CASE REPORTS

Sheehan's syndrome and anterior hypopituitarism

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Abstract

A case of Sheehan's syndrome and anterior hypopituitarism was collected in Geriatric department of the third clinical college of Inner Mongolia medical university. Due to atypical clinical symptoms, it is easy to be delayed in its diagnosis and treatment. The paper aims to investigate the difference of clinical characteristics and treatment outcome of anterior hypopituitarism through case analysis.

Key Words: Hypopituitarism, Postpartum hemorrhage, Signs and symptoms

1 Medical record

1.1 General information

A 26-year-old female patient was admitted to our hospital mainly because of intermittent anorexia, nausea and vomiting, diarrhea for 5 years and aggravation of 6 days on December 4, 2009. In 2004, the patient experienced massive hemorrhage during childbirth, was treated with blood transfusion and achieved good outcome. Later, the symptoms of poor appetite, nausea, vomiting, diarrhea, fatigue, mental indifference, drowsiness, unresponsive, and loss of libido appeared intermittently. She underwent a thyroid function examination in 2007 and the results showed that: s-TSH 1.7 IU/L (normal 0.3-5.0 IU/L), T_3 < 0.7 pmol/L (normal 1.1-3.4 pmol/L), T_4 < 13.2 pmol/L (normal 64-165 pmol/L). Low cortisol rhythm, 8 am 28.01 ng/ml (normal 70-280 ng/ml), 5 pm 32.74 ng/ml (normal 40-180 ng/ml), 12 pm 28.01 ng/ml (normal 28-80 ng/ml). Follicle stimulating hormone < 0.5 mIU/ml (normal 3-22 mIU/ml), Luteinizing hormone < 0.5 mIU/ml (normal 0.7-78.9 mIU/ml), Estradiol 38.5 pg/ml (normal 25-309 pg/ml). The diagnosis of anterior hypopituitarism was confirmed then. She took replacement therapy of prednisone 5 mg/d and Thyroxine tablet 50 μg/d and the symptoms were relieved. The examination results in 2008 were as follows: s-TSH 1.7 IU/L (normal 0.3-5.0 IU/L), T3 2.1 pmol/L (normal 1.1-3.4 pmol/L), T4 140 pmol/L (normal 64-165 pmol/L). The patient were manifested as fever with chills, sore throat, headache, cough, less sputum 6 days prior to her admission and received intravenous anti-inflammatory medication in private clinics with good result. She had nausea, vomiting of stomach contents 8 times, diarrhea, passed loose stools 6 times, spiritual diet, poor sleep but normal urine 1 day before admission. Past medical history included hysterectomy due to postpartum hemorrhage in 2004.

1.2 Physical examination

Data on the physical examination revealed her temperature 36°C and blood pressure 110/80 mmHg. She was conscious, with dry and rough skin, and apathy. Areola pigmentation was pale, with sparse eyebrows. Double lung breath sounds resonance, and no abnormal breath sound was heard. The heart rate was 67 times per minute, showing regularity in the force and rhythm of the heartbeat. Her bulging abdomen was soft with tenderness. No enlargement of liver, spleen

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and kidneys beneath the rib was found, nor edema of lower limbs. She had no pubic hair or armpit hair.

1.3 Auxiliary examination

The pituitary gland MRI disclosed an empty sella. Na^+ 139.1 mmol/L, Cl^- 100.9 mmol/L, K^+ 3.67 mmol/L, plasma glucose 5.0 mmol/L. Cortisol rhythm were low: 8 am 3.1 μg/dl (normal 6.2-19.4 μg/dl), 5 pm 2.0 μg/dl (normal 2.3-12.3 μg/dl), 12 pm 0.8 μg/dl (normal 1.2-6.2 μg/dl), FSH < 0.5 mIU/ml (normal 3-22 mIU/ml), LH < 0.5 mIU/ml (normal 0.7-78.9 mIU/ml), E_2 38.5 pg/ml (normal 25-309 pg/ml), PRL 5.6 ng/ml (normal 2.7-26 ng/ml), P 0.22 ng/ml (normal 0.11-30.9 ng/ml), GH 1.72 ng/ml (normal 1.0-3.0 ng/ml). Thyroid function: s-TSH 0.3 IU/L (normal 0.3-5.0 IU/L), FT_3 3.8 pmol/L (normal 3.2-9.2 pmol/L), FT_4 10.8 pmol/L (normal 8.6-25.8 pmol/L).

