RECURRENT ISCHEMIC STROKE AND RECENT MENHORRAGIA IN A PATIENT AFFECTED BY ANTIPHOSPHOLIPID SYNDROME AND SLE: A DIFFICULT THERAPEUTIC CHOICE

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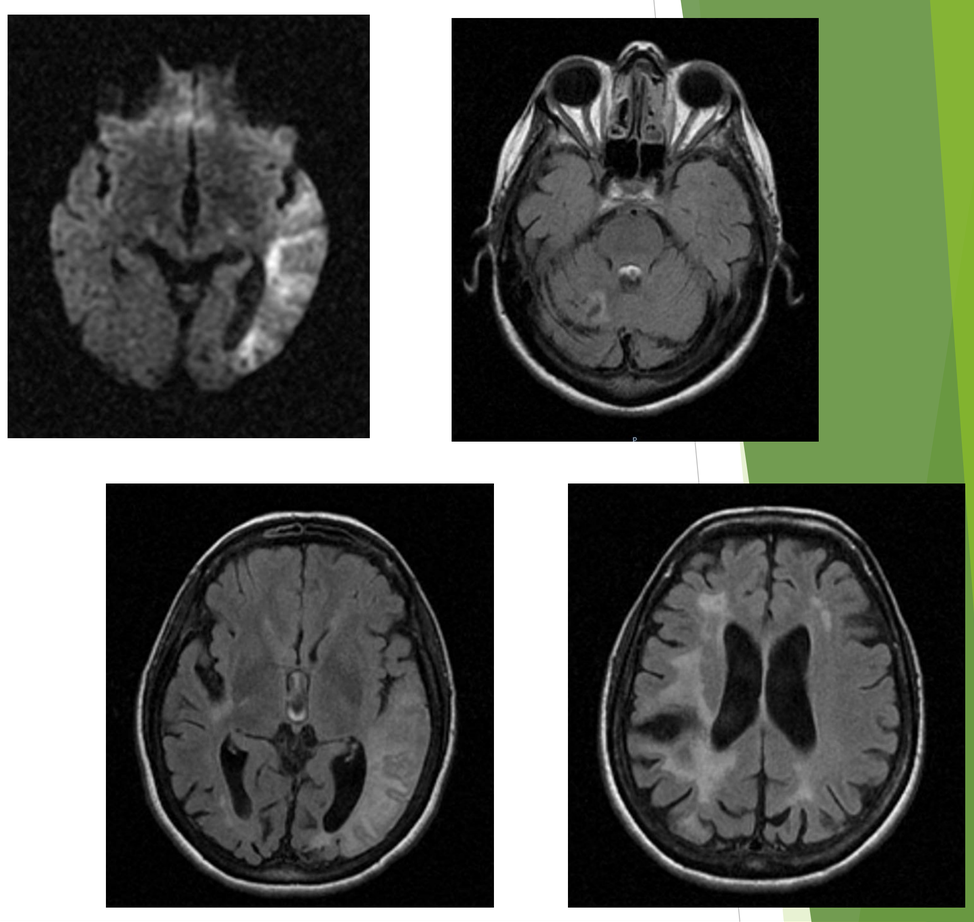
Background

Antiphospholipid syndrome (APS) is defined by the occurrence of an episode of venous or arterial thrombosis or recurrent fetal losses and the presence of antiphospholipid antibodies (aPL), anticardiolipin antibodies or anti-ß2-glycoprotein I (aß2GPI) antibodies, isolated or in any combination. APS can be primary if isolated, or secondary if associated to an underlying autoimmune disease. Treatment of APS consists in secondary prevention of thrombotic events with long-term anticoagulation.
We present a case of a 47 year-old woman with a definite diagnosis of APS secondary to systemic lupus erythematosus (SLE), presenting to our attention for ischemic stroke. The management of this case was particularly challenging.

Case presentation

The patient had a diagnosis of SLE in 2008. In 2015 she had an episode of ischemic stroke. During hospitalization high levels of aPL were found and other causes of stroke were excluded. She received a diagnosis of APS secondary to SLE. After stroke, since 2015, she was treated with warfarin, with a target INR between 2 and 3. In may 2017 the patient presented to the Emergency Department complaining headache and confusion. Symptoms began two days before. Brain CT showed a large ischemic stroke localized in the left hemisphere. INR ratio at admission was under therapeutic range (INR=1.32). A brain MR with MR angiography was done to exclude signs of arterial or venous thrombosis. MRI showed a subacute ischemic temporo-parieto-occipital lesion in the left emisphere and multiple old infarcts localized in the right temporo-parietal region and in the cerebellum. Other sites of thrombosis were excluded with lower limbs echocolordoppler and abdominal ultrasonography. The patient reported voluntary interruption of anticoagulant therapy four days before symptoms onset, due to menhorragia. She had an history of menhorragia and she cyclically discontinued anticoagulant therapy during menstrual flow. Complete blood count showed hypochromic normocitic anemia with thrombocytopenia (HB: 9.9 g/dL; MCV: 86.8 fL; PLT: 71.000/mmc). aPL levels were high (345 U/mL; range: 0-10 U/mL). A transvaginal ultrasonography and an hysteroscopy were requested to find the cause of menhorragia. The exams showed the presence of a pelvic mass compatible with a leiomyoma, which was the cause of recurrent bleeding. The gynecology consultant suggested a miomectomy, but the patient refused surgery. She was treated with low molecular weight heparine 6000 UI bid and, after a week, with warfarin.



On the left: Subacute ischemic lesion localized in left temporo-parietal region visible on DWI and Flair
On the right: old infarcts in the cerebellum and in the right parietal lobe; diffuse leukoencephalopaty

Discussion

Secondary thromboprophylaxis with long-term anticoagulation therapy is currently recommended for patients with definite APS. There is consensus for the treatment of a patient affected by APS and a venous thrombotic event, but there is some uncertainity in the choice of treatment for a patient with an arterial thrombotic event. Some treatments have been proposed for this category of patients: antiplatelet therapy alone, anticoagulants with a target INR of 2-3, anticoagulants with a target INR of 3-4 or an association of antiplatelet and anticoagulant therapy.
In our case the patient was already under anticoagulant therapy, but she had not a good compliance. She usually did not take the therapy during menstrual flow, because she had menhorragia. So there was presumably a window of about five days a month out of the time in therapeutic range (TTR) .
The cause of menhorragia was identified, but the patient refused surgery. We considered the hypothesis of switching to a direct oral anticoagulant (DOAC), in order to reduce the days in which the patient was not protected. Infact, after a temporary interruption of anticoagulant treatment, with a single dose of DOAC the patient is already protected, but with warfarin some days are necessary to reach the target INR. We finally did not switch to a DOAC because the lack of evidence of efficacy in APS. Actually there are several clinical trials investigating the efficacy and the safety of DOACs for secondary prevention in patients with APS.

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XLVIII CONGRESSO NAZIONALE
14-17 OTTOBRE 2017 – NAPOLI
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