·临床病理讨论·

Clinicopathological Conference (the 48th case)

Adult gland pituitary hypofunction in an elderly female patient

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Case presentation

A female patient(a retired worker), 68 years old, who complained mainly of "repeated episodes of dizziness, fatigue, vomiting in 6 years, chest tightness, chest pain for 1 year", was admitted to Heart Center, Chaoyang Hospital, Capital Medical University on February 24, 2010. The patient suffered from dizziness and fatigue with unknown cause 6 years ago. She ever experienced sudden syncope and loss of consciouness during visiting Xuanwu Hospital, when she presented with blood pressure of 62 /? mmHg and slower heart rate, then her consciousness recoverd spontaneously 1-2 minutes later with no treatment. The head CT and electrocardiogram(ECG) showed no significant abnormality, and she was discharged after symptomatic treatment. Since then, the patient presented with intermittent anorexia, dizziness, nausea, vomiting, non-visual rotation, which were not affected by different body positions. All these symptoms appeared more frequently in winter, lasted for several days, relieved without any treatment. One year ago, the patient began to suffer from chest tightness and chest pain at physical activities. Each attack lasted for 3-5 minutes and relieved by rest. In Xuanwu Hospital, the diagnosis of "coronary heart disease, angina pectoris " was established. After oral administration of "Wan Shuang Li" and other meidcations, chest tightness and chest pain appeared accidentally. Ten days ago, the patient experienced dizziness and vomiting(stomach contents, 4-5 times a day on average). No visual rotation or tinnitus was accompanied. Twenty-nine hours before admission, the patient suffered from chest distress and chest pain again after 100 meters walking, accompanied with shoulder dispersion and sweating; the symptoms relieved after resting for 3-5 minutes. For further treatment, the patient visited Heart Center, Chaoyang Hospital. ECG showed "sinus bradycardia", and she was admittied for "arrhythmia". Since the onset, the patient displayed low blood pressure, slow heart rate, susceptibility to coldness, frailty, poor appetite and sleep, normal stool. The body mass decreased by about 5kg over the past decade.

Past history The patient had a 30-year history of cervical vertebra disease, chronic superficial gastritis, and one-year of lipid abnormality. Hypertension, diabetes and chronic kidney disease were denied. She received lumbar intervertebral disc protrusion operation 47 years ago. In recent 2 months, hyponatremia was observed. She also denied trauma and blood transfusion history. She had been living in Beijing since she was born. She got married at marriage age and gave birth to a healthy daughter by cesarean section. No postoperative bleeding was ever reported. The age at menopause was 52 years. She denied smoking and drinking history.

Family history Her mother suffered from hypertension and coronary heart disease. Her sister received permanent pacemaker implantation because of "arrhythmia". Her brother underwent coronary stenting because of coronary heart disease.

Physical examination Body temperature was 36.2 degrees; pulse rate 50 beats/min; respiratory rate 12 times/min; blood pressure 120/80mmHg (1mmHg= 0.133kPa). The patient was conscious, independent control of body position, and cooperative with examination. She had normal physical development, moderate nutrition condition, light skin color without pigmentation, normal skin temperature, dry skin, sparse eyebrows, light nipple areola color, absence of armpit hair and pubic hair, no enlargement of systemic superficial lymph nodes and jugular vein engorgement, clear bilateral breath sounds, and no evidence of cardiac dilatation. The heart rate(50 beats/min) pattern was regular. The abdomen was soft without palpable mass. No edema of limbs was observed.

Auxiliary examination (1) Blood routine: WBC 2.81×10^9, NE 42.7%, EO 12.6%, HBG 101g/L, PLT 118×10^9, ESR 33mm/h. (2)Biochemical examinations: normal liver function, renal function and HbA1c; serum potassium 4.9mmol/L, sodium 119.7mmol/L, chloride 90.8mmol/L; normal four coagulation factors and D-dimers. Hs-CRP 2.28mg/L, NT-BNP 301.3pg/ml;

