Familial hypokalemic periodic paralysis and Wolff-Parkinson-White syndrome in pregnancy

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Purpose: To describe the anesthetic and obstetrical management of a pregnant patient with co-existing Familial Hypokalemic Periodic Paralysis (FHPP) and Wolff-Parkinson-White syndrome (WPW).

Clinical Features: A 29 yr-old primigravida with FHPP and WPW presented to the antenatal clinic at 18 wk gestation, for consideration of her anesthetic and obstetrical management during labour and delivery. A plan was constructed to avoid the known precipitating factors of FHPP including carbohydrate loading, cold, mental stress and exercise, which could lead to acute attacks of weakness. She presented for induction of labour at 41 wk and three days. An epidural catheter was sited early in labour. The second stage was limited to less than one hour. She had a rotational forceps delivery for which the epidural was extended to provide anesthesia. A healthy male baby was delivered. The patient made an uncomplicated recovery and was discharged home on the second postnatal day. The peripartum potassium was kept within the normal range with intravenous as well as oral potassium supplementation. No arrhythmias were reported.

Conclusion: Assessment of the patient at an early stage in her pregnancy allowed for a multidisciplinary approach to this patient and her medical problems. A plan was made to avoid known precipitating factors during labour, delivery and the postnatal period well in advance of her date of confinement, leading to a successful outcome for mother and child.

Objectif : Décrire le traitement anesthésique et obstétrical d'une patiente enceinte atteinte d'une paralysie périodique hypokaliémique familiale (PPHF) et du syndrome de Wolff-Parkinson-White (WPW).

Éléments cliniques : Une primigeste de 29 ans atteinte de PPHF et du syndrome de WPW a été vue à la clinique prénatale à 18 sem de grossesse pour que soit envisagé le déroulement anesthésique et obstétrical du travail et de l'accouchement. Cette planification visait à prévenir les facteurs déclenchants de la PPFH, comme la charge glucidique, le froid, le stress mental et l'exercice, qui pourraient entraîner une faiblesse aiguë. À 41 sem et 3 jrs de grossesse, on a procédé à l'induction du travail. On a placé un cathéter péridural tôt pendant le travail actif. Le deuxième stade a duré moins d'une heure. L'accouchement a nécessité une rotation par l'application de forceps et une extension de l'anesthésie. La patiente a donné naissance à un garçon en santé, a connu une récupération sans complications et a quitté l'hôpital le deuxième jour postnatal. Pendant la période périnatale, le potassium a été maintenu dans les limites de la normale grâce à des suppléments intraveineux et oraux. Aucune arythmie n'a été notée.

Conclusion : L'évaluation de la grossesse à un stade précoce a permis le traitement multidisciplinaire de la patiente et de sa condition médicale. Le plan élaboré, bien avant la date prévue de l'accouchement, pour prévenir les facteurs déclenchants de la maladie pendant la période périnatale a mené à d'heureux résultats pour la mère et l'enfant.

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Case Report

A 29 yr-old primigravida, with familial hypokalemic periodic paralysis (FHPP) and Wolff-Parkinson-White syndrome (WPW), presented to the antenatal clinic at British Columbia Women's Hospital at 18 wk gestation, where she was seen by the Departments of Anesthesia and Maternal Fetal Medicine.

Familial hypokalemic periodic paralysis was diagnosed at the age of six. Her father had the disease that resulted in permanent weakness of his proximal lower limb muscles. The patient, herself, complained of mild weakness of the proximal lower limb muscles, which increased during the pregnancy. Typically, she reported 2-3 episodes of severe weakness per year, which were precipitated by fatigue, stress, heavy meals, monosodium glutamate, cold and codeine. On such occasions, she was unable to climb stairs. Her regular treatment included 250 mg acetazolamide in divided doses, and 24 potassium chloride (KCl) tablets per day. She took additional KCl whenever she felt weak. In 1990, a severe episode of weakness occurred following general anesthesia for dental extractions. After treatment with intravenous potassium, she made a full recovery.

