Puerperal ovarian vein thrombosis accompanied by hydronephrosis

Poporodna tromboza ovarialne vene in hidronefroza

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Ključne besede:
poporodno obdobje; venska tromboza; bolečina v trebuhu; faktorji strjevanja krvi; obstrukcija ureterja

Key words:
puerperal period; venous thrombosis; abdominal pain; blood coagulation factors; ureteral obstruction

Izvleček

Tri tedne po porodu je bila 22-letna ženska sprejeta na urološki oddelek zaradi vročine in bolečin ledveno ter v trebuhu. Z intravensko urografijo je bila ugotovljena hidronefroza, ki smo jo drenirali z nastavitvijo notranjega drena (DJ), ter uvedeno antibiotično zdravljenje. Po treh dneh je prišlo do otekanja nog, kar je spodbudilo nadaljne preiskave. Računalniška tomografija (CT) je pokazala trombozo ovarijske vene kot vzrok za hidronefrozo in še trombozo votle vene v višini vtoka ledvičnih ven, trombozo iliakalnih in proksimalnih globokih ven obeh spodnjih udov. Uvedeno antikoagulantno zdravljenje z nizkomolekularnim heparinom in kasneje trajno antikoagulantno zdravljenje z varfarinom so omogočili pretežno rekanalizacijo s trombi utesnjenih ven.

Bolnica je heterozigotna nosilka mutacij za faktor V Leiden in protrombin. Čeprav literatura v zadnjem času navaja zanemarljivo povečano tveganje za globoko vensko trombozo pri dvojnih heterozigotih, je bolnica imela več očitnih dejavnikov tveganja (spontani splavi, mirovanje, kajenje, debelost, krvna skupina ne-O ...). Vse to bi moralo spodbuditi podrobnejšo oceno tveganja za trombozo in razmislek o tromboprofilaksi.

Na tromboflebitis ovarialne vene je potrebno pomisliti pri bolnicah v poporodnem obdobju z nepojasnjeno vročino in bolečino v trebuhu.

Abstract

Three weeks after delivery, a 22-year old woman presented to urology with fever, abdominal and right-sided flank pain. Hydronephrosis was diagnosed with iv-pyelography and treated with JJ-stent drainage and antibiotics for suspected pyelonephritis. On the third day oedema of the right leg appeared, which prompted further investigations. CT identified ovarian vein thrombosis as a cause of hydronephrosis, and further thrombosis of the inferior vena cava, iliacal and deep veins of both upper legs. Anticoagulant treatment with low-molecular-weight-heparin and later warfarin resulted in partial recanalisation of thrombi.

The patient is double heterozygous for factor V Leiden and prothrombin mutation. Although recent literature negates this as a significant risk factor, presence of other, more obvious and easily recognizable risk factors (previous spontaneous abortions, smoking, bed rest, obesity, non-O blood group...) should have prompted detailed risk evaluation and consideration of thromboprophylaxis.

Ovarian vein thrombophlebitis should be suspected in any postpartum patient with unexplained fever and abdominal pain.

Citirajte kot/Cite as:
Zdrav Vestn 2014;
83 supl: I-39–44

Prispelo: 15. jul. 2013,
Sprejeto: 7. nov. 2013

Introduction

Ovarian vein thrombosis can present as asymptomatic or severely symptomatic (acute abdomen) and can have–with development of sepsis or progression of venous thrombus to pulmonary embolism–severe consequences.[1-3] It is most often identified in the postpartum period, but can appear also with other precipitating factors such as thrombophilia, surgical procedures, malignancies and inflammatory conditions.[4]

Key factors in the pathogenesis of thrombosis (Virchow triad) are blood flow stasis, altered coagulation and intimal injury. After childbirth, blood flow in the ovarian veins rapidly decreases, leading to venous collapse and stasis. Hypercoagulability is present for 6 weeks postpartum. Furthermore, intrauterine bacterial infection post partum may cause local sepsis, producing inflammation and leukocyte infiltration that result in venous intimal injury.[5]

Thrombosis of the ovarian vein post-partum occurs most often on the right side.[2] However, recent report of predominantly non-pregnancy-related causes found equal frequency of left and right sided cases.[6]

The most common presenting symptoms of ovarian vein thrombophlebitis include fever and lower abdominal discomfort.[7] Frequency of ovarian vein thrombosis related to pregnancy is estimated to be around 0.04 %[8] after vaginal birth or 0.1 % after caesarean section.[2] A lot of cases go undetected. The diagnostic method of choice is CT or MR imaging, ultrasound being appropriate for follow up of thrombosis which also extends in other veins.[9,10] Most patients with post-partum ovarian vein thrombophlebitis can be treated with antibiotics and anticoagulation therapy.

