

## Deep Vein Thrombosis in the Second Trimester of Pregnancy: A Case Report and Literature Review

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### ABSTRACT

**Introduction:** Deep vein thrombosis (DVT) is diagnosed in about 1 in every 500 to 2000 pregnancies. Pregnancy increases the risk of pulmonary embolism (DVT), a leading cause of maternal deaths and fetal death. Several risk factors include advanced age, multiple pregnancies, lower limb varicose veins, and obesity.

**Clinical case:** A 21-year-old with a 26-week pregnancy experienced sudden pain in her lower left limb, causing increased volume and difficulty walking. Doppler ultrasound revealed thrombosis in the common and deep femoral veins, thrombophlebitis of the great saphenous vein, and soft tissue edema. A multidisciplinary approach was employed.

**Discussion:** Deep vein thrombosis (DVT) is a thromboembolic disease in pregnancy, affecting up to 50% of cases. Diagnosis involves high clinical suspicion, risk factors, time of gestation, venous Doppler ultrasound images, and D-dimer test. Treatment should be based on a comprehensive evaluation, considering thrombophilia type, history of DVT, and family history.

**Conclusion:** Early identification, biomarker use, and education about DVT symptoms are crucial for optimal treatment and preventing complications.

**KEYWORDS:** Deep vein thrombosis, pregnancy, fetal death, doppler ultrasound, deep femoral veins, D-dimer test, biomarker, treatment.

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### INTRODUCTION

Deep vein thrombosis (DVT) is diagnosed in about 1 in every 500 to 2000 pregnancies; pregnant or postpartum women have a four- to five-fold higher risk of embolism than non-pregnant women. <sup>(1, 2)</sup>

Approximately 80% of thromboembolic events in pregnancy are venous, with a prevalence of 0.5-2.0 per 1,000 pregnant women. <sup>(3)</sup> Based on data from the Pregnancy Mortality Monitoring System conducted by the Centers for Disease Control and Prevention (CDC) between 2017 and

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2019, thrombotic pulmonary embolism or other embolism contributed to 10.5% of all pregnancy-related deaths. <sup>(4)</sup>

Pulmonary embolism is the second leading cause of death in the fetus and is the cause of 20% of maternal deaths. <sup>(5)</sup> DVT in pregnant women occurs at the ileo-femoral level, unlike non-pregnant women, whose usual presentation is popliteal-femoral. <sup>(2, 5)</sup>

Risk factors include age > 35 years, multiple pregnancies, lower limb varices, inflammatory bowel disease, urinary tract infection, diabetes, hospitalization for non-obstetric reasons (>3 days), and body mass index (BMI) 30 kg/m<sup>2</sup>. <sup>(6)</sup> The most important risk factor for a pregnant woman to suffer a thrombotic event is having experienced one previously, and the next most notable risk factor is suffering from thrombophilia. <sup>(7)</sup>

On the other hand, during pregnancy and the postpartum phase, the Virchow triad (venous stasis, endothelial injury, and hypercoagulability) becomes more pronounced. <sup>(1, 7)</sup>

Pregnancy conditions a state of hypercoagulability by progressive increase in several coagulation factors, including factors I, II, VII, VIII, IX, and X, while protein S and fibrinolytic activity levels decrease. <sup>(7)</sup>

In addition, there is an increased venous stasis in the lower extremities due to venous compression caused by the pregnant uterus. <sup>(6)</sup> All of this promotes a greater susceptibility to thrombus formation during pregnancy and the puerperal period. <sup>(8)</sup>

### CLINICAL CASE.

A 21-year-old female, with a 26-week pregnancy, Mexican, without chronic diseases or allergies; with a history of anorectal malformation at birth, resolved by postnatal colostomy and sagittal anorectoplasty, who went to the emergency obstetric service because of a sudden pain of moderate intensity in the lower left limb, initially located at the left inguinal region and later extended to the left leg, as well as increased volume and difficulty for walking; with a clinical picture of 8 hours of evolution.

