

# Ovarian Vein Thrombosis in Two Postpartum Women

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Ovarian vein thrombosis is an uncommon condition that has been estimated to occur in 500 to 2000 postpartum women.<sup>1,2</sup> This condition is classically a puerperal process, but it may also arise in nonpuerperal settings such as endometritis, pelvic inflammatory disease, malignancy, thrombophilia, inflammatory bowel disease, and pelvic and gynecologic surgeries.<sup>3-5</sup> Complications of ovarian vein thrombosis most frequently occur in the postpartum period, the most serious being systemic sepsis and pulmonary embolism. Up to one third of postpartum cases may result in pulmonary embolism, and mortality estimates approach 5%.<sup>6</sup> Ovarian vein thrombosis often has a vague and variable presentation, and a high index of suspicion is required to make the diagnosis. This article presents a case of concurrent postpartum ovarian vein thrombosis and retroperitoneal hematoma, the first described in the literature to our knowledge, as well as a second case of postpartum septic ovarian vein thrombophlebitis complicated by pulmonary embolism. A review of this disorder, including presentation in the nonpuerperal setting, diagnosis, association with hematologic disorders, and treatment controversies, is also provided.

## CASE 1

### Initial Presentation and History

A 24-year-old G2 P2002 woman reported right-sided abdominal pain approximately 12 hours after delivery. Labor had been induced at 41 weeks' gestation with dinoprostone and oxytocin. After induction, the patient progressed to an uncomplicated vaginal delivery of a 6-lb 10-oz boy. She was a nonsmoker and had no significant past medical, surgical, or family history.

### Clinical Evaluation

On physical examination, the patient demonstrated a minimal amount of vague lower abdominal pain with a

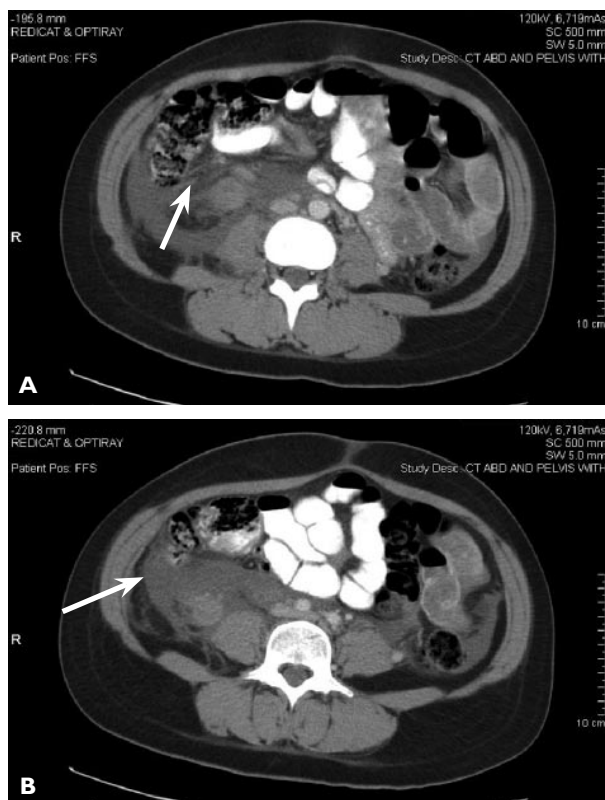
temperature of 101.1°F, leukocytosis of 12,500 cells/ $\mu$ L (normal, 4500–11,000 cells/ $\mu$ L), and a hemoglobin level of 11.7 g/dL (normal, 14.0–17.0 g/dL). The patient was observed during the night, and when her pain did not resolve the next morning, abdominal computed tomography (CT) with intravenous contrast was ordered to evaluate for a surgical source for her persistent pain, such as appendicitis. This scan revealed a large right-sided retroperitoneal hematoma and right ovarian vein thrombosis (Figure 1).

