Management of the postpartum ovarian and partial cava inferior vein thrombosis

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Summary
Objective: Postpartum ovarian vein thrombosis (POVT) is a rare but very dangerous complication with possible lethal outcome. Here the authors present a case of POVT with propagation in cava inferior vein, which was diagnosed fourth day after delivery by cesarean section. Case Report: A 27-year-old female with fever complained of pain in the area of the right side of the abdomen, in the ileocecal region three days after premature delivery by caesarean section. Right ovarian venous thrombosis and partial cava inferior vein thrombosis was demonstrated on sonography and confirmed with computed tomography. She was treated with antibiotics and anticoagulation therapy with good response. Conclusion: If women after delivery have an elevated temperature with abdominal pain and leukocytosis in laboratory analyzes, it is always necessary to think of the POVT. Early recognition and therapy are crucial.

Key words: Ovarian vein thrombosis; Deep venous thrombosis; Postpartum thrombosis.

Introduction
Postpartum ovarian vein thrombosis (POVT) is a rare but very dangerous complication with possible lethal outcome. It was recognized, described, and published for the first time by Austin in 1956. [1]. The cluster of non-specific symptoms and the clinical picture is masked by the symptoms of other diseases which makes the diagnosis proverbially delayed. Frequency of the POVT varies between 0.05% and 0.16% after the delivery, while after the cesarean delivery it reaches up to 2% [2].

The risk of venous thrombosis is increased during peripartum and postpartum periods due to venous stasis, an increase in the concentration of I, II, VII, IX, X coagulation factors, von Willebrand factor, and occurrence of endometritis. During pregnancy, dilatation of the ovarian vein (OV) is possible up to three times in comparison to its physiological width. There are three leading factors in POVT genesis: decelerated venous blood flow, endothelial injury, and hypercoagulability (Virchow’s triad). The incidence of venous thrombosis in the right OV is 90%. [3]

Pelvic pain, fever, and palpable mass in the right hypochondrium, make up the main triad of symptoms. In addition, nausea, vomiting, hypotension, tachycardia, tachypnea, and clinical picture of intestinal obstruction may occur. The main complications of unrecognized vein thrombosis are ovarian abscess, ovarian infarction, development of septic thrombophlebitis, lower vein thrombosis (VCI), uterine necrosis, ureteral compression, and even pulmonary embolism with an incidence of up to 13% and mortality up to 4%. The initial and basic diagnostic method is ultrasound. Imaging techniques such as contrast CT or MRI are required to set the precise and accurate diagnosis.

Antibiotic and anticoagulant therapy is the basic treatment in the POVT. Due to relapse the POVT it is recommended to administer them for up to six months after the end of hospital treatment. [5].

The authors present a patient who developed postpartum OV thrombosis with symptoms on the fourth day after the cesarean delivery, and the diagnosis was set on the tenth day after delivery.

Case Report
A 27-year-old woman, G1, P0, on the third day after premature delivery by cesarean section complains of pain in the area of the right side of the abdomen, in the ileocecal region. Laboratory analyzes indicate leukocytosis of 20 × 10^9 /L with high CRP values of 150 mg/dL, D-dimer 4.14 mg/L FEU, and slightly higher fibrinogen values of 6.9 g/L. The patient was febrile up to 38.1°C, in the absence of vaginal bleeding, nausea, vomiting, and urinary disorders. Postoperatively, the patient received prophylactic doses of low molecular weight heparin (LMWH) 0.6 ml s.c./24 hours with antibiotic protection by ceftriaxone and metronidazole. There is no history of previous coagulation disorders and previous thromboses.

At the ultrasound examination, a hypoechogenic mass was observed in the right horn region of the uterus, suspected with an inflammatory process, well-vascularised, in the presence of an inflammatory process, well-vascularised, in the presence of a smaller amount of free fluid around the inflammatory complex, as well as dilated OV and cava inferior thrombus [Figures 1-3]. On contrast-enhanced CT, a dilated right OV with lumen width up

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Figure 1. — Ultrasound transverse cross-section at small pelvis with hyperechoic adnexal mass in the area of right adnexa is well-vascularized.

Figure 2. — Ultrasound cross-section at right enlarged ovary vein.

Figure 3. — Ultrasound cross-section at cava inferior vein with partial occlusion and thrombus within.

Figure 4. — Computed tomography coronal cross section of the abdomen and small pelvis with contrast application shows a hypodense right ovary vein with the presence of a blood clot and perivascular hyperechoic and varicose pelvic veins.

Figures 5 and 6. — An axial and coronary section of the computed tomography image of the abdomen and small pelvis with contrast application revealing the presence of thrombus in the VCI and propagation into its intrahepatic segment.
to 2.3 cm with complete venous thrombosis and a thrombotic mass of 43x10.5 mm in the VCI was observed, which filled one-third of its lumen with the propagation of thrombus into the intrahepatic segment VCI [Figures 4-6].