1.4 Primary diagnosis

(1) Sheehan's syndrome, anterior hypopituitarism pituitary crisis
(2) Upper respiratory tract infection

1.5 Treatment

The patient has a steady administration of prednisone 5 mg/day for a year once it is prescribed. She had fatigue, weight loss, nausea, vomiting, diarrhea, sweating of upper respiratory tract infection incentives during the past 3 months. The diagnosis of pituitary crisis was established on the day of admission. Hydrocortisone 100 mg was added to per 100 ml of saline for intravenous infusion to relieve acute adrenal insufficiency crisis after admission. The prednisone tablets were adjusted to 3.32 mg in the morning and 1.68 mg at 16 o'clock orally, and levothyroxine tablets 50 μg. She was manifested as nausea and vomiting meat water-like substance and occult blood (+). Therefore, acid suppression, bleeding, anti-infective therapy was treated and good outcome was obtained. Moreover, estrogen, progesterone replacement in order to maintain female characteristics and bone metabolism was maintained.

1.6 Confirmation of the diagnosis

(1) Sheehan's syndrome, anterior hypopituitarism pituitary crisis
(2) Upper respiratory tract infection

2 Discussion

2.1 Dr. Ruijing Yan

Dr. Ruijing Yan is a doctor at the Third Affiliated Hospital of Inner Mongolia Medical University.

The etiology for hypopituitarism is complex, which may result from disorders involving the pituitary gland, hypothalamus, or surrounding structures. It is classified into primary cause and secondary cause. The primary causes include: (1) Pituitary ischemic necrosis: postpartum hemorrhage (Sheehan's syndrome), diabetes, temporal arteritis and eclampsia; (2) Pituitary tumors: primary in the saddle within a variety of pituitary adenoma, chromophobe cell tumors, craniopharyngiomas, meningiomas, optic glioma; (3) Pituitary apoplexy: associated with pituitary; (4) Iatrogenic nasopharynx or sellar radiation therapy, surgical trauma destruction; (5) Other infectious diseases, autoimmune diseases, cavernous sinus thrombosis and primary empty sella syndrome. Secondary causes include: (1) The pituitary stalk damage: trauma, tumor or aneurysm oppression and trauma surgery; (2) The hypothalamus or other central nervous system disease, trauma, cancer, sarcoidosis, ectopic pineal tumors and neurological anorexia and so on, wherein postpartum pituitary adenoma and pituitary ischemic necrosis are the most common cause.[1]

Pathogenesis of hypopituitarism can be summarized as the following three points: (1) The decreased secretion of pituitary hormones due to pituitary lesions. (2) Releasing hormone secretion (or factors) under hypothalamic pituitary hormone is impeded due to hypothalamic lesions. (3) Hypothalamic–pituitary (the pituitary portal system) contact breaks, releasing hormone of hypothalamic pituitary stimulating hormone does not reach the pituitary gland so that pituitary cells dysfunction appears due to lack of excitement.[2]

Pituitary gland normally weighs 0.5 g, adenohypophysis and neurohypophysis own independent blood supply. Pituitary is mainly supplied by superior hypophysial artery, one branch of the carotid artery, forming arterial ring at the base of the pituitary stalk artery. Many branches of the arterial ring will enter into hypothalamus and media eminence, which is also the first capillary plexus of pituitary portal system. The portal system not only connects with media eminence of media eminence but also associates with adenohypophysis, functioning as an intermediary to deliver neuroendocrine substance by hypothalamus to adenohypophysis. The volume of pituitary is extended significantly about 2-3 times during pregnancy due to increased secretion of Prolactin (PRL) stimulated by human placental lactogen (HPL) and estrogen. The enlarged pituitary gland is easily to be damaged during acute ischemic swelling because of bone restrictions. In addition, there is no overlap within pituitary portal system, establishment of collateral circulation, therefore, is not allowed in case of ischemia. In summary, the symptoms that affect pituitary insufficiency, damage the central hypothalamic neuroendocrine, pituitary stalk integrity, and occupy space pituitary fossa may stimulate the disease. Sheehan's syndrome is pituitary avascular necrosis induced by postpartum hemorrhage, may produce crisis if remains uncured or infected by other stresses, such

