor for stroke in young. Neurosyphilis now rarely present in its classical form, but presents atypically with subtle signs and symptoms. APLA, Hyperhomocystinemia due to B12 deficiency and neurosyphilis are treatable causes in order to prevent the recurrent episodes.

Key Words:
APLA, Hyperhomocystinemia, Neurosyphilis, CSF VDRL

Introduction

Hyperhomocystinemia due to lack of vit B12 and folic acid is one of the common causes of stroke in young. Hyperhomocystinemia is associated with carotid intimal medial thickness. In screening studies of blood donors, 8% of normal people will have APLA, which was an co finding in this case but with elevated titres apl antibody and negative acl antibody. It’s known to get false positive Serum VDRL positivity in APLA but CSF VDRL when reactive and in absence of substantial contamination of CSF with blood is diagnostic of Neurosyphilis.

Case report

28 year old male presented with right side hemiplegia with aphasia. CT brain showing massive left MCA infarct. Carotid artery Doppler showed critical narrowing and Echo was normal without any vegetations or shunt. Blood Homocyseine levels were elevated, apl by liquid phase coagulation assay was positive and acl by solid phase coagulation assay was negative. The apl titre remained significantly elevated (>40 international units) even with 6 weeks gap. The aPTT was normal, ANA negative, HIV 1 & 2 negative, platelet count normal, Serum VDRL and CSF VDRL are positive along with positive TPHA and positive RPR (low titres) so a diagnosis
of neurosyphilis was made. Co risk factors were smoking and dyslipidemia. Diagnosis of Hyperhomocysteinemia APLA was made and oral anticoagulants with aspirin was started for APLA. Neurosyphilis was treated. Physiotherapy continued for hemiplegia.

**Discussion**

Homocystinemia an amino acid disorder that causes an excess of homocystine in blood. It can be due to disruption of Methionine metabolism- Deficiency in cystathionine beta synthase enzyme, defective methyl cobalamin synthesis and abnormality in MTHFR. Above abnormalities can be nutritional/ genetic/environmental. An abnormal gene on chromosome 1 has been proposed as the cause of reduction in MTHFR. Lesser increase of homocystine in serum is seen in heterozygots, with decreased folic acid and B12, renal failure and after heart transplantation. Increase homocystine level is associated with higher risk of stroke. Carotid stenosis appears to have a graded response to increase level of homocystine. Increased carotid plaque thickness has been associated with high homocystine and low B12 levels. In patient with baseline homocystine level with exceeding 9.1µm/ ltr, supplementation with B vitamins resulted in slowed progression of carotid intimal medial thickness (CIMT).

APLA are antibody directed against certain phospholipids. They are found in variety of scenarios. Patients without lupus or other autoimmune diseases can have symptomatic APLA (primary APLA). In screening study of blood donors, 8% of normal people will have APLA (however APLA in these people are usually low titre and most often occur in young women). Many patients with APLA will have normal APTT and therefore one cannot exclude APLA by just doing APTT. ACL antibody actually react with a complex of cardiolipin and protein known as âglycoprotein. One is very suspicious of APLA must do panel of tests like anti cardiolipin antibody, Kaolin clotting time, dRVVT, Lupus inhibitor screen. There are no prospective trials of therapy in APLA, one can draw several lessons from what has been found in retrospective studies. Although APLA is autoimmune disease, still immunosuppressives, steroids donot benefit.

Neurosyphilis now rarely presents in its classical form of tabes/GPI, but presents atypically with subtle signs and symptoms for eg; neurosyphilis can masquerade as a stroke like syndrome, intracranial SOL, dementia, Psychosis other than chronic meningitis. CSF VDRL when reactive and in absence of substantial contamination of CSF with blood is diagnostic of Neurosyphilis. The VDRL will be falsely positive only if blood contamination is sufficient to tinge the CSF pink. CSF studies are reactive in only approximately 70-75% of neurosyphilis cases. CSF fluorescent treponemal antibody absorption test may be the only serological evidence of neurosyphilis. If the CSF VDRL is negative, a positive FT Abs in an appropriate clinical setting, associated with raised CSF cell count, protein/ IgG index is a useful method of identifying neurosyphilis. Since the antibiotic era, the spectrum of neurosyphilis reported to have changed. Of the 241 new cases of neurosyphilis studied by Hooshmand et al, the majority were asymptomatic and the remainder had atypical syndrome, with only 49% having a reactive nontrephonemal serological test for syphilis. A study from South Africa reported that majority of patients with neurosyphilis presented with subtle clinical signs and weakly positive or even negative serology. The atypical presentation has been emphasized in an editorial in the BMJ. However a study from UK in 1979, 17 cases of neurosyphilis were found that the presentation was not atypical.

Penicillin remains the drug of choice for the treatment of syphilis. Ceftriaxone is effective for
treatment of syphilis when used in multiple dose regimen. Macrolide resistance has been widely documented among strains of treponema pallidum and treatment failures have been reported.

**Conclusion**

Increased Homocysteine in blood is associated with increased risk of stroke. APLA is found in 10-46% of young patient with stroke and in 10% of stroke patient overall. Stroke patient with APLA tend to be younger. Small vessel block is most common than large vessel block in APLA. Early neurosyphilis unlike meningovascular syphilis has only CSF VDRL positivity but not late enough to cause classical neurological symptoms like meningovascular syphilis.

**References**