The management of Cesarean delivery in a parturient with paroxysmal nocturnal hemoglobinuria complicated by severe preeclampsia

[Césarienne chez une parturiente souffrant d’hémoglobinurie nocturne paroxystique compliquée d’une pré-éclampsie sévère]

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Purpose: To describe the anesthetic and peripartum management of a parturient with paroxysmal nocturnal hemoglobinuria complicated by severe preeclampsia, review the pathophysiology of this condition, rationale for thromboembolic prophylaxis, and its implications on the choice of labour analgesia and anesthesia.

Clinical features: A 35-yr-old primigravida was diagnosed with paroxysmal nocturnal hemoglobinuria at 18 weeks gestation following new onset pancytopenia. Venous thromboembolic prophylaxis with low molecular weight heparin (LMWH) was started, and continued despite a persistent thrombocytopenia. At 34 weeks, labour was induced after she developed signs of severe preeclampsia, and intravenous magnesium sulfate therapy was commenced. The use of a twice daily dosing regime of LMWH, along with severe thrombocytopenia contraindicated neuraxial anesthesia. As a result, labour analgesia was provided with an intravenous patient-controlled analgesia system with fentanyl. The patient subsequently had an uneventful Cesarean delivery under general anesthesia. Anticoagulation with LMWH was restarted postoperatively, and continued for six weeks postpartum. She was discharged home on day 20 postpartum, on oral prednisolone under the care of the hematologists.

Conclusion: Paroxysmal nocturnal hemoglobinuria is associated with an increased risk of venous thromboembolism, and so anticoagulation therapy assumes primary importance. The use of LMWH for prophylaxis in combination with thrombocytopenia may contraindicate neuraxial anesthesia. General anesthesia should be aimed at preventing or exacerbating complement mediated intravascular hemolysis.

Objectif: Décrire la prise en charge anesthésique et peripartum d’une parturiente souffrant d’hémoglobinurie nocturne paroxystique compliquée d’une éclampsie sévère, rendre compte de la physiopathologie de cet état, des raisons justifiant la prophylaxie thromboembolique et de son influence sur le choix de l’analgésie et de l’anesthésie du travail.

Éléments cliniques: Une primigeste de 35 ans a reçu un diagnostic d’hémoglobinurie nocturne paroxystique à 18 semaines de grossesse suite à une pancytopenie de novo. Une prophylaxie thromboembolique veineuse avec de l’héparine à bas poids moléculaire (LMWH) a été débutée et continuée malgré une thrombocytopenie persistante. Le travail a été provoqué à 34 semaines, après que la patiente a développé des signes de pré-éclampsie sévère, et une thérapie intraveineuse de sulfate de magnésium a été débutée. L’anesthésie neuraxiale était contre-indiquée à cause de l’administration deux fois par jour de LMWH et la thrombocytopenie sévère. C’est pourquoi l’analgésie pour le travail a été fournie à l’aide d’un système intraveineux d’analgésie contrôlée par le patient au fentanyl. La patiente a eu un accouchement par césarienne sans complications sous anesthésie générale. L’anticoagulation à base de LMWH a été reprise après l’opération, et maintenue pendant six semaines post-partum. La patiente a quitté l’hôpital le vingtième jour post-partum, et a suivi un traitement oral de prednisolone prescrit par les hématologistes.

Conclusion: L’hémoglobinurie nocturne paroxystique est associée à un risque accru de thromboembolie veineuse, c’est pourquoi l’anticoagulation joue un rôle primordial. L’anesthésie neuraxiale peut être contre-indiquée à cause du recours à une prophylaxie à base de LMWH combinée à une thrombocytopenie. L’anesthésie générale devrait avoir pour objectif d’empêcher d’exaspérer une hémolyse intravasculaire médicée par le complément.
Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired hemolytic anemia associated with complement mediated intravascular hemolysis, bone marrow failure and thrombophilia. Paroxysmal nocturnal hemoglobinuria is rare with a reported incidence of 1–10 per 1,000,000, and is mainly seen in adults, especially women of reproductive age. Pregnancies complicated by PNH are associated with increased maternal and perinatal morbidity and mortality, possibly related to a 14.4% incidence of venous thrombosis. The management of anticoagulation to reduce the risk of venous thromboembolism (VTE) and the severity of the thrombocytopenia may have anesthetic implications.

