

Anaesthetic Management of a Dwarf with Hypopituitarism Presenting for Epigastric Hernioplasty: A Case Report

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Abstract

Hypoplastic pituitary, a rare entity in itself and when presented to us requires a detailed evaluation and postoperative follow up. We are presenting a 48 year old lady who is short statured posted for epigastrichernioplasty. Detailed evaluation revealed secondary hypothyroidism, difficult airway, cardiomegaly, pericardial effusion, secondary adrenocortical insufficiency, growth hormone deficiency. CT scan of brain revealed cerebrospinal fluid filled sellar region and magnetic resonance imaging proved hypo plastic pituitary. After optimization with L-thyroxine she was planned for balanced general anaesthesia with epidural analgesia under steroid coverage. Peroperatively we faced resistant hypotension and due to inadequate reversal she was shifted to intensive care unit on ventilator. Subsequently we proved that her postoperative adrenocorticotrophic hormone and cortisol level were low. However 24 hours later she could be extubated and finally she was discharged one week after the operation. However such cases are a challenge to the attending anaesthesiologist and as there is no strict protocol for anaesthetizing such a rare entity we have thought for detailing the case.

Keywords: Adrenocortical insufficiency; Balanced general anaesthesia; Epidural analgesia; Hypoplastic pituitary; Resistant hypotension

Introduction

The anterior pituitary often referred to as the 'master gland' orchestrating the complex regulatory functions of multiple other endocrine glands along with hypothalamus and the hormones produced by this gland elicit specific responses in peripheral target tissues [1]. Congenital hypoplastic pituitary is a very rare entity and the diagnosis is often elusive, emphasizing the importance of recognizing subtle clinical manifestations and performing the correct laboratory diagnostic tests. Hypopituitarism is not a common encounter that we as anaesthesiologists face in our day to day practice. Associated anomalies, short stature, difficult airway, secondary hypothyroidism and hypothalamo-pituitary-adrenal axis suppression require vigilant management and are a real challenge for anaesthesiologists.

Here we are presenting such a case of Hypopituitarism, who presented to our pre-anaesthetic check up clinic with a 5 year history of Epigastric hernia now posted for epigastrichernioplasty.

Case Report

A 48 year old lady presented to the preanaesthetic check up clinic with congenital dwarfism, gradually progressive uncomplicated ventral hernia for 5 years and hoarseness of voice since several years. She had history of premature menopause (at 40 years) and cold intolerance. Her father was short statured and her birth and maternal history were unremarkable.

On examination, her weight was 20 kg and height was 98 cm. Proportionate shortening of limb and trunk, coarse skin, hoarse voice

were noted. Airway assessment revealed small nostrils, interincisor distance-3 cm, Mallampati class-3, thyromental distance-4 cm, atlanto-occipital Extension >35°, short thick neck. Her heart rate was 86/min. and blood pressure was 110/72 mm. of Hg.

Examination of back revealed very short interspinous spaces without kyphoscoliosis.

The routine investigations: chest x-ray (CXR) postero-anterior view showed cardiomegaly, electrocardiogram (ECG) showed low voltage complex, Echocardiography findings were left ventricular ejection fraction (LVEF)-66%, Concentric left ventricular hypertrophy (LVH) and mild pericardial effusion.

Hormonal assays preoperatively revealed tri-iodothyronine (T3)-0.29ng/ml (Normal range: 0.8-2.0 ng/ml), thyroxine (T4)-3.29 µg/dl (Normal range: 4.6-12 µg/dl), thyroid stimulating hormone (TSH)-3.23 µIU/ml (Normal range: 0.27-4.2 µIU/ml), free T3-1.8 pg/ml (Normal range: 2.3-4.2 pg/ml), free T4-0.5 ng/L (Normal range: 0.8-1.8 ng/L), prolactin-8.3 ng/ml (Normal range: 1.9-25.9 ng/ml), luteinizing hormone (LH)-37.4 µIU/ml (Normal range: 8.2-40.8 µIU/ml), follicle stimulating hormone (FSH)-83.3 µIU/ml (Normal range: 35-151 µIU/ml), morning cortisol (7-9 A.M.)-17.14 µg/dl (Normal range: 4.3-22.4 µg/dl), adrenocorticotrophic hormone (ACTH)-11.0 pg/ml (Normal range: 6-46 pg/ml), GH-0.2ng/ml (Normal range: 0.5-17.0 ng/ml).

