

The importance of clinical reasoning in the recognition of septic pelvic thrombophlebitis after ruptured ectopic pregnancy: case report

A importância do raciocínio clínico no reconhecimento da tromboflebite pélvica séptica após gestação ectópica rota: relato de caso

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ABSTRACT

Septic Pelvic Thrombophlebitis (SPT) is a potentially fatal complication of pregnancy, being a possible cause of refractory fever during the postpartum period. Early diagnosis reduces morbidity and mortality, but is challenging, because the clinical manifestations and the propaedeutics are nonspecific. Generally, this hypothesis is raised after excluding other more common diseases that must be investigated with caution and critical sense. We describe the case of a 32-year-old patient, secundigravida, obese, diabetic and poorly controlled hypertensive who continued to spike fevers despite antibiotic therapy after a complicated ruptured ectopic pregnancy. Laboratory and imaging tests were nonspecific and the hypothesis of SPT was suggested after treating all the usual infectious foci. After anticoagulation in conjunction with broad-spectrum antibiotic therapy, the patient became afebrile and improved her general condition. We emphasize the importance of clinical reasoning in case management, from investigating differential diagnoses to suspecting and managing SPT.

Keywords: Thrombophlebitis; Fever of unknown origin; postpartum Period; Clinical reasoning; Clinical competence.

RESUMO

A Tromboflebite Pélvica Séptica (TPS) é uma complicação potencialmente fatal da gravidez, sendo uma possível causa de febre refratária durante o puerpério. O diagnóstico precoce reduz a morbimortalidade, mas é desafiador, pois as manifestações clínicas e a propedêutica são inespecíficas. Geralmente, esta hipótese é aventada após a exclusão de outras doenças mais comuns que devem ser investigadas com cautela e senso crítico. Descrevemos o caso de uma paciente de 32 anos, secundigesta, obesa, diabética e hipertensa mal controlada com febre refratária à antibioticoterapia após gestação ectópica rota complicada. Exames laboratoriais e de imagem eram inespecíficos e, após o tratamento de todos os focos infecciosos usuais, suspeitou-se de TPS. Após a anticoagulação, a paciente apresentou achatamento da curva térmica e melhora clínica. Enfatizamos a importância do raciocínio clínico na condução do caso, desde a investigação de diagnósticos diferenciais à suspeita e ao manejo da TPS.

Palavras-chave: Tromboflebite; Febre de causa desconhecida; Período pós-parto; Raciocínio clínico; Competência clínica.

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INTRODUCTION

Septic Pelvic Thrombophlebitis (SPT) is an inflammatory condition that causes the formation of infected thrombi in the pelvic vessels, especially in the ovarian vessels¹. It is considered a rare complication of pregnancy and a possible cause of fever and abdominal pain in the postpartum period². Typically, patients with SPT present non-specific clinical findings and have persistent fever despite antibiotics³. SPT can lead to pulmonary thromboembolism, septic shock, and death⁴.

By the 19th century, SPT was described for the first time by Von Recklinghausen. Later, in the 50s, the disease was elucidated through a cohort of 70 women who had fever after gynecological-obstetric procedures who had palpable intravenous thrombi and/or seropurulent fluid in the pelvis. Initially, ligation of the thrombosed vein was the preferred treatment, although drug therapy became the preference since then. At the beginning of the 20th century, the mortality rate was approximately 50%, mainly due to lack of knowledge about the condition³. Over the years, mortality rates have been declining, but even today, SPT is a hypothesis that is little discussed and rarely considered, even after more likely diagnoses have been excluded. Delay in treatment directly impacts morbidity and mortality, therefore, it is essential to understand when to suspect this clinical entity.

The following report describes the case of a patient who developed persistent and refractory fever after management of a ruptured ectopic pregnancy complicated with hemodynamic instability. The patient had many risk factors for SPT. After adequate treatment of overlapping infections and exclusion of other hypotheses, SPT was considered as a differential diagnosis. We highlight the importance of clinical reasoning in the face of a complex case of a patient in critical condition and with multiple comorbidities.

CASE REPORT

A 32-year-old patient, secundigravida, obese (BMI 40 kg/m²), diabetic and poorly controlled hypertension previously seen in another service with vaginal bleeding and positive beta hCG (2.800 mIU/ml) that was conducted as inevitable pregnancy loss. Upon admission, she presented vomiting, sweating, chills, light vaginal bleeding and tachycardia (125 bpm). During the gynecological examination, it was noted open cervical os and externalization of amorphous material. Uterine curettage was performed without prior imaging examination, with habitual bleeding and no infectious complications. However, the patient progressed with hemodynamic instability and required blood transfusion.

The patient was admitted to the intensive care center of our service presenting tachycardia (165 bpm), tachypnea (35 bpm), and cold extremities. After initial support, the patient was intubated, with a difficult airway, and referred to exploratory laparotomy. It was visualized massive hemoperitoneum due to a ruptured ectopic pregnancy on

the left and a salpingectomy was performed. During the transoperative, two bags of packed red blood cells and 2.5L of crystalloid were administered.

