Case Series

Familial Dysautonomia, Report of 3 Cases from Iran and a Discussion about Their General and Anaesthesia Care

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Abstract

Background: Familial Dysautonomia (FD) is a rare hereditary syndrome which is an autosomal recessive trait that typically affects Jewish children. Important signs and symptoms of the disorder include; diminished pain perception, absence of overflow tears, hypotonia, fainting cardiac arrhythmias and autonomic crisis.
Cases Report: In this article we reported 3 cases of FD syndrome which had presented for surgical operation followed by a discussion about general care of these patients as well as Anesthesia considerations.
Keywords: Familial Dysautonomia, Pain, Anesthesia care

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Introduction

Dysautonomia may be congenital, Idiopathic or secondary to systemic disease[1]. Congenital or familial dysautonomia (FD) also named as riley-day syndrome is an autosomal recessive disorder that typically affects Jewish children[1]. Incidence of this disease is 1 in 3700 persons, so it is rare in general population. The disease caused by mutation in chromosome 9[2]. Peripheral nerve biopsy reveals a decrease in the number of small myelinated and unmyelinated fibers, post-morten examination of sympathetic, para -sympathetic and dorsal root ganglion cells demonstrates reduced numbers of cell bodies. Associated and potentially related biochemical changes are reported including significant decreases in serum dopamine ß hydroxylase and urinary vanillylmandelic acid (VMA) and increase urinary homovanillic acid (HVA). This suggests that FD patients have a deficiency related to an enzyme defect and an excess of catecholamine precursors[3]. Sings and symptoms of FD is variable and include: absence of overflow tears and corneal drying, poor suck at birth, drooling, swallowing and feeding problems, hypotonia and poor muscle tone, short stature, delayed motor language and social developmental milestones, inappropriate temperature controls, wide swings in blood pressure, gastro esophageal reflux, frequent lung infections or pneumonias, episodic vomiting decreased and no reaction to pain and temperature (no pain and no tears in patient life), excessive sweating, blotchy reddening of skin with exercise and/or feeding. Smooth tongue and lack of tastes, spinal curvature, poor weight gain and growth, impaired renal function, osteoporosis and osteopenia, fainting and cardiac arrhythmias, sleep

apnea, restrictive lung disease and signs of autonomic crisis. FD is often associated with a shortened life span[1,2].

General care of theses patients is difficult and also is more difficult when they underwent an invasive procedure like as anesthesia and surgery because autonomic crisis are one of the most devastating symptoms of the disease[4,5].

Hereby, we present three cases of FD which presents for surgical operation and have a discussion about general medical and anesthetic care of these patients.

Cases Report

Case A:

A 6 year-old girl presented to Anesthesia pre-operative evaluation clinic (APEC) for scheduling blepharorrhaphy surgical operation. She complained from corneal drying and lack of lacrimation since neonatal period. On the past medical history, she has had lack of tears, sever sweating, failure to thrive (<10 percentile), inappropriate pain sensation and diminished tendon reflexes (floppy baby). She has had also 2 faint experiences at 3 and 4.5 years old intermittent attacks of tachycardia/bradycardia. She has had a previous surgical operation at which severe bradycardia and hypotension was mentioned.

On examination smooth tongue without papillae, diminished deep tendon reflexes, orthostatic hypotension and unstable pulse rates is noted. Genetic consultation confirmed FD syndrome at this patient.

After pre-operative evaluation and preparing for operation, the patient scheduled for surgery. Precise continuous monitoring including blood pressure temperature, heart rate, respiratory rate, pulse oxymetry and capnography was done. Anesthesia was induced using standard doses of thiopantal, atracurium and alfentanil, ventilation was secured by using a laryngeal mask airway due to face and mandibular deformity and probability duration of difficult airway. Anesthesia maintained using continuous infusion of propoful, atracurium and remifentanil of surgery was about 75 minutes in which one crisis of severe bradycardia and hypotension was occurred which managed properly by using intravenous atropine and diminuting

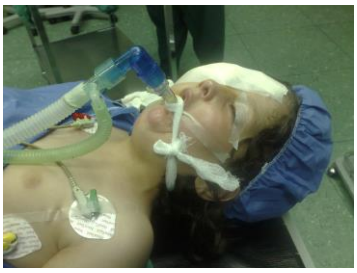

Figure 1 .Case 1, patient under general Anesthesia, Labbafinejad Medical Center, Tehran, IRAN

surgical (occulo-cardiac) reflex at end of operation. The patient transferred to recovery room, there were no problems and she was discharged 24 hours later with excellent general conditions.