The diagnosis of venous thromboembolism during pregnancy is a challenge because the classic symptoms are less specific during this state than in non-pregnant women. <sup>(9)</sup> Normal symptoms during pregnancy that may simulate thromboembolic disease include leg pain, edema or swelling, dyspnea, tachypnea, tachycardia, and palpitations. <sup>(1,9)</sup>

There is still much controversy regarding medical and surgical treatment in pregnancy; for example, the use of non-fractional heparin (HNF) has been suggested in initial management since it allows rapid reversal of anticoagulation. <sup>(8)</sup>

Other authors recommend using low molecular weight heparins because they have a half-life of 4 to 5 hours, are not associated with fetal adverse effects, have greater activity against factor Xa, and bind less to plasma proteins, endothelial cells, and macrophages; increasing their bioavailability, half-life and anticoagulant activity. <sup>(9)</sup>

In this document, we present the case of a 21-year-old female, 26 weeks pregnant, with no history of chronic diseases or allergies, with a history of anorectal malformation corrected at birth, who went to the emergency department for sudden pain in the lower left limb, with swelling and difficulty walking, establishing diagnosis of deep venous thrombosis, receiving appropriate treatment. The objective of this case is to conduct a review of the published literature on the current diagnosis and treatment of DVT in pregnant patients.

At physical examination, the patient was oriented, hemodynamically stable, without respiratory distress, with a fetal heart rate of 134 beats per minute, without cervical dilatation. The right lower limb was measured: thigh 54 cm, calf 30 cm, ankle 19 cm, with peripheral pulses present and normal temperature. The left lower limb had a significant increase in volume: thigh 58 cm, calf 37 cm, ankle 22 cm; with peripheral pulses decreased and capillary filling delayed and, a positive Homans sign [**Image 1**].



**Image 1. Left lower limb with deep vein thrombosis. There is a marked increase in volume and circumference compared to the right lower limb, plus edema. These clinical findings are indicative of a possible venous obstruction.**

Laboratory studies reported: hemoglobin 12.4 g/dl, hematocrit 36.7%, platelets 275,000/ mcL, D-dimer >10,000 ng/ml, fibrinogen 368.5 mg/dl, TP 12.2 seg, INR 1.08, TTP 21.3 seg, procalcitonin 0.24 ng/mL, PCR of 48 mg/L. Glucose of 94 mg/dl, creatinine of 0.5 mg/dl, liver profile, and serum electrolytes without alteration. Antiphospholipid antibodies, anti-DNA, ANA and ANCA, were negative.

The venous doppler ultrasound on the left lower limb indicated a thrombosis in the common and deep femoral veins, thrombophlebitis of the great safenic vein, and soft tissue edema. The same image study was carried out the following week, with no significant changes compared to the previous report.

The patient was assessed by the angiology and internal medicine team. They recommended management with enoxaparin at a dosage of 60 mg SC every 12 hours and the use of elastic compression stockings with a pressure of 15-20 mmHg. At that time, there were no clinical signs of pulmonary thromboembolism, and the patient was not considered a candidate for vascular surgery due to the absence of phlegmasia.

During hospitalization, the patient had a proper evolution, with a final quantification of D-dimer of 4323.71 ng/ml, consequently, hospital discharge was decided two weeks after admission [Image 2].



**Image 2. Clinical improvement in the patient's left lower limb was observed after one week of treatment.**

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The patient was readmitted to the obstetrics department at 39 weeks of pregnancy. She was in the latent phase of labor and exhibited a cephalopelvic disproportion. During the examination, fecal impaction was noted, with the dilated rectum palpated against the posterior wall of the vagina, obstructing the vaginal canal.