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as infection, trauma, surgery, childbirth, overwork, excessive sweating, vomiting, diarrhea, dehydration, which may cause severe cases coma and death.[3]

2.2 Dr. Yan Feng

Dr. Yan Feng is an attending doctor at the Third Affiliated Hospital of Inner Mongolia Medical University.

Clinical manifestations of hypopituitarism are described in the following two aspects: (1) Etiology and clinical manifestations: The symptom of postpartum pituitary necrosis can result from dystocia while childbirth bleeding, fainting, shock history, or concurrent infection during childbirth. The patient was extremely weak after childbirth, manifested as no bulging breasts and no milk secretion, accompanied by the hypoglycemia, weak and rapid pulse rate, and oliguria. In addition, the patient had not been fully recovered, gradually the symptoms of sexual dysfunction, thyroid and adrenal insufficiency, and loss of periods occurred. The following manifestations may appear when the lesion is involved with hypothalamus:[4] 1) Anorexia nervosa or polyphagia, or both alternating; 2) An increase in drinking water, but also showed a diminished sense of thirst or no thirst; 3) Tends to daytime sleepiness, insomnia at night; 4) Unexplained fever or hypothermia; 5) Loss of libido or hyperthyroidism; 6) Sphincter dysfunction (constipation); 7) Psychopathia; 8) Intermittent epilepsy or convulsion; 9) Sweat or no sweat; 10) Cyanosis at hand and foot; 11) Tachycardia, arrhythmias or insufficient blood supply of coronary artery; 12) Physical exercise ability is low or don't want to move. Other medical causes of surgery, trauma, inflammation may drive the primary disease to crisis. (2) Hypopituitarism performance. Most multiple pituitary hormone deficiency phenomenon usually start with prolactin, gonadotropin, growth hormone deficiency symptoms, followed by thyroid stimulating hormone, and adrenocorticotropic hormone finally, sometimes the symptoms of adrenal insufficiency may occur earlier than thyroid dysfunction. 1) Prolactin secretion: manifested as no bulging breasts and no milk secretion. 2) Secretion of growth hormone deficiency, hypoglycemia in adults. 3) Decreased secretion of gonadotropin. Amenorrhea, loss of libido or disappear, breast and genital obvious atrophy, loss of fertility in female patients. Male patients showed degradation of secondary sexual characteristics, such as pubic hair sparse, the sound becomes soft, underdeveloped muscles, subcutaneous fat increased, as well as testicular atrophy, sperm development stopped, scrotum hypopigmentation, external genitalia, shrink the prostate, loss of libido, impotence, *etc*. 4) Thyroid-stimulating hormone deficiency: pale complexion, aged appearance, sparse eyebrow hair, armpit hair and pubic hair loss, dry skin, thin and shrink, edema, apathy, unresponsive, low tone, mental deterioration, crouching for cold, sometimes hallucinations, delusions, mental disorders, and even mania. 5) Adrenocorticotropic hormone deficiency: weakness, fatigue, loss of appetite, nausea, vomiting, abdominal pain, weight loss, heart sounds weak, slow heart rate, blood pressure, hunger, intolerance, easy hypoglycemia performance, prone to infection, followed by shock and coma. 6) Melanocyte stimulating hormone secretion deficiency: a lighter complexion, skin pigmentation will not deepened even was exposed to sunlight. Deeper pigment in normal parts will fade, such as areola and medioventral line. A small number of patients may have dark brown spots of irregular edges at anywhere. Sometimes there may appear yellow pigmentation at (toe) end.

2.3 Dr. Ying Wang

Dr. Ying Wang is a resident doctor at the Third Affiliated Hospital of Inner Mongolia Medical University.

