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Anaesthesiological and surgical considerations in a patient with ectopic adrenocorticotropic hormone syndrome

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Abstract
Background: An ACTH-producing tumor is a rare type of endocrine pathology. This case report highlights the importance of a multidisciplinary approach in the diagnosis, surgical management, and anesthesia care for a patient with ectopic ACTH-producing tumor. Laparoscopic mono- or bi-lateral adrenalectomy under general anesthesia is the gold standard for treating Cushing's syndrome. However, preoperative assessment and preparation, intraoperative management of electrolyte and homeostasis corrections, difficult airway management, and postoperative glucocorticoid supplementation are essential to prevent life-threatening complications, such as arrhythmias and adrenal crisis.
Case presentation: Female, 41 years old presented to the emergency department with symptoms of progressive weakness, pressuring sensation in the head and eyes, fogginess and swelling of legs. Diagnostic tests revealed severe hypokalaemia 2, 37 mmol/l, increased ACTH 393.0 pg/ml and cortisol 73.1 mkg/dl plasma levels with pituitary microadenoma in MRI scan were discovered. Consequently, diagnosis were: ectopic ACTH-producing tumor, Cushing's syndrome. Severe hypokalaemia. Glucocorticosteroid-induced diabetes mellitus, secondary transient hypothyroidism, secondary hyperparathyroidism. Vitamin D deficiency.
Even though ACTH producing site was not localised, there was made decision to perform bilateral laparoscopic adrenalectomy, because her condition and laboratory tests worsened with persistent hypokalemia. Preoperatively, potassium supplementation was not successful and with sever hypokalemia 2.06 mmol/L mmol/l and metabolic alkalosis Ph 7.53 the patient underwent general anaesthesia. Continuous infusion of Potassium and Hydrocortisone was provided. Overall, patient's condition during the surgery was stable and after the extirpation of both adrenal glands, hemodynamic fluctuations were not observed. However, the patient developed hemorrhagic shock and underwent emergency splenectomy in the intensive care unit. Afterall, Potassium, ACTH and cortisol plasma levels started to improve in the next postoperative days. The patient was discharged from the hospital at 7th postoperative day.
Conclusion: This case demonstrates that the diagnosis and treatment of ectopic ACTH - producing tumor requires the involvement of multidisciplinary team and extraordinary decisions can be helpful. Bilateral laparoscopic adrenalectomy without identification of the primary ectopic ACTH-producing tumor under general anaesthesia with precise electrolyte and glucocorticoid supplementation was the right decision in this case.

Keywords: Cushing's syndrome, hypokalaemia, anaesthesia, adrenal disorders

Introduction
The hypothalamic-pituitary-adrenal axis contributes to the regulation of cortisol, a hormone of the adrenal cortex. The hypothalamus secretes corticotropin releasing hormone (CRH), which is a pituitary regulatory hormone. Adenohypophysis receives hormonal influences from the hypothalamus through the capillary wall and the adrenocorticotropic hormone (ACTH) is synthesized and secreted [2]. ACTH regulates the secretion of cortisol. Hormonal regulation is based on the negative feedback: the increase in cortisol concentration inhibits ACTH and CRH and vice versa. The secretion of ACTH and cortisol is pulsatile. The highest secretion peak is reached between 5 a.m. and 6 a.m. [4].
Cortisol is a steroid hormone, and has the widest range of biological effects: it participates in carbohydrate, protein and fat metabolism. It promotes gluconeogenesis, and insulin resistance, as well as increases blood glucose concentrations, stimulates the release of free fatty acids, and stimulates fat cell differentiation. It reduces cell division and collagen synthesis in the skin.

In the musculoskeletal system, it inhibits osteoblast function, decreases the absorption of calcium in the gastrointestinal tract, and increases calcium excretion in the kidney, leading to osteopenia and osteoporosis, and reducing linear skeletal growth via IGF-1 [4]. In the cardiovascular system, it increases arterial blood pressure. In the blood vessels, smooth muscle sensitivity to adrenergic stimuli increases, and in the kidneys, sodium retention and potassium excretion increase. In the immune system, cortisol functions as a suppressor of immunological response: it inhibits inflammatory mediators, prostaglandin, NO, cytokines, histamine, and plasminogen, and reduces the activity of phagocytes. In the central nervous system, it contributes to the regulation of emotions and formation of one's perception and promotes neuronal death [5]. In the eyes, cortisol increases intraocular pressure. In the endocrine system, it inhibits the secretion of thyroid-stimulating hormone (TSH), luteinizing hormone (LH), follicle-stimulating hormone (FSH) and growth hormone (GH) [2, 4].