Wolff-Parkinson-White syndrome (WPW) was diagnosed five years previously. Electrocardiographically there was a short PR interval and wide QRS complexes with a slurred upstroke. She had experienced several episodes of paroxysmal supraventricular tachycardia, sometimes precipitated by fasting. Treatment of these episodes with ß blockers exacerbated her weakness and was discontinued. An accessory pathway was identified and laser ablation attempted, unsuccessfully. Following this, she aborted any palpitations with a Valsalva maneuvre and did not require any pharmacological therapy.

After discussion between the patient and her care team, a management plan was proposed. This included vaginal delivery with Cesarean section reserved for obstetric reasons. In an effort to balance the need to avoid fasting, carbohydrate and sodium overload and maintain potassium homeostasis to prevent paralysis and arrhythmias, intravenous fluid therapy would be started early in labour. The solutions proposed were dextrose 5% and normal saline 0.25% run at 125 $ml \cdot hr^{-1}$. In addition, 40 $mmol \cdot l^{-1}$ potassium chloride added to one litre of a solution consisting 2/3 dextrose 5% (3.3 g) and 1/3 normal saline (Na 51 $mmol \cdot l^{-1}$, Cl 51 $mmol \cdot l^{-1}$) would be run at 60 $ml \cdot hr^{-1}$. The electrolyte concentrations were to be monitored six hourly during labour and postnatally.

Continuous ECG monitoring would be instituted when active labour was established. In the event of an arrhythmia, the plan was to administer intravenous ß blockers after ensuring normal serum potassium levels. If there were no response, intravenous lidocaine would be administered.

Epidural analgesia was considered beneficial to decrease the stress of labour and potentially prevent an attack of weakness. It was planned to limit the second stage of labour to less than one hour by vacuum extraction or forceps delivery. In the event that she required a Cesarean section, the risks and benefits of regional and general anesthesia were discussed. Both could have detrimental effects on the FHPP; namely, weakness and excess motor blockade with regional anesthesia and the potential problem of prolonged weakness induced by muscle relaxants with general anesthesia. On balance, however, a regional technique was preferred. It was considered important to maintain normothermia to decrease the possibility of precipitating an attack of weakness.

The patient had an uneventful pregnancy other than for an increasing need for extra oral potassium and acetazolamide to combat weakness. As spontaneous labour did not occur she presented for induction at 41 wk plus three days gestation. Cervical ripening was accomplished with two insertions of vaginal prostaglandin 2 mg. Spontaneous rupture of membranes occurred at 1 cm dilation with clear amniotic fluid identified. An oxytocin infusion was commenced at 4 to 8 $milliunits \cdot min^{-1}$ and ECG monitoring was instituted. Serum potassium was measured six hourly and ranged between 3.8 $mmol \cdot l^{-1}$ and 4.2 $mmol \cdot l^{-1}$. An epidural catheter was inserted. After a test dose of 3 ml lidocaine 1.5%, a loading dose of 12 ml bupivacaine 0.125% with epinephrine (1:800,000) was administered. A bupivacaine (0.08%) and fentanyl (2 $\mu g \cdot ml^{-1}$) infusion was commenced at 10 $ml \cdot hr^{-1}$. Two top ups were given (15 ml bupivacaine 0.125%) as labour progressed.

The first stage of labour was 23 hr. After 45 min of pushing in the second stage, the presenting part was in the left occipito-transverse position 2+ at the ischial spines. The decision was to perform a rotational forceps delivery. The epidural was judiciously extended with carbonated lidocaine 1.75%, by incremental doses of 2 ml, to a total of 6 ml. This produced a motor and sensory block to T_6. A healthy male baby was delivered weighing 3.18 kg with Apgar scores of 9 at one and five minutes. Examination of the newborn was normal. One milligram of epidural morphine was given prophylactically for episiotomy pain.

The motor block gradually regressed over the following four hours and there was no residual weakness. The post delivery potassium was kept within the normal range using oral and intravenous supplementation.

The patient reported no peripartum palpitations, and no arrhythmias were recorded. She made an

uncomplicated recovery and was discharged home on the second postnatal day.