Treatment for hypopituitarism includes: (1) General therapy: The patient should pay more attention to rest and warmth, avoid infection, mental stimulation, overwork and incentive activities, and maintain a good mood, meanwhile nutrition therapy should be strengthened, such as high protein, high energy, vitamin-rich foods. (2) Cause-based treatment: The root factor for the disease should be dealt with first once the cause is conformed, for example, surgery is advisable for tumor. (3) Endocrine therapy: hormone replacement therapy should be performed in a timely manner once the diagnosis is established, and be based on the principle of supplying the shortage.[5] Thyroid hormone, adrenocorticotropic hormone (Ach), estrogen, progesterone and other hormone replacement therapy is employed as various hormone replacement therapy, depending on the type of hormone deficiency. The therapy starts with a small dose and adjusts according to personal condition, while arbitrary-withdrawal is not allowed. Generally the dose of prednisone was 5-15 mg/d, once a day, oral maintenance dose is 5 mg/d. Extra administration of thyroid hormones, once a day, should be taken as long-term maintenance doses after the use of Ach for 5-7 days. Artificial female hormones menstrual cycle may be used as a long-term treatment for young female patients. Moreover, the patient should observe drug efficacy and side effects closely and alert the potential gastrointestinal stress ulcer during the course of the treatment. In addition to that, additional drugs to protect the gastric mucosa is necessary, and observe appetite, bowel sounds, abdominal distension, vomit and test results of feces color and occult blood. The symptoms, such as irritability, upper abdominal fullness, frequent hiccups, increased bowel movements, heart rate, blood pressure, are highly suggestive of gastrointestinal bleeding so that timely treatment is crucial. If the diagnosis of gastrointestinal bleeding is confirmed, the patient should immediately withdrawal or reduce dose, and use hemostatic agents, meanwhile paying attention to water, electrolyte, acid-base balance and peri-

odic review.

2.4 Dr. Qinxue Li

Dr. Qinxue Li is the deputy director of geriatrics department of the Third Affiliated Hospital of Inner Mongolia Medical University, specializing in endocrine diseases of the elderly.

Hypopituitarism refers to the pituitary hormone secretion, which can be a single hormone such as growth hormone (GH) deficiency or multiple stimulating hormone deficiency at the same time. Sheehan's syndrome results from postpartum hemorrhage that induces large areas of pituitary ischemic necrosis, and finally leads to hypothyroidism syndrome. The patient in the case underwent massive bleeding during childbirth, gradually appears intermittent anorexia, nausea, vomiting, diarrhea, fatigue, mental apathy, somnolence, dull reaction, loss of libido. Examination revealed that adrenal, thyroid and gonadal function were reduced because of hypopituitarism. The secretion of pituitary cells is directly affected by various hormones (factor) in the hypothalamus. It may induced by the pituitary disease or secondary to hypothalamic disease, manifested as thyroid, adrenal gland, gonads and other target gland dysfunction.[6] When partial or all the pituitary gland is destroyed, it can produce a series of endocrine dysfunction performance. The clinical symptoms appear when the damage is up to 50%, then it is obvious when it is up to 75%, finally aggravates when it is 95%. The clinical symptoms of the disease vary widely, and bring about long delay in diagnosis or misdiagnosis due to its atypical performance. The reasons are as follows: (1) Medical history is not comprehensive. Menstruation, reproductive history and sexual function may be ignored by the clinician, without careful examination, especially in the distribution of body hair and pudendum. Only local symptoms are noted, without systems integration analysis of the disease, so the disease is misdiagnosed as hypoglycemia, irregular menstruation, abdominal pain of unknown origin and many other diseases, which results in long-term delay in proper treatment. (2) Atypical clinical manifestations. Hypopituitarism carries complicated performance and lacks of specific symptoms. Patients with decreased secretion of pituitary hormones would show secondary atrophy and dysfunction of gonads, thyroid, and adrenal cortex. Pituitary necrosis is rapid onset, but hypopituitarism may appear after many years, which is often misdiagnosed by non-specialist doctors. (3) The possibility of hypopituitarism should be taken into consideration for unexplained fatigue, sleepiness, apathy, loss of hair, loss or disappearance of libido or other symptoms and digestive system during clinical practice. Timely tests for gonads, thyroid, and adrenal function are imperative for early diagnosis and reducing misdiagnosis rate. The presence of pituitary crisis should be ruled out for unexplained hypoglycemia, uncorrected hyponatremia or shock, unexplained coma, *etc*. (4) Narrowed diagnostic thinking. The incidence of postpartum hemorrhage is lower with the improvement of the overall health care level in our country, and the pituitary disease induced by the disease is even rare. As a clinician, we should have a wide range of knowledge, detailed medical history and careful examinations are imperative for expand ideas so that our thinking will not be limited to a professional range. Appropriate checks are the key to make a correct diagnosis of the disease, so as to reduce misdiagnosis and delayed treatment.

