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A RARE PRESENTATION OF MALE ANTIPHOSPHOLIPD SYNDROME

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ABSTRACT :

Antiphospholipid syndrome (APS) is an autoimmune pathological disorder which is most common in females. We report a case of 33 year old male with no co-morbidities who is a non-alcoholic, non-smoker presented with aphasia and MRI brain revealed acute infarct in occipito parietal lobe. On further evaluation for young stroke, hypercoagulation work-up was done and diagnosed to have Anti phospholipid antibodies (APLA) triple positivity (β_2 glycoprotein Ig G, Cardiolipin antibody Ig G, lupus anticoagulant). He was treated with anticoagulation, single antiplatelet.This case reports highlights the importance of evaluation of all thrombotic events for its underlying etiology and therefore prevents its recurrence which can sometimes even be fatal.

KEYWORDS : Male APLA, Aphasia, Triple positivity

INTRODUCTION :

Antiphospholipid syndrome (APS) , which is also known as Hughes syndrome, is primarily thought to be an autoimmune pathological disorder. It is characterised by arterial and/or venous thrombosis and/or recurrent pregnancy loss in the prsence of antiphospholipid antibodies[(1)]. The thrombosis and recurrent pregnancy loss that characterise antiphospholipid antibody syndrome are linked to antiphospholipid antibodies. There is evidence that both genetic and environmental variables were involved in the development of these pathogenic antibodies, even though their ontogeny has not yet been fully elucidated. The ability of aPL to induce a procoagulant phenotype in APS patients plays a central role in the development of arterial and venous thrombotic manifestations typical of the disease[(2)].

Diagnosis of the anti-phospholipid syndrome (APS) requires patient to have both a clinical event (thrombosis or pregnancy morbidity) and the persistent presence of the anti-phospholipid antibody (aPL), documented by a solid- phase serum assay (anti-cardiolipin antibody [aCL] or anti– β-2-glycoprotein I antibody [aβ2GPI] IgG or IgM), a coagulation assay (inhibitor of phospholipid-dependent clotting—the lupus anticoagulant test), or both. The prevalence of positive aPL tests increases with age. Positive aPL tests are seen in 10% to 40% of SLE[(3)] patients and 20% of people with rheumatoid arthritis[(4)] patients; nonetheless, the incidence of APS is rather low. Clinical manifestations range from asymptomatic aPL positivity (no prior history of vascular or pregnancy events) to catastrophic APS (multiple

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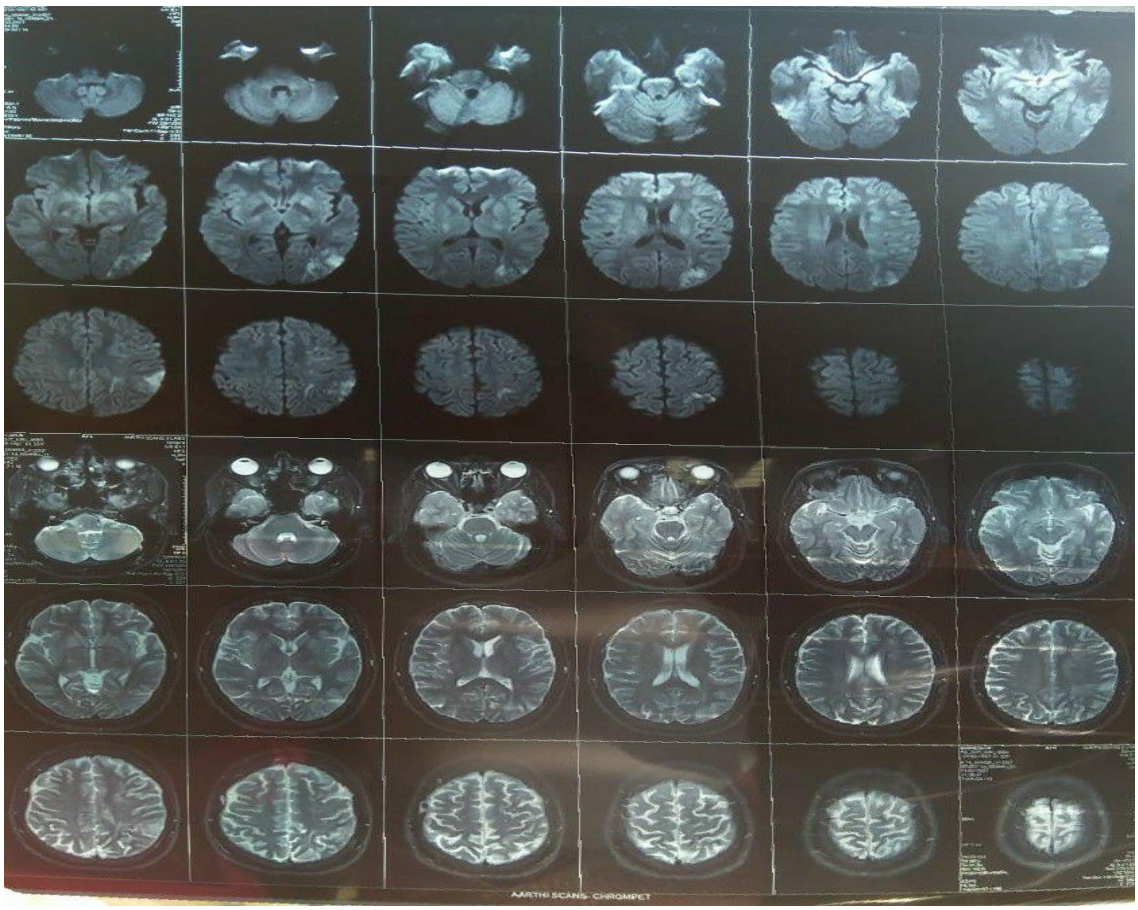
thromboses occurring over days). The cause of the thrombotic event needs to be evaluated and should not be treated as a single entity. It affects primarily females. Here we report a case of Male APS with rare presentation of aphasia.

CASE DESCRIPTION :

A 33 year old male presented to us with difficulty in speech. On examination his speech was non-fluent, comprehension was intact, repetition, reading and writing were preserved. He had no other neurological deficit. Clinically diagnosed to have transcortical motor aphasia and further evaluation was done. MRI brain was done which showed acute infarct in left occipito-parietal lobe (invovlving cortical and subcortical white matter) and left periventricular white matter.

Young stroke work-up was done. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were normal. Autoimmune profile was negative. In APLA profile found to have triple positivity (β_2 glycoprotein Ig G, Cardiolipin antibody Ig G, lupus anticoagulant). Other hypercoaguble work-up (protein-c, protein-s, antithrombin-III, serum homocysteine levels, factor – V) was done and negative. After 12 weeks APLA profile was repeated and found to have persistent triple positivity ((β_2 glycoprotein Ig G, Cardiolipin antibody Ig G, lupus anticoagulant). He was diagnosed to have primary Antiphospholipid syndrome and treated with vitamin-k antagonist - Acitrom and single antiplatelet. Target INR was maintained between 2 to 2.5.



MRI brain showing infarct in left occipito-parietal lobe

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DISCUSSION :

APS was initially identified in a subset of patients with systemic lupus erythematosus (SLE) and related connective tissue disorders (CTD) that had abnormal LA tests. It was then divided into "primary" and "secondary" APS, depending on whether or not these conditions were present[5]. Both in vitro studies and in vivo animal models have provided compelling evidence of aPL's ability to induce thrombosis. The main targets of aPL action, β2GPI and prothrombin (PT), are proteins that interact with many factors involved in hemostasis making the central role that aPL-mediated thrombosis plays in APS unsurprising[5]. Single thrombus or multiple occlusions of veins, arteries and the microvasculature may give rise to a wide range of clinical pictures. While deep vein thrombosis, particularly of the lower limbs, is the most frequently reported clinical manifestation (39%), thrombocytopenia (30%), livedo reticularis (24%), stroke (20%), pulmonary embolism (14%), heart valve lesions (10%), epilepsy (7%), myocardial infarction (6%), leg ulcers (5%) and amaurosisfugax (5%) may also occur and are categorised as "non-criteria features of APS"[6].

The relationship between aPLs and the neurological system has been cosidered to be most significant. Evidences suggested that aPLs may interfere with endothelial cell function and increase their procoagulant activity of endothelial cells.[7] IgG fractions increase mononuclear cell adhesion to human umbilical vein endothelial cells (HUVEC) in aPL-positive patients. Recently, it was discovered that the adhering cofactor β2GPI serves as a bridge for anti-2GPI antibodies to bind to and activate endothelial cells[8]. These studies indicate that aPLs targets the endothelium and damages the vasculature, making it more susceptible to leukocyte adhesion and thrombosis. It is not known why the brain and CNS are particularly vulnerable in APS patients. Cerebrovascular disease (CVD) is the most frequent neurological manifestation in aPL-positive patients[9]. It was also suggested that aCL and LA represent a kind of aPLs leading to cerebral vascular injury and thrombosis which results in cerebral infarction. The cerebral ischaemia, which is mainly focal, can be transient or persistent. Our case initially presented as aphasia without any other neurological deficit which was rare presentation.

Initial anticoagulation with unfractionated heparin or low molecular weight heparin followed by a vit-k antagonist, typically warfarin, is the standard treatment for thrombotic APS. This treatment is continued indefinitely because most studies indicate that patients with APS have a high rate of recurrent thrombosis. A target international normalized ratio (INR) of 2.5 (2.0–3.0) is recommended[10]. Theoretically, direct oral anticoagulants (DOACs) offer a desirable substitute. Several studies published data regarding their use in APS was limited to anecdotal reports in case studies and case series with variable results[10]. Direct -acting oral anticoagulants (DOACs) are not recommended in patients with antiphospholipid syndrome, particularly those who test positive for all 3 antiphospholipid tests – (lupus anticoagulant, anticardiolipin antibodies and anti-beta 2 glycoprotein I antibodies) since they were at high risk for recurrence. Our patient had triple positivity and initiated on Vitamin-k antagonist.

Initial presentation of our case is aphasia and found to have triple positivity on APLA work-up which was not reported so far to the best of our knowledge.

CONCLUSION :

Despite the fact that APS is one of the most prevalent thrombocytophilias, it is not recognised often. Thrombotic events shouldn't be just treated as a single entity rather must be evaluated for underlying disease. APS can be one of the cause for thrombotic events in males too. All thrombotic events should be screened for all three antiphospholipid antibodies. Recurrence of thrombotic events may cause several complications which can be even fatal at times so prevention of recurrence is necessary by appropriate anticoagulation.

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