Diagnosed OV thrombosis with thrombotic mass propagation in the VCI required the transition from preventive to therapeutic doses of LMWH, namely, 0.6 ml s.c. at 12 hours with continued antibiotic therapy. As the condition was not worsened, treatment was continued with oral anticoagulant medication with Rivaroxaban at a dose of 15 mg/day with a reduction in the dose of 10 mg/day of ten days for six months. Investigations of congenital and acquired thrombophilia included D-dimer, protein S, the values of which were within the reference levels, while protein C was reduced (53.5%). 

Analyzes of anticardiolipin at IgM and IgG, anti-beta2 IgG, and IgM were negative, and lupus anticoagulant was reduced (53.5%). A homozygous mutation for methylene-tetrahydrofolate reductase gene (MTHFR) and a heterozygous mutation for the Pai-1 gene were established, while mutations for factors II and V were excluded.

Discussion

Pregnancy as a physiological condition can affect the change in viscosity and hypercoagulability of blood. Women are 4-6 times more prone to thromboembolism and the risk increases in puerperium [6]. Platelet adhesion increases, as well as the concentration of fibrinogen (factor I) even up to 50%, with simultaneous increase in prothrombin (factor II). At the same time, the level of fibrinolysin decreases with increasing fibrinogen, factor VII, VIII, IX, XII and von Willebrand’s factor [7]. During pregnancy, the volume of blood increases, and the diameter of the vein is three times greater than in non-pregnant women. Anatomical and physiological differences between the right and the left OVs are the reason why, in 90% of cases, thrombosis of the right OV is more common. The right OV is longer than the left, has more incompetent valves, and the acute angle of junction with the VCI increases the sensitivity of uterine pressure, which causes additional rotation of the uterus to the right. The left OV runs under the right angle to the left renal vein, it is shorter and has less valves. The flow in the left OV is retrograde, which protects it against bacterial infection and injury versus anterior flow at the right where the possibility of infection and the formation of phlebothrombosis are increased [8]. The most common infectious agents are anaerobic bacteria such as Streptococcus, Staphylococcus, Proteus species, Bacteroides species, and gram negative: Escherichia coli, Enterobacter and Klebsiella species [9].

In about 19% of cases, OV thrombosis is detected on the tenth day after delivery [10]. The main symptoms are abdominal pain, elevated temperature, nausea, vomiting, and sometimes there are symptoms similar to ileus. Leukocytosis is present in 70-100% of cases, as well as elevated sedimentation and C-reactive protein. This disease should be suspected in case there is no improvement in general and local conditions even after 48-72 hours from administration of antibiotics. A wide range of symptoms not only de- fines the OV thrombosis, but also more commonly diseases, such as: acute appendicitis, tubo-ovarian abscess, pelvic inflammatory disease, adnexa torsion, and intraligamental hematoma. Hydroureter and hydronephrosis are more pronounced on the right side due to the aforementioned gravity uterus dextropositions and possible enlargement of the right OV. The most serious complication may be pulmonary embolism [2].

Diagnosis can be confirmed by US, CT or MRI. Gaseous distension of the intestine may mask the POVT, which is why the wrong diagnosis of acute appendicitis, tubo-ovarian abscess or hydroureter is often established [11]. The suspected POVT itself requires CT diagnosis or MRI due to sensitivity that reaches 100%, and specificity up to 99%. The diagnosis is based on the presence of Zerhouni criteria: enlarged vein, decreased lumen density of the vein, and well-defined vein wall with perivascular edema. At the same time, contrast CT method diagnostics also makes it possible to differentiate ureter and OVs at the stage of excretion [10].

In more than 50% patients diagnosed with the POVT, there has been a predisposition for its occurrence, therefore it is advised to test for inherited and acquired thrombophilia in patients with postpartum OVT [3].

The basic POVT therapy involves the use of anticoagulant therapy and antibiotics [8, 10]. Antibiotics are administered 7-10 days, while long-term use of antibiotics is carried out only in rare cases of positive hemoculture [3]. In case of suspected septic fleshthrombosis, the therapy of choice is antibiotic ampicillin-sulbactam, piperacillin-tazobactam, ticarcillin-clavulante, or ceftriaxone-metronidazole [12].

There are no clear recommendations for duration of anti-coagulant therapy. Thrombus withdrawal and complete re-canalisation can be established within 7-14 days after administration of anticoagulant therapy. Some studies have shown a high probability of OVT recurrence, which significantly increases mortality, when compared to the DVT. For this reason, the British Committee for Standards in Haematology recommends the application of anti-coagulant therapy 3-6 months after diagnosed POVT. For successful treatment of the POVT, the use of LMWH and rivaroxaban over a period of six months is recommended, followed by antiagregation suloxide therapy to prevent the risk of relapse [13]. In patients with postpartum POVT, the use of prophylactic doses of anticoagulant drugs is advised during the next pregnancy and six weeks postpartum [14].

In conclusion, although rare, POVT is a serious state of puerperium due to possible serious complications. Pain in right hypochondria, elevated temperature and leukocytosis, as well as high sedimentation, are the cause of suspected postpartum venous thrombosis. Since POVT is not a common complication in puerperium and there is not enough of the described and treated cases associated with
the use of new oral anticoagulants, the presentation of this case can contribute to the success in treating unwanted complications in puerperium.

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