### Management

The patient could not be started on anticoagulation therapy for ovarian vein thrombus due to the concurrent retroperitoneal hematoma. After discussing the potential risk for pulmonary embolism from the ovarian vein thrombus, she elected to have a nonremovable inferior vena cava filter placed. During hospitalization, the patient's hemoglobin level decreased to 10.2 g/dL but stabilized without the need for blood product transfusion. A full hematologic evaluation for hypercoagulable disorders and disorders of both bleeding and clotting was pursued. The only laboratory abnormality revealed was a heterozygous methylenetetrahydrofolate reductase (MTHFR) allele. Although her homocysteine level was normal, a consulting hematologist recommended folic acid supplementation due to the heterozygosity of the MTHFR allele. Three months following discharge, the patient reported intermittent abdominal pain at clinical follow-up. Surveillance abdominal CT scan demonstrated near resolution of

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**Figure 1.** Abdominal computed tomography scan of patient 1 demonstrating (A) retroperitoneal hematoma (arrow) and (B) ovarian vein thrombus (arrow).

the retroperitoneal hematoma but persistence of the ovarian vein thrombus (Figure 2). Because the patient continued to have intermittent abdominal discomfort, anticoagulation therapy was instituted for the persistent ovarian vein thrombosis after the retroperitoneal hematoma had completely resolved. At 6 months postpartum, the patient had experienced nearly complete resolution of her symptoms.

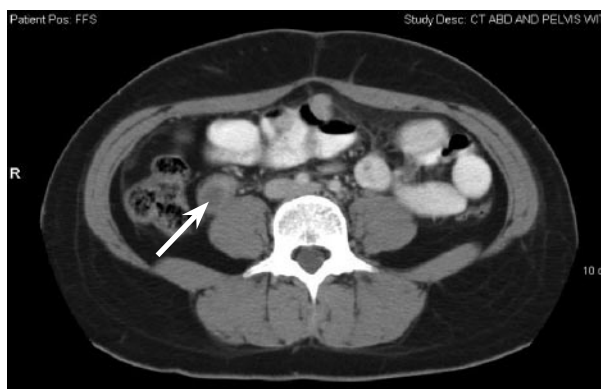
## CASE 2

### Initial Presentation and History

A 36-year-old G3 P3003 woman presented to the emergency department complaining of cough, minor hemoptysis, malaise, and a temperature of 104°F. She was 5 days postpartum from an uncomplicated term vaginal delivery. She was a nonsmoker who had no significant past medical, surgical, or family history.

### Clinical Evaluation

The patient's physical examination was remarkable for tachycardia to 105 bpm, an oxygen saturation of 95% on 2 L oxygen supplementation via nasal can-



**Figure 2.** Abdominal computed tomography scan of patient 1 demonstrating resolution of retroperitoneal hematoma and organized ovarian vein thrombus (arrow).

nula, clear lungs, and abdomen that was minimally tender to palpation in the deep pelvis. A pelvic examination performed by the obstetrician revealed a nontender uterus and normal brown-red lochia. The white blood cell count was 15,700 cells/ $\mu$ L. The presence of hemoptysis raised concern about the possibility of pulmonary embolism, and a spiral CT scan of the chest confirmed a right lower lobe pulmonary embolism (Figure 3). Doppler ultrasound of the legs did not reveal deep venous thrombosis. Additional evaluation with an abdominopelvic CT was then obtained, which demonstrated right ovarian vein thrombosis.

### Management

Anticoagulation therapy with heparin was initiated along with intravenous antibiotics for pulmonary embolism and systemic sepsis resulting from the right ovarian vein thrombosis. The patient's leukocytosis and fever resolved after 48 hours of intravenous antibiotic therapy. A hypercoagulability work-up revealed no abnormalities. Heparin was discontinued, and a 6-month course of oral warfarin was initiated. The patient was discharged home 2 days later in good condition. At follow-up 6 months later, she had not experienced recurrence of her symptoms while being maintained on therapeutic anticoagulation.

