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Treatment of Catastrophic Antiphospholipid Syndrome to Pregnant Woman: A Case Report

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Abstract

The research aimed to study and analyze the life-threatening complication of antiphospholipid syndrome by acute thrombotic microangiopathy, which can lead to multiorgan damage. The progression of catastrophic antiphospholipid syndrome during pregnancy creates a lot of problems in diagnostic due to its extended clinical manifestations and coincidence with additional obstetric intricacies and microangiopathic diseases. Early diagnosis and aggressive treatment (anticoagulants, glucocorticoids, and plasma metabolism (or intravenous immunoglobulins) remain key factors for favorable. In cases of refractory CAPS, cyclophosphamide or monoclonal antibodies (rituximab, eculizumab) should be considered.

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1 Introduction

In medical literature, the antiphospholipid syndrome (hereinafter APS) refers to a complex of auto-immune disorders with increased production of antibodies to phospholipids and related glycoproteins (β2-glycoprotein-1, annexin, and prothrombin) (Sammaritano, 2020). The presence of aPL is associated with miscarriages preeclampsia, preterm labor, fetal developmental delay, and fetal death (Silver, 2018). The most severe degree of APS belongs to a separate nosological form – catastrophic antiphospholipid syndrome – CAPS (Asherson, 1992; Bucciarelli et al., 2006; Berman et al., 2013). The latter is characterized by the development of thrombotic microangiopathy, numerous thrombosis of vital organs with the development of multiple organ failure, and in some cases even by tissue necrosis. It is life-threatening and requires immediate treatment (Carmi et al., 2017; El-Said et al., 2020).

According to the literature, APS occurs in 5% of the population, and among all cases, APS CAPS is approximately 1% (Sene et al., 2009). Mortality in CAPS patients, despite therapy, reaches almost 36-50% (more often from heart and lung failure or cerebrovascular complications) and pregnancy can act as a trigger (Espinosa et al., 2011). The maternal mortality rate among patients with CAPS reaches one-third (Bucciarelli et al., 2006; Gomez-Puerta et al., 2013), which emphasizes the need for urgent and correct diagnosis of APS as a key factor of successful treatment. In this paper, we describe the case of treatment of catastrophic APS in the pregnant woman.

2 Materials and Methods

We presented a result of the examination and treatment of a pregnant woman with a history of multiple venous thromboembolism and APS at 23 weeks of gestation. She has developed CAPS with right upper quadrant pain, the multifocal bilateral impression of the brain with areas of secondary hemorrhage, thrombus in the small intrahepatic vessels thrombocytopenia, elevated creatinine, liver enzymes. She has significantly elevated antiphospholipid antibodies. Current CAPS management recommendations are based on a case studies analysis from the International CAPS Registry, which was created in 2000 according to the APS European Forum initiative (Kazzaz et al., 2016; Santi et al., 2021).

3 Results and Discussions

A nulliparous pregnant (23+2 weeks of gestation) a 33-year-old woman was admitted to Vinnytsia Regional Perinatal Center. At the age of 22+6 weeks of gestation, the pregnant woman complained of epigastric pain and pain in the right hypochondriac region (day 0, Fig. 1).

Laboratory analysis showed hemoglobin 10.3 g / dL, new-onset thrombocytopenia (platelet count 67 x 109 / L), absence of proteinuria, slightly elevated WBC and fibrinogen, APTT 56 sec, serum creatinine 81 μmol / L, serum amylase 32 U / L, alanine aminotransferase (ALAT) 95 U / L (ref 0-35), aspartate aminotransferase (ASAT) 202.9 U / L (ref 0-35), lactate dehydrogenase (LDH) 539.3 U / L (ref 120-246), alkaline phosphatase (AP) 195.6 U / L (ref 30-120), C-reactive protein 20.7 mg / L (ref <10), procalcitonin <0.10 μg / L (ref <1.0). Analysis for SARS-CoV-2 by PCR: negative. Test for aPL: aCL > 100 U / ml (ref <10), ab2GPI> 160 U / ml (ref <20), LA – 2.5887 (ref 0.8-1.2) (day 7).