Other routine investigation findings were haemoglobin (Hb)-9.7 gm%, total leukocyte count (TLC)-8600/cu.mm. (Normal range: 4000-11000/cu.mm.), differential leukocyte count (DLC)-N₇₂L₁₇M₁E₈B₂, fasting blood sugar (FBS)-68 mg/dl (Normal range: 80-110 mg/dl), postprandial blood sugar (PPBS)-96 mg/dl (Normal range:<140 mg/dl), urea-32 mg/dl (Normal range: 20-40 mg/dl), creatinine-0.46 mg/dl (Normal range: 0.5-1.5 mg/dl). So, the patient was also hypoglycemic, as it is not uncommon in hypopituitarism.

CT scan of brain showed physiological calcifications in globipallidi and dentate nuclei, cerebrospinal fluid (CSF) filled sellar region. Pituitary gland was not visualized. Magnetic resonance imaging (MRI) of brain revealed hypoplastic pituitary. There were bilateral small ovaries on ultrasonography (USG) of abdomen.

Preoperative Optimisation

L-thyroxine 12.5 µg once daily for 10 days followed by 25 µg for 10 days and then 37.5 µg for next 3 weeks. After 6 weeks of optimization thyroid hormone levels improved (T3: 0.56 ng/ml; T4: 4.82 µg/dl; TSH: 2.1 µIU/ml).

Clonidine (100 µg orally) stimulation test showed 60 minutes later GH value of 0.26 ng/ml and 90 minutes later GH level was 0.27 ng/ml. Pre-anaesthetic airway evaluation could not be done by indirect laryngoscopy. Hence it was done by fiberoptic bronchoscope which revealed edematous vocal cords, narrow glottic opening but no mass was obstructing the glottic aperture.

Anaesthetic Management

After adequate optimization, obtaining informed written consent, keeping the difficult airway cart and resuscitative drugs and equipments ready, the patient was taken for anaesthesia. Intra-venous (IV) access was done in both hands. Early in the morning patient was administered 37.5 µg of L-thyroxine. Airway anaesthesia was done by nebulisation with 4% xylocaine for 20 mins after injection glycopyrrolate (0.2 mg) in intra-muscular (IM) route. Superior laryngeal nerve and recurrent laryngeal nerve blocks were given by 2% xylocaine around 1 ml at each site. Monitors were attached. Besides routine monitoring, neuromuscular monitoring and bi-spectral index (BIS) monitoring were done in this case. Blood glucose was also monitored. Plan of anaesthesia was balanced general anaesthesia combined with thoracic epidural analgesia. After preloading the patient with 10ml/kg of balanced salt solution, thoracic epidural catheterization was done at T8-T9 intervertebral space using 18G Tuohy needle with patient in sitting posture followed by 2 ml of test dose of 2% Xylocaine with adrenaline. Premedication was with inj. hydrocortisone 50 mg (IV) 30 minutes before intubation, Ondansetron 2 mg. (IV) 30 minutes before intubation, metoclopramide 10 mg (IV) and glycopyrrolate 0.2mg (IM) 20 mins before intubation, fentanyl 50 µg (IV) 6 mins before intubation, midazolam 2 mg. (IV) 2 mins before intubation. Pre-oxygenation was done with 100% oxygen (O₂) for 5 mins.

Awake fiberoptic guided tracheal intubation was done by 5.5 mm. internal diameter (ID) poly vinyl chloride (PVC) cuffed endotracheal tube after adequate airway anaesthesia and preparation. Muscle relaxant atracurium (0.5mg/kg) administered after confirmation of tube placement, dose titrated as guided by neuromuscular monitors. Maintenance of anaesthesia was done with O₂:N₂O = 33:67 and isoflurane (0.4-0.6 minimum alveolar concentration). Intermittent positive pressure ventilation (IPPV) was provided with respiratory rate (RR)-12/min, tidal volume (TV)-160 ml, inspiration and expiration ratio=1:2.5. Epidural analgesia was maintained with 0.125% bupivacaine and fentanyl (2 mcg/ml) as infusion at a rate of 4ml/hr. IV fluid ringer lactate 700 ml was given in 1 hour. 20 mins after induction of anaesthesia there was sudden hypotension with bradycardia nonresponsive to IV fluids though heart rate was stabilized with atropine 0.3 mg (IV). The epidural infusion rate was then halved and another 150 ml of IV fluid was infused. Dopamine (200 mg/50 ml

normal saline) infusion was started at a rate of 2 ml/hr via infusion pump. Operation was done successfully and patient was sent to intensive care unit (ICU) with endotracheal tube in-situ after hemodynamic stabilization with inotrope. Urine output, capillary blood glucose (CBG), arterial blood gas (ABG) analysis were within normal limits in the immediate postoperative phase.