Case report

A 22-year-old woman was admitted to urology with right-lower-quadrant abdominal pain, right flank pain and high-grade fever (39 degrees C) for suspected ureterolithiasis with pyelonephritis three weeks after her first, full term vaginal delivery of a healthy infant.

She was a smoker and moderately obese. Her blood group was B positive. There had been no complications during birth, but she was advised bed rest during the second half of pregnancy. Regarding family history, her father had cerebrovascular insult at the age of 44. The patient's medical history was unremarkable, except for appendectomy five years earlier and two previous spontaneous abortions. Results of cardiorespiratory examination were unremarkable. On pelvic examination, the cervix and uterus were non-tender. There was no calf or thigh swelling or tenderness. Laboratory evaluation showed a white blood cell count of 13.000/uL, CRP of 171 mg/L. On urine sediment microscopy, 50 red blood cells, 25 white blood cells and few bacteria were found per high power field. An abdominal ultrasound examination revealed a right-sided hydronephrosis. Intravenous urography showed obstruction of the right ureter at L3/L4 level (Figure 1). Our initial diagnosis was a right-sided ureterolithiasis with pyelonephritis. We drained the right kidney with a JJ stent. Insertion of the stent was unexpectedly smooth and without resistance. Blood and urine cultures were obtained and antibiotic treatment was started.

On the third day we noticed oedema of the right leg. Colour-Doppler ultrasound examination revealed proximal femoral thrombosis on the right side. Anticoagulant therapy with low- molecular-weight heparin in a therapeutic dose (enoxaparine – Clexane 0.6/12h) was started. Blood and urine cultures remained sterile. Despite antibiotic treatment, the patient still had a high-grade fever, which followed a spiking pattern for more than one week. Therefore, a contrast-enhanced abdominal computed tomography was performed. The examination revealed right ovarian vein thrombosis and obstruction of the right ureter at the level L3/L4, where the right ovarian vein crosses the right ureter. The thrombus extended into the inferior vena cava up to the level of renal veins, and down into the common iliac, external and internal iliac and femoral veins on both sides. All these veins were completely obstructed (Figure 2). The patient was maintained on enoxaparin 0.6 ml/12h and an-