### DISCUSSION

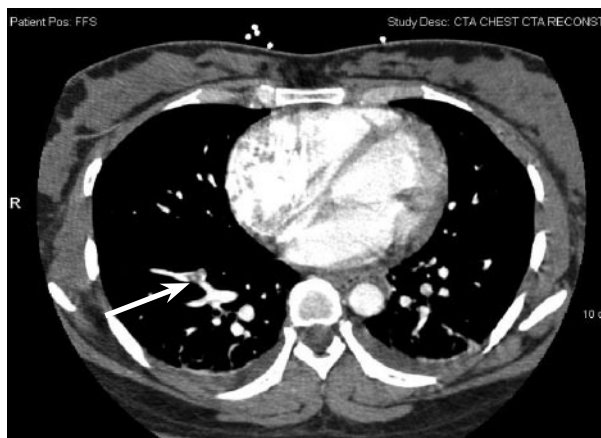
The first case reported in this article was notable for the concurrent presentation of ovarian vein thrombosis and retroperitoneal hematoma, which altered the patient's management as anticoagulation was not appropriate in the setting of bleeding. Thrombosis accompanied by bleeding might result from several etiologies, including acquired or hereditary coagulation

disorders, use of oxytocin and dinoprostone for inducing labor, or the trauma of labor itself.

Disseminated intravascular coagulation (DIC) is an acquired disorder that manifests as diffuse systemic bleeding coupled with microvascular thrombosis. Patients in gram-negative septic shock or who have suffered severe trauma or massive blood transfusions are at risk for DIC. DIC can occur during pregnancy and may be precipitated by severe preeclampsia, intrauterine death with retained fetus, placenta abruption, or amniotic fluid embolism.<sup>7</sup> In addition, either bleeding or thrombosis may occur in the chronic myeloproliferative disorders (essential thrombocythemia, polycythemia rubra vera, myelofibrosis, and chronic myelogenous leukemia) as a result of abnormal platelet function.<sup>8</sup> Finally, dysfibrinogenemia and paroxysmal nocturnal hemoglobinuria (PNH) are 2 rare congenital disorders that should be considered in the setting of bleeding and thrombosis. Dysfibrinogenemia is an autosomal dominant inherited abnormality of fibrinogen that results in defective clot formation and bleeding. Abnormal thrombin time and reptilase time tests are indicative of dysfibrinogenemia.<sup>9</sup> PNH manifests with red blood cell breakdown and hemoglobin release in the urine; the classic triad of symptoms is hemolytic anemia, pancytopenia, and thrombosis.<sup>10</sup> A defect of the glycoprophosphatidylinositol-anchored cell membrane protein in bone marrow stem cells results in increased red cell sensitivity to complement, thereby increasing intravascular hemolysis. Pregnancy in patients with PNH is considered very high risk, with a maternal mortality rate of up to 10%, mostly secondary to thromboembolic events, and a significant risk of fetal wasting or prematurity.<sup>11</sup>

Dinoprostone, which contains prostaglandin E<sub>2</sub>, results in cervical thinning and dilation as well as uterine contraction and may have smooth muscle-induced vasodilatory effects. Dinoprostone may be useful in controlling postpartum hemorrhage, which theoretically could have caused thrombosis in this patient, but a definitive association with thrombosis has not been described.<sup>12</sup> Oxytocin may be used to stimulate uterine smooth muscle contraction via release of intracellular calcium and is also used to control postpartum hemorrhage through uterine contraction. Oxytocin has been shown to cause afibrinogenemia, potentially resulting in increased blood loss during labor.<sup>13</sup> It is possible that the administration of oxytocin in case patient 1 contributed to the development of her retroperitoneal hematoma.

The process of vaginal delivery itself may result in both hemorrhagic and thrombotic states. Postpartum hemorrhage can be caused by uterine atony, lacera-



**Figure 3.** Chest computed tomography scan of patient 2 demonstrating right lower lobe segmental pulmonary embolism (arrow).

tions, retained products of conception, uterine rupture, and hereditary coagulopathies.<sup>14</sup> Initially, labor trauma is a bleeding state, but in patients who are resuscitated with blood products and medications such as dinoprostone, DIC with vascular thrombosis can result.