Increased cortisol synthesis and secretion leads to endogenous Cushing's syndrome, characterized by weight gain, central obesity, exophthalmos, fat accumulation in the thoracocervical area (*buffalo hump*), proximal myopathy, moon face (*facies lunata*), hirsutism and acne, facial plethora, thinning of the skin, stretch marks (red-purple), skin pigmentation, wound healing is impaired, peripheral edema, fatigue, depression, behavioural changes, problems with concentration and memory, oligomenorrhea, polycystic ovary syndrome (POS), hypertension, decrease in libido, diabetes mellitus, kidney stone formation promoted by hypercalciuria, osteoporosis and pathological fracture, recurrent infections, hypokalaemia [4, 6]. From the pathophysiological perspective, endogenous Cushing's syndrome is divided into ACTH - dependent, and ACTH - independent. ACTH-dependent reasons: pituitary Cushing's syndrome (Cushing's disease), ectopic ACTH/CRH production. ACTH-independent reasons: adrenal adenoma and carcinoma, primary pigmented nodular adrenal hyperplasia, Carney syndrome, McCune-Albright syndrome, abnormal receptor expression. [4].

Ectopic production of ACTH

Epidemiology

Ectopic production of ACTH occurs in 15% of all Cushing's syndrome cases [4]. The most common tumors causing ectopic ACTH syndrome are small cell carcinoma in the bronchi or neuroendocrine tumor (NET) in the lung, pancreas, thymus, etc. Less commonly pheochromocytoma, medullary thyroid carcinoma. Very rarely prostate, gallbladder, ovarian, breast, or large bowel carcinoma [4].

Clinical presentation

The clinical presentation can be variable, depending on the malignant potential of the tumor and its localisation; however, in Cushing's syndrome with more pronounced ACTH production, the clinical presentation will be dominated by symptoms of Cushing's syndrome. If this syndrome has been caused by NET, it is characterised by sudden weakness, skin pigmentation, very high levels of ACTH and cortisol in the blood, weight loss, impaired glucose tolerance. Typical symptoms include hypokalaemia, metabolic alkalosis and peripheral oedema [12].

Diagnostics

Diagnostics includes at least 2 of the following criteria

- Spontaneous hypokalaemia (< 3.2 mmol/L),
- Plasma cortisol > 600 nmol/L (absence of circadian rhythm and/or dexamethasone suppression),
- Plasma ACTH > 22 pmol/L,
- Free cortisol 24 h urine >400 nmol/day [8].

To find the localization of the tumor, radiological diagnostics are used: ultrasonography, computed tomography, magnetic resonance imaging, somatostatin receptor scintigraphy. Somatostatin receptor PET (e.g. 68Ga DOTATATE PET/CT) should be optimally used for NET diagnosis.

Additionally, biochemical markers, the carcinoid syndrome-specific serotonin metabolite 5-HIAA in 24h urine and the syndrome-nonspecific Chromogranin A, can be used for NET diagnosis [11]. These markers have low sensitivity and various factors can often lead to a false positive result [12].

Treatment

If the localization of an ACTH-producing tumor has been identified, surgical treatment methods ranging from radical resection to volume reduction surgery are recommended. In rare cases, radiotherapy, chemotherapy, somatostatin analogues, biological preparations and radionucleotide therapy can be combined [12]. Therapy depends on the size of the tumor, its localisation, metastases, prognosis, origin, and treatment options in the hospital.

If the localization of an ACTH-producing tumor has not been identified, bilateral adrenalectomy [8] followed by lifelong hormone replacement or the less effective "medical adrenalectomy" using ketoconazole, metyrapone, mitotane or etomidate is the choice of action; however, their efficacy is not high and there are numerous side-effects [13].

Anaesthesiological aspects in a patient with Cushing's syndrome

Laparoscopic mono- or bi-lateral adrenalectomy is the gold standard for operative treatment of Cushing's syndrome, during which general anaesthesia is provided. During and after surgery, attention should be paid to certain stages that may cause complications [Table 1].

