

General anesthesia for patient with Fahr's syndrome

A case report

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Abstract

Rationale: Fahr's syndrome (FS) is a rare neurological and psychiatric disorder characterized by bilateral brain calcifications when a secondary cause of the calcification is found.

Patient concerns: A 53-year-old female patient diagnosed with FS for laminectomy because of ossification of posterior longitudinal ligament. She had a history of generalized tonic-clonic (GTC) seizure and medication with anticonvulsant drugs. She had gait disturbance, spasticity, bradykinesia, and diffuse calcifications in the basal ganglia, thalamus, cerebellum, and cerebral hemispheres on the brain computed tomography. On the preoperative examination, the serum and ionized calcium (Ca) were decreased to 3.7 and 2.22 mg/dL. Hypomagnesemia is combined with hypocalcemia. Furthermore, the level of parathyroid hormone was decreased to 2.18 pg/mL.

Diagnoses: Due to the radiologic findings and laboratory test results, she was diagnosed with FS with primary hypoparathyroidism.

Interventions: The Ca and magnesium (Mg) had been corrected before surgery but the electrolytes revealed low level at the intraoperative period. The 300 mg of calcium chloride was administered at 2 times and 1200 mg of it were infused for 1 hour during intraoperative periods. In addition, total 4 g of Mg sulfate intravenously administered. We used rocuronium as a neuromuscular block and checked neuromuscular function by train-of-four monitoring.

Outcomes: Residual neuromuscular blockade was reversed with pyridostigmine and her muscle power completely recovered. The patient was extubated successfully and no unpredictable events occurred. On the day following transfer, serum electrolytes remained low, and although Ca was continuously supplied, serum Ca did not recover to a normal level. The patient was medicated with anticonvulsant drugs but experienced GTC seizure 2 weeks after surgery.

Lessons: We presume that the pathophysiology of FS was related to primary hypoparathyroidism and hypomagnesemia. FS raises concerns associated with neuromuscular problems, spasticity, and seizure, and concerns of hypotension, heart failure, cardiac arrhythmia, and cerebrovascular attack during perioperative periods, among anesthesiologists because of hypocalcemia and vessel calcification. During the perioperative period, Ca levels should be closely monitored, and titrated Ca replacement therapy is recommended. The simultaneous correction of hypomagnesemia is of considerable importance when correcting hypocalcemia.

Abbreviations: BP = blood pressure, Ca = calcium, CPK = creatine phosphokinase, ECG = electrocardiography, FS = Fahr's syndrome, GTC seizure = generalized tonic-clonic seizure, HR = heart rate, Mg = magnesium, OPLL = ossification of the posterior longitudinal ligament, PFBC = primary familial brain calcification, PTH = parathyroid hormone, TOF = train-of-four.

Keywords: Fahr's syndrome, general anesthesia, hypocalcemia, hypomagnesemia, hypoparathyroidism

Editor: N/A.

Informed written consent was obtained from the patient for publication of this case report and accompanying images.

This work was supported by the 2018 Yeungnam University Research Grant.

The authors have no conflicts of interest to disclose.

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Medicine (2019) 98:17(e15390)

Received: 6 December 2018 / Received in final form: 26 March 2019 /

Accepted: 2 April 2019

<http://dx.doi.org/10.1097/MD.0000000000015390>

1. Introduction

Fahr's syndrome (FS) is a rare neurological and psychiatric disorder characterized by bilateral brain calcifications when a secondary cause of the calcification is found,^[1] which may be due to various medical conditions including inflammatory, metabolic, autoimmune, and genetic disorders.^[2] Clinical symptoms of FS include parkinsonism, hyperkinetic movement disorder, cognitive impairment, laryngospasm, seizure, cardiac irritability, and decreased cardiac contractility. The symptoms are related to hypocalcemia with widespread calcification of the nervous system and vessels. During perioperative periods, FS also raises concerns associated with neuromuscular problems, such as myopathy, abnormal response to neuromuscular blocking agents, spasticity, and concerns of hypotension, heart failure, cardiac arrhythmia, and cerebrovascular attack because of hypocalcemia and vessel calcification.