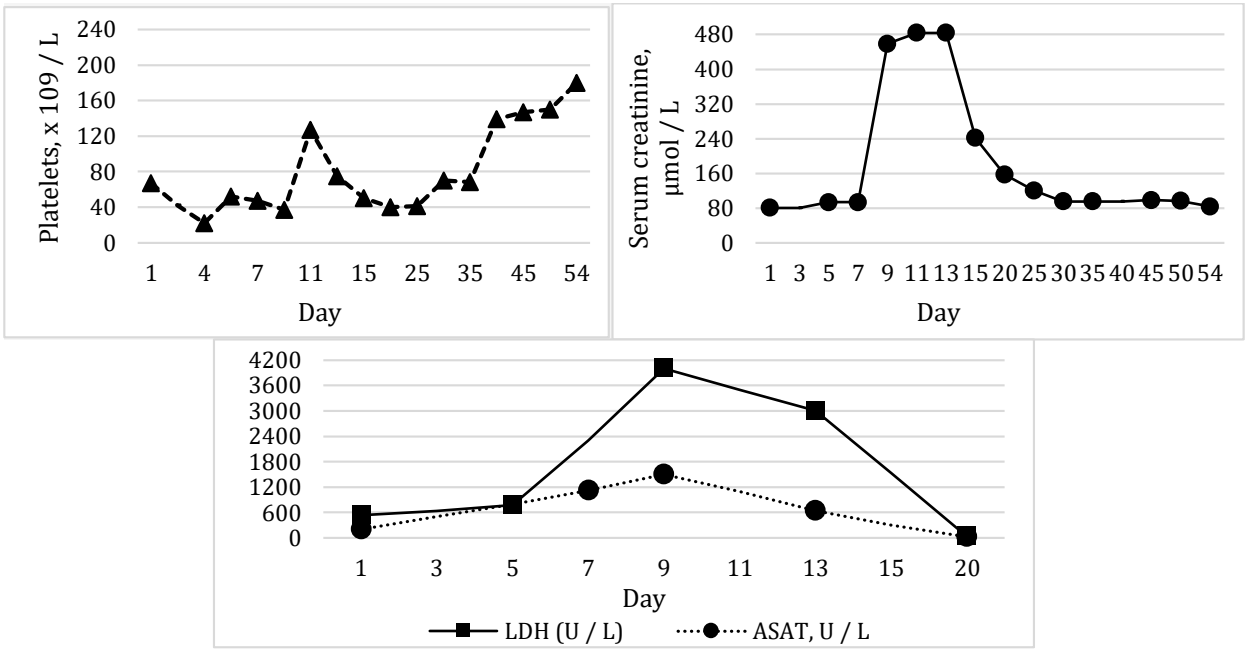


Figure 1. A course of laboratory parameters*
*LDH: lactic dehydrogenase. ASAT: aspartate aminotransferase.

On admission ultrasound examination (US) of the abdominal cavity showed signs of thickening of the walls with increased blood flow, congestion in the lumen of the gallbladder, minor bilateral pyelectasis (Fig. 2).

