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CASE REPORT
Coronary heart disease

Perioperative management in a patient with panhypopituitarism – evidence based approach: a case report

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Background Hypopituitarism is characterized by partial or complete deficiency of vital endocrinological hormones such as steroid and thyroid hormones. Generally, normal individual can exhibit 2- to 10-folds rise in serum cortisol levels during stressful period. But patients with panhypopituitarism are more prone to develop metabolic and haemodynamic instability particularly during stressful perioperative period. This can potentially increase significant morbidity and mortality.

Case summary A 62-year-old female patient presented with breathlessness on exertion. Her coronary angiography revealed critical triple vessel coronary artery disease, and she was scheduled for coronary artery bypass grafting surgery. She had been diagnosed with Sheehan's syndrome (postpartum hypopituitarism) since 20 years. She was taking steroid and thyroxine regularly. After uneventful off-pump coronary artery bypass grafting surgery, patient had severe haemodynamic compromise with Addisonian crisis in the post-operative phase. Left ventricular dysfunction was refractory to maximal inotropic therapy. Addisonian crisis was treated with higher 'Stress doses' of intravenous hydrocortisone and routine oral thyroxin.

Discussion Acute Addisonian crisis after stressful surgery is a life-threatening complication. Evidence-based approach plays an important role in appropriate biochemical assessments and specific therapeutic decisions regarding hormonal over-replacement or under-replacement in the perioperative period.

Keywords Hypopituitarism • Cardiac surgery • Perioperative management • Case report

Learning points

- Hypopituitarism is a complex disease with various hormonal deficiencies and diverse manifestations. It can be really difficult to manage such patients perioperatively particularly after cardiac surgery. Acute Addisonian crisis after stressful surgery is a life-threatening complication.
- Previous reports mentioned empirical treatment in such cases. Recently published guidelines definitely provide evidence-based approach which plays an important role in appropriate biochemical assessments and specific therapeutic decisions regarding hormonal over-replacement or under-replacement in the perioperative period.

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Introduction

Hypopituitarism is associated with higher morbidity and mortality due to cardiovascular and/or cerebrovascular diseases. In these cases, perioperative management presents a unique set of challenges due to potential risk of metabolic and haemodynamic instability particularly during stressful perioperative period.[1–3] A few anecdotal case reports in the literature described their individual experiences.[4] Recently published evidence-based recommendations can be very helpful in managing patients of hypopituitarism undergoing major surgery.

Timeline

Time	Events
Initial presentation	Admitted for coronary artery bypass grafting surgery for critical triple vessel coronary artery disease. Known case of Sheehan's syndrome. Already on oral medication—prednisolone and thyroxine.
Day 0 (intraoperative)	On the day of surgery, patient was administered intravenous injection of hydrocortisone 100 mg and thyroxine orally in the same preoperative dose. Uneventful operative course of off-pump coronary artery bypass grafting surgery.
Day 1	Hypotension and severe metabolic acidosis. Intravenous hydrocortisone 200 mg stat followed by 200 mg 8 hourly was administered. Thyroxine in the same preoperative doses. Thereafter, haemodynamics started improving.
Day 3	Extubated on post-operative Day 3 in haemodynamically and metabolically stable condition.
Day 5	Intravenous hydrocortisone dose was gradually tapered.

Case presentation

A 62-year-old female patient (weight 98 kg, height 158 cm) presented with complaints of breathlessness on exertion since 2 months. She also had chest discomfort on regular activities and patient feels better after taking rest. Patient had multiple comorbidities like diabetes, hypertension, obesity, hypothyroidism, and hypopituitarism. She had been diagnosed with Sheehan's syndrome (postpartum hypopituitarism) since 20 years. Physical examination revealed heart rate 68/min, regular pulse, and blood pressure of 130/60 mmHg with no signs of congestive heart failure. Jugular venous pulsation was not elevated and there was no peripheral oedema. On examination, she had a respiratory rate of 16/min with peripheral O_2 saturation of 97%. Auscultation did not reveal any abnormal breath sounds, rales, or rhonchi. Cardiac examination revealed a regular rhythm with no murmurs, gallops, or rubs. Her laboratory investigations were—haemoglobin 10 g/dL (normal range 12.0–15.5 g/dL), serum creatinine 1.1 mg/dL (normal range 0.6–1.1 mg/dL), and troponin I 0.06 ng/mL (normal <0.034 ng/mL). Electrocardiogram was suggestive of left ventricular (LV) hypertrophy. Transthoracic 2D echocardiographic examination revealed left ventricular ejection fraction (LVEF) 65% with no other abnormality detected. Considering the history of angina pain and risk factors for coronary artery disease, coronary angiography was performed. It was suggestive of critical triple vessel coronary artery disease and patient was scheduled for coronary artery bypass grafting surgery. At the time of admission, she was on following medications-prednisolone 5 mg orally in morning and 2.5 mg in the evening, and thyroxine 125 μg orally once daily. At the time of admission, thyroid hormones levels were—free T3-2.450 pg/dL, free T4-1.140 ng/dL, TSH-0.130 mIU/L, and serum cortisol level at 8 am—37.08 mcg/dL.