Patient 2 was diagnosed with pulmonary embolism caused by ovarian vein thrombosis. Differentiating between septic pelvic thrombophlebitis and ovarian vein thrombosis is difficult, with some considering these entities to be part of a clinical spectrum of symptomatology. Septic pelvic thrombophlebitis typically involves small caliber pelvic veins but can progress to larger named veins with signs of sepsis, whereas ovarian vein thrombosis is progression of the clot to the larger ovarian veins, with or without sepsis.<sup>15</sup>

### OVARIAN VEIN THROMBOSIS

Pregnancy is a hypercoagulable state in which there is increased platelet adhesion and decreased fibrinolysis coupled with increasing levels of factors I, II, VII, VIII, IX, and X.<sup>1</sup> Erythrocyte mass increases approximately 20% to 30%, while plasma volume increases by 40% to 50%. This relatively hemodilutional state during pregnancy serves to limit maternal blood loss at delivery.<sup>16</sup> In addition, these changes along with relative venous stasis at the vena cava due to uterine compression can predispose pregnant women to thromboembolism.

### Presentation

Classically, ovarian vein thrombosis arises in the first 7 days postpartum.<sup>1</sup> In the postpartum period, up to 80% of patients will present with fever, but only half will experience right lower quadrant abdominal pain.<sup>17</sup> Importantly, many patients will have nonspecific symptoms,

including malaise, vague diffuse abdominal pain, or shortness of breath. In rare cases, a mass may be palpable, but this is an unusual finding.<sup>1,2,15,17</sup> Other conditions associated with ovarian vein thrombosis include endometritis, pelvic inflammatory disease, malignancy, inflammatory bowel disease, and pelvic surgery.<sup>2</sup> Symptoms are similar in the nonpuerperal setting, but many patients may be asymptomatic with findings of ovarian vein thrombosis noted incidentally on imaging conducted for other conditions.<sup>3–5</sup>

Up to 90% of cases involve thrombosis of the right ovarian vein.<sup>18</sup> Several physiologic and anatomic factors predispose the right vein ovarian to thrombosis. During pregnancy, the diameter of the ovarian vessels increases due to increased blood flow and hormonal changes, resulting in substantially increased pressure on both the vessel walls and the valves within the veins. This increased pressure at the valves results in venous incompetence, compounding venous stasis in the pelvis.<sup>19</sup> In addition, the gravid uterus may undergo physiologic dextrorotation, potentially compressing the already engorged right ovarian vein. Also, the right ovarian vein enters the inferior vena cava at an acute angle, making it more susceptible to compression, whereas the left typically enters the left renal vein at a right angle. Finally, in the postpartum period, blood flow in the right ovarian vein is antegrade as compared with retrograde in the left vein, potentially predisposing to right-sided thrombosis.<sup>3,15</sup>

### **Diagnostic Imaging**

A high index of suspicion for ovarian vein thrombosis is needed to establish the diagnosis, regardless of the setting. Abdominopelvic CT scan with intravenous contrast has a sensitivity and specificity nearing 100% in some studies and should be considered the initial investigative step because it is readily obtainable and is more cost-effective than magnetic resonance imaging (MRI).<sup>20–22</sup> On CT, differentiation of the thrombosed ovarian vein from the appendix can be difficult; visualization of a tubular retroperitoneal mass with central low attenuation extending cephalad to the inferior vena cava is characteristic of ovarian vein thrombosis.<sup>23</sup> The accuracy of ultrasound in confirming the diagnosis of ovarian vein thrombosis is highly operator dependent, which should limit its role in obtaining the initial diagnosis.<sup>21,22</sup> Additionally, overlying bowel gas may limit visualization in ultrasound, which oftentimes causes the operator to confuse ovarian vein thrombosis with the appendix or hydroureter.<sup>21</sup> However, ultrasound may have a role for follow-up imaging in patients previously diagnosed with the condition. MRI can provide additional information in patients with a strong clinical sus-

picion for the diagnosis but equivocal CT findings or in patients with a contrast dye allergy.<sup>20,21</sup> In 1 study, magnetic resonance angiography was found to have 100% sensitivity and specificity for diagnosing ovarian vein thrombosis in patients with inconclusive initial studies, superior to ultrasound and CT.<sup>22</sup>