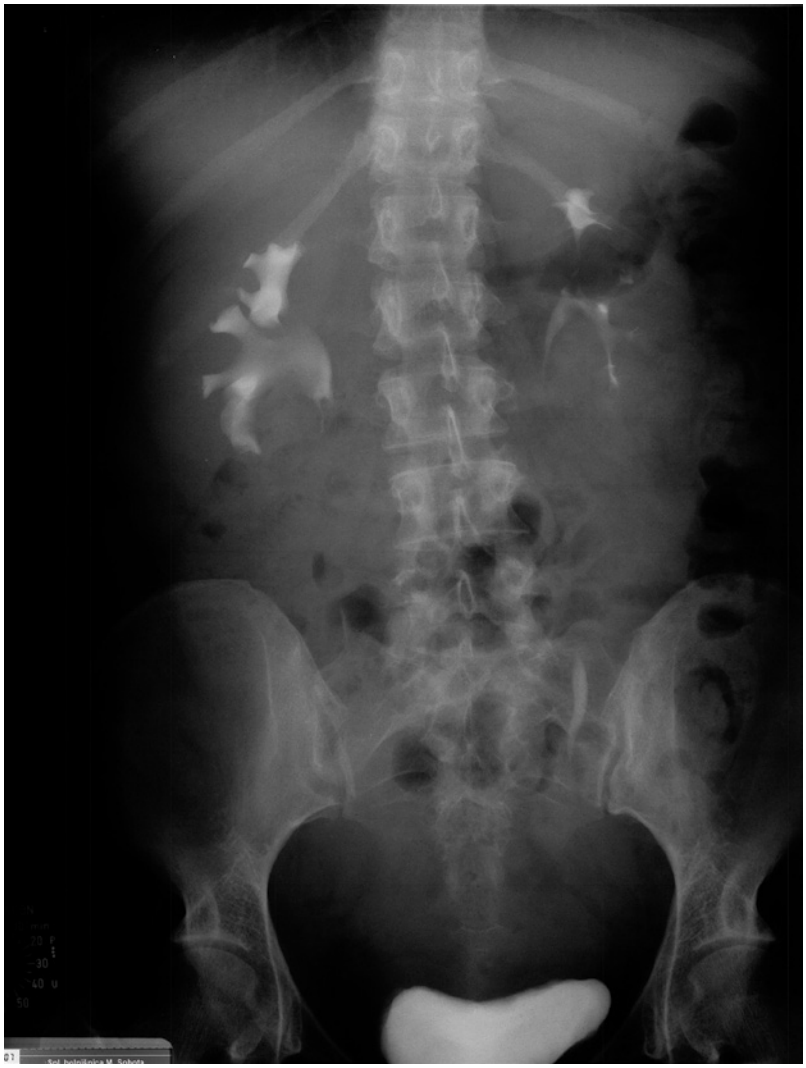

Figure 1: Intravenous urography showing an obstruction at L3/L4 level on the right side.

tibiotics (cefuroxime initially (500 mg/12h); after hydronephrosis was established, gentamicin was added and after the diagnosis of thrombophlebitis of the ovarian vein was established, metronidazole 400mg/8h was added). Fever subsided in 10 days. Laboratory parameters: WBC normalized, CRP first increased to 202 mg/L on day 12 and then started to decrease (96 mg/L on day 17). The patient was referred to the Clinical Department of Vascular Diseases for further investigation. Genetic analysis documented a prothrombin and coagulation factor V Leiden heterozygous gene mutations. A life-long anticoagulant therapy was advised and oral anticoagulation with warfarin instituted before discharge.

Two months later we removed the JJ stent. One week after JJ stent removal, all veins were still partially obstructed, but there was no hydronephrosis.

After two years, veins are patent, but rests of thrombi are still seen in the iliac and femoral veins. The patient works as waitress, has no pain or swelling and has (against advice) stopped using elastic stockings. However, she is on oral anticoagulant treatment with INR strictly controlled between 2 and 3.

Discussion

The differential diagnosis of ovarian vein thrombophlebitis includes endometritis, appendicitis, pyelonephritis, ureterolithiasis, adnexal torsion and tubo-ovarian abscess. A suspicion of the condition should arise when fever, which usually follows a spiking pattern, fails to respond to standard broad-spectrum antibiotic therapy. Blood cultures provide identification of a microorganism in less than 35 % of cases.[11,12] In the event of extension of thrombus to other veins, respective symptoms appear. The diagnosis is best confirmed by abdominal CT with contrast, but can be detected by MRI or, in the case of thrombus extending to other veins, ultrasound studies. Thrombosis may extend into the vena cava[5] or other veins, for example the renal vein on the left.[13,14] The incidence of pulmonary embolism has been reported to be from 13 % to 33 %. Of these cases, 4 % are fatal.[5,11] The described case is among more serious presentations of ovarian vein thrombophlebitis. Flank pain from hydronephrosis was a result of obstruction caused by the thrombosed ovarian vein at the level where it crosses the ureter. Such presentations are very rare and always surprising. We found three reports of hydronephrosis as a result of ovarian vein thrombosis in the recent literature.[15-17]

Regarding treatment, in mild cases, some observational studies questioned the efficacy of anticoagulation therapy, like Brown and associates who prospectively randomized 14 patients to receive either antimicrobial therapy or antimicrobial therapy plus heparin. The duration of fever and hospital stay was similar in both groups. Furthermore, neither thromboembolic events nor reinfection were reported.[18] In cases with extensive thrombosis, anticoagulation is not questionable, however, the optimal duration