On the day of surgery, patient was administered intravenous injection of hydrocortisone (HC) 100 mg and thyroxine orally in the same preoperative dose. After uneventful anaesthesia induction, off-pump coronary artery bypass grafting (CABG) was performed with left internal mammary artery graft anastomosed to left anterior descending, saphenous venous grafts anastomosed to obtuse marginal, and posterior descending artery. Operative course was uneventful. Perioperatively, blood sugar was maintained between 100 and 200 mg/dL by titrated continuous intravenous insulin infusion. Postoperatively, patient had hypotension and severe metabolic acidosis. Echocardiography revealed LV dysfunction LVEF 40%. Despite adequate volume resuscitation and high dose of vasoactive agents (intravenous infusions of epinephrine 0.2 μg/kg/min and norepinephrine 0.15 μg/kg/min), mean arterial pressure could not be maintained optimally. Intra-aortic balloon pump was inserted considering LV dysfunction. Intravenous (i.v.) sodium bicarbonate infusion was started and intravenous hydrocortisone 200 mg stat followed by 200 mg i.v. 8 hourly was administered. Oral thyroxine was continued in the same preoperative dose. Thereafter haemodynamics started improving. Patient could be extubated on post-operative day (POD) 3 in haemodynamically and metabolically stable condition. Intravenous hydrocortisone was gradually tapered after POD 5 till it was replaced by oral prednisolone as in the preoperative regimen on POD 14. Patient was discharged from the hospital in a stable condition on POD 20. At 1-month follow-up after surgery, patient was clinically well. She resumed her regular activities, and her serum cortisol level and thyroid hormones were within normal level on her routine steroid and thyroxine medications.

Discussion

Hypopituitarism is a disorder characterized by a complete or partial deficiency of pituitary hormone secretions, such as thyroid-stimulating hormone or thyrotropin, growth hormone, adrenocorticotropic hormone, luteinizing hormone, follicle-stimulating hormone, and prolactin. Adults with hypopituitarism generally have risk factors for cardiovascular diseases such as central obesity, dyslipidaemia, insulin resistance, hypertension, and prothrombotic state with reduced fibrinolytic activity.[1,2] Patients with panhypopituitarism are more prone to develop cardiovascular-related mortality as compared with the normal population.[3] Hypercholesterolaemia, due to growth

hormone deficiency, was supposed to be the major reason in such patients.[4]

Perioperative course of any patient is influenced by major hormones—glucocorticoids and thyroid hormones. Cortisol is an important stress response hormone having metabolic, vasoactive, and anti-inflammatory effects on cardiovascular system. Besides, it also exerts inotropic action and regulates free water distribution within the vascular compartment. Patients with normal hypothalamic-pituitary-adrenal axis function exhibit 2- to 10-folds increase in serum cortisol levels during the periods of stress or serious illness.[5] Clinical implication of this physiological phenomenon is that patients with hypopituitarism can easily land up in adrenergic crisis if adrenal insufficiency is not successfully managed post-operatively. This can manifest with hypotension, fever, sepsis, vomiting, and toxic psychosis.[6] Similarly, deficient thyroid hormone can potentially cause dysfunction of cardiovascular, pulmonary, renal, and central nervous system, and make patients susceptible to surgical complications.[7]

Nevertheless, perioperative thyroid hormone replacement in patients with coronary artery disease should be done cautiously because it may exacerbate myocardial ischaemia and affect the sensitivity of vascular smooth muscle for catecholamine.[8] Therapeutic thyroxine dosage can raise myocardial contractility, heart rate, and myocardial oxygen consumption.[4] Perioperative low-dose thyroxin to maintain suboptimal blood concentrations of free T3 and free T4 has been suggested as a safe and appropriate thyroxin replacement in such patients.[4,6,8] Maintenance of serum thyroxine and cortisol levels in the normal range is of paramount importance in such patients in order to prevent likely adverse outcomes owing to surgical stress.

