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Case Report

Chorea and Basal Ganglia Hypermetabolism as Indicators of "APS" and "Probable APS": A Case Report

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Abstract

A 77-years old female patient was admitted for subacute onset of choreiform movements affecting the limbs of the left side of the body associated with dystonic contracture of the homolateral hemiface.

Introduction

Chorea is a hyperkinetic movement disorder that can be determined by several conditions, including inherited, neurodegenerative, autoimmune, metabolic, structural disorders as well as pharmacological treatments [1]. Antiphospholipid Syndrome (APS) is an acquired autoimmune disease which most commonly causes vascular thrombosis or pregnancy morbidity. Chorea is a rare neurological manifestation of APS [2]. In terms of etiopathology, two mechanisms have been proposed: on one hand autoimmune recognition of antigens exposed by endothelial cells resulting in thrombosis of the small vessels that irrorates the basal ganglia. On the other hand, non-thrombotic direct interaction of the antibodies with antigens exposed by nigrostriatal dopaminergic neurons; such link may result in membrane depolarization with hyperactivation of the direct pathway that would ultimately result in the clinical manifestation of chorea; such selectivity could depend on a particular asset of phospholipid exposed by dopaminergic neurons of the pars compacta of the substantia nigra [3,4]. In such conditions, emato-encephalic blood-brain barrier lesions may be essential to increase the permeability of the antibodies allowing the bond with the neural antigens [5].

A diagnosis of APS, according to the revised Sapporo criteria [6] requires the combination of at least one clinical and one laboratory criterion. The fulfilment of the clinical criterion requires the presence of either one or more clinical episodes of arterial, venous or small vessels thrombosis in any tissue organ or pregnancy morbidity intended as (a) three or more unexplained consecutive spontaneous abortion before 10th week of gestation, (b) one or more unexplained deaths of a morphologically normal fetus at or beyond 10th week of gestation, (c) one or more premature births of a morphologically normal neonate before 34th week of gestation because of eclampsia or placental insufficiency. On the other hand, the fulfilment of the laboratory criterion requires the presence of medium-high titres of at least two out of three antiphospholipid antibodies (aPL) that mast is confirmed on two or more occasion at least 12 weeks apart. However, several potential manifestations of APS have not been included in the diagnostic criteria, including neurological manifestation such as chorea cases caused by a potential direct non-thrombotic interaction of aPL with basal ganglia neurons. That poses the issue of classifying cases with non-criteria clinical manifestation of APS and aPL positivity. In such scenario the term of "probable APS" [6] have been proposed to classify cases that fulfils laboratory criteria and manifest "clinical feature associated with APS" and "non-criteria features" of APS.

Traditional neuroleptics, such as haloperidol, have proven effective in correcting the disfunction of neural circuits responsible for choreic disorder. The treatment should not last more than 4-8 weeks to avoid the risk of irreversible tardive dyskinesia. Otherwise, the autoimmune etiology justifies the use of immuno suppressants, particularly steroids [7]. In absence of remission, a multidrug treatment should be started; combination therapy with haloperidol and steroids has often proven effective in cases of monotherapy failure [8]. Isolated case reports suggest the use of intravenous immunoglobulins, plasmapheresis, and treatment with rituximab as additional therapeutic options for patients who do not respond to conventional drugs [9,10].

No clinical trials support the necessity of starting a primary preventive treatment of ischemic stroke in cases of "probable-APS", such as cases of chorea in absence of sign of thrombosis. According to Ruffini, et al. [11], the use of antiplatelet therapy may be useful in individuals with persistently high levels of aPL, especially those with other cardiovascular risk factors.

Case Presentation

A 77-years old female patient was admitted for subacute onset of choreiform movements affecting the limbs of the left side of the body

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associated with dystonic contracture of the homolateral hemiface. The neurological examination also showed a mild slowdown of the ideomotor processes. Patient's medical history revealed hypertension in adequate treatment, and one miscarriage at fourth month but also a full-term pregnancy in absence of complications. Family history was not relevant. A brain CT showed no significant abnormalities (Figure 1).

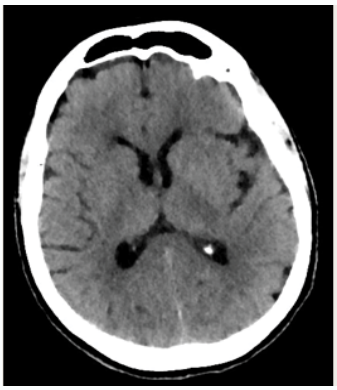

Figure 1: Brain CT: no significant abnormalities.

