

# Protein S Deficiency

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## Abstract

Protein S is a vitamin K dependent co-factor of protein C. Deficiency of Protein S results in a hypercoagulable state, which is treated with anticoagulation. This is the first report of a patient with Protein S deficiency, who underwent a Cesarean section under spinal anesthesia.

## INTRODUCTION

Protein S is a vitamin K-dependent plasma protein discovered in 1977.<sup>1</sup> It functions to express the activated form of protein C, which inhibits the blood clotting cascade at the levels of Factor V and Factor VIII.<sup>1</sup> Patients who are either deficient in protein S, or express a dysfunctional protein S, are at risk for repetitive thrombosis.<sup>1</sup> Under normal circumstances, pregnancy is associated with a hypercoagulable state.<sup>2</sup> We describe the use of neuraxial anesthesia for cesarean section in a parturient who presented with Protein S deficiency.

## CASE REPORT

A 45 year-old gravida VI para 0 woman with a past medical history significant for protein S deficiency presented to the labor floor at 35 weeks gestation in premature labor. Since she had been having labor pains over the past week, her aspirin had been stopped 9 days earlier. Her last dose of SQ Heparin was the previous day; her membranes were intact, and the decision was made by the obstetrician to proceed with Cesarean section.

The patient had 2 elective abortions and 1 spontaneous abortion in her first three pregnancies. Over the past year she had two donor eggs implanted in her uterus, both of which were spontaneously aborted. After the second miscarriage, she was worked up for hypercoagulable conditions that commonly lead to loss of implanted, young donor eggs. She was diagnosed with Protein S deficiency 2 months later. She denied any history of deep venous thromboses or pulmonary emboli. Her past surgical history was significant only for an appendectomy at eight years old without anesthetic complications. Her only medications were one 81 mg aspirin daily and 5000 units of subcutaneous Heparin once daily.

She was allergic to Penicillin and Advil, the former causing swelling, the latter hives. The patient was 58 inches tall and weighed 61 kg. Her lungs were clear to auscultation bilaterally and her heart was regular rate and rhythm, a normal S1 and S2, with no rubs, murmurs, or gallops appreciated. A coagulation profile was obtained prior to beginning the case. Her PT was 11.1, PTT was 28.3, and INR was 1.1.

The patient was brought to the operating room and placed in the sitting position. A spinal anesthetic was performed at the L3-L4 level using a 27 gauge Whitacre needle. The patient received 1.5 cc of 0.75% Bupivacaine with 0.25 mg of preservative free morphine. A T4 level of anesthesia was obtained. The patient was placed in the left uterine displacement position and had an uneventful Cesarean section. She was monitored in the post anesthesia care unit for two hours. She had by this time recovered motor and sensory function bilaterally and was discharged from the recovery room and sent to the floor. She was restarted on aspirin and heparin on post operative day #2. She was discharged after an uneventful hospital stay on post operative day #4.

## DISCUSSION

Protein S is a vitamin K dependent co-factor of protein C. Protein C acts by neutralizing activated factors V and VIII, and by exhibiting an inhibitory action of plasminogen activator.<sup>3</sup> Deficiency of protein S results in increased incidence of venous thrombosis. Deficiency of protein S may be hereditary or acquired. Hereditary disease is an autosomal dominant disorder, with homozygotes generally dying in infancy due to massive thrombosis. Heterozygotes generally have their first thrombotic event by their mid-twenties.<sup>4</sup> Acquired disease is usually due to hepatic

disease.<sup>4</sup>

Patients with protein S deficiency may develop lower extremity thrombosis, pulmonary embolisms, and superficial thrombophlebitis.<sup>5</sup> The frequency of venous thromboembolism from protein C and S deficiency ranges from 7 to 17%.<sup>3</sup> There is also risk of spontaneous abortion, as had previously occurred in our patient.

Pregnant patients with protein S deficiency can be managed with either a combination of aspirin and subcutaneous heparin or with low molecular weight heparin. Patients should not be offered neuraxial anesthesia unless the PTT is within the normal range if they are managed with aspirin and heparin.<sup>6</sup> The effect of low molecular weight heparin cannot be determined by a lab test, so the patient must be off it for at least 24 hours prior to neuraxial anesthesia.<sup>6</sup> Tachycardia, hypotension, and hypothermia also increase the likelihood of thrombosis and should also be avoided.<sup>6</sup> The risk of DVT among healthy pregnant women undergoing elective cesarean section is low and general medical thromboprophylaxis is probably not justified.<sup>7</sup>

To the best of our knowledge, this is the first report of a patient with protein S deficiency, who underwent a Cesarean section under spinal anesthesia. Our search revealed only two previous case reports of patients with protein S deficiency, who presented in labor.<sup>5,8</sup> In one, the patient had been on heparin, also. The coagulation studies were normal, and a combined spinal/epidural anesthetic was administered for labor. The patient also had had a positive stress test, and an arterial catheter was used for monitoring blood pressure continuously. This patient delivered vaginally.<sup>5</sup>

The only other case report was of a patient with protein S deficiency, who had been treated with heparin subcutaneously, who presented for a Cesarean section. Rather than recheck the PT and PTT following a heparin subcutaneous dose, a general anesthetic was administered.

These authors recommended avoiding spinal anesthesia in patients who have received heparin.<sup>8</sup> We disagree with these recommendations. Patients presenting for Cesarean section are at increased risk for aspiration prior to intubation for general anesthesia, and there is an increased risk of difficult intubation. A regional anesthetic should be administered whenever possible, and general anesthesia should be avoided.

In summary, we describe a successful anesthetic in the parturient with hereditary protein S deficiency. Neuraxial techniques can be used safely in these patients as long as appropriate laboratory workup is completed and the patient has been off anticoagulants for an adequate period of time.

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