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Protein S deficiency presenting with portal vein thrombosis in a non-cirrhotic pregnant woman: Case report and review of literature

Ahmed Alshammari

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Author Affiliation:
Department of Internal Medicine, College of Medicine, University of Hail, Hail, Saudi Arabia; Email: alshammari.md@gmail.com

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ABSTRACT

A 27-year-old primigravid patient presented with severe abdominal pain during the 10th week of gestation. Blood test results, including those of lipase and liver enzymes, were unremarkable. However, doppler ultrasonography of the abdomen revealed left portal vein thrombosis. Therapeutic enoxaparin was initiated, resolving the pain. At week 25 of gestation, the patient went into labor and delivered, vaginally, a single, live male infant. The newborn died within one week. Postpartum, she underwent further investigation to identify the cause of portal vein thrombosis. A thrombophilia workup revealed low protein S activity. This case highlights the importance of performing a thrombophilia workup in women with portal vein thrombosis during pregnancy.

Keywords: portal vein thrombosis; protein S deficiency; pregnancy; thrombophilia; enoxaparin; abdominal pain

1. INTRODUCTION

Protein S deficiency is an inherited or acquired thrombophilia that is associated with high risk of venous thrombosis. Protein S is synthesized primarily in the liver and endothelial cells. Protein S is dependant on vitamin K for its activity and circulates in the blood in a free state (40%) and bound to C4b-binding protein (60%), (ten Kate & van der Meer, 2008). Portal vein thrombosis (PVT) is an uncommon condition in the general population, with a prevalence of approximately 3.7 per 10,000 persons. PVT is also rare in pregnancy, and it is usually associated with thrombophilias, myeloproliferative disorders, intra-abdominal infections or inflammation, and liver cirrhosis. PVT can lead to spontaneous abortion, premature birth, or perinatal death. Anticoagulation and timely recognition are crucial to prevent complications during pregnancy (Rodríguez-Leal et al., 2014; Handa et al., 2014).

In this article, we report a case in which a young patient developed PVT during her first pregnancy, resulting in premature delivery and neonatal death. Postpartum thrombophilia screening confirmed the presence of protein S deficiency. During the subsequent pregnancy, the patient was treated with enoxaparin, delivering a full-term healthy baby.

2. CASE PRESENTATION

A 27-year-old healthy woman (G1P0) presented to the emergency room at the Maternity and Children Hospital in Hail, Saudi Arabia, with a history of abdominal pain for 2 weeks. The pain was initially intermittent, sharp, and radiating to her back, but progressed and became very severe and persistent, and associated with nausea and vomiting the day before presentation. She denied other symptoms, such as diarrhea, constipation, hematemesis, hematochezia, vaginal bleeding, dysuria, leg swelling, leg pain, or fever, and a review of the systems was unremarkable.

Physical examination showed a tachycardic, distressed woman due to severe abdominal pain. Her abdomen was soft, and there was no rebound tenderness or rigidity. Vital signs, system examinations, and past medical history were unremarkable. Other than multivitamins, she was not taking any medication before or during pregnancy. She is a lifelong non-smoker who denied alcohol intake or illicit drug use. Her family history was unremarkable. Complete blood count, kidney function, liver function tests, and lipase levels were unremarkable. Doppler ultrasound of the abdomen revealed a gravid uterus with a single viable fetus at 10 weeks of gestation. Echogenic filling was observed within the proximal part of the left portal vein, consistent with partial left portal vein thrombosis (Figure 1A and B).