Case B:

A 8 year-old girl was presented to anesthesia pre-operative evaluation clinic (APEC) for scheduling PK and blepharorrhaphy, she complained from corneal drying, lack of tears and subsequent blurred vision, on past medical history she was delivered by normal vaginal delivery without any mentioned important problem, but she has had failure to thrive, inappropriate sucking and weight gain at neonatal period. Hearing loss and diminished pain sensation is noted when she was 2 years. Ventricular dysrhythmia and intermittent attacks of tachycardia/bradycardia has been reported which has supervised and has managed by pediatric cardiologist. Several pulmonary infections (pneumonias) were also noted in few last years. Laboratory examinations had not important abnormal findings. After precise pre-operative evaluation and preparations the patient scheduled for operation. Premedication were administered by intravenous injection of fentanyl and midazolam. General anesthesia was induced by using of intravenous

Figure 2. Case 2, patient before anesthesia at operative room, Labbafinejad Medical Center, Tehran, Iran

propofol and atracurium. After tracheal intubations, anesthesia maintained by total intravenous anesthesia (TIVA) via continuous infusion of propofol, remifentanil and Atracurium. Duration of anesthesia was about 2 hours and everything were under precise control without any important problems except an attack of severe bradycardia due to direct pressure on the globe by the surgeon and activation of occulo-cardiac reflex. After termination of operation the patient transferred to recovery room with normal vital and general conditions and discharged from hospital with good general conditions after next 24 hours.

Case C:

An 11 year–old girl referred to APEC for scheduling blepharoplasty and PK Her chief complaint at presentation was corneal dryness and blurred vision. On past medical history she was second sibling of family who the first one had no medical problem she has suffered from lack of lacrimation, diminished neurologic reflexes from early at birth. Failure to thrive was not noted during infancy and new born periods. She has had 4 episodes of fainting at about 3 to 7 years in her life. She has also had diminished pain sensation from early childhood (about 1.5 years old). Automatic dysfunction and trophic ulcers were noted several times during pre-school age. She had also 2 surgical operations for eye and abdominal problems which was with severe attacks of bradycardia and hypotension especially in the second operation. She has had a genetic consultation for her problems and after precise evaluation diagnosis of FD was confirmed.

After preparation for anesthesia, and administration of premedication, anesthesia is induced by intravenous injection of alfentanil, propofol and cisatracurium. Air way security was established by use of a no. 3 laryngeal mask airway and anesthesia maintained by TIVA method using propofol, remifentanil, cisatracurium. Surgical time was about 100 minutes without any autonomic and or hemodynamic problems.

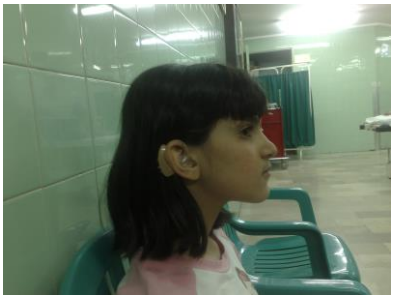

Figure 3. Case 3. Patient before anesthesia, Notice the assist Hearing device

At the end of operation and after insuring the stability of patient, she was transported to recovery room and subsequently to the ward and discharged from hospital 2 days later without any important problems.

Discussion

Congenital or familial dysautonomia (Riley-day syndrome) is an autosomal recessive disorder that typically affects Jewish children[1,5]. FD syndrome is an inherited disorder that affects nerve function throughout the body. Symptoms are present at birth and grow worse over time[2]. It is a rare genetic disease that affects the autonomic and sensory nervous system from birth. The most striking symptoms of FD are reduced sensitivity to pain and temperature, and the inappropriate tears. But FD is much more than "no pain and no tears", it affects every major system of the body, causing respiratory, cardiac, orthopedic, digestive and vision problems[2,6]. Children with FD lack the most basic reflexes and instincts that we take for granted. As they cannot control their blood pressure or heart rate, and they lack the ability to suck at birth and swallow properly. Because they often swallow into their lungs rather than their stomachs, they are prone for aspiration. Most FD patients have a feeding tube, so they can be fed directly into their stomachs and reduce risk of pneumonia. Advances in treatment have dramatically extended life expectancy, but children with FD still suffer debilitating symptoms that prevent them from leading normal lives[1,7].