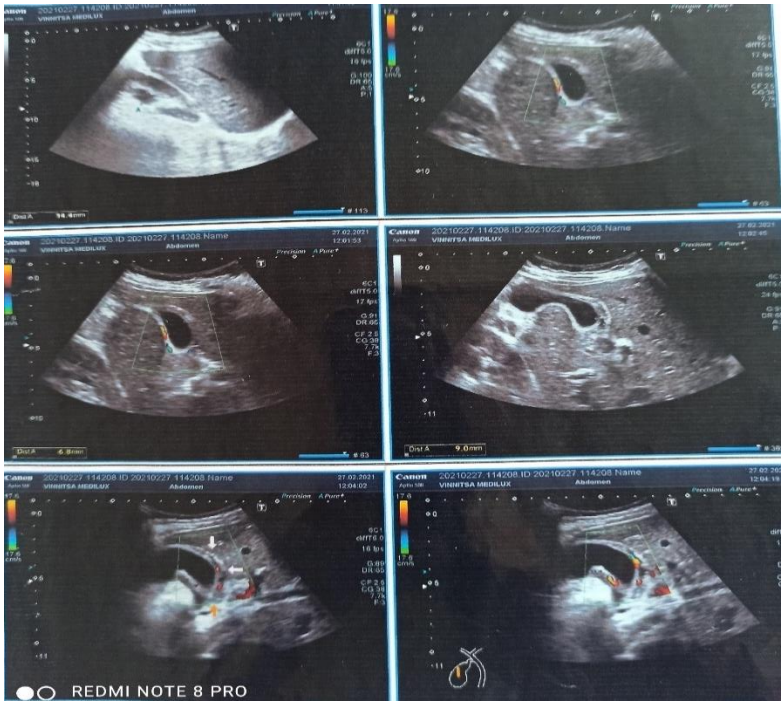
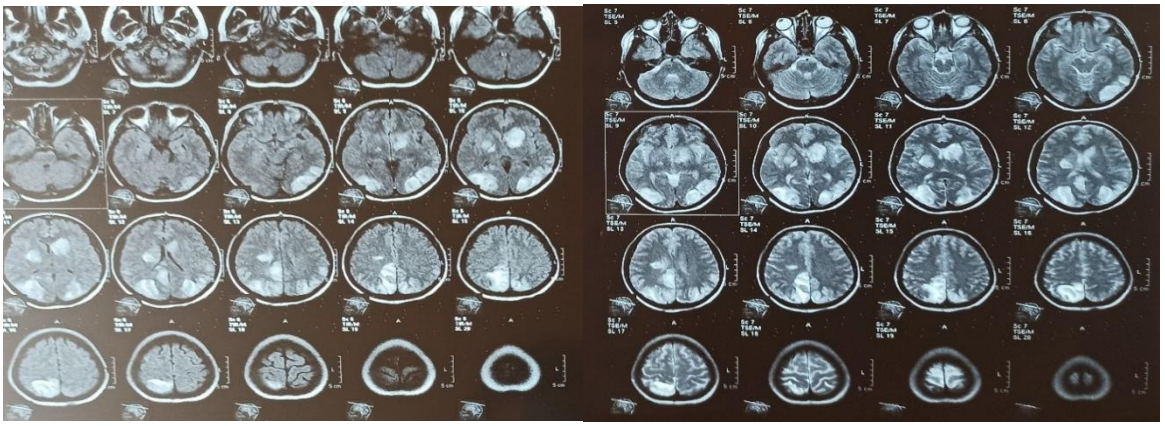


Figure 2. Ultrasound examination of the abdominal cavity on admission

On the 23+6 wg there was a sudden deterioration in general condition, decreased level of consciousness – 9 according to Glasgow Coma Scale, the appearance of the right-sided hemiparesis (day 7, Fig. 1). According to the results of the brain MRI: multifocal lesions in both hemispheres of the brain, mostly in the posterior and parietal areas with areas of secondary hemorrhage (Fig. 3).



(A) T2 mode FLAIR (A). (B) W / TSE

Figure 3. *Magnetic resonance imaging of the brain*

Multislice computed tomography (MSCT) of the brain with intravenous contrast and fetal protection showed the signs of acute cerebrovascular accident in the form of multiple foci of mixed ischemic-hemorrhagic nature in the projection of the basal ganglia in both hemispheres on the background of cerebral edema (Fig. 4-A). Chest MSCT revealed the signs of local pulmonary fibrotic changes of the lung parenchyma (Fig. 4-B). MSCT of the abdomen showed signs of hepatomegaly with the presence of pathological volumetric hypodense areas in the right and left lobes of the liver as a type of infarction and thrombotic lesion in small branches of the portal vein, minor ascites, chronic cholecystitis, right-sided pyeloectasis (Fig.4-C).

