Case Report

Combined mucopolysaccharidosis type VI and congenital adrenal hyperplasia in a child: Anesthetic considerations

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Abstract

We present a child posted for magnetic resonance imaging of brain under general anesthesia with the rare combination of mucopolysachharidosis type VI and congenital adrenal hyperplasia. The presence of both these disorders has important anesthetic implications. The pathophysiology of this rare combination of disease is reviewed with emphasis on the anesthesia management.

Key words: Congenital adrenal hyperplasia, mucopolysaccharidosis, steroid supplementation, stress dose

Introduction

Mucopolysaccharidosis type VI (MPS VI) and congenital adrenal hyperplasia (CAH) are autosomal recessive disorders with multisystem involvement and may present an anesthetic challenge. Airway problems are frequently encountered in patients with MPS VI and CAH. Valvulopathy, skeletal involvement (in MPS VI) and steroid dependence and salt wasting (in CAH) compound the problems. Delivery of anesthesia to such patients in the hostile environment of magnetic resonance imaging (MRI) suite needs adequate backup and expertise. We report successful conduct of anesthesia in a child with MPS VI and CAH scheduled for MRI. We could not find any report on anesthetic management of patients with MPS VI and CAH in an extensive search of literature and Medline.

Case Report

A 12-kg, 3-year old girl born of consanguineous marriage, a known case of MPS VI (Maroteaux Lamy disease) and CAH, was scheduled to undergo MRI brain under anesthesia. The developmental milestones were delayed for age. The child was unable to stand or walk but was able to sit with support. The child had coarse facial features, corneal clouding, depressed nasal bridge, large tongue and high arched palate with a 2-cm mouth opening [Figure 1]. Parents did not reveal any history of snoring or apneic episodes while sleeping. Patient had virilization of the external genitalia with hirsutism and masculine voice. Patient had ambiguous genitalia. There was history of unexplained sibling death in the family at 1 year of age. She was on oral androstenedione (to keep the levels between 1 and1.5 nmol/l), hydrocortisone 10 mg/day, prednisolone 1.5 mg/day, and levothyroxine 20 μg/day. Hemogram, urine routine and microscopic examination, and kidney and liver function tests were within normal limits. Ultrasound abdomen was normal. Echocardiogram revealed myxomatous mitral valve with normal biventricular function and pulmonary artery pressure. X-ray skull showed craniomegaly with J-shaped sella [Figure 2]. X-rays of both hands revealed beaking and irregularity of proximal portions of 2nd to 5th metacarpals, mild widening of the distal radial metaphyses, and generalized osteopenia [Figure 3]. Kyphosis with ovoid-shaped vertebra and anterior beaking of L1 vertebral body was present on dorsolumbar spine X-ray. Chest X-ray displayed mild cardiomegaly, with cardiothoracic ratio of 0.55 [Figure 4]. Urine screening test for glycosaminoglycan dermatan sulfate was positive with deficient *N*-acetylgalactosamine-4-sulfatase in isolated leukocytes. 17-OH pregnenolone, 11-deoxycortisol, deoxycorticosterone, testosterone, and androstenedione levels were elevated.

General inhalational anesthesia with laryngeal mask airway was planned and informed consent was taken from the father

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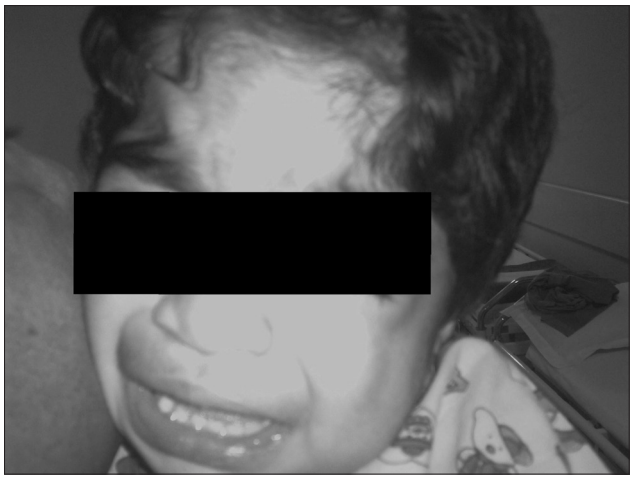