Due to the history of anorectal malformation, the decision was made to terminate the pregnancy through an abdominal procedure, suspending low molecular weight heparin upon

### DISCUSSION

Deep vein thrombosis (DVT) is part of a group of thromboembolic diseases of pregnancy, which include pulmonary embolism.<sup>(7)</sup> Pregnancy, as mentioned above is a physiological state that increases the risk of thrombosis.<sup>(3, 6)</sup>

In this case, the patient presented with acute symptoms of pain and edema in the left lower limb, along with physical findings and laboratory studies that confirmed the presence of DVT, which is consistent with the literature documenting the frequency of this condition in pregnant women.<sup>(1, 8, 10)</sup>

The venous flow rate is reduced in the legs at 25 - 29 weeks of gestation and lasts up to 6 weeks after delivery.<sup>(6)</sup> Up to 50% of venous thromboembolism (VTE) in pregnant women is associated with inherited or acquired thrombophilia, and antiphospholipid syndrome must be ruled out, which causes about 20% of cases of deep venous thrombosis, with or without pulmonary thromboembolism.<sup>(6, 8)</sup>

While autoimmune factors like antiphospholipid antibodies and hematological changes that could increase thrombotic risk were not detected, the hypercoagulability associated with pregnancy and potential anatomical sequelae plays a crucial role in the development of deep vein thrombosis (DVT) in this patient.

The diagnosis includes a high clinical suspicion, considering risk factors and the time of gestation, venous Doppler ultrasound images, and a D-dimer test.<sup>(2, 8, 9)</sup>

In a study of 60 pregnant patients with a first episode of DVT, almost all (97%) had isolated DVT in the left lower limb; only two patients had bilateral DVT.<sup>(12)</sup> In another retrospective study involving 96 pregnant patients with DVT, in which the affected side was known, 88% had left-side DVT.<sup>(13)</sup> This surprising distribution has been attributed to an increase in venous stasis in the left leg related to compression of the left iliac vein by the right iliac artery, together with compression of the inferior vena cava by the pregnant uterus.<sup>(6)</sup>

On the other hand, D-dimer becomes less useful with gestational age and many patients will still require ultrasound.<sup>(13)</sup> D-Dimer levels increase during a normal pregnancy and slowly decrease after delivery, making D-Dimer less specific than in non-pregnant patients, particularly when traditional cut-off values are used, for example, <500 ng/mL.<sup>(13,14)</sup>

admission. A male newborn was delivered, weighing 2,430 grams and measuring 48 centimeters, with an APGAR score of 8/9 and a Capurro assessment indicating 39 weeks of gestation. Post-surgical bleeding was quantified at 400 milliliters.

The patient was discharged 48 hours after surgery without complications and was prescribed low molecular weight heparin treatment for an additional 6 weeks.

There is currently no universally accepted pregnancy-adjusted reference range or a single cut-off limit for D-dimer levels.<sup>(14)</sup> Preliminary data suggest that using higher cut-off values for D-dimer may maintain a high sensitivity (80-100%) and improve specificity (62-79%) for diagnosing deep vein thrombosis (DVT), however, further studies are necessary before this approach can be routinely implemented.<sup>(8, 13)</sup> Until more definitive data establish an ideal cut-off value, we will continue to use the traditional cut-off value of 500 ng/mL.<sup>(8)</sup>

In this case, the laboratory findings indicated a high D-dimer level (>10,000 ng/mL), which was consistent with an acute thrombotic process. The significant elevation, along with clinical and imaging findings, provided conclusive evidence.

The diagnosis of deep vein thrombosis (DVT) during pregnancy and the postpartum period is determined by performing a compression ultrasound.<sup>(6)</sup> This involves assessing the compressibility of the proximal veins or calf; a lack of compressibility indicates thrombosis in these areas. Additionally, poor blood flow observed in Doppler images of the femoral-iliac vein suggests iliac vein thrombosis.<sup>(6)</sup>

These are considered the first-line techniques in suspected DVT, however, the sensitivity and specificity of Doppler ultrasound alone in confirming or excluding iliac vein thrombosis are not well-established and have not been rigorously evaluated.<sup>(8)</sup>

Therefore, if Doppler ultrasound suggests the possibility of iliac vein thrombosis, treatment should be initiated.<sup>(8)</sup> When considering treatment, the decision to use anticoagulant therapy for the prevention of thromboembolic disease in pregnant women should be based on a comprehensive evaluation that should consider the type of thrombophilia, any history of deep vein thrombosis (DVT) or pulmonary embolism, and the family history of thromboembolic events.<sup>(1, 2, 7)</sup>