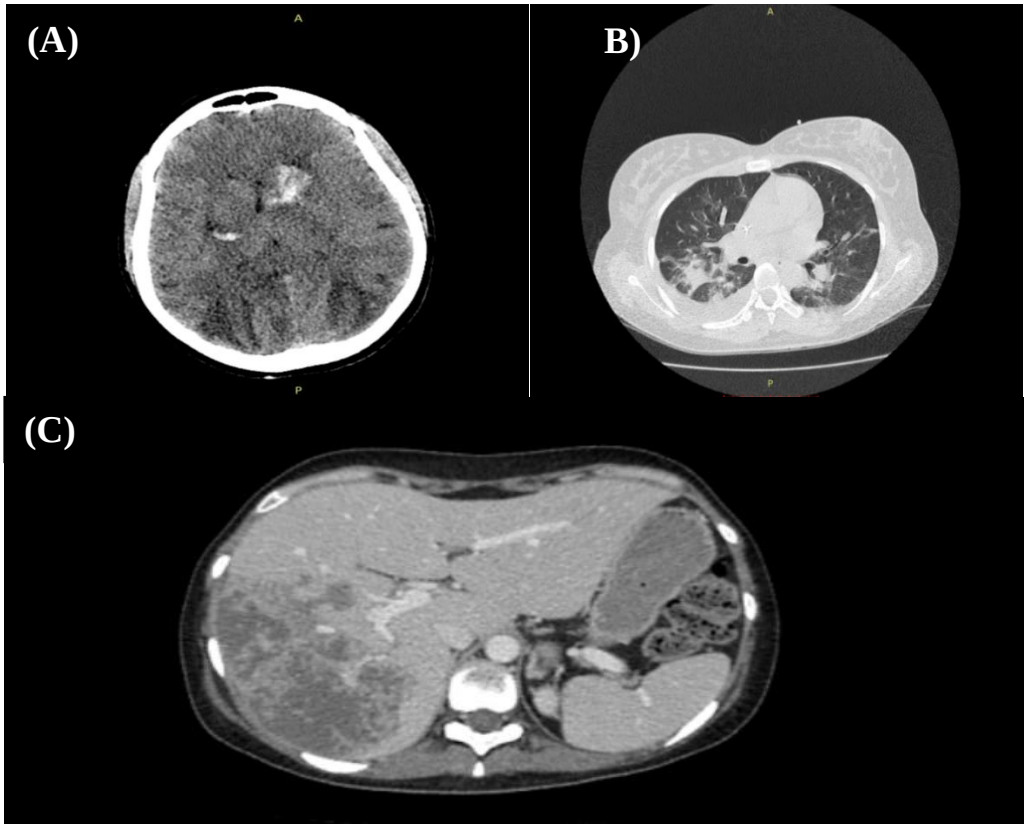
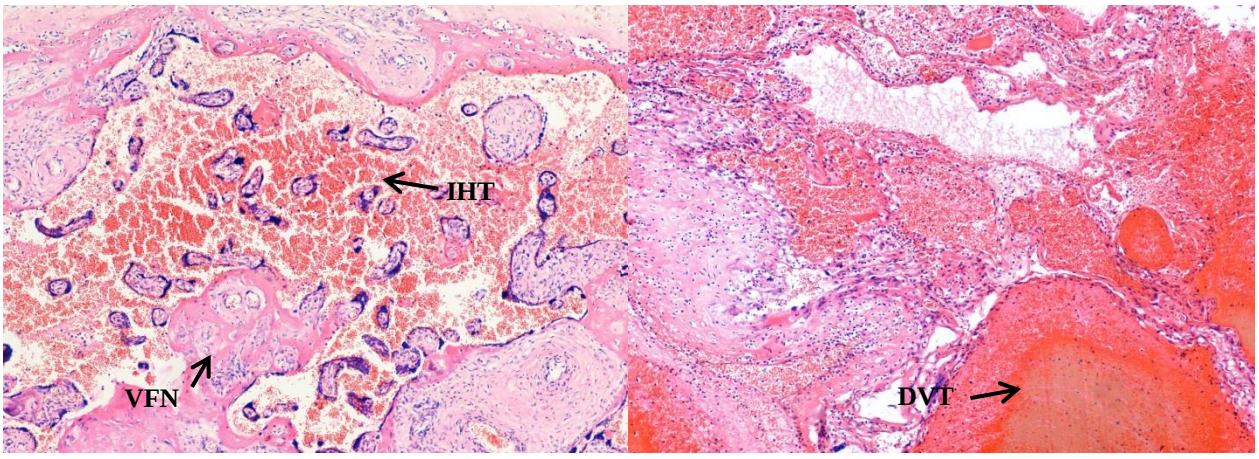


Figure 4. Multislice computed tomography with intravenous contrast and fetal protection of the: (A) brain, (B) chest, (C) abdominal organs

Diagnosis: the first pregnancy at 24 weeks. CAPS. Acute ischemic strokes with secondary hemorrhagic infiltration (Gibson et al., 2001). Brain edema. Intrahepatic thrombosis of small hepatic vessels. Multiple organ dysfunction syndromes (cerebral, respiratory, renal, hepatic). Anemia. Post-thrombotic syndrome. Placental dysfunction. Intrauterine growth restriction. Post-COVID condition with the formation of pulmonary fibrosis of the lungs. The prescribed treatment included: LMWH (enoxaparin 0.5 mg/kg twice a day with a dose reduction to 0.25 mg/kg/day with a decrease in platelets to 20 x 109/L), glucocorticoids pulse therapy, plasmapheresis, a broad-spectrum antibiotic, symptomatic management of cerebral edema, secondary arterial hypertension, hyperthermic syndrome, hepatic and renal dysfunction, respiratory support, parenteral and subsequent enteral nutrition (James et al., 2005).