The anaesthetist, together with the surgeon and endocrinologist draws up the perioperative treatment plan:

Before surgery, anaesthesia is safe if before surgery are controlled hypercortisolism, arterial hypertension, hyperglycaemia, hypokalaemia, hyperhydration, hypercoagulation and infection prophylaxis. The patient receives necessary treatment until the morning of the surgery and strictly adheres to a fasting protocol, as gastric motility can often be disturbed.

During the surgery, the anaesthetist should be aware about difficult airways due to the central obesity and proximal muscle weakness, as well as about difficult ventilation, due to restrictive-type respiratory failure with reduced functional residual capacity (FRC). Hypoventilation, atelectasis, and hypoxia can be the consequences of reduced FRC. Therefore, adequate preoxygenation, rapid sequence intubation with the Sellick Maneuver and protective ventilation should be provided. The anaesthetist must be prepared to refer to colleagues in case of difficult ventilation and/or intubation and have a clear and well thought-out

extubation plan; often this should be done under monitoring in the intensive care. The pneumoperitoneum created during laparoscopy may contribute to endobronchial intubation, so the position of the endotracheal tube should be re-checked again [1].

Standard anaesthetic monitoring includes non-invasive/invasive monitoring of the arterial blood pressure, body temperature, capnography, pulse oximetry, and electrocardiography monitoring. Large-sized peripheral intravenous catheters or a central venous catheter are necessary as well. As an additional method to multimodal analgesia, epidural analgesia is recommended. Hydrocortisone should be available during surgery to prevent potentially rapid glucocorticoid deficiency after adrenalectomy [1].

After the surgery, aggressive analgesia, early mobilization of the patient, control and correction of hypokalaemia, hypertension, hyperglycaemia, hypokalaemia, and other clinical/laboratory parameters are cornerstones of enhanced patient recovery.

Table 1: Management of perioperative complications in patients with Cushing's syndrome

Cushing's syndrome	Treatment
Before surgery	
Cortisol inhibition	Adrenal enzyme inhibitors
Hypertension	Applying the PAH therapy, except for AKE-I and ARB
Hyperglycaemia	Cancel oral therapy and start insulin therapy
Hypokalaemia	Start spironolactone and potassium replacement
Perioperative hypercoagulation	MMH, lower limb compression techniques, early postoperative mobilisation
During surgery	
Detailed anaesthesia plan	General endotracheal anaesthesia, additional epidural analgesia may be considered
Positioning	Careful and gentle positioning, avoid bone fractures
Premedication	Avoid deep sedation
Risk of aspiration	Medication, the Sellick Maneuver, rapid sequence induction
Provision of airways	Adequate preoxygenation, select the most suitable endotracheal intubation method, ensure correct intubation
Venous access	Large peripheral venous catheter and central venous catheter
Invasive monitoring	Radial artery catheter, Swan-Ganz if necessary
Biochemical tests	Monitor glycaemia, electrolytes, and pH
Postoperative respiratory insufficiency	Awake extubation, patient monitoring
After surgery	
Acute pain therapy	Aggressive therapy, systemic/epidural opioids
Biochemical tests	Monitor glycaemia, electrolytes, cortisol, pH
Postoperative respiratory insufficiency	Breathing exercises, analgesics, mobilization
Venous thrombosis	LMWH, early mobilization
Infection, inflammation	Preventive antibacterial therapy before/after surgery

Abbreviations: PAH – primary arterial hypertension, ACE-I – angiotensin-converting enzyme inhibitors, ARB – angiotensin receptor blockers, LMWH – low-molecular-weight heparin.

Key massage: The main objective is to demonstrate the work of a multidisciplinary team and its importance in the care of this patient. The non-standard therapeutic approach for a patient with suspected ACTH-producing tumor was individually tailored to the patient and aimed at saving their life due to electrolyte imbalance.