The most recommended anticoagulants are low molecular weight heparins, while vitamin K antagonists can cross the placenta and are teratogenic, making their use in pregnant women contraindicated.<sup>(7)</sup> New oral anticoagulants have not been tested for safety in pregnant women, so their use should be avoided.<sup>(7, 15)</sup>

According to the international consensus based on expert opinion, it is mentioned that treatment should be

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continued up to six weeks postpartum and with a minimum duration of 3 months. <sup>(16)</sup>

When low molecular weight heparin is used, weight-based dose adjustment is recommended, although changes in weight, the glomerular volume of distribution, or filtration occur as the pregnancy progresses, and the need for dose adjustment is controversial; some authors support the need for progressive dose adjustments based on weight gain, while other studies have shown that few women require dose adjustment throughout pregnancy. <sup>(7)</sup>

Similarly, there has been no evidence of an increased risk of recurrence with once-daily low molecular weight heparin versus twice-daily. <sup>(5, 6)</sup> Routine anti-Xa levels for monitoring the effectiveness of anticoagulant therapy are not indicated, given the high cost of the test and the absence of studies showing that dose adjustment concerning its determination increases safety, efficacy, or decrease in hemorrhagic complications. <sup>(3, 7)</sup> Therefore, this study was not conducted in this patient, but the same dose of low molecular weight heparin was maintained as the pregnancy progressed.

It is important to note that there were no hemorrhagic complications or new thrombotic events during the follow-up period. In the case of a recurrence, despite proper anticoagulant treatment, several factors should be evaluated. <sup>(7)</sup> First, it must be confirmed that this is a genuine episode of thrombosis, as it can easily be mistaken for post-thrombotic syndrome. <sup>(7)</sup> Additionally, it is crucial to ensure that the patient is adhering to the treatment plan and receiving the appropriate doses of medication adjusted according to their weight. <sup>(7)</sup> In addition, situations that increase the risk of recurrence, such as underlying tumor disease or antiphospholipid syndrome should be ruled out. <sup>(7, 17)</sup>

Despite the complexity of the thrombosis, the patient showed a good response to the therapy administered, indicating that the treatment was appropriate and timely. The gradual reduction of D-dimer levels during their hospital stay indicated a positive response to treatment, although long-term follow-up is essential to assess any possible sequelae.

It is important to note that the patient did not present signs of pulmonary thromboembolism, which was a key criterion for ruling out the need for vascular surgery. The absence of serious complications such as *phlegmasia cerulea dolens* (severe form of DVT) justified conservative management.

However, the outcome of the pregnancy, in this case, was a cesarean delivery, it should be known that cesarean delivery doubles the risk of venous thromboembolic disease. <sup>(18)</sup> The use of anticoagulant therapy during surgery does not increase the risk of bleeding. <sup>(18)</sup> It is notably associated with a lower rate of surgical site infections. Therefore, it should not be considered a contraindication for cesarean sections in emergencies when there are obstetric indications. <sup>(18)</sup>

Anticoagulation during peripartum has been associated with up to 12.8% of obstetric hemorrhagic complications, including increased postpartum bleeding

(10%) and perineal hematomas (3%). <sup>(19)</sup> However, these risks do not contraindicate its use; it should be reduced with the change to unfractionated heparin with a pre-delivery suspension according to half-life to reduce these risks, as was done in this patient, which immediately suspended the use of heparins upon admission, and pending resolution by abdominal route. <sup>(18)</sup>

Management of DVT in pregnant women requires not only effective treatment but also adequate follow-up to prevent recurrence, a critical aspect given the persistent risk of thrombosis in this population.

### CONCLUSION

Multidisciplinary care involving obstetrics, angiology, and internal medicine was crucial for the successful management of this patient, ensuring the safety of both mother and fetus. This case underscores the need for timely assessment and management of DVT in pregnant women.

Early identification of symptoms, along with the use of appropriate biomarkers and imaging studies, is crucial for accurate diagnosis. Therefore, ongoing training for healthcare professionals, as well as research in this area, is essential to optimize treatment and ensure timely care. Additionally, educating pregnant patients about the signs and symptoms of deep vein thrombosis (DVT) is important for preventing this complication.

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