Discussion

There are three different subtypes of familial periodic paralysis (FPP); hypokalemic, hyperkalemic and normokalemic.[1] Hypokalemic periodic paralysis (FHPP) is inherited as an autosomal dominant disorder with a male preponderance (male to female ratio of 3-4:1). The disease is linked to chromosome 1q 31-32, a region containing the gene encoding the α 1 subunit of the L-type calcium channel of skeletal muscle.[2] Attacks of muscle weakness accompany low serum potassium concentrations. The attacks can be severe and prolonged, and are counteracted by the ingestion of potassium.[3] Forearm arteriovenous blood studies reveal that the hypokalemia is generated by the insulin dependent uptake of potassium from the extracellular space into muscle fibres.[2] Administration of insulin and glucose to the patient is a certain way of inducing an attack.[4]

The attacks of weakness are classically precipitated by large carbohydrate-containing meals, especially large evening meals that lead to paralysis on rising the next morning. Other precipitants include cold, mental stress, infection, exercise, menstruation and sodium loading. The paralysis is generally incomplete, involving the arms, legs and trunk, but often sparing the diaphragm and muscles supplied by the cranial nerves.[1,5] During attacks, the blood pressure rises and arrhythmias can occur.[1]

The primary treatment of acute episodes is the administration of potassium. Acetozolamide is also prescribed as the associated metabolic acidosis leads to a rise in serum potassium and the amelioration of symptoms.[6]

Most of the literature regarding the anesthetic management of FHPP is old, however it elucidates several important principles. These are:

1. Close monitoring of potassium levels, as these patients often have very high requirements.
2. Use of a nerve stimulator to monitor neuromuscular block is mandatory if general anesthesia is to be administered.
3. Keeping patients warm during general or regional anesthesia.
4. Post-anesthetic care should be in a high dependency area for 24-48 hr or until the patient is stable with a normal potassium level.

General anesthesia has been successfully administered to patients with hypokalemic periodic paralysis. Horton[7] described 21 general anesthetics in eight members of one family with hypokalemic periodic paralysis. Muscle weakness occurred postoperatively related to the use of muscle relaxants. On three occasions in two patients, muscle relaxation had been provided by either succinylcholine (infusion or intermittent doses to a total of 70 mg) or tubocurarine (21 mg total).[7] Two additional patients experienced postoperative weakness without the use of muscle relaxants.

There are two reports of general anesthesia for Cesarean section in patients with FPP. In one, the patient had an emergency Cesarean section for pre-eclampsia. Anesthesia was induced with thiopentone, succinylcholine, tubocurarine and maintained with nitrous oxide and oxygen. Postoperatively there was no residual muscle weakness.[8] The second reported general anesthesia for Cesarean section in a patient with immune thrombocytopenia and a history of normokalemic or hypokalemic FPP.[9] This patient was also given thiopentone and succinylcholine but no other muscle relaxants during the procedure. This case, however, was complicated by the presence of myotonia and plasma cholinesterase deficiency, previously unknown. The authors found a prolonged recovery (38 min) of the single twitch response after succinylcholine that was attributed to plasma cholinesterase deficiency.[9] If muscle relaxants are used a nerve stimulator is a mandatory piece of equipment. Atracurium has also been used successfully. In one report, an intravenous induction was followed by a small dose of atracurium (2.5mg). Careful use of a nerve stimulator, (train of four response of the ulnar nerve affixed to a strain gauge), guided the anesthesiologist's administration of incremental doses for muscle relaxation and recovery prior to extubation.[10]

One case report[11] describes an episode suggestive of malignant hyperthermia (MH) during general anesthesia, induced with thiopentone and succinylcholine, in a patient who had FHPP. A muscle biopsy performed four months after the episode revealed features consistent with a diagnosis of FHPP. Halothane caffeine contracture testing was reported as MH equivocal. None of the known mutations of MH were detected. The gene encoding FHPP has been proposed to be in the same locus as that encoding the muscle dihydropyridine-sensitive calcium channel subunit. An abnormality of this channel could lead to an increase in cytosolic calcium in FHPP patients closely resembling MH, but without the hyperkalemia.[11] To the authors knowledge no other reports have linked the two disorders.

There is no evidence to contraindicate the use of regional anesthesia in FHPP. A paravertebral field block has been used to provide anesthesia for incisional hernia repair with a successful outcome.[12] There is a

single case report of uncomplicated epidural analgesia for labour in a nulliparous woman with FHPP.[13] There are no reports of spinal anesthesia. The concerns with regional anesthesia are the development of an excessive motor block possibly requiring ventilatory support or permanent muscle weakness. In our case, a significant motor block occurred with minimal local anesthetic for forceps delivery, but no residual motor weakness was observed. Although epinephrine can decrease serum potassium levels, we felt this was not clinically important when given in low concentration as part of the epidural loading dose.