Figure 1: Photograph of the child with MPS VI and CAH

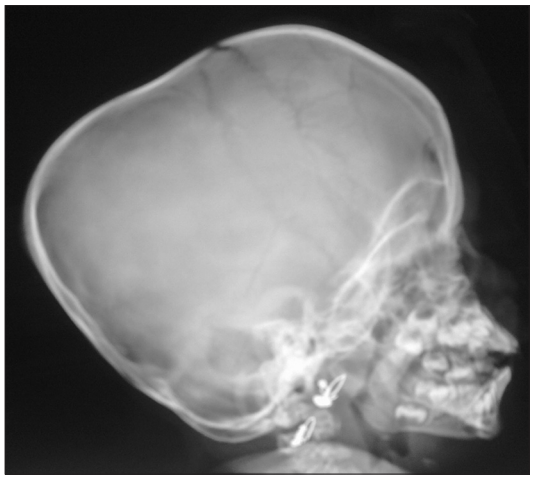

Figure 2: X-ray skull showing craniomegaly and J-shaped sella

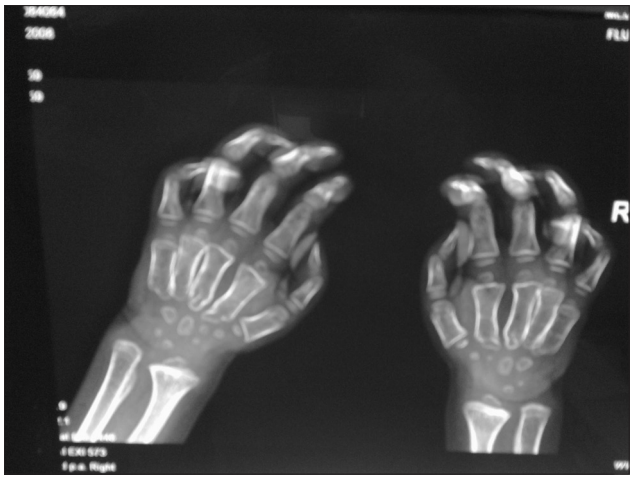

Figure 3: X-ray both hands with bony changes found in MPS VI

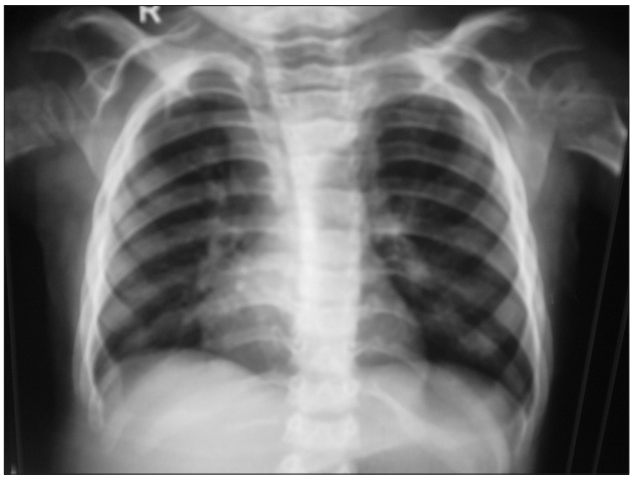

Figure 4: Chest X-ray showing mild cardiomegaly

of the child. Anesthesia was delivered by an MRI compatible anesthesia machine with vaporizers, monitors, airway equipment, and drug-delivery systems. Monitoring in the form of ECG, non-invasive blood pressure, and SpO_2 was done. Sedative premedication was avoided. Patient was induced with sevoflurane and a 24-G intravenous (IV) cannula secured. Fentanyl 20 μg and glycopyrrolate 50 μg administered IV. Laryngeal mask airway (LMA), size 2, could be placed in the second attempt and $EtCO_2$ monitoring initiated. Anesthesia was maintained on oxygen in air with sevoflurane. Hydrocortisone 25 mg IV was given. Patient was able to generate a spontaneous tidal volume of 90–100 ml with a pressure support of 5 cmH_2O. Patient remained hemodynamically stable throughout the procedure. At the end of the procedure, LMA was removed. The post procedure period was uneventful and patient was discharged after 4 h of observation.

Discussion

MPS VI is an autosomal recessive disorder with progressive multisystem involvement, first described by Pierre Maroteaux and Marice Lamy in 1963.[1] Patients with this disease lack the enzyme *N*-acetylgalactosamine-4-sulfatase with the accumulation of dermatan sulfate in skin, bones, neurons, liver, spleen, heart, cornea, and the airways. Patients with MPS VI have severe impairment of the intellectual function.[2] Cardiac involvement with valvulopathy, commonly of the mitral valve, is seen.[3] Presentation with endocardial fibroelastosis[4] or cardiomyopathy[5] has also been reported. Accumulation of glycosaminoglycan in the tissues results in coarse facies, corneal deposits, and skeletal involvement affecting the bones of skull, vertebra, hands, and feet. Umbilical and inguinal hernias frequently occur in MPS due to abdominal protuberance from hepatosplenomegaly and ineffective connective tissue support of the anterior abdominal wall. Patients commonly present for surgery and anesthesia due to multisystem involvement. The overall operative mortality in patients with mucopolysaccharidoses has been reported to be 20%.[6]

Airway difficulty is frequently encountered.[7] Narrow

foramen magnum with atlantoaxial instability limits the direct laryngoscopy which was present in our patient. Patients are prone to upper airway obstruction because of large tongue, thick gums, thick nasal mucosa, and large adenoids,[8] which is worsened by frequent upper respiratory tract infections. Progressive obstruction may lead to sleep apnea with severe hypoxemia and finally corpulmonale.[9] Thus, airway handling should be in expert hands and the equipment required for managing pediatric airway should be available.