We describe our experience of general anesthesia in a patient with FS and a calcium metabolism disorder. There are a few

reports about anesthetic experience of patient with FS. Therefore, we summarized FS and introduced our anesthetic process with consideration. The patient has provided informed consent for publication of the case

2. Case report

We anesthetized a 53-year-old female patient with a diagnosis of FS for laminectomy because of thoracic ossification of the posterior longitudinal ligament (OPLL). She had putatively diagnosed with FS 3 years previously based on brain computed tomography (CT) scan findings with a history of generalized tonic-clonic (GTC) seizure and was on anticonvulsant medication. In addition, she had gait disturbance, spasticity of both lower and upper extremities, bradykinesia in upper limbs. We confirmed diffuse calcifications in basal ganglia, cerebellum, thalamus, and cerebral hemispheres by brain CT scan after admission for surgery (Fig. 1). Preoperative examination revealed abnormal serum calcium and magnesium levels, that is, serum and ionized calcium and magnesium levels were low at 3.7 mg/dL (Normal range [NL]: 8.6–10.6), 2.22 mg/dL (NL: 4.6–5.16), and 1.4 mg/dL (NL: 1.9–3.1), respectively, indicating hypomagnesemia combined with hypocalcemia. In addition, serum parathyroid hormone (PTH) was low at 2.18 pg/mL (NL: 15–65) and creatine phosphokinase (CPK) was high at 657 IU/L (NL: 1–145), and electrocardiography (ECG) showed a prolonged QT interval (QTc 556 ms). Electroencephalography revealed mild encephalopathy with a slight beta wave excess. Cardiac and renal echography findings were normal.

On her arrival in the operating room, her blood pressure (BP) was 146/86 mm Hg and her heart rate (HR) 83 bpm. Standard anesthetic monitoring, including ECG, pulse oximetry, noninvasive BP, and end-tidal CO₂, was initiated with bispectral index, esophageal thermometry, and train-of-four (TOF) monitoring. On this occasion, ECG did not show a prolonged QT interval. General anesthesia was induced and maintained with 70 mg of propofol and sevoflurane in air and oxygen with continuous

intravenous remifentanyl. About 2 minutes after administering 25 mg of rocuronium, TOF decreased to 2. After administering an additional 10 mg of rocuronium, tracheal intubation was performed without airway trauma or hemodynamic instability. Arterial catheterization was performed for continuous BP monitoring and frequent laboratory corrections.

Serum calcium and magnesium had been corrected before surgery, but initial intraoperative laboratory findings revealed low electrolyte levels, that is, pH 7.44, PaCO₂ 44 mm Hg, PaO₂ 248 mm Hg, HCO₃ 29.9 mmol/L, K⁺ 4.1 mmol/L, Na⁺ 137 mmol/L, and Ca²⁺ 3.81 mg/dL, and thus, 2 g of magnesium sulfate hydrate and 600 mg of calcium chloride were intravenously administered. Following blood gas analysis showed pH 7.44, PaCO₂ 45 mm Hg, PaO₂ 240 mm Hg, HCO₃ 30.6 mmol/L, K⁺ 4.2 mmol/L, Na⁺ 137 mmol/L, and Ca²⁺ 3.73 mg/dL. For further correction, calcium chloride (600 mg) was administered i.v. and an additional 1200 mg was slowly infused over 1 hour. After completing the calcium infusion, 2 g of magnesium sulfate hydrate was administered. Blood laboratory tests then showed; pH 7.43, PaCO₂ 44 mm Hg, PaO₂ 243 mm Hg, and HCO₃ 29.2 mmol/L, K⁺ 4.1 mmol/L, Na⁺ 132 mmol/L, Ca 9.3 mg/dL, Ca²⁺ 4.81 mg/dL, Mg²⁺ 4.2 mg/dL, serum phosphorus (IP) 7.8 mg/dL, and CPK 286 IU/L. Blood laboratory testing at the end of surgery showed; pH 7.38, PaCO₂ 47 mm Hg, PaO₂ 225 mm Hg, and HCO₃ 27.8 mmol/L, K⁺ 3.8 mmol/L, Na⁺ 134 mmol/L, Ca 8.2 mg/dL, Ca²⁺ 4.63 mg/dL, Mg²⁺ 2.6 mg/dL, IP 8.1 mg/dL, myoglobin 337.2 ng/mL, creatine kinase-muscle/brain (CK-MB) 8.5 ng/mL, and CPK 326 IU/L. Observed changes in electrolyte levels are summarized in Table 1.

Electrocardiograms were recorded hourly, and prolonged QT was not observed. Residual neuromuscular blockade was reversed with pyridostigmine and her muscle power completely recovered. The patient was extubated successfully and no unpredictable events occurred. Anesthesia lasted 5 hours 15 minutes and was completed uneventfully. No significant hemodynamic or respiratory system changes occurred during emergence except for mild reductions in BP and HR. No other adverse symptoms were observed in the postanesthetic care unit and the patient was transferred to a general ward. On the day following transfer, serum calcium and magnesium remained low, and although calcium was continuously supplied, serum calcium did not recover to a normal level. The patient was medicated with anticonvulsant drugs to prevent convulsions but experienced GTC seizure 2 weeks after surgery. The blood laboratory tests showed Ca²⁺ 4.7 mg/dL, Mg²⁺ 1.5 mg/dL, IP 7.2 mg/dL, and CPK 171 IU/L on the day of the seizure. The patient continued to take oral medications with calcium and magnesium after discharge.

