Psychiatria Danubina, 2015; Vol. 27, No. 3, pp 280-282 *Case report*

ACUTE PSYCHOTIC SYMPTOMS: A MANIFESTATION OF ANTIPHOSPHOLIPID SYNDROME OR INFARCTION OF CORPUS CALLOSUM

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INTRODUCTION

The antiphospholipid syndrome (APS), which is an autoimmune disorder, is characterized by recurrent arterial or venous thrombosis in the presence of circulating antipshospholipid antibodies (Khamashta et al. 2004). The patients are considered to have the APS if they have at least one clinical and at least one labaratory criterion at the same time (Miyakis et al. 2006). APS may be an isolated disease (primary APS) or it may be associated with systemic lupus erythematosus or another autoimmune condition (secondary APS) (del Rio Casanova et al. 2014). APS is seen mostly in young-to-middle-aged adults, but it may also occur in children and elderly people. The prevelance of antiphospholipid antibodies was reported to be 2%-5% present in general population (Levine et al. 2002). One of the most prominent feature of APS is Central Nervous System involvement (Hughes 2003, Sanna et al. 2003). Either thrombotic or nonthrombotic neurological symptoms can be associated with APS. Stroke and migrane are the most common clinical features and are seen 20% of the patients. Epilepsy, dementia, chorea, multiple sclerosis-like syndromes, Guillain-Barre-like syndrome and sensorineuronal hearing loss have also been reported associated with APS (Sanna et al. 2003). Some psychiatric disorders/symptoms clusters like depression, anxiety, and psychosis have been reported in association with APS. In addition, increased levels of anticardiolipin antibodies and lupus anticogulants have been reported in untreated psychotic patients (Schwartz et al. 1998). The presenting symptoms of APS can also be psychotic symtoms, and the somatic symptoms may appear later (Kurtz & Multer 1994). Raza et al. (2008) have also reported manic disorder as a psychiatric manifestation of AFS. In addition, Del Rio-Casanova et al. (2014) have reported psychosis as debut of antiphospholopid syndrome. However, the precise pathophysiological mechanisms underlying the association between APS and psychosis have not been identified yet. The circulating antibodies or the thrombotic events may be the key pathological feature. We aimed to discuss the possible association between APS and psychosis with a case report.

CASE REPORT

A 25 years-old female patient with confusion and fever had admitted to the emergency department of a research hospital. Mrs. H. is a primary school graduate and she has one child. Her symptoms started one week ago as sleeplessness, talking too much, persecutory paranoid symptoms auditory hallucinations, and agitation. She was hearing commentary voices and voices discussing with each other. There were no other first rank symptoms such as thought insertion, thought withdrawal and thought broadcasting. She was alert and she was thinking that her husband's mother will give harm. She had not any psychiatric problems in the history and did not specify any prominent psychosocial stressor. She was hospitilized with the diagnosis of acute psychotic disorder. Olanzapin 30 mg/day, ketiapin 400 mg/day, and diazepam 10 mg/day were prescribed in the hospital for four days. Her psychotic symptoms did not disappear in this period and she had confusion as well.

When the patient was brought to the emergency unit, it was not possible to form therapeutic alliance with her and she was severely agitated. In the neurological examination there was not any positive finding such as neck rigidity, focal neurological signs, and muscular rigidity. Her body temperature was measured to be 39.7ºC. Her leucocyte counts were 19850/mm^3. The creatine kinase levels were 951IU/L. INR level was in normal limits. Lumber puncture has been applied and there was not any abnormal finding. She was hospitilized in the intensive care unit. Neuroleptic treatment has been stopped. She was hydrated. Paracetamol was given to decrease her body temperature. In Magnetic Resonance İmaging (MRI) T2 weighted sagittal sections hyperintense lesion is seen in the splenium of corpus collosum which is compatible with acute infarction (Figure 1). In the third day of hospitilization, her orientation and cooperation was normal. However, paranoid psychotic symptoms and auditory hallucinations were prominent. To treat the psychotic symptoms we have started olanzapin and it has been titrated up to 20 mg/day. Her psychotic symptoms disappeared in two weeks. In the investigation of the etiology of the infarction, the anticardiolipin antibodies have been found positive.

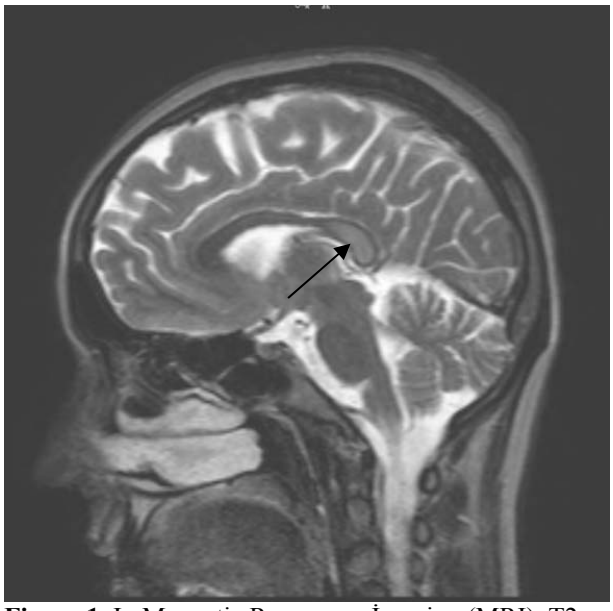

Figure 1. In Magnetic Resonance İmaging (MRI), T2 weighted sagittal sections hyperintense lesion is seen in the splenium of corpus collosum which is compatible with acute infarction

The patient did not smoke and had no any other vascular risk factor. No history of abortus. The electrocardiogram, cervical Doppler, intracranial and cervical magnetic resonance angiography, and transthoracic and transoesophageal echocardiography were normal. Routine blood tests were normal. Thrombophilia panel results were positive for MTHFR mutation, PAI-SERPINE 1 mutation, Factor XIII V34L and also Anticardioplipin IgM. We started acetylsalicyclic acid because of the increased risk of thrombosis in the antifosfolipid syndrome. The patient is now on remission for one year and she has not been using olanzapin so far. The brain magnetic resonance imaging was also normal after one year (Figure 2).