FD causes a mysterious syndrome called "autonomic crisis" in which patients experience extreme swings of heart rate and heart rate, along with dramatic personality changes, and a complete shutdown of the digestive system of patients go into crisis, they cannot engage in any normal activity until hours or days later, and they may requires to hospitalization for observation, sedation and hydration until the crisis abates[1].

There is no cure for FD. Treatments are supportive and preventative. Therapies include medication to maintain

and regulate cardiovascular respiratory and gastrointestinal system. Surgical interventions include: fundoplication, gastrostomy, spinal fusion, and tear duct cautery are used to promote strength and speech development. There are some supportive therapeutic modalities for these patients and most used supportive methods include: artificial, tears, special feeding techniques, special therapies (feeding, occupational, physical, speech), special drug management of autonomic manifestations, respiratory care, protecting the child from injury (coping with decreased taste, temperature and pain perception), treatment of orthopedic problems (tibial torsion and spinal curvature), compensating for labile blood pressures.

The anesthetic management of familial dysautonomia is both complex and challenging. Decreased autonomic innervation of blood vessels and organs and variable baroreceptor sensitivity to circulating catecholamine's lead[1] to blood pressure liability. Baseline systemic vascular resistance is low. Cardiac output responds poorly to increased demand and is very dependent on preload, owing to a relatively fixed inotropy and chronotropy[1].

Patients are extremely sensitive to direct-acting vasopressors and have erratic responses to indirect-acting sympathomimetics, owing to diminished sympathetic innervation. Respiratory function is often compromised by aspiration pneumonia. Poor respiratory muscle function and varying degrees of scoliosis contribute to the restrictive lung disease. In addition, the centrally and peripherall mediated responses to hypoxia and hypercalfbia are diminished, a finding that implies greater sensitivity to CNS depressants[1].

Preoperatively, the major goals are to optimize respiratory function, ensure adequate hydration and reduce patient anxiety. Since chronic dehydration is common, hydration with intravenous crystalloid should before induction of anesthesia[1].

Preoperative medication with benzodiazepine is recommended because it is the treatment for dysautonomic crisis. Narcotic administration should be minimal or omitted, owing to the increased sensitivity manifested by dysautonomic patients. Antisialagogues should not be administered routinely, to avoid inspissated secretions. Before surgery, chest physiotherapy and prophylactic antibiotics should be given, as necessary. Acid aspiration prophylaxis should be utilized in this patient group at risk.

Severe hypotension has been reported to follow administration of thiopental and inhalational anesthetics to familial dysautonomia patients. However, adequate preoperative hydration can prevent significant hypotension with thiopental, narcotic or volatile[1] anesthetic administration. Dysautonomic patients require smaller doses of anesthetic drugs, perhaps owing to decreased pain sensation or an inability to release catecholamines in response to painful stimuli. Continuous appropriate monitoring should be instituted before induction. Because of the gastrointestinal effects of the disease, rapid sequence induction should be considered. Controlled ventilation via an endotracheal tube should be maintained during surgery owing to a tendency for atelectasis in these patients. There have been no reported adverse or prolonged responses to succinylcholine or nondepolarizing muscle relaxants, whereas adequate preload, both of which are more response to muscle relaxant reversal agents is unpredictable[1,6,7]. Atropine is effective in the treatment of bradycardia. If hypsion is unresponsive to fluid challenge, small, incremental doses of direct-acting a-adrenergic agents are indicated. Theoretically, regional anesthetic techniques should be tolerated well for the appropriate surgical procedure. Temperature should be monitored during the perioperative period owing to poikilothermic tendencies in dysautonomia.

Postoperatively, the goals are to maintain adequate ventilation, control pain and reactive blood pressure responses, and prevent aspiration. Postoperative pain, if present, should be treated to avoid provoking a dysautonomic crisis. Mechanical ventilation is advised until narcotics are discontinued. Vigorous pulmonary toilet and Prophylactic antibiotics should be administered appropriately[1,7,8].

Conclusion

FD is a rare hereditary disorder in which signs and symptoms of dysautonomia suspects these patients for disastrous problems. With advances in diagnosis and treatment modalities as well as general and anesthetic cares continues to improve their survival.

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