Clinical case

Patient – female, 41 years old. In August 2022, she suddenly developed severe fatigue, pressuring sensation in the forehead, edema in both legs, and worsening of chronic polyarthritis, which she attributed to overheating and increased physical exertion. She turned to the general practitioner. In laboratory tests leukocytosis (14.45 10x9/L), neutrophilia (12.58 10x9/L), slightly increased D-dimers (0.56 mg/L) and hyperglycaemia (6.96 mmol/L), lactate dehydrogenase (LDH) 435 U/L, alanine aminotransferase(ALT) 97 U/L, creatine kinase 328 U/L, gamma-glutamyl transferase (GGT) 154 U/L, hypokalaemia (2.51 mmol/L), thyroid stimulating hormone(TSH) 0.081 mU/L, glycosuria (17 mmol/L) were presented. She started to receive – Spiramycin (Rovamycin, sanofi-aventis Zrt., Hungary), Omeprazole (Omeprazole-ratiopharm, TEVA Pharma S.L.U., Spain), Magnesium and Potassium (Panangin, Gedeon Richter Plc., Hungary), pancreatic supplements (Pangrol, Berlin-Chemie AG (Menarini Group), Germany) and Diclofenac (Diclomenal retard, G. L. Pharma GmbH, Austria). Emergency is called a week later because her condition worsens with progressive weakness, pressuring sensation in the head and eyes, fogginess and swelling of the legs. The patient is urgently admitted to Regional Hospital with suspected disturbances of cerebral blood circulation. Additionally, patient's medical history suggests, that she had a stomach ulcer ~20 years ago, contracted Covid-19 on 02.2022, chronic initial polyarthritis, denies surgery during life, there are no known allergies or medication intolerance. The patient denies taking medication on a daily basis.

At Regional Hospital

In the emergency department, a CT scan of the head was performed, without any acute changes in the brain, however a pathological substrate was observed in the both upper jaw cavities - a chronic sinusitis. In ECG sinus rhythm was detected with 77 x/min, left atrium overload, non-specific ST-T changes, no acute pathology. As mentioned before, patient had severe hypokalaemia (2.37 mmol/l), also blood tests showed significantly increased ACTH and cortisol plasma levels, therefore an ACTH-producing tumor was suspected. Additionally, abdominal and thyroid ultrasound (US) and CT with intravenous (IV) contrast for the chest and abdominal cavity were performed. Results found not conclusive data on oncological processes: US presented a slightly dilated urinary output; other organs were without pathology and thyroid gland was with homogeneous parenchyma of normal echogenicity, TIRADS1. CT scan with IV contrast not found significant pathological findings either - in the chest organs, and several small cortical areas of hypoperfusion were seen in the abdominal cavity on both sides of the kidneys; bone hemangioma in the body of the L1 vertebra, adrenal hyperplasia.

Blood tests were carried out

Complete blood count: WBC ↑ 12.99 10^3/uL, RBC 4.28

10^6/uL, HGB 13.3 g/dL, HCT 39.2%, RDW-CV ↓12.3%, PLT 169 10^3/uL, PDW ↓8.3 FL, NEU ↑11.45 10^3/uL, ↑88.1%, LYM ↓0.87 10^3/uL, ↓6.7%, MONO 0.65 10^3/uL, 5.0 %, EO ↓0.00 10^3/uL, ↓0.0%, BASO 0.02 10^3/uL, 0.2.

Clinical chemistry: ALT ↑105.8 U/l, CK ↑ 884.5 U/L, GGT ↑ 210.5 U/L, Creatinine 65.5 umol/l, GFR 92 mL/min/1.73m^2, Glucose ↑14.88 mmol/l, CRO 0.71 mg/L, Troponin – T ↑39.12 ng/L, CK-MB fraction ↑18.10 ng/ml.

Electrolytes: Sodium 142 mmol/l, Potassium ↓2.37 mmol/l, Calcium 2.14 mmol/L, Chlorides 88.8 mmol/L

Hormones: TSH ↓0.079 uIU/mL, FT4 ↓0.860 ng/dL, FT3 ↓1.60 npg/mL, C-peptide 3.63, Parathyroid hormone ↑96.77 pg/mL, Cortisol ↑73.1 mkg/dl, ACTH ↑393.0 pg/ml, Aldosterone <3.7 ng/dl

Immunohematology and autoantibodies: ANA IgG 0.2 index, Anti CCP <8.0 U/ml, Antibodies against TPO 12.2 IU/ml, TSH receptor antibodies 1.4 IU/L