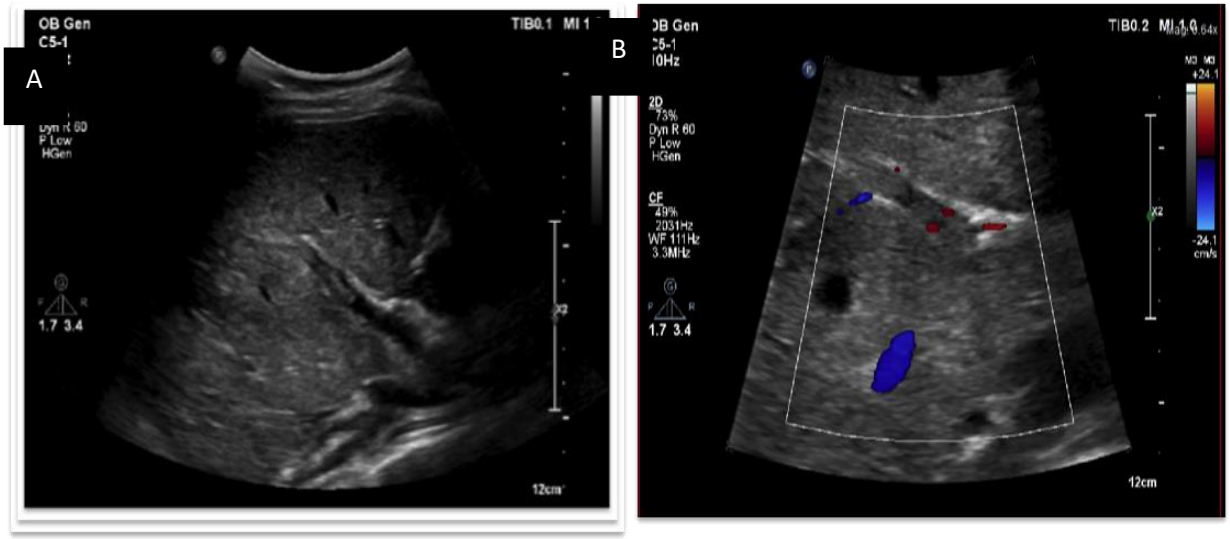

Figure 1 Doppler ultrasound of the abdomen. A) Left portal vein thrombus with a diameter of 11 mm. B) No blood flow is seen.

She was initiated on therapeutic enoxaparin 60 mg twice daily. At week 25 of gestation, she delivered, vaginally, a single, live male infant. The newborn, weighing 670 g, was transferred to the neonatal intensive care unit where he died within 1 week. Enoxaparin was continued post-partum for 7 weeks and then discontinued. Two months postpartum, a thrombophilia workup was performed and revealed a low protein S activity of 24.1% (normal 55%–140%). Screening for protein C, antithrombin level, factor V Leiden, lupus anticoagulant, anti-cardiolipin immunoglobulin M (IgM), and IgG were all unremarkable. The international normalized ratio and partial thromboplastin time were also normal. Abdominal computed tomography (with contrast) showed resolution of the PVT. The patient had a second pregnancy and was prescribed anticoagulation prophylaxis (enoxaparin 40 mg daily) at the beginning of the pregnancy. Her pregnancy was unremarkable, and she delivered a healthy infant at the 38th week of gestation.

3. DISCUSSION

Deficiency of protein S can be inherited or acquired thrombophilia that is associated with high risk of thrombosis. Protein S major function is to reduce thrombin generation and to enhance fibrinolysis by working with activated protein C, which inactivates factors Va and VIIIa. It also interact with other coagulation factors to inhibit prothrombin activation. Hereditary protein S deficiency results from *PROS1* gene mutations on chromosome 3 and it has an autosomal dominant inheritance pattern. Acquired protein S

deficiency is caused by many conditions, such as pregnancy, liver cirrhosis, nephrotic syndrome, disseminated intravascular coagulation, and medications, including oral contraceptive pills and some chemotherapeutic agents. In women, protein S levels are significantly lower than those in men (Zhu et al., 2011).

PVT secondary to protein C and S deficiencies was reported in a 66-year-old man who presented to the hospital with a history of myalgia and anorexia lasting for 2 weeks with fever, nausea, and vomiting. Complete portal vein occlusion was seen on doppler ultrasound of the abdomen, and a thrombophilia workup revealed low protein C and S levels (Choi et al., 2011). There is also a rare case of PVT secondary to protein S deficiency, where a 38-year-old male presented to the hospital with frequent esophagogastric variceal bleeding (EGVB) as a complication of PVT. The patient underwent endoscopic therapy and was then prescribed rivaroxaban to reduce the risk of thrombosis. The patient did well without further EGVB or thrombotic event at a 1-year follow-up (Zhou et al., 2018).

PVT during pregnancy is uncommon. Pregnancy can precipitate PVT in patients with underlying thrombophilic disorders (Bissonnette et al., 2015). Gomes (2020) reported a case of a 23-year-old female at 35 weeks of gestation with distended and painful abdomen. She was diagnosed with decompensated chronic cryptogenic liver disease with PVT as a result of protein S deficiency. In a case series of three women with PVT during pregnancy, one patient had a mutation in factor V Leiden and another patient had protein S deficiency (Anbazhagan et al., 2010).

Recommendations by the American College of Obstetricians and Gynecologists include a thrombophilia workup when the results will change pregnancy management (ACOG, 2018). Screening for antithrombin, protein S and protein C deficiencies is recommended by the Canadaian Society of Obstetricians and Gynaecologists if thrombosis occurs in an unusual vascular beds (Chan et al., 2014).

4. CONCLUSION

In our case, thrombophilia workup after her pregnancy revealed protein S deficiency, placing her at a high risk for pregnancy-associated thrombosis. Because of this, the patient was placed on anticoagulation prophylaxis at the beginning of her second pregnancy. In conclusion, thrombophilias are major risk factors for pregnancy-associated thrombosis, and we strongly recommend screening for inherited thrombophilias in women who were diagnosed with PVT during pregnancy.

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Author Contributions

Data collection, analysis and interpretation of results, review of literature, and draft manuscript preparation by Dr. Ahmed Alshammari.

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

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Conflict of interest

The authors declare that there are no conflicts of interest.

Data and materials availability

All data associated with this study are present in the paper.

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