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negative hepatitis B and hepatitis C antigen and antibody, negative HIV and TP antibody. (3)Urine routine: ERY 25/μL, SG 1.013; the left items normal. (4) Stool routine and fecal occult blood: occult blood in feces was positive on February 28 and March 6, and negative on March 10. (5) Blood osmotic pressure: 246mosm/L. (6) 24-hour urinary sodium 230.6mmol/L, urinary potassium 59.1mmol/L, serum beta 2 microglobulin 1780.8ng/ml, urine beta 2 microglobulin 131.1ng/ml. (7) 9 items related to tumor surveillance: sFerr 357.2-709.7ng/ml, NSE 17.38- 18.85ng/ml, others normal. (8)Thyroid function: FT3 1.39pg/ml, FT4 0.73 pg/ml, thyroid-stimulating hormone (TSH) 3.915pg/ml, serum cortisol 3.66μg /dl at 8:00 am, 2.26μg/dl at 4:00pm,3.9μg/dl at 12:00am; 24-hour urinary free cortisol: 36.1μg/24h (10-100); adrenocorticotropic hormone (ACTH) 3.02pmol/L at 8:00am, 3.26pmol/L at 4:00pm, 2.12pmol/L at 12:00am; Sex hormones: estradiol 7.81pg/ml, follicle-stimulating hormone (FSH) 3.86IU/L, luteinizing hormone (LH) 0.8IU/L, prolactin (PRL) 53.88ng/ml, progesterone < 0.08ng/ml, testosterone 0.46 ng/ml; Recumbent Food & P conditions: renin activity 0.09ng/ml, angiotensin II 8.2pg/ml, aldosterone (ALD): 0.07ng/ml. (9)ECG: sinus bradycardia, atrioventricular block degree I, 0.05mV down-slopping of ST_{V3-4}, flat $T_{III,}$ avF, and V2. Supersonic and enchanted graph: segmental wall motion abnormalities, LVEDD 45.7mm, LVEF 58%. (10)Abdominal B-mode ultrasound: normal hepatobiliary, pancreatic, spleen, and renal images; normal uterus, uterine appendages at menopause, no obvious effusion. (11)Gastroscopy: chronic atrophic gastritis accompanied with an erosion, Helicobacter pylori negative, mild chronic inflammation of gastric mucosa, concave of small intestinal epithelium. (12) Cervical vertebra radiographs: cervical vertebra disease, disappearance of cervical vertebra physiological curvature, mild backward of C3 vertebra. (13)Carotid artery ultrasound: double carotid artery intima coarseness. (14)Vestibular function examination: caloric test normal. (15)Head CT: mild senile brain change, empty sella. (16)Pituitary MRI: saddle abnormal signals in the shadow, no exclusion of empty sella, extreme pituitary atrophy.

Diagnosis and treatment After admission, blood pressure fluctuated at 120-90/70-60mmHg, and was 100/70mmHg generally. Electrocardiogram showed sinus bradycardia, with heart rate of 43-60 beats/min. The patient presented with intermittent dizziness, nausea, and poor appetite. Continuous intravenous sodium administration for correction of hyponatremia, even maximum 12g sodium daily, yielded poor results. The patient still had frequent nausea and vomiting. On February 26, the patient complained of chest tightness and heavy sweating. ECG revealed no obvious change. Blood glucose was 2.24mmol/L. Following intravenous injection of 50% glucose 40ml, blood glucose increased to 5.5mmol/L, and the symptoms relieved. On March 8, coronary angiography showed stenosis of left anterior descending artery(LAD) by 50%. Coronary heart disease, single branch lesion, involving the LAD, was considered. Diagnosis: adult gland pituitary hypofunction; coronary heart disease, angina pectoris; dyslipidemia; cervical spondylosis; chronic superficial gastritis; postoperative lumbar intervertebral disc protrusion.

For treatment, prednisolone 2.5-5.0mg was given orally once daily. Thyroid hormone accelerates the metabolism of the cortical hormone and aggravates cortraical hormone deficiencies, so euthyrox 50μg was additionally given orally once daily since one week after prednisone application, and the dosage increased to 75μg later because of the presence of bradycardia and low levels of T3 and T4. Routine treatment for coronary heart disease was also given. Gonadal hormone was not given to the patient, because she has been 68 years old and in menopause. Growth hormone was not given either, because it was expensive, and additionally, as an old female, she doesn't need replacement therapy. At the 4 months follow-up visit, the patient's symptoms, including dizziness, anorexia, nausea, vomiting, chills, fatigue, dry skin, were improved significantly, and the anginal symptoms disappeared. Physical examination revealed that the patient had eyebrows growth, light areola color, absence of armpit hair and pubic hair, ruddy complexion, and weight gain. Blood pressure still fluctuated at 90-100/60-70mmHg. Heart rate increased to 55-60 beats/min. Blood sodium returned to normal (137.2mmol/L). The changes in biochemical test results after treatment are shown in Table1.

Clinical discussion

Dr. CHI Hongjie from Heart Center of Chaoyang Hospital The patient presented with syndromes caused by insufficiency of multiple anterior pituitary hormones. (1)Hypogonadism: light nipple areola, sparse hair, absence of armpit hair and pubic hair. (2)Hypothyroidism: susceptibility to coldness, dry, rough, and pale skin with poor elasticity, less sweating, loss of appetite, slow heart rate, and decreased memory. (3)Adrenal cortical hypofunction: physical weakness, fatigue, anorexia, nausea, vomiting, weight loss, susceptibility to infection, episodes of hypoglycemia, light skin color due to reduced secretion of ACTH, pale complexion, and light nipple areola. (4)Growth hormone deficiency: muscle weakness, fatigue, poor appetite, dizziness, hypotension, hypoglycemia, low blood serum sodium, and atherosclerosis.