On postoperative day 1, she developed hemodynamic instability and presented a drop in hematimetric levels, requiring norepinephrine and a new blood transfusion. She presented the first record of high fever (39°C) refractory to antipyretics and maintained a high temperature curve in the subsequent days.

Initially, the patient was secretive, with diffuse wheezing on respiratory auscultation. On gynecological examination, the cervix was firm and there was little vaginal discharge. The operative wound was showing serous drainage, without phlogosis. Profuse watery diarrhea. The patient still had profuse watery diarrhea.

Furthermore, she presented leukocytosis without deviation and elevated C-reactive protein (CRP), but both parameters were stable. Liver function tests, transaminases and canalicular enzymes were unremarkable. Fibrinogen of 39 mg/dL. Fluorescent antinuclear antibody (FANA) and rheumatoid factor were non-reactive, erythrocyte sedimentation rate (ESR) was normal, complements proteins C3 and C4 were also normal. Negative serologies and blood cultures. Tracheal aspirate culture with *Acinetobacter* growth. Urine culture showed growth of 100,000 CFU/mL of *Candida albicans*. *Clostridium* toxins A and B were negative.

The use of imaging diagnostic tools was limited and difficult to perform due to obesity. Even so, pelvic ultrasound (USG) revealed a heterogeneous image in the right adnexal region to be clarified. The computed tomography (CT) of the chest showed consolidation in the right lung base and the CT of the abdomen showed a small amount of fluid in the abdominal cavity, without collections.

Throughout the entire hospitalization, the patient used: Clindamycin, Ceftriaxone, Piperacillin + Tazobactam, Doxycycline, Meropenem, Vancomycin, Metronidazole, Polymyxin B, Fluconazole, and Miconazole.

Despite treatment of all the usual infectious foci, the patient maintained a continuous and refractory fever. Faced with fever of undetermined origin in the context of postoperative pelvic surgery with consumed fibrinogen, the hypothesis of TPS was raised. Therapeutic anticoagulation was started in conjunction with broad-spectrum antibiotic therapy and the patient became afebrile and her general condition improved.

DISCUSSION

EPIDEMIOLOGY

SPT is a rare pregnancy complication. In the United States, it is estimated to occur in approximately 0.03% of peripartum women; 98% of cases occurring after cesarean sections. Other relevant risk factors include: endometritis, chorioamnionitis, pre-eclampsia, multiparity, maternal age <20 years, black race, obesity, peripartum blood transfusion¹,

and body mass index $> 25 \text{ kg/m}^2$. The right ovarian vein is the most commonly affected⁴. In the present case report, the patient presents more than one risk factor, reinforcing the diagnostic hypothesis.

SPT has been reported more rarely in non-pregnant women and men. In these cases, the condition is often associated with other pelvic infections (pelvic inflammatory disease, for instance), pelvic surgery, uterine fibroids, hormonal stimulation with gonadotropins, and underlying malignancy^{6,9}. SPT occurs in a context of pelvic vein endothelial damage, venous stasis, and hypercoagulability. This pathogenesis will be elucidated in detail below.

PATHOGENESIS

Physiological changes in the maternal organism during pregnancy and postpartum predispose to thrombus formation, resulting in an increased risk of SPT. The mechanism can be explained by Virchow's Triad, composed of three changes that lead to a thrombogenic state: abnormal blood flow (stasis or turbulence), endothelial injury, and blood hypercoagulability¹⁰. During pregnancy, stasis is caused by a collapse of the pelvic veins due to uterine dextrorotation, dilation of the ovarian vein, and increased blood volume¹¹. The retrograde ovarian venous flow (from left to right) resulting from these changes explains why thrombus formation is more frequent on the right side^{12,14}.

In addition, due to the greater blood flow, blood turbulence favors endothelial damage. This intravascular vessel wall damage is aggravated in infectious or traumatic contexts (surgery or intrapartum trauma). In itself, pregnancy is a state of hypercoagulability, due to changes in platelet adhesion and clotting factors caused by hormonal changes. Therefore, there is a thrombogenic environment in the ovarian vasculature during and after the gestational period¹⁰.

CLINICAL FINDINGS

Patients with SPT can present two spectrums of the same disease: ovarian vein thrombophlebitis (OVT) and deep septic pelvic thrombophlebitis (DSPT)¹⁰.

Postpartum women with OVT manifest an acute illness, with fever and abdominal pain within a week after delivery or pelvic surgery^{14,16}. Gastrointestinal symptoms such as nausea and ileus may occur, but they are usually mild. The pelvis is sensitive to palpation and, rarely, a tender rope-shaped mass extending from the uterus to the superolateral region of the abdomen is palpated. In general, the diagnosis is made by visualizing the obstructed ovarian vein in the CT scan¹⁰.