Molecular biology: HLA B27 negative

Therapy with potassium chloride 7.45% (Potassium Chloride Braun 7,45%, B. Braun Melsungen AG, Germany) 20 ml 2 x/day was immediately started in Regional hospital, Torasemide 5mg (Torasemide Hexal, Salutas Pharma GmbH, Germany) was prescribed for 3 days, which is subsequently cancelled, Spirinolactone (Spirinolactone Accord, Accord Healthcare Limited, United Kingdom) 50mg 2x/day, Omeprazole (Omeprazole-ratiopharm, TEVA Pharma S.L.U., Spain), Ramipril (Ramipril Actavis, Actavis hf., Iceland), Metformin (Metformin-ratiopharm, Merckle GmbH, Germany), Vildagliptin (Vildagliptin Galenicum, SAG MANUFACTURING, S.L.U., Spain), Magnesium sulfate (Magnesium sulfate -Kalceks., AS KALCEKS, Latvia). Hypokalaemia fails to be corrected with the prescribed therapy; therefore, the patient with diagnosis - ACTH hypersecretion of unspecified etiology (Cushing's syndrome) with severe accompanying hypokalaemia - is transferred to the endocrinology department of Riga East Clinical University Hospital for further examination, clarification of the diagnosis, and correction of therapy.

Riga East Clinical University Hospital (RAKUS)

After 7 days the patient was transferred to the the Clinical University Hospital.

Upon admission, the patient's condition was severe but stable; in laboratory tests no significant dynamic improvement was detected for the patient. Critical hypokalaemia remains (1.68 mmol/l) with an increase in cortisol and ACTH plasma levels. Upon admission, a central venous catheter (CVC) was inserted to provide high doses of potassium replacement.

The patient is repeatedly subjected to a CT scan of the abdominal cavity and chest with IV contrast. There are no data on hormonally active oncological processes. An MRI of the pituitary gland detected a pituitary microadenoma. After that, long Dexamethasone suppression test was used to rule out the hormonal activity of a pituitary microadenoma. Suppression of cortisol and ACTH was not observed. A percutaneous biopsy in the nodule of the right lobe of the thyroid gland was performed under local anesthesia for histological examination. Pathological histological opinion: adrenal glands - adrenal cortex hyperplasia, spleen - spleen tissue with extensive hemorrhages, red pulp hyperplasia, small hyalinosis of trabeculae, hemorrhages in periadrenal fatty tissue. The morphological presentation may be consistent with splenic rupture.

In 24h urine collection excessive amount of cortisol 11003.20 mkg/24h is verified (normal 4.30-176.00).

In the hospital initially the patient received 100 mmol potassium substitution following by KCl 7.45% 15ml/h continuous infusion. Additionally, the patient received Spirinolactone 50 mg (Verospiron, Gedeon Richter Plc., Hungary) 4x/day, Omeprazol 20 mg 1x/day on an empty stomach in the morning, Levothyroxin 25 mcg (L-Thyroxin Berlin-Chemie, BERLIN-CHEMIE AG, Germany) 1x/day, Ramipril 5mg 1x/day; insulin therapy and regular determination of glucose levels were also started.

Given that the NET tumor had not yet been detected, a Concilium was duly convened. In light of the protracted symptoms, the ineffectiveness of conventional therapies, the persistent hypokalemia coupled with severe liver damage, and the characteristic markers of hypercortisolism evident in the patient's blood tests, the possibility of a pituitary microadenoma serving as the source of ACTH production was effectively ruled out. Consequently, it was determined that a bilateral adrenalectomy would be the appropriate course of action. With informed consent provided, the patient underwent laparoscopic bilateral adrenalectomy under general anesthesia, with a lifelong hormone replacement therapy plan established.

Preoperative period

Anesthesiologyst assessment: At anaesthesia, the patient's general condition was stable. Standard anthropometric parameters of the patient: height 175 cm, body weight 83 kg. The patient had no history of previous surgery. She was fully conscious, oriented in time, space and person. According to the Glasgow Coma Score, 15 points. Vital signs were stable: arterial blood pressure 130/80 mmHg, pulse 70 x/min. On the auscultation of heart valves, no murmur is heard. Sinus rhythm 60 x/min, ventricular hypertrophy, signs of overload shown in ECG. Transthoracic echocardiography: myocardial hypertrophy, myocardial contractions are good with ejection fraction 50%.

Respiratory rate 16x/min. Auscultation: bilateral vesicular breathing. X-ray, CT scan with IV contrast without pathological changes. Mallampati II in sitting position (possible mild tracheal intubation).

