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Case Report

An Unusual Case of Protein S Deficiency Presenting as Splenic Infarction and Poor Pregnancy Outcome

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Abstract

Splenic infarction is rare and is usually kept at the bottom of our differential diagnosis list for abdominal pain. Splenic infarction due to Protein S deficiency makes it an even more rare case. It may be symptomatic or asymptomatic and can occur either with venous or arterial compromise. We report a case of Protein S deficiency who delivered a baby with Intra-Uterine Growth Restriction (IUGR) and later presented as acute abdomen - splenic infarction. A thorough literature review using google and Medline revealed no similar case.

Keywords: Splenic infarction; IUGR; Protein S deficiency

Introduction

Splenic infarction is a rare clinical condition whose presentation can mimic other causes of acute abdominal pain. The pathognomonic sign for splenic infarction is Left Upper Quadrant (LUQ) tenderness, which is seen in only 35% of the patients and the final diagnosis depends on clinical presentation and imaging studies. It is mostly seen in conjunction with hematologic disorders, atrial fibrillation, cardio-vascular and thromboembolic disorders [1,2].

Protein C and S are essential in limiting the activation of coagulation in vivo and their deficiencies carries an approximately 10-fold increase risk for venous thrombosis, often at unusual sites. Arterial thrombosis is however rarely observed [3]. Our patient was found to have Protein S deficiency, which remained undetected on first contact with the healthcare team but later manifested as splenic infarction - both arterial as well as venous.

Materials & Methods

Upon the patient's informed consent, a fully-detailed medical, surgical, family, obstetrical and social histories were obtained along with a systemic physical examination. The patient's medical records, investigations and imaging results were accessed while maintaining her confidentiality. A thorough review of literature was done to look for similar cases.

Case Report

A 21 years-old female, para 1, who delivered a male baby 6 weeks back, presented with a sudden, severe left abdominal pain. The pain was severe (6/10 on a Stanford pain scale-SPS) and associated with anorexia, vomiting and high-grade fever. She was managed with analgesics and discharged on the same day. However, her pain did not subside and progressed to 10/10 in the next 2 days. She reported to the emergency room again and was admitted as abdominal pain under evaluation. There was no significant history of trauma, hemoglobinopathies, autoimmune disorders, previous thrombo-embolic events or use of oral contraceptives. However, her first and recent pregnancy outcome was an IUGR, which was delivered by an uneventful cesarean section. In addition, she had a positive family history of stroke and Rheumatoid arthritis.

Her examination was unremarkable, except for the conjunctival pallor and mild tenderness in the LUQ, with spleen palpable 1 cm below the costal margin. Initial lab work-up showed notable findings (Table 1). Ultrasound and urine analysis ruled out renal causes, and chest x ray was inconclusive. However, a Computed Tomography (CT) angiogram revealed an isolated splenic vein thrombosis and splenic artery occlusion, thus pointing to the diagnosis of splenic infarction (Figure 1a and 1b).

This prompted further hematologic evaluation to elucidate the etiology, which revealed decreased protein S levels (41%). There were no positive findings in her hemoglobin electrophoresis, sickle cell solubility, rheumatoid factor, antinuclear antibodies or cytomegalovirus antibodies screening.

She was started on intravenous acetaminophen (analgesia), enoxaparin (low molecular weight heparin), clopidogrel (antiplatelet) and domperidone (antiemetic). A possibility of splenectomy was discussed with her in case of no clinical improvement, or complications. During her 10-days hospital stay, her pain subsided, inflammatory markers reduced, and platelet count normalized. She was discharged on subcutaneous enoxaparin and domperidone. Upon follow-up, she was switched to dabigatran (oral anticoagulant), and immunized with *pneumococcal* 23-valent & hemophilus b conjugate vaccines. She was counselled on contraception, as her future pregnancies would be at high risk, but she preferred natural method. Her repeat Protein S levels were also low (43%).