### **Risk for Complications**

The risk for developing complications of ovarian vein thrombosis correlates with the clinical setting in which the condition arises. In a small review involving 6 patients diagnosed with ovarian vein thrombosis in the setting of a malignant solid tumor, none developed pulmonary embolism or localized abdominal pain.<sup>3</sup> Additionally, this study showed that several patients had resolution of the ovarian vein thrombosis during follow-up without anticoagulation therapy. A second study revealed that 40 out of 50 patients (80%) undergoing total abdominal hysterectomy with bilateral salpingo-oophorectomy and retroperitoneal lymph node dissection for carcinoma had documented ovarian vein thrombosis on postoperative surveillance CT scanning.<sup>4</sup> None of these patients had abdominal or pulmonary symptoms to suggest any complications from the ovarian vein thrombus, and none were treated with anticoagulation. Furthermore, a small study that included both male and female patients found that the development of gonadal vein thrombosis after diverticulitis, inflammatory bowel disease, perforated appendicitis, and pseudomembranous colitis more commonly occurred on the left side.<sup>5</sup> Although the body of literature is still quite small, it appears that in the setting of malignancy or recent pelvic surgery, observation of ovarian vein thrombosis on either side without anticoagulation is appropriate.

Complications of ovarian vein thrombosis are more common in the postpartum period. Extension of the clot into the inferior vena cava or renal veins, acute ureteral obstruction, sepsis, pulmonary embolism, and death have been documented as a consequence of the ovarian vein thrombosis in the postpartum period.<sup>2,15,24–28</sup> The incidence of pulmonary embolism after puerperal ovarian vein thrombosis varies widely, ranging from 0%<sup>28</sup> to 33%<sup>6</sup> in the highest reports, with a resultant mortality rate up to 4%.<sup>25,26</sup>

### **Treatment**

There is no clear consensus in the literature regarding optimal treatment of this condition. A small randomized study demonstrated no episodes of pulmonary embolism and no outcome differences among 14 women diagnosed with septic pelvic thrombophlebitis who were randomized to intravenous antibiotics alone

(n = 8) or intravenous antibiotics plus heparin (n = 6).<sup>29</sup> However, because of the increased risk of a potentially lethal pulmonary embolism, most reviews support treatment of postpartum ovarian vein thrombosis with intravenous anticoagulation.<sup>25,28,30,31</sup> Most patients will present with fever, and antibiotic therapy is typically initiated for the presumptive diagnosis of endometritis, prior to securing the true diagnosis of ovarian vein thrombosis.

The duration of anticoagulation therapy is controversial. Resolution of ovarian vein thrombosis has been documented after only 7 to 14 days of therapy.<sup>31</sup> Others have shown that ovarian vein thrombosis may not resolve with short anticoagulation therapy, and 3 to 6 months of anticoagulation is indicated until there is radiologically confirmed resolution of the thrombus.<sup>28,30</sup>

An association of puerperal ovarian vein thrombosis with inherited hypercoagulability disorders has been noted, which may predispose these patients to ovarian vein thrombosis. Puerperal ovarian vein thrombosis remains an uncommon condition, and most patients will not have a heritable coagulation disorder; given the ease of testing and serious consequences if hereditary disorders are missed, some have recommended screening for these conditions.<sup>1,27,28</sup>

## CONCLUSION

Although ovarian vein thrombosis is uncommon, it should be included in the differential diagnosis for postpartum women presenting with vague symptoms given the potentially fatal outcome associated with this condition. The case patients demonstrate 2 different presentations of postpartum ovarian vein thrombosis: a complex case with concurrent retroperitoneal hematoma treated with inferior vena cava filter placement, and a case of septic ovarian vein thrombosis resulting in pulmonary embolism that was successfully treated with anticoagulation. The published literature clearly indicates that complications such as pulmonary embolism, sepsis, and thrombus extension are more likely to occur in the puerperal setting and thus seems to support use of anticoagulation therapy, given the difficulties in predicting the development of these complications. The evaluation for congenital hypercoagulable disorders appears warranted in this setting, even though pregnancy itself is a hypercoagulable state. **HP**

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