Prior to her hospitalization, the patient has not taken any medication on a daily basis. She denied harmful habits, such as regular alcohol consumption and drug use.

Changes in significant laboratory indicators before the surgery: potassium in blood serum 2.06 mmol/L, despite potassium replacement therapy with 200 mmol of potassium IV per day and therapy with Spirinolactone in a total dose of 200 mg per day.

Before the surgery, the patient had received an IV antibacterial therapy Cefazolini 2g (Cefazolin-BCPP, PJSC SIC “Borshchahivskiy Chemical-Pharmaceutical Plant”, Ukraina) for the prevention of infection.

Diagnosis: ectopic ACTH-producing tumor, Cushing's syndrome. Severe hypokalaemia. Glucocorticosteroid-induced diabetes mellitus, secondary transient hypothyroidism, secondary hyperparathyroidism, probably on the background of vitamin D deficiency. The assessment of the patient's physical condition according to the *ASA* scale (American Society of Anaesthesiologists) is III (patient with a severe systemic disease that limits their physical activity), which correlates with perioperative mortality of 1.8% to 4.3%.

Surgery and anaesthesia

The patient was planned to undergo bilateral laparoscopic adrenalectomy under general anaesthesia with the endotracheal intubation. During anaesthesia, standard monitoring parameters were used to monitor vital signs: 3-lead ECG, SpO_2, invasive arterial blood pressure (by inserting an *a. radialis dx* monitoring catheter intra-arterially, in aseptic conditions). The patient had previously been provided with v. *jugularis interna dx* centra access with 3-lumen venous catheter. The depth of the anaesthesia is monitored with the Bispectral index in the range of 60-40%, and adjusted, if necessary. A warming airflow blanket is used to maintain an optimal body temperature. Blood gas tests were performed intraoperatively (Table 2).

For induction of anaesthesia Oxygen - by inhaling O_2 at a flow rate of 6 l/min, an IV infusion of Remifentanil (Remifentanil Kabi, Fresenius Kabi Deutschland GmbH, Germany) at 0.0025 mg/kg/h was started; IV Fentanyl (Fentanyl citrate-Kalceks, AS KALCEKS, Latvia) 0.1 mg, Propofol (Propofol Fresenius, Fresenius Kabi Austria GmbH, Austria) 150 mg, Atracurium (Atracurium besilate Kalceks, AS KALCEKS, Latvia) 40 mg, Dexamethason (Orlixon, KRKA, Slovenia) 12 mg were administered.

To secure the airways, the endotracheal intubation by direct laryngoscopy was used with a Macintosh-type laryngoscope and an endotracheal tube ID 7.0 mm, depth a 22 cm. Mechanical lung ventilation was started in SIMV PCV VG mode (*Synchronized intermittent mandatory ventilation pressure controlled ventilation-volume guaranteed*) with the following parameters: ventilation volume 475 ml, respiratory rate 14 x/min, positive end-expiratory pressure (PEEP) 4 cmH_2O, inhalation-exhalation ratio 1:2, Pmax (peak inspiratory pressure 30 cmH_2O), maintaining end-expiratory CO_2 between 35 and 40 cmHg.

For maintenance of anaesthesia: Sevoflurane with MAC 0.8 to 1, IV infusion of Remifentanil from 0.0025 to 0.006 mg/kg/h as necessary, IV infusion of Atracurium 0.53 mg/kg/h, as well as IV potassium substitution with Potassium 7.45% - 10 mmol/h to avoid life-threatening hypokalemia.

Table 2: Electrolyte and pH changes in the patient during bilateral adrenalectomy.

Time	0h	1h	2.5h
pH	-	7.53	7.47
Na+, mmol/L	142	143	144
K^+, mmol/L	1.9	2.2	2.4
Ca2+, mmol/L	1.04	1.03	1.03
Glucose, mmol/L	9.1	10.0	10.8

50 min after intubation, IV Atropine (Atropine Sopharma, SOPHARMA AD, Bulgaria) 0.5 mg was administered intraoperatively due to bradycardia up to 38 x/min, which subsided immediately. Additionally, 2h and 50 min after the intubation, Ephedrine (Ephedrine Sintetica, Sintetica GmbH, Germany) 10 mg was administered IV due to hypotension 78/48 mmHg, which resulted in an increase in blood pressure.