Table 1 Biochemical changes after treatment

Item	Before treatment	At 4 months after treatment
WBC($\times 10^9$)	2.81	9.46
NE(%)	42.7	62.7
EO(%)	12.6	2.4
HGB(g/L)/	101	132
FT3(pg/ml)	1.39	1.74
FT4(pg/ml)	0.73	1.15
TSH(p/ml)g	3.915	0.215
Serum cortisol at 8:00am(μg/L)	3.66	6.7
Serum cortisol 4:00pm(μg/L)	2.26	2.46
Serum cortisol 12:00am(μg/L)	3.9	1.18
Renin(ng/ml)	0.09	0.54
AngII(pg/ml)	8.2	81.9
ALD(ng/ml)	0.07	0.03
Estradiol(pg/ml)	7.81	24.49
Follicle stimulating hormone(IU/L)	3.86	4.38
LH(IU/L)	0.8	1.29
PRL(ng/ml)	53.88	38.48
Progesterone(ng	< 0.08	0.24
Testosterone/ml)	0.46	0.47
ACTH 8:00am(pmol/L)	3.02	2.33
ACTH 4:00pm(pmol/L)	3.26	< 1.11
ACTH 12:00am(pmol/L)	2.12	< 1.11

ACTH secretion is in an intermittent increase pattern, leading to rapid rise of blood cortisol. It shows a circadian rhythm: peak at hours before and after the awakening, gradually falling during morning, afternoon and evening, and lowest at 1 to 2 hours after falling asleep. Because the plasma ACTH half-life is short, and in an intermittent secretion pattern, so the plasma ACTH cannot be used as a reliable indicator of pituitary function of ACTH reserve. This patient displayed low levels of serum cortisol and ACTH at many time points, and the circadian rhythm disappeared(no peak in the morning). Patient with pituitary hypofunction has normal or low levels of TSH, T3 and T4. This patient had normal level of TSH, low level of T3 and T4. Pituitary gonadotropic cells secret LH and FSH respectively, which may change during menstruation. These two kinds of gonadotropins are secreted in an irregular, pulse pattern, so it is difficult to monitor their secretion. This patient had low levels of gonadotropin and sex steroid. After hormone replacement therapy, her condition was improved significantly. The patient's condition was in accordance with the diagnosis of adult gland pituitary hypofunction.

Prof. WU Xingli from Institute of Geriatric Cardiology of Chinese PLA General Hospital: The patient's head CT examination showed mild senile brain change and empty sella. Pituitary MRI revealed abnormal signals in the saddle, suggesting the possibility of cyst, no exclusion of empty and extreme pituitary atrophy. It has been 6 years since her first attack. She responded well to the treatment, so the sella turcica occupying lesion was considered cyst or nonfunctional adenoma. Any cause of anterior pituitary or hypothalamus injury can lead to anterior pituitary hypofunction, either primary or secondary disorder. The primary disorders included the following. (1)Benign or malignant tumor of pituitary and adjacent tissues. (2) Postpartum hemorrhage and other vascular disorders. For example, diabetic vascular disease can induce pituitary necrosis. Besides, there is pituitary hyperplasia in late gestation. Hemorrhage at delivery can cause hypotension, followed by pituitary gland arteriolar spasm, which also causes vascular necrosis of pituitary mesophyll. (3) Pituitary involved infection(pituitary tuberculosis, meningitis or encephalitis), operation and trauma, pituitary stroke, and some infiltrative lesions(leukemic infiltration), *etc*. The secondary disorders included (1)Damage of pituitary stalk, such as trauma, pituitary or sellar operation, *etc*; (2)Hypothalamus and other central nervous system lesions, such as sarcoidosis, tissue cell disease, and drug toxicity (vincristine) , *etc*. This disease can be divided into two categories: partial or complete impairment. For partial impairment, not all anterior pituitary hormones were synthesized and secreted inadequately. In this patient, prolactin level was high, so her situation belongs to partial impairmemt.

Prof. YANG Zhongsu from Heart Center of Chaoyang Hospital: Low level of hormones induced by primary diseases of endocrine glands is usually complicated by significant elevation of trophic hormones synthesized and secreted by anterior pituitary. If trophic hormone levels were not elevated, or on the contrary, lowered, especially if multiple trophic hormones were affected simultaneously, adult pituitary hypofunction should be considered. The clinical signs of this patient meet the diagnosis of this disease. It needs to be differentiated from some other diseases. (1)Anorexia nervosa. Angular and amenorrhea are the frequently seen symptoms. Pituitary function may be affected by anxiety and malnutrition, so as to induce some symptoms similar to hypopituitarism. But it is usually seen in young females around the age of 20 years, who ever had a previous mental stimulation history, was more marasmic than those with pituitary hypofunction, rarely shed armpit hair and pubic hair, and urinary 17 - ketone sterol and urinary 17 - hydroxyl corticosteroids were normal or lightly decreased. (2)Primary hypothyroidism. Except hypothyroidism, other