3. Discussion

FS is characterized by symmetrical calcifications within basal ganglia, the cerebral cortex, and cerebellar,^[3] though the locations of these calcifications vary. FS has a slow, progressive course and usually an onset from the fourth to sixth decades of life. The common symptoms of FS include Parkinson's disease-like movement disorder, epilepsy, syncope, ataxia, and dementia. In addition, FS has been shown to be sometimes associated with cerebrovascular disease and myopathies, including cardiomyopathy.^[3] The etiology of FS is widespread calcification within brain and blood vessels due to inflammatory, metabolic, autoimmune, genetic disorders, and others.^[2] The inheritance of FS has been reported to be related to 4 genes, that is, *SLC20A2*, *PDGFR*,



Figure 1. The brain computed tomography of the patient. Symmetric calcification was observed in both cerebral hemispheres, and involved basal ganglia, thalamus, and cerebellum.

Table 1**The laboratory findings of electrolytes during perioperative period.**

Electrolytes (normal range)	Preop.1	Preop.2	Intraop.1	Intraop.2	Intraop.3	Intraop.4	Postop.1	Postop.2
Ca (8.6–10.6 mg/dL)	3.7	6.7			9.3	8.2	5.7	7.1
Ca ²⁺ (4.6–5.16 mg/dL)	2.22	3.58	3.81	3.73	4.81	4.63	2.93	3.43
Mg ²⁺ (1.9–3.1 mg/dL)	1.4	2			4.2	2.6	2	2.2
IP (2.5–4.5 mg/dL)	7.7	8.6			7.8	8.1	6.8	6.8
PTH (15–65 pg/mL)	2.18							
Myoglobin (12–76 ng/mL)	93.6					337.2		
CK-MB (0.6–6.3 ng/mL)	2.6					8.5		
CPK (1–145 IU/L)	657				286	326		
pH (7.35–7.45)			7.44	7.44	7.43	7.38		
pCO ₂ (35–45 mm Hg)			44	45	44	47		
pO ₂ (80–100 mm Hg)			248	240	243	225		
BE (0.0–4.0 mmol/L)			5	5.6	4.3	2.2		
HCO ₃ (23–29 mmol/L)			29.9	30.6	29.2	27.8		
Supplement	Continuous correction of Ca, Mg		2 g of MgSO ₄ 600 mg of CaCl ₂	2 g of MgSO ₄ 600 mg, 1200 mg (for 1 h) of CaCl ₂			Continuous correction of Ca, Mg	

Preop.1: 1 wk before operation; Preop.2: 1 d before operation; Intraop.1: Initial laboratory findings during intraoperative period; Intraop.2: Second laboratory findings during intraoperative period; Intraop.3: Third laboratory findings during intraoperative period; Intraop.4: Final laboratory findings at the end of operation; Postop.1: Laboratory findings of postoperative 1 day; Postop.5: Laboratory findings of postoperative 5 d. CPK = creatine phosphokinase, PTH = parathyroid hormone.

PDGEE, and *XPR1*,^[2] and thus, inherited FS is also referred to as Fahr's disease or primary familial brain calcification. However, Fahr's disease has been associated with idiopathic cerebral calcification, which differentiates FS from Fahr's disease.^[4] Savino et al encouraged the use of "secondary basal ganglia calcification" instead of FS to describe Fahr's disease attributable to secondary causes.^[5]

The majority of syndromes observed in parathyroid diseases involve disruptions of calcium and phosphorus homeostasis. Hypoparathyroidism is a rare endocrine disorder usually with an etiology of inadvertent parathyroid gland injury due to neck surgery. In addition, when there is a family history, familial isolated hypoparathyroidism may occur without surgical damage to glands. Autoimmune and metabolic disease, such as autoimmune polyglandular syndrome 1, mitochondrial neuromyopathies, and Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency, are also rare causative factors.^[6] Above all things, magnesium plays a central role in adenylate cyclase activity, which mediates PTH secretion and the organ effects of PTH, and magnesium deficiency alters the function of adenylate cyclase and results in the suppression of PTH release to blood and peripheral resistance.^[7]

Our patient had a history of GTC seizure, gait disturbance, spasticity of both lower and upper extremities, and bradykinesia of upper limbs, and these upper motor neuron signs were attributable to the OPLL and/or brain calcifications. Moreover, she exhibited continuously low levels of PTH and electrolytes, including calcium and magnesium, and although calcium and magnesium were repeatedly administered during the preoperative period, electrolytes were not corrected to normal ranges. Accordingly, calcium and magnesium administrations were continued postoperatively. The patient displayed hypocalcemia, hyperphosphatemia, hypomagnesemia, and hypoparathyroidism throughout her hospital stay, despite the provision of adequate treatment. Although we were not able to obtain genetic information related to causative factors, we presume that the pathophysiology of FS was related to primary hypoparathyroidism and hypomagnesemia.