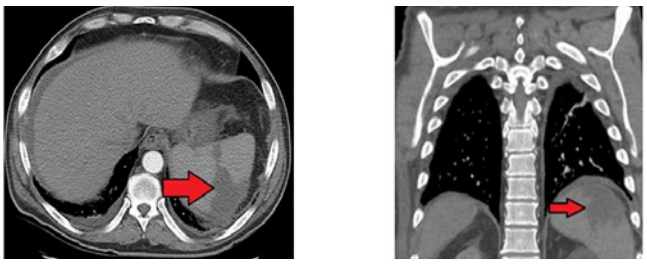

Figure 1a & 1b: CT Abdomen showing a splenic infarct with a left pleural effusion and left lower lobe atelectasis.

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Table 1: Lab results.

Parameter	Value	Interpretations
RBC	3.61 million	Low
Hemoglobin	9090g/dL	Low
Hematocrit	30.30%	Low
Monocytes Absolute	14.40%	High
Platelates	1,855	Critical
Albumin	25.3 g/L	Low
ALP	205 IU/L	High
C-RP	36 mg/L	High
Prothrombin Time	13.70 seconds	High
Partial Thrombiplastin Time	138 seconds	High

Table 2: Hemostatic changes in pregnancy.

Anticoagulation/fibrinolysis	Procoagulation
Peotein S ↑	Prothrombin (Factor II) ↑
Activated protein C ↓ in third trimester	Factor V ↑
Plasminogen activator	Factor VII ↑
inhibitor - I ↓	Factor VIII ↑
	Factor IX ↑
	Factor X ↑
	Fibrinogen ↑
	D-dimer ↑
	Sustemic platelet activation ↑ in late pregnancy

Discussion

Splenic infarction is an uncommon condition that usually presents to the emergency department as an acute abdomen.

Although some may be asymptomatic with so called "silent splenic infarction". These infarctions may be segmental (involving a part of spleen) or it may involve the whole spleen. The splenic infarctions are associated with a heterogenous group of disorders such as bacterial endocarditis (10%), thrombo-embolism secondary to atrial fibrillation (22%), hematological diseases (10%) or hypercoagulable states (22%) [4].

Protein C and S deficiency represents a small percentage of cases of inherited thrombophilia and is associated with more uncommon findings of warfarin associated skin necrosis, neonatal purpura fulminans and pregnancy complications. Establishing a diagnosis of hereditary Protein C or S deficiency may be difficult, particularly in the setting of an acute thrombosis.

Protein S is a vitamin K dependent glycoprotein synthesized by hepatocytes. It serves as a cofactor for activated Protein C, which inactivates procoagulant factors Va and VIIIa, reducing thrombin generation [5].

Protein C and S deficiency has been linked to adverse pregnancy outcomes which includes miscarriage, fetal loss, preeclampsia and fetal growth impairment (IUGR) (See Table 2).

In a report from European Prospective Cohort on Thrombophillia, that compared pregnancies in 843 women with thrombophilia and 541 controls (unaffected partners of men in the cohort), the risk of fetal loss (miscarriage or still birth) was significantly increased in the thrombophillic women (odds ratio{OR} 1.35: 95% CI 1.01-1.82) [6].

For the 162 women in this cohort with protein C/S deficiency, the numbers were too small to reach statistical significance {OR 1.4: 95% CI 0.9-2.2} [6].

Thus, it is imperative to screen any women with a poor pregnancy outcome, for thrombophillic conditions in absence of other risk factors. Our patient was discharged at first without screening for the thrombophillic conditions and, unfortunately she presented with a thrombo-embolic phenomenon in the form of splenic infarction in her puerperium. Had she been thoroughly investigated during her hospital admission, her splenic infarction could have been easily prevented.

Treatment of Inherited thrombophilia include prophylactic anticoagulation postoperatively, during pregnancy and postpartum period in addition to the routine care and education. The choice between Direct Oral Anticoagulants (DOAC) and warfarin depends on the patient preference, adherence to the therapy, and potential drug and dietary interactions.

Conclusion

Splenic infarction, though rare, should always be kept as a differential diagnosis of a left hypochondriac pain and tenderness. A thorough history (including obstetrics history in females), examination and relevant investigations (CT abdomen and coagulation profile) must be carried out to come to an early diagnosis in order to reduce morbidity and mortality associated with the disorder and more importantly to improve pregnancy outcomes.

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