At 24+1 weeks of gestation, the clinical condition of the mother was deteriorating and termination of pregnancy was performed (day 9, Fig. 1). Was born a dead newborn. The fetal autopsy revealed disseminated intravascular coagulation syndrome (plethora of internal organs, thrombosis of the vessels of the microcirculatory tract, focal hemorrhage in the internal organs) (Liston et al., 2007). Histological examination of the placenta showed signs of placental insufficiency, the presence of unevenly dilated vessels with the development of erythrocytosis, vascular thrombosis, and the formation of common ischemic and hemorrhagic infarctions (Chiou et al., 1997; Tibballs & Russell, 2009). The histological picture of placental infarction is very heterogeneous due to the various periods of the isolated nature of the necrosis of villi or the occurrence of an ischemic focus on the periphery of the intervillous hemorrhage and thrombosis (Fig. 5).



(A) Placental villus (B) Decidual plate

Figure 5. Placental histology. Hematoxylin-eosin staining (A and B, obj. 10x)*

*IHT: intervillous hemorrhage and thrombosis. VFN: villous fibrinoid necrosis. DVT: decidual vessel thrombosis

Due to the progressive deterioration of the patient's condition, plasma exchange was performed with replacement of 50% of the patient's removed plasma with fresh-frozen donor plasma and the remaining 50% was with solutions of balanced crystalloids (day 11, Fig. 1), cyclophosphamide 500 mg, duration of intravenous infusion was 2 hours (day 13, Fig. 1). Over the next 7 days, the patient's condition improved with a gradual regression of neurological symptoms, speech, movements, and levels of liver markers were within the normal range (day 20). Renal function showed stabilization on the 25th day of treatment (serum creatinine was 121 μmol / L and after the stage of polyuria the diuresis was of normal range). At the same time, the platelet level returned to the normal range only on the 54th day after the development of CAPS. In 56 days the woman was discharged in a satisfactory condition (Primadewi & Diwyami, 2021).

Discussions

Early recognition and treatment of CAPS may prevent fatal outcomes (Gomez-Puerta et al., 2007; Hakman & Mikhael, 2018). In our patient manifestation of the disease fit into the picture of definite CAPS (Asherson's syndrome) (Asherson et al., 2003; Widana et al., 2021), because our patient met all four of the four criteria for the classification of CAPS: multifocal thrombosis with a multiple organ failure: lesions of the central nervous system, liver, kidneys, and placenta. Signs and symptoms of the liver, the central nervous system, and renal lesions development in less than a week:

- 3) signs of thrombosis of vessels and intervillous space during the histological study of the placenta (Fig. 5);
- 4) our patient is triple positive for aPL: aCL > 100 U/ml, ab2GPI > 160 U/ml, LA 2.5887.

Unlike HELLP syndrome, termination of pregnancy did not improve patients' clinical condition. This correlates with the other cases data (Gomez-Puerta et al., 2007). The current treatment of CAPS involves therapy with anticoagulation, corticosteroids, and plasma exchange or intravenous immunoglobulins (Bucciarelli et al., 2006; Wang et al., 2019). Our patient received all methods of treatment according to the recommendations of CAPS, except for the intravenous immunoglobulins. Due to the acute deterioration of the mother's clinical condition the premature delivery was performed (Silver et al., 2018). In these circumstances refractory CAPS rituximab and eculizumab must be taken into account (Espinosa et al., 2017).

4 Conclusion

The presence of CAPS in any pregnant woman with multiple organ thromboses, suspicious laboratory results, and a positive apL should be carefully evaluated. early diagnosis and the beginning of rapid treatment can be considered the main components of a positive outcome of treatment. In cases of refractory CAPS, cyclophosphamide or monoclonal antibodies (rituximab, eculizumab) should be considered.

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