After the extirpation of both adrenal glands, Hydrocortisone (Hydrocortison-Richter, Gedeon Richter Plc., Hungary) 100 mg IV, Paracetamol (Paracetamol B. Braun, B. Braun Medical S. A., Spain) 1 g IV, Ketarolax (Ketorolac-Grindeks, AS GRINDEKS., Latvia) 30 mg IV, and Ondansetron (Ondansetron Accord, Accord Healthcare Limited, United Kingdom) 8 mg IV were administered. In total, 1600 ml of IV fluids was administered, diuresis was 1400 ml. Blood loss was 100 ml. From the hemodynamic point of view, the surgery was stable and after the extirpation of both adrenal glands, hemodynamic fluctuations were not observed. At the end of the surgery, 1 drain with the tip in the lodge on the left side was placed.

Total time of anesthesia was 4h and 40 min, duration of the surgery was 3h and 5 min.

After the surgery, the patient was transferred to the intensive care clinic for further treatment. In approximately 1 h 40 min in the intensive care clinic, 400 ml of fresh blood suddenly appeared in the drain system and symptoms of haemorrhagic shock developed with a drop in arterial blood pressure to 55/24 mmHg; the patient became pale, sweating profusely, with impaired consciousness. The patient immediately was taken to the operating room for upper median laparotomy and general anaesthesia with Ketamine (Esketamine Kalceks, Kalceks, A/S, Latvia) 100 mg IV, Atracurium 40 mg, Fentanyl 0.1 mg and Rapid sequence endotracheal intubation was provided. Additionally to Tranexamic acid (Tranexamic acid Baxter, Baxter Holding B.V., Netherlands) 1 g IV administration, crystalloids, continuous infusion of noradrenaline (Norepinephrine Kalceks, Kalceks, A/S, Latvia) and haemotransfusions (2 doses of red blood cells, 2 doses of Fresh frozen plasma) are used to stabilize hemodynamics.

Fresh blood and blood clots were detected mainly in the upper abdomen cavity, more in the left subdiaphragmatic space. After the evacuation of blood and clots with a total blood loss of 2 L, bleeding was visualized from the portal area of the spleen. Considering the mentioned finding, splenectomy was performed by suturing the *a. lienalis*, as well as the perilienal tissue is ligated. The abdominal cavity was rinsed with 7 L of saline solution until the water is clean; the hemostasis test was repeated, there are no data on profuse bleeding. The lobe of the right adrenal gland was visualized and profuse bleeding was not observed. 2 drains were inserted into the surgical incisions of both adrenal glands. Sanation of the pelvis was performed, as well as revision of the intestines for their entire length. There were no data on palpable formations in the intestines. Laparotomy wound was closed in layers. After the surgery, the patient continued further treatment in the intensive care unit.

Post-operative period

After a bilateral adrenalectomy, an infusion of Hydrocortisone 200 mg was prescribed for 2 days, changing to 45 mg Hydrocortisone p/o on the third postoperative day, with the addition of the mineral corticoid Fludrocortisone (Cortineff, Adamed Pharma S.A., Poland) 0.1 mg. The patient continued to receive IV antibacterial therapy with Cefazolin 1g 4x/day and Enoxaparin (Clexan, Sanofi-

aventis groupe,France) 0.4 s/c for the prevention of thrombosis. K substitution and Verospirone were discontinued. On the fifth postoperative day, the patient is transferred from the ICU to the surgical unit.

Patient's blood tests at discharge

Complete blood count: WBC ↑10.96 10^3/uL, RBC ↓2.69 10^6/uL, HGB ↓8.20 g/dL, HCT ↓25.0%, MCV 92.9 fL, MCH 30.50 pg, MCHC 32.80 g/dL, PLT 192 10^3/uL, ↑3.8 %, NEU ↑7.99 10^3/uL, 73%, LYM 1.68 10^3/uL, ↓15.3%, MONO ↑0.75 10^3/uL, 6.8 %, EO 0.08 10^3/uL, 0.7%, BASO 0.04 10^3/uL, 0.4 %

Clinical chemistry: ALT ↑50.70 U/l, Creatinine ↓30 umol/l, Glucose 4.9 mmol/l, CRO ↑57.70 mg/L