On the other hand, patients with DSPT present the later form of the disease, with high fever usually three weeks after delivery or surgery. It is important to highlight that abdominal pain may be minimal or absent and fever may be the only symptom^{17,19}. Imaging diagnosis is difficult, once a thrombosis of a specific vein is not normally identified. The suspicion begins due to the persistence of the fever, despite adequate antibiotic therapy for the supposed infection

(endometritis or other pelvic infection, for example). In many cases, the diagnosis is only made after a good clinical response to empirical anticoagulation¹⁰.

DIAGNOSTIC APPROACH

Clinical suspicion of SPT should be raised in patients who present with persistent fever lasting at least three to five days, despite antibiotic therapy, and without evidence of abscess after vaginal delivery, cesarean or pelvic surgery¹⁰. During physical examination, pelvic and pouch of Douglas sensitivity should be assessed. Masses may or may not be palpated. The presence of a cord extending centrally from the uterus to the superolateral part of the abdomen increases the suspicion of TPS, however it is an uncommon finding. Anamnesis should not be neglected and, in most cases, imaging tools will be necessary to evaluate other possible diagnoses.

Basic laboratory tests for the initial evaluation of postpartum fever include a complete blood count, urine summary, and urine and blood cultures. Although blood cultures are often negative, positive results may lead to an alternative diagnosis and/or guide antimicrobial therapy. The microbiology is not yet well defined, but in general it reflects a spectrum similar to that of other pelvic infections and includes streptococci, *Enterobacteriaceae*, and anaerobes. Leukocytosis greater than 12,000/microL occurs in 70 to 100% of patients, although it is not a specific finding and can also be observed in the uncomplicated postpartum period^{14,15}.

Unless the initial evaluation reveals an obvious cause for the fever, it is recommended to request pelvic CT or magnetic resonance imaging (MRI) with contrast. There is no consensus regarding the ideal imaging test, but it is certain that pelvic USG is limited for diagnosing TPS. Pelvic CT and MRI are useful for identifying OVT, however, a negative imaging study cannot exclude DSPT as the deep pelvic vessels are not well visualized^{20,22}. There are typical tomographic findings associated with TPS, such as an enlarged thrombosed vein and a filling defect in the vessel lumen^{23,26}. On MRI, thrombosed vessels appear bright^{26,27}.

Therefore, the case should be treated as a possible SPT when the patient presents with persistent fever after vaginal birth, cesarean section or pelvic surgery, despite antibiotic therapy (for presumed endometritis, for example), excluding other apparent causes. Anticoagulation should be started even if no thrombus is identified on imaging tests. The diagnosis of SPT can then be presumed if the fever resolves within 48 hours after empiric systemic anticoagulation^{14,15,17,19,28,30}.

TREATMENT

Surgical excision or ligation of the thrombosed vein was the preferred treatment in the past. However, currently, antibiotic therapy combined with systemic anticoagulation has become the first-line approach^{32,34}.

Although there are no well-defined recommendations on antibiotic therapy, it is suggested a parenteral regimen that covers streptococci, *Enterobacteriaceae*, and anaerobes,

that is, similar to that for intra-abdominal infections in general. Commonly, patients are already using Gentamicin with Clindamycin or Ampicillin-Sulbactam, for example, to treat endometritis or other presumed pelvic infections involving the same microbial spectrum. If it is impossible to use beta-lactams, alternative regimens include fluoroquinolone (Ciprofloxacin or Levofloxacin) with Metronidazole^{3,15,17,19,35,36}.

In turn, anticoagulation prevents the formation of new thrombi and reduces the risk of septic embolism. Initial anticoagulation is performed with unfractionated heparin (UFH) or low molecular weight heparin (LMWH), according to the doctor's preferences and depending on the patient. The standard dosage of UFH for treatment of SPT is an initial bolus of 5,000 units followed by continuous infusion of 16 to 18 units/kg for a goal partial thromboplastin time (PTT) of 1.5 to 2.0 times the patient's baseline value. The dosage of LMWH is standard, for example, Enoxaparin 1 mg/kg subcutaneously every 12 hours. The ideal duration is also uncertain and should be individualized, and may even be guided by tomographic study^{3,15,17,19,35,36}.

CONCLUSION

Although uncommon, the hypothesis of TPS should be considered in the case of puerperal fever of undetermined origin refractory to antibiotic therapy. The clinical manifestations are varied and can be less exuberant, mainly in a serious context, and the propaedeutics is nonspecific. Therefore, critical and evidence-based judgment must guide the case from the investigation of possible differential diagnoses to the suspicion and management of TPS. We emphasize that valuing clinical history can avoid delays in treatment and improve outcomes. We hope that this report illustrates the importance of clinical reasoning in the face of a complex case in which the propaedeutics was not very informative.

AUTHORS' CONTRIBUTION

We describe contributions to the papers using the taxonomy (CRediT) provided below: *Conceptualization, Investigation, Methodology, Visualization & Writing – review & editing*: Isadora Bevilaqua Fernandes Hosken; Gabriela Santos Soares. *Project administration, Supervision & Writing – original draft*: Isadora Bevilaqua Fernandes Hosken; Gabriela Santos Soares; Marta Luisa Palomero Bueno. *Data curation & Formal Analysis*: Marta Luisa Palomero Bueno.

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