Hypocalcemia is classically related to hyper-excitability at neuromuscular junctions, resulting in tetany, muscle cramps, laryngospasm, and seizures.^[8] Tracheal intubation and neuromuscular blocking agent use are 2 of the most concerning aspects of general anesthesia in FS. During induction, laryngeal dystonia and spasm may induce life-threatening dyspnea, and thus, it is important this airway component be carefully examined and that preoxygenation is adequate. Furthermore, hypocalcemia primarily induces functional changes in muscle membranes that result in creatinine kinase (CK) leakage, which suggests hypocalcemic myopathy may be asymptomatic hyper-CK-anemia. Policepatil et al reported a case of hypocalcemic myopathy secondary to hypoparathyroidism,^[8] and found muscle fibers exhibited type 2 fiber atrophy and focal myofibrillar degeneration. Hypoparathyroidism resulting in the development of myopathy with elevated CK probably remains minimally symptomatic due to the slow development of hypocalcemia and the remarkable ability of the body to adapt to chronically low serum calcium levels.^[9] However, it has been reported massive hyperkalemia developed after the administration of succinylcholine in a patient with myopathy. Therefore, we used rocuronium as a neuromuscular block and checked neuromuscular function by TOF monitoring, which is also essential for confirming neuromuscular function recovery and for detecting spasticity.

Patients with FS are prone to cardiovascular problems, such as, prolonged QT on ECG and hypocalcemia cardiomyopathy. Furthermore, because calcium is essential for myocardial contractile function, permanent hypocalcemia may result in cardiac dysfunction. In severe cases, hypocalcemia may cause heart failure when accompanied by renal sodium reabsorption and sodium retention.^[10] In addition, vascular calcium deposits compromise arterial elasticity and vasomotor responses and increase risks of cerebrovascular and coronary attacks.^[11,12] The vascular calcifications are a different type of atherosclerotic change because calcium first deposits on the outer layers of vessels and intima are spared.^[13] Anesthesiologists should pay strict attention to cardiovascular monitoring including BP, HR, CVP, and ECG, and a preoperative echocardiographic examination is essential.

Seizure may occur in FS, but no definite correlation exists between seizure and anatomical locations of calcifications, though calcium deposits in subcortical white matter are thought to be related to seizure development.^[14] In addition, although vascular and perivascular calcifications in central nerve system (CNS) may be correlated with seizure, its occurrence is considered to be mainly due to hypocalcemia. Hypocalcemia and hypomagnesemia cause neuronal irritability and CNS seizures. In the presence of such electrolyte imbalances, seizures are usually GTC, although other types can occur. The degree and rapidity of hypocalcemia onset affect ensuing symptoms.^[15] Magnesium is used for anticonvulsant treatment because it inhibits N-methyl-D-aspartate glutamate receptors and increases prostaglandin production in brain. Additionally, magnesium may stabilize neuronal membranes. Hypomagnesemia may result from various states such as antimicrobial, antibiotic, or chemotherapeutic treatment that may have increased magnesium renal excretion. But our patient had no history to cause a hypomagnesemia. The medical team, which included an endocrinologist, nephrologist, and neurologist, discussed the cause of hypomagnesemia, we did not figure out the exact causes of hypomagnesemia and decided to continue the conservative treatment.

In conclusions, anesthetic considerations in FS include laryngeal dystonia or spasm, unpredictable response to neuromuscular blocking agents, seizure, cerebrovascular attack, and myopathy, including symptoms of myalgia, weakness, and cardiovascular dysfunction, which are closely related to serum electrolytes, including calcium and magnesium. We considered several anesthetic problems such as laryngeal dystonia or spasm, seizure, myopathy, cerebrovascular attack, and cardiovascular dysfunction during general anesthesia in our patient. During the perioperative period, calcium levels should be closely monitored, and titrated calcium replacement therapy is recommended. The simultaneous correction of hypomagnesemia is of considerable importance when correcting hypocalcemia. Furthermore, we recommend invasive artery catheterization be performed for continuous arterial BP monitoring to prevent ischemic organ injury.

Author contributions

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