2.5 Dr. Gaisheng Tian

Dr. Gaisheng Tian is director of geriatrics department of the Third Affiliated Hospital of Inner Mongolia Medical University, specializing in endocrine diseases of the elderly.

Etiology and pathogenesis of hypopituitarism is complex. This may result from disorders involving the pituitary gland, hypothalamus, or surrounding structures, leading to decreased secretion of most pituitary hormones. The disease is easily to be misdiagnosis due to its large differences in the clinical manifestations, and lack of specificity. The cause for hypopituitarism in this case is postpartum hemorrhage. The disease, once diagnosed, should be treated immediately. It may induce a variety of incentives crisis in the later stage, such as coma, if timely diagnosis and treatment are not provided. Pituitary crisis is a rare but potentially life-threatening situation, whose diagnosis and survival rate rely on the suspicion of the potential of the disease, the rapid diagnosis and treatment.

Hypophysis function decline crisis hereby refers to pituitary crisis. Based on the symptoms of hypopituitarism, it may be induced by a variety of factors, such as nfection, sepsis, diarrhea, vomiting, dehydration, hunger, cold, acute myocardial infarction, cerebral vascular accident, surgery, trauma, anesthesia and the use of sedatives, hypnotics, hypoglycemic drugs. The clinical manifestations are as follows: (1) fever type ($> 40°C$); (2) low temperature ($< 30°C$); (3) low blood type; (4) low blood pressure, circulatory collapse type; (5) water intoxication type; (6) mixed type. Each type is characterized by the corresponding symptoms, of which digestive system, circulatory system and neuropsychiatric symptoms stand out the most, such as fever, circulatory failure, shock, nausea, vomiting, headache, confusion, delirium, convulsions, coma and other critical condition. Clinical postpartum hemorrhage caused by Sheehan's syndrome cause pituitary crisis, and thus life-threatening if not prompt treatment is not performed. Therefore, the treatment of pituitary crisis hinges on early and correct diagnosis. Treatment of pituitary crisis includes: an intravenous bolus injection of 50% glucose solution 40-60 ml to correct hypoglycemia, followed by 10% glucose solution, hydrocortisone 50-100 mg intravenous infusion per 500 ml were then added to relieve acute adrenal insufficiency crisis. The treatment for circulatory failure is on the basis of shock therapy and sepsis infection should be treated with anti-infection. Hypothermia

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is much associated with hypothyroidism so that a small dose of thyroid hormone is required, together with warm blanket for gradually warming. Anesthetics, sedatives, hypnotics, or hypoglycemic drugs should be used with caution or disabled.

3 Conclusion

What we learn from the case is that: as a clinician, we should have a wide range of knowledge, detailed medical history and careful examinations are imperative for expand ideas so that our thinking will not be limited to a professional range. Appropriate checks are the key to make a correct diagnosis of the disease, so as to reduce misdiagnosis and delayed treatment. Replacement therapy in the treatment of anterior pituitary hypothyroidism is mainly to the corresponding target gland hormones, tailored for individual condition, which could improve systematic metabolism and sexual function. It is long-term maintenance therapy for life, appropriate increase of the dose or and even intravenous infusion is essential in case of stress. While self-withdrawal is inadvisable as it may progress to critical condition or induce the crisis.

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