Wolff-Parkinson-White syndrome is one of the preexcitation syndromes in which activation of an accessory atrio-ventricular conduction pathway leads to early and rapid ventricular contractions. The ECG typically shows a short PR interval, anomalous QRS complexes and a delta wave. In the majority of cases there is no underlying heart disease. The arrhythmia most commonly associated with WPW is paroxysmal supraventricular tachycardia. An increase in the frequency of paroxysmal supraventricular tachycardia has been observed in the obstetric population without any evidence of preexcitation, as well as in patients with WPW.[14] This put our patient with WPW and FHPP in a high-risk category for development of arrhythmias, especially during labour and delivery.

Several mechanisms have been suggested to account for arrhythmias in pregnancy; these include hemodynamic, hormonal and emotional changes. An increase in the plasma volume leads to an increase in left ventricular end diastolic volume, which can lead to irritability of the myocardium. The increase in heart rate observed in pregnancy, along with an underlying WPW syndrome, might induce a unidirectional block in the re-entrant circuit resulting in atrioventricular tachycardias.[14] Very fast tachyarrhythmias, which cause serious hemodynamic changes, must be treated immediately. Several methods of terminating these arrythmias have been described. These include vagal stimulation, sedation, and drugs such as propranolol, digoxin, calcium antagonists and adenosine. Adenosine is the preferred treatment for patients with supraventricular tachycardia and its very short half-life has potential advantages in pregnant women. There now are several reports of its use in pregnancy with no ill effects to the fetus.[15–18] Electrical cardioversion during pregnancy has also been documented in several case reports. Transient fetal arrhythmias rarely occur during cardioversion and usually resolve with delivery of a normal infant.[19–21]

Patients with hypokalemic periodic paralysis are prone to develop ventricular arrhythmias (ventricular premature beats, ventricular bigeminy and fusion beats). These occur during hypokalemic episodes. Bidirectional ventricular tachycardia can also occur and is independent of potassium levels. The major concern in our patient was that she might develop malignant ventricular arrhythmias as well as SVT because of her two medical disorders. In the event of a life-threatening ventricular arrhythmia in the peripartum period the cardiologist recommended potassium first (increasing the rate of the potassium infusion), followed by beta blocker therapy. If beta blocker therapy was unsuccessful in converting the rhythm, lidocaine would be used. Although beta blocker therapy might increase her weakness it was considered safer and easier to provide mechanical ventilation, if required, than to manage a life threatening arrhythmia that might respond to beta blockers. Adenosine could have been used if she developed a narrow complex tachycardia secondary to her Wolff-Parkinson-White syndrome.

In our patient we faced the dilemma of balancing her fluid and potassium requirements. As fasting had precipitated episodes of supraventricular tachycardia, in the past it was felt that some carbohydrate was required during labour and delivery, even though a carbohydrate load might precipitate an episode of weakness. As sodium loading has also been implicated in the development of muscle weakness the choice of intravenous fluids was problematic. There was little in the literature to provide firm recommendations regarding ideal fluid and potassium supplementation for stressful situations such as labour. At the multidisciplinary case conference, it was decided to balance these needs with a constant infusion of dextrose 5% in normal saline 0.25% at 125 $ml \cdot hr^{-1}$ and a separate infusion of potassium chloride to maintain potassium homeostasis. Further intravenous supplementation of potassium was to be based on her clinical condition and her serum potassium concentrations. If weakness occurred, the rate of the potassium infusion would be increased and titrated to her response. In a report, published after our patient delivered, the authors administered lactated Ringer's solution containing 40 mEq $KCl \cdot l^{-1}$ at 200 $ml \cdot hr^{-1}$. No rationale was provided for their management.[13]

To our knowledge, this is the first reported case of both WPW syndrome and FHHP in a pregnant patient. The key to successful management of these complex patients is careful planning, a multidisciplinary approach and institution of clear guidelines prior to admission.

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