She regained consciousness almost after 4 hrs; reflexes were normal, hemodynamics adequately stabilized. She was extubated after a successful weaning trial 24 hrs later. Postoperative ACTH level was 8.0 pg/ml which was low and cortisol was also in the low normal range of 8.2 µg/dl, despite in a stressful scenario. Her haemoglobin did not alter significantly in the postoperative period.

The next day i.e. 2nd post-operative day she was transferred to surgical ward and was discharged with good health with the advice of tapering steroid dosage and continuation of thyroid hormone replacement therapy 7 days after the operation.

Discussion

Hypopituitarism, an underactive pituitary gland results from impaired production of one or more of the pituitary trophic hormones. Reduced pituitary function can result from inherited disorders, more commonly it is acquired and reflects mass effects of tumours or the consequence of trauma, infiltrative disorders, vascular and infectious aetiologies [1-3].

Our patient had a congenital inherited disorder, aetiology of which was unknown as evidenced by Low TSH and ACTH in the period of stress, a low GH with a secondary hypothyroid background, secondary adrenocortical insufficiency. MRI also suggested a hypoplastic pituitary. Pituitary gland development from Rathke's pouch involves a complex interplay of lineage specific transcription factors expressed in pluripotent stem cells and gradients of locally produced growth factors [1].

The clinical manifestations of hypopituitarism depend on which hormones are lost and the extent of hormone deficiency. GH deficiency causes growth disorders in children and leads to abnormal body composition in adults. Gonadotrophin deficiency causes menstrual disorders and infertility in women and decreased sexual function, infertility and loss of secondary sexual characters in men. Somatotrophin and gonadotrophin seem to be affected first. TSH and ACTH deficiency usually develop later in the course of pituitary failure [3].

TSH deficiency causes growth retardation in children and features of hypothyroidism in children and in adults. The secondary form of adrenal insufficiency caused by ACTH deficiency leads to decreased production of cortisol with relative preservation of mineralocorticoid production. Prolactin deficiency causes failure of lactation. When lesions involve posterior pituitary, features like polyuria and polydipsia reflect loss of vasopressin secretion. Epidemiological studies have documented an increased mortality rate in patients with long standing pituitary damage primarily due to increased cardiovascular and cerebrovascular disease.

Our patient had a low free T3 and free T4 with a low TSH indicating a secondary hypothyroid state. This was the laboratory finding along with clinical suspicion which prompted us to investigate further.

The diagnosis of ACTH deficiency is difficult [2]. Partial ACTH deficiency may be unmasked in the presence of an acute medical or surgical illness when clinically significant hypocortisolism reflects diminished ACTH reserve [1]. Under surgical and anaesthetic stress, the adrenal glands secrete 116-185 mg of cortisol daily [4]. Under maximum stress, they may secrete 200 to 500 mg/day [4]. Good correlation exists between the severity and duration of the operation and the response of the adrenal gland. Major surgery would be represented by procedures such as major vascular, skeletal, neurologic repair or major reconstruction of the gastrointestinal tract and minor surgery by procedures such as herniorrhaphy. In one study of 20 patients during major surgery, the mean maximal concentration of cortisol in plasma was 47 µg/dl (Range 22 to 75 µg/dl). During minor surgery, the mean maximal concentration of cortisol in plasma was 28 µg/dl (Range 10 to 44 µg/dl) [3].

In our case the hormonal assay of ACTH and cortisol postoperatively reflected a secondary adrenocortical insufficiency. Also preoperative ACTH level was in low normal range in a stressful situation, which depicted a pituitary pathology. The diagnoses of GH deficiency can be made by GH assays before and after stimulation tests such as clonidine test, Arginine test and insulin provoked hypoglycaemia test [2]. Our patient had a pre-existing hypoglycemia.

Glucocorticoid replacement therapy improves most features of ACTH deficiency [1].