Apart from mechanical hurdles in the management of anesthesia, our patient also had metabolic alterations in the form of CAH. CAH is an inherited, autosomal recessive disorder presenting in females as virilized external genitalia at birth due to prenatal exposure to androgens.[10] The incidence of CAH, in the United States, ranges from 1 in 15000 to 18000 live births; however, its incidence statistics for Indian population are not available. CAH involves a deficiency of an enzyme (21-, 11-, or 17-hydroxylase) involved in the synthesis of cortisol, aldosterone, or both.[11] In the most common 21 hydroxylase deficient form, seen in 90% of the cases, there is excess secretion of corticotrophin releasing hormone (CRH) and adrenocorticotropin hormone (ACTH) from hypothalamus and pituitary respectively due to deficient cortisol synthesis. This result in diversion of cortisol precursors to adrenal androgen synthesis, which does not require 21 hydroxylation.[12] Most patients with CAH have inadequate aldosterone secretion with consequent salt wasting.[13] Lack of both cortisol and aldosterone predispose to adrenal crisis, manifested as dehydration, hypotension, shock, acute abdomen, unexplained hypoglycemia, fever, hyponatremia, hyperkalemia, azotemia, and hypercalcemia. Medical management of CAH consists of administration of glucocorticoid to suppress the increased production of ACTH and CRH by negative feedback loop and also supplementation with mineralocorticoid and salt in salt wasters.[14] Long-term therapy with steroids may be associated with Cushingoid habitus, glucose intolerance, hypertension, hypokalemia, weight gain, and impaired wound healing. A clear understanding of the pathophysiology is important for the management of such patients.

Both regional as well as general anesthesia can be safe in patients presenting with this rare combination, lest the anesthesiologist is aware of the challenges presented. A thorough preoperative examination and work up is necessary. Hemogram, urine routine examination, chest and cervical spine X-ray, and serum electrolytes should be done. Any cardiac anomaly should be fully elucidated by an echocardiogram and chest and upper respiratory tract infections should be treated preoperatively.[7] Preoperative pulmonary function tests may be helpful to elucidate the risk of postoperative pulmonary complications in patients with long-term sleep apnea with pulmonary hypertension and/or corpulmonale. Due consideration should be given to positioning while performing a procedure under regional anesthesia due to the fragile skeletal system. Central neuraxial anesthesia should be performed with caution due to involvement of vertebral column in MPS and steroid induced obesity in CAH. Patient cooperation and consent may herald the provision of regional anesthesia in patients suffering from MPS due to intellectual decline.

Sedative premedication should be avoided for fear of upper airway obstruction. Use of antisialogogue may help reduce copious secretions. Antibiotic prophylaxis is recommended in all patients with MPS.[15] Establishment of a secure airway can be difficult owing to bony and soft-tissue abnormalities found in MPS VI and this is compounded by obesity-related difficult airway in steroid-dependent patients of CAH. In our patient, narrow foramen magnum and unstable atlantoaxial joint made airway management even more challenging. Considering the anticipated difficulties in securing the airway, adequate backup plan and expertise should be available. Hak Suh *et al*., reported successful intubation in a 9-month-old child with rare MPS VI. The authors feel that since repeated surgeries may be required in such patients, successive management of airway becomes increasingly difficult due to progressive nature of the disease.[16]

American Society of Anesthesiologists issued guidelines for anesthesia outside the operating room[17] are strictly adhered to in our set up. An inhalational induction with sevoflurane provides a controlled situation since the patient remains on spontaneous ventilation. We preferred putting an LMA over a tracheal tube with spontaneous ventilation, in view of her cervical spine anomaly. Steroid induced osteopenia should be addressed while positioning the patient.

Maintenance steroid therapy intraoperatively prevents adrenal crisis. Daily cortisol production ranges from 9 to 11 mg/ m^2/day.[18] Stress causes ACTH mediated increase in the cortisol production. During the perioperative period, it can rise depending on the severity, duration of surgery, and the technique and depth of anesthesia. CAH patients on supplemental steroid therapy cannot elicit this response and are candidates for "stress dosing" of glucocorticoids. Patients taking more than 10 mg prednisone daily, or taken such regimen within past 3 months, are candidates for stress dosing perioperatively and should be supplemented with psychological replacement or subjected to testing for exclusion of adrenal suppression.

To conclude, children with MPS and CAH pose an anesthetic challenge. A multidisciplinary approach and

thorough knowledge of the pathophysiology, symptomatology, and management of such patients helps in reducing the perioperative morbidity.

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