DISCUSSION

The precise mechanism underlying the central nervous system (CNS) involvement of APS has not been identified yet (Raza et al. 2008). The CNS involvement can be the result of cerebral ischemia secondary to thrombosis. The blood coagulation regulation is altered because of antiphospholipid antibodies, this state leads to a procoagulant state (Levine et al. 2002). It is reported that 5-10% of APS patients has also deep vein thrombosis. This finding also confirms the increased risk of thrombosis in APS.

We found an infarction area in the caudal part of corpus callosum in radiological imaging. This finding can be attributed to hypercoagulability in APS. Corpus callosum is the largest fiber bundle that connects cortical and subcortical regions of the brain (Murphy et al. 2013). It also interconnects both cerebral hemisphres, promoting functional integration sensory and motor functions (Hofer & Frahn 2006). The infarction of corpus callosum is not commonly seen, because it has a rich

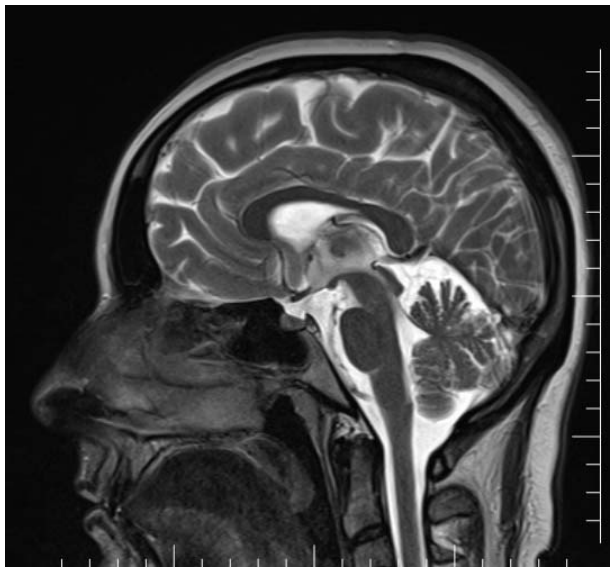

Figure 2. Normal cranial imaging after one year

blood supply from the three main arterial systems (Saita et al. 2006). The clinical manifestation of acute corpus callosum infarction has no specifying symptom and it can be easily misdiagnosed (Murphy et al. 2013, Ishızaki et al. 2012). Yang et al. (2014) reported movement disorders (84%), cognitive and mental abnormality (40%), mood lability (20%), and alien hand syndrome (8%) in patients with corpus callosum infarction. They also reported improvements in cognitive and mental problems after proper treatment. On the other hand, Whitford & Kubicki (2010) have reported corpus callosum abnormalities and their association with psychotic symptoms in patients with schizophrenia. In addition, corpus callosum complete or partial agenesis, and also abnormal callosal dimensions and abnormal pattern of interhemispheric transfer have been reported in psychotic patients (David 1994). These finding support that abnormality in corpus callosum may give rise to psychotic symptoms. In our case, the onset of acute psychotic symptoms can be the result of corpus callosum infarction secondary to increased thrombosis risk in APS.

Some symptoms such as optic atropy, epilepsy, depression, and chorea which are seen as CNS involvement of APS cannot be the result of hypercoagulability (Sanna et al. 2003). This findings suggest that hypercoagulability can not be the only reason of these manifestations (Chapmann et al. 2003). Antiphospholipid antibodies may have direct effects; they may bind neurons or glial cells and disrupt their function. Sun et al. (1992) reported that anticardiolipin antibodies bind to mouse brain tissue and may inhibit astrocyte proliferation in vitro. Khalili & Cooper (1991) also reported that patients with systemic lupus erythematosus (SLE) with elevated anticardiolipin antibodies have high binding to myelin. Jankowski et al. (2003) injected isolated antibodies from patients with APS into hamsters. They reported a direct link between the presence of antipshopsholipid antibodies and increased risk of thrombosis as a result. Some studies also emphasizes the important role of β_2 glyco-

protein 1 in APS (Wilson et al. 1999, de Laat et al. 2004). The best explanation the role of β_2 glycoprotein 1 in APS is that the autoantibodies that are present in APS induce a new function for this glycoprotein (Tropidi et al. 2011). However there is also a need for better in vivo models to understand the underlying mechanism.

CONCLUSION

Further studies are needed to understand the pathophysiology of antiphospholipid syndrome induced neuropsychiatric symptoms. The intensity of treatment should be aimed at an international normalized ratio (INR) of 2.0-3.0 (Tropidi et al. 2011). In our case INR result was in normal range. We also used asetilsalisilic acid to decrease the risk of thrombosis. In our case positive psychotic symptoms were also prominent. We used antipsychotic treatment for the symptom management. Treatment of psychotic symptoms in APS only with anticogulant therapy has not been previously examined. This case report also emphasizes the importance of investigation of medical or systemic etiology of abrubt onset of psychotic symptoms.

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