Because these patients cannot respond to stressful situations, it was traditionally recommended that they may be given a stress dose of glucocorticoids preoperatively [5].

However, Symreng and colleagues gave 25 mg of hydrocortisone intravenously to adults at the start of the operative procedure followed by 100 mg intravenously over the next 24 hours and this regimen did not worsen the situation. As minimum dosage was required in our patient to avoid the side effects of steroid, this regimen became more attractive [6].

The total daily dose of hydrocortisone replacement should not exceed 300 mg divided into 2-3 doses. Prednisolone 5 mg (morning dose) and 2.5 mg (evening dose) having fewer mineralocorticoid action and long duration of action is preferred in patients who are orally allowed to intake. Doses are increased several folds during periods of acute illness or stress [1]. Hence our patient was administered a steroid dosage regimen i.e. 50mg hydrocortisone which might have been inadequate considering dosage and duration but is an issue of debate due to lack of strict guidelines.

In a well controlled study of glucocorticoid replacement in primates, the investigators clearly defined the life-threatening events that can be associated with inadequate perioperative corticosteroid replacement [7]. L-thyroxine is recommended in 0.075-0.15 mg daily dose till patient is euthyroid [1]. Replacement of GH is indicated only if the diagnosis of adult GH deficiency is unequivocally established. If evolved GH < 0.3 ng/ml then, in adults somatotrophin 0.1-1.25 mg subcutaneously four times daily and in children 0.02-0.05 mg /kg/day administered for around 6 months [1]. In our case as adult growth hormone deficiency (AGHD) was not established, GH replacement was not considered. Difficult airway management, hypotension not responding to standard regimen, decrease in core body temperature in spite of active warming, very low concentration of anaesthetic drug requirement due to reduced metabolism, higher incidence of postoperative gastrointestinal and neuropsychiatric complications, electrolyte and coagulation disturbances, delayed emergence from

anaesthesia, perioperative stress management, steroid management are the main highlights of perioperative vigilant anaesthetic care [8-11]. In patients with concurrent thyrotrophin and corticotrophin deficiency, thyroxine must not be given without cortisol as this may precipitate a pituitary crisis [2].

The response to surgical and traumatic stress is triggered by hypothalamic activation secondary to afferent neuronal input from an area of injury or emotional activity centered in the limbic system and humoral factors such as inflammatory cytokines (interleukins, tumour necrosis factor and interferon). This is characterized by an increase in plasma levels of cortisol, ACTH, antidiuretic hormone/ vasopressin (ADH), renin, catecholamines, endorphins and by metabolic changes such as hypoglycemia and negative nitrogen balance [12-14]. Regional anaesthesia and general anaesthesia appears to blunt the release of various stress hormones [15]. Hence in this case epidural analgesia was considered.

Since it was a predicted difficult airway with history of hoarseness and as indirect laryngoscopy by otorhinolaryngologists was inconclusive we planned to evaluate the airway preoperatively so that preoperative airway management can be planned accordingly [16-18].

After excluding any major upper airway problem, we decided to go for awake fiberoptic intubation as per difficult airway algorithm, keeping in mind all the required precautions and keeping all the resuscitation drugs and equipments ready [19,20]. Maximum secretion of ACTH occurs during reversal of anaesthesia, during extubation and in immediate postoperative period [21]. In the postoperative stressed state ACTH and cortisol increases 2-3 folds with circadian rhythm disruption more in women [3,22-24].

This lady postoperatively revealed a low normal cortisol and ACTH which showed that secondary adrenocortical insufficiency might have been one of the probable causes of intraoperative hypotension though epidural analgesia induced hypotension can't be negated or proved.

Conclusion

Hypoplastic pituitary, though a rare entity but when presents to us, requires thorough evaluation including step wise hormonal assays with close eye on clinical presentation. A planned optimization plan should be sought out and only after adequate optimization we should proceed with such patients anticipating the risks of cardiovascular and cerebrovascular instability. Further it requires a vigilant anaesthetic management even in the post operative period regarding ventilatory support and postoperative hormonal evaluation. Proper guideline is still lacking regarding hormone replacement therapy in perioperative phase and the use of regional analgesia. But a keen eye, proper preparation and anticipation of complications can help to overcome the difficulties. So we can conclude that perioperative anaesthetic care in patients with hypopituitarism requires careful preoperative assessment and meticulous perioperative management.

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