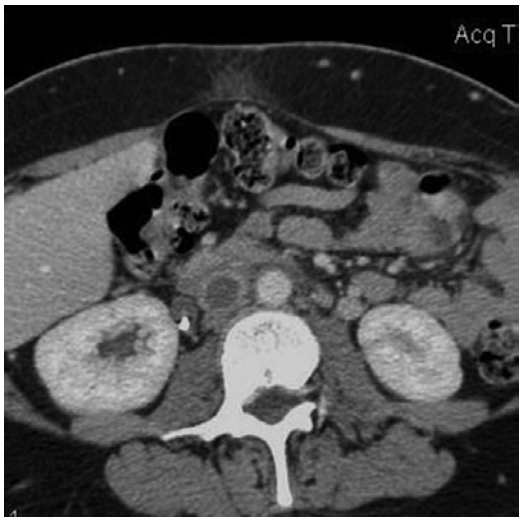

Figure 2: Cross sectional computed tomographic scan of the abdomen shows a filling defect in the right ovarian vein and in the inferior vena cava. Behind the ovarian vein is the right ureter, which contains a JJ stent.

of anticoagulation is unknown, but with the thrombus in the vena cava it should last for at least 6 months.[8]

Historically, treatment was surgical. In 1951, Collins proposed a pathogenic model for suppurative pelvic thrombophlebitis and advocated ligation of the inferior vena cava and ovarian veins. He published his experience with 202 women who underwent surgical intervention and reported a 90 % survival rate.[12] Such treatment was frequently associated with significant complications (postoperative oedema, recurrent thrombophlebitis, leg ulcers, stasis dermatitis and venous claudication). The introduction of antibiotics, heparin and oral anticoagulation therapy into the treatment regimen led to a dramatic shift from surgical to pharmacological management. This approach has produced post-treatment outcomes and long-term results equivalent or better compared to those of surgery. Surgical treatment, which consists of insertion of a vena cava filter, open ligation of vein or thrombectomy, is generally reserved for patients in whom anticoagulation is contraindicated, for those who have recurrent pulmonary emboli despite medical management, complications related to medical management, and for patients with a free-floating thrombus.[5,19,20]

With such serious cases, the need for search and identification of risk factors and prevention of venous thromboembolism is obvious. Looking retrospectively, it is now easy to see a number of risk factors that our patient presented with. Three are universally recognized and could be easily identified: immobilization during pregnancy, smoking and obesity.[21]

The question of thrombophilia risk factors is less clear. First, it is not clear whether one should screen for them or not, and second, the role of "double heterozygosity" was questioned. It seems guidelines do not advise screening for thrombophilia in pregnant women without previous venous thromboembolism.[22,23] However, our patient had family history of embolic event (brain stroke, father at age 44) and she had two previous miscarriages (three should prompt for antiphospholipid antibody screening)[22] – should this not, in combination with three established risk factors, prompt screening for thrombophilia? If it would– double heterozygosity (factor V Leiden and prothrombin) – would be found. Is this important? Although each heterozygosity itself increases the risk, recent analyses, show double heterozigosity by itself not being a very strong risk factor.[24,25] However, our patient had an additional, only recently recognized as relatively stronger compared to factor V Leiden, but very easily identified genetic risk factor – her blood group was B (non-O).[26] It was recently found that non-O blood group presents further risk in addition to factor V Leiden and prothrombin.[27]

According to present knowledge and guidelines, due to three classical risk factors (obesity, immobilization and smoking) this patient would be considered for prophylaxis with low-molecular-weight heparin.[21] However, most probably she would only receive 7 days of prophylaxis and this would be probably not enough. If her genetic risk factors were known, she would be considered for longer time and higher dose prophylaxis. But–it is estimated that general screening for thrombophilia is not advised.[22,23] Perhaps women with presence of two or more established risk factors in combination with non-O blood group (blood group is known in all pregnant women) represent a group at higher risk, where detailed evaluation of risk and screening for thrombophilia would be justified and would improve chances to prevent such serious cases, as described in this report.

Early diagnosis and treatment of postpartum ovarian vein thrombosis is important to prevent progression of thrombosis with potentially disastrous consequences, but requires a high degree of suspicion, as many other, more straightforward reasons for abdominal pain and fever seem more obvious. Strict evaluation of every woman during pregnancy and at the time of delivery for risk of thrombosis with application of thromboprophylaxis, as required by guidelines, may significantly reduce risk for the occurrence of serious cases and prevent most of them. Perhaps new, only recently recognized genetic risk factor – blood group status, which is easily available, should also be taken into account and used to help detecting women at risk, who would benefit from thrombophilia screening.

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