Recently clinical practice guidelines by an endocrine society have suggested the following specific recommendation regarding perioperative hormonal replacement in patients with hypopituitarism.[9] Related aspects of these recommendations can be summarized in three parts.

How to diagnose adrenergic insufficiency?

Central adrenergic insufficiency (AI) should be diagnosed by measuring serum cortisol levels at 8–9 a.m. Random cortisol level should never be used to diagnose the condition. Serum cortisol level less than 3 g/dL is suggestive of AI and a cortisol level more than 15 g/dL likely rules out an AI diagnosis. Hydrocortisone (HC) is the most common glucocorticoid used for replacement, followed by prednisone, cortisone, and dexamethasone. Patients with suspected adrenergic crisis due to secondary AI should be treated with an immediate intravenous injection of 50–100 mg HC.

How should steroids be replaced?

It has been observed that cortisol secretion per day is 75–100 mg in response to a major surgery and 50 mg in response to a minor surgery. Cortisol secretion is correlated with the duration and extent of surgery, and it rarely exceeds 200 mg in the first 24 h after surgery. In patients with central AI, the lowest tolerable dose of HC is recommended for replacement to potentially reduce the risks of cardiovascular and metabolic disease. Patients receiving daily HC doses higher or equal to 30 mg are prone to have endothelial dysfunction and raised overall cardiovascular mortality.[10] Lower hydrocortisone dose (15 mg/day) is associated with clinical improvement by reducing mean body weight, may result in lowering arterial stiffness and maintaining a more physiological nocturnal blood pressure dip.[11] Clinical practice guidelines by an endocrine society have suggested 25–75 mg of hydrocortisone per 24 h (usually for 1–2 days) in cases of minor to moderate surgical stress. In cases of major surgical stress, a 100 mg of intravenous hydrocortisone followed by a continuous i.v. infusion of 200 mg HC per 24 h is recommended (alternatively 50 mg every 6 h i.v. or i.m.).

(Dose equivalence of glucocorticoids: Hydrocortisone 20 mg = Prednisone 5 mg = Dexamethasone 0.75 mg = Methylprednisolone 4 mg = Cortisone 25 mg.)

How should thyroid hormones be replaced?

It is very essential to note that adrenal insufficiency should be conclusively excluded before initiating L-T4 therapy for hypopituitarism. Thyroid hormone speeds up the clearance of endogenous cortisol and this could potentially unmask insufficient cortisol production resulting in adrenal crisis. L-T4 in doses adequate to achieve serum fT4 levels in the mid to upper half of the reference range is recommended. Appropriate L-T4 dose advocated in hypopituitarism is about 1.6 μg/kg/day, with dose adjustments based on age, clinical context, and fT4 levels. Thyroid extracts, L-T3 or other formulations of thyroid hormones should not be used for treatment in hypopituitarism cases. Serum TSH levels are not preferred to guide thyroid hormone replacement dosing in such patients.

In the present case, patient had severe haemodynamic compromise with LV dysfunction refractory to maximal inotropic therapy. Intra-aortic balloon pump seemed to be a justifiable option in such scenario of post-operative low cardiac output unresponsive to usual inotropic supports.[12] However, the main culprit was post-operative Addisonian crisis resulting in a severe haemodynamic and metabolic deterioration. Such acute Addisonian crisis was treated with higher 'Stress doses' of intravenous hydrocortisone and routine oral thyroxin.

Rarely, hypopituitarism can also develop after cardiac surgery. This can present acutely as neuro-ophthalmological complications secondary to necrosis, Haemorrhage or acute swelling in a pre-existing pituitary tumour[13] and delayed presentation may be in the form of hypogonadism. Non-pulsatile flow, microemboli during bypass and haemodynamic changes in the brain during bypass are supposed to be the contributory causes of pituitary infarction after CABG.[14]

Conclusion

Hypopituitarism is a complex disease with various hormonal deficiencies and diverse manifestations. It can be really difficult to manage such patients perioperatively particularly after cardiac surgery. Acute Addisonian crisis after stressful surgery is a life-threatening complication. Evidence-based approach plays an important role in appropriate biochemical assessments and specific therapeutic decisions regarding hormonal over-replacement or under-replacement in the perioperative period.

Lead author biography

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Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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