Only a few cases highlighting the management of pregnant women with PNH have been described in the literature. The anesthetic management for Cesarean delivery was reported in only one of these cases. In this case report, we report the anesthetic management for Cesarean delivery of a parturient newly diagnosed with PNH and superimposed preeclampsia. Approval for the use of personal health information contained in this manuscript has been obtained in accordance with Duke University Medical Center Institutional Review Board guidelines.

Case report
A 35-yr-old primigravida female was referred to the Division of Hematology at our institution at 18 weeks and five days gestation with a progressive pancytopenia. She had a pulmonic valvulotomy for congenital pulmonary stenosis and an atrioseptal defect (ASD) closure at four years of age. At age 32, she developed progressive pulmonary valve insufficiency associated with right ventricular enlargement and decreased right ventricular function. Subsequently, she underwent a right ventricular outflow tract reconstruction and a pulmonary valve replacement with a porcine Hancock valve. In addition, she had a past history of a thoracic aortic valve. In addition, she was noted to have elevated blood pressure on admission was 179/93 mmHg (151/85 mmHg), with no associated proteinuria, and she had become increasingly symptomatic.

Anticoagulation therapy was monitored by measuring monthly anti-factor Xa activity levels aiming for a therapeutic range of 0.5–1.0 u·mL⁻¹.

A transthoracic echocardiogram performed at 26 weeks confirmed normal left ventricular function, a functioning bioprosthetic pulmonary valve, repaired ASD and mild pulmonary, tricuspid and mitral regurgitation. On this visit laboratory results revealed a further fall in hemoglobin to 6 g·dL⁻¹, a platelet count of 68 × 10⁹·L⁻¹, serum LDH of 4283 U·L⁻¹, anti-factor Xa level of 0.79 u·mL⁻¹, and a normal serum haptoglobin level. It was felt at this point that blood transfusion was not indicated, since she only complained of occasional fatigue with mild shortness of breath on climbing stairs. Anticoagulation therapy was continued despite a falling platelet count as this was thought to be due to PNH rather than heparin induced thrombocytopenia (HIT).

At 31 weeks gestation, her hemoglobin was 5.4 g·dL⁻¹ and she had become increasingly symptomatic. She was transfused 3 U of packed red blood cells. A PNH screen was repeated and was again positive. In addition she was noted to have elevated blood pressure (151/85 mmHg), with no associated proteinuria, and no other symptoms or signs of preeclampsia.

She was admitted to hospital at 34 weeks gestation after developing signs of severe preeclampsia. Her blood pressure on admission was 179/93 mmHg and remained elevated. Laboratory results were consistent with ongoing hemolysis with a hemoglobin of 7.3 g·dL⁻¹, platelet count of 47 × 10⁹·L⁻¹, serum LDH of 5217 U·L⁻¹, and new onset hemoglobinuria. Coagulation studies were normal. She also had an elevated aspartate transaminase (135 U·L⁻¹; reference value 10–60 U·L⁻¹), significant proteinuria (1.7 g over 24 hr estimated by protein/creatinine ratio), and an elevated serum uric acid level (7.9 mg·dL⁻¹; reference value < 5.5 mg·dL⁻¹). She received a total of hydralazine 20 mg iv, in 5-mg aliquots for the control of hypertension. Magnesium sulfate at 2 g·hr⁻¹ was started intravenously for seizure prophylaxis. Enoxaparin was discontinued, and unfractionated heparin (UFH)