Electrolytes: Sodium 142.50 mmol/l, Potassium↓ 2.95 mmol/l, Calcium ↓1.84 mmol/l

The patient was discharged from the hospital at 7th postoperative day. Adrenal cortex hormone replacement therapy should be implemented at home: Hydrocortisone 20mg in the morning and 10 mg at noon, Fludrocortisone 0.1 mg once a day. Additionally, vitamin D 4000 IU 1x/day, calcium citrate 500mg 2x/day. It is recommended to be under the supervision of a family doctor and an endocrinologist; a wholesome, balanced diet, adequate protein intake, following the basic principles of eating with a low glycemic index, increase the salt intake in the diet (~5g/day); currently rest mode, regular physical activities after stabilization of the health condition. It is recommended for repeated admission in endocrinology department for dynamic monitoring after 5-6 months, to rule out Nelson's syndrome. Somatostatin scintigraphy is considered to determine the location of an ectopic ACTH tumor.

Summary

An ectopic ACTH-producing tumor is a rare endocrine pathology. The diagnosis and treatment is complex, time-consuming and requires the involvement of multidisciplinary team. Hypokalemia can be life-threatening if its compensation fails despite high doses of potassium replacement. In this case, there was an vital indication for bilateral adrenalectomy, without identification of the primary ectopic ACTH-producing tumor. The main anaesthetic considerations included provision of airways, protective ventilation, stable arterial and venous access, and precise electrolyte control. The present case shows that a successful outcome is achieved when multidisciplinary approach is involved in the diagnosis and treatment. The patient is currently in her daily routine with a lifelong therapy under the supervision of an endocrinologist and a general practitioner; however, the final diagnosis and etiotropic therapy is still ahead.

Conflict of Interest Not available

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References

1. Vanags I, Sondore A. Clinical Anesthesiology and Intensive Therapy. Riga: Medicīnas apgāds; c2017.
2. Tretjakovs P. Regulation of Endocrine Functions [lecture].
3. Nieman LK. Overview of the treatment of Cushing's syndrome [Internet]. 2021 Nov 21 [cited 2024 Jun 13]. Available from: https://www-uptodate-com.db.rsu.lv/contents/overview-of-the-treatment-of-cushings-syndrome?search=cushing+syndrome&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H1
4. Melmed S, Koenig R, Rosen C, Auchus R, Goldfine A. Williams Textbook of Endocrinology [Internet]. Elsevier; c2020 [cited 2024 Jun 13]. Available from: https://www-clinicalkey-com.db.rsu.lv/#!/content/book/3-s2.0-B9780323555968120017
5. Sroykham W, Wongsawat Y. Effects of brain activity, morning salivary cortisol, and Emotion Regulation on cognitive impairment in elderly people [Internet]. Medicine; c2019 Jun [cited 2024 Jun 13]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6616250/
6. Ferri FF. Cushing Disease and Syndrome [Internet]. 2022 Jan 1 [cited 2024 Jun 13]. Available from: https://www-clinicalkey-com.db.rsu.lv/#!/content/derived_clinical_overview/76-s2.0-B9780323755702002514
7. Nieman LK, Biller BMK, Findling JW, Newell-Price J, Savage MO, Stewart PM, *et al*. Diagnosis of Cushing's syndrome: An endocrine society clinical practice guideline [Internet]. OUP Academic. 2008 May 1 [cited 2024 Jun 13]. Available from: https://academic.oup.com/jcem/article/93/5/1526/2598096
8. Wells T, Day A, Hilman S. Ectopic ACTH production: Diagnosis, treatment and Prognosis [Internet]. J Cancer Prev Curr Res. 2016 Dec 14 [cited 2024 Jun 13]. Available from: https://medcraveonline.com/JCPCR/ectopic-acth-production-diagnosis-treatment-and-prognosis.html
9. Domi R, Sula H, Kaci M, Paparisto S, Bodeci A, Xhemali A. Anesthetic considerations on adrenal gland surgery [Internet]. J Clin Med Res. 2015 Jan [cited 2024 Jun 13]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4217745/
10. Mihai R. Bilateral adrenalectomy-simultaneous or delayed? [Internet]. Laparoscopic Surgery. 2019 Oct 8 [cited 2024 Jun 13]. Available from: https://ls.amegroups.com/article/view/5398/html

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