The patient was then hospitalized. Lab analysis showed no abnormalities in blood cell count, renal and hepatic function, copper metabolism, anti-neuronal antibodies, antinuclear antibodies, prolonged PTT, absence of complement consumption and high titres of (aCL) anticardiolipin antibodies and anti-β2 glycoprotein I (a β2GPI) antibodies. Lupus Anticoagulant (LAC) antibodies resulted negative. Anti-double strand DNA antibodies also resulted negative.

A brain MRI with gadolinium showed a mild periventricular bilateral chronic vasculopathy, and moderate bilateral frontoparietal atrophy (Figure 2). Brain 18F-FDG PET scan showed a bilateral hypermetabolism of the basal ganglia (SUVmax 18.54 for the right putamen and 14.88 for the left one) in absence of significant alterations of metabolic activity of the neocortex (Figure 3).

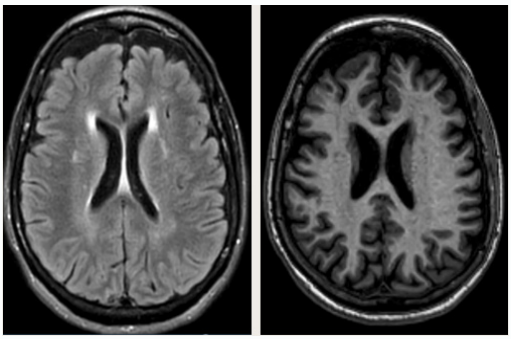

Figure 2: Brain MRI with and without gadolinium: mild periventricular bilateral chronic vasculopathy, and moderate bilateral frontoparietal atrophy; no evidence of vascular lesions within the basal ganglia.

CT total body scan with contrast showed no signs of thrombosis neither etero-formative lesion. Lower extremity venous ultrasound showed no evidence of deep vein thrombosis.

Based on the high titres of aPL antibodies in absence of medical history of thrombosis, PET hypermetabolism of the basal ganglia, and the lack of imaging findings suggestive for thrombosis a diagnosis of "probable APS" was made.

A symptomatic treatment with haloperidol was started determining a complete remission of motor symptoms. The treatment was maintained for four weeks. The remission of motor symptoms persisted even after symptomatic treatment discontinuation at a 24th month follow-up evaluation, thought blood analysis revealed the persistence of aCL and a β2GPI antibodies at a 12-week revaluation.

A preventive antiaggregant therapy with aspirin was also started in absence of further thrombotic complications after a 24-month follow-up.

Discussion

Movements disorders associated with brain hypermetabolism of the basal ganglia can be features of APS and "probable APS"; in such conditions brain MRI alone may prove inconclusive or negative. This case report underlines the importance of performing a brain 18F-FDG PET to evaluate the presence of basal ganglia hypermetabolism. In absence of a medical history characterized by criteria clinical manifestations such assessment would support only a diagnosis of "probable APS". Given a similar diagnosis, it remains unclear whether is necessary to start a preventive treatment with antiaggregant with the purpose of anticipating thrombotic complications of APS, such as cerebral infarction.

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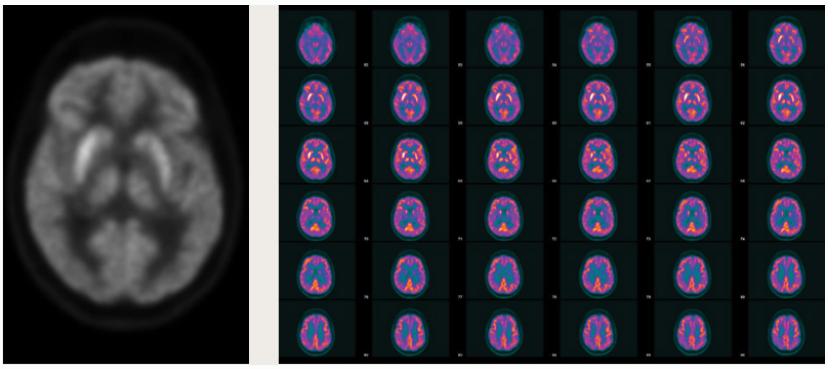

Figure 3: Brain 18F-FDG PET scan: bilateral hypermetabolism of the basal ganglia (especially in the right putamen); no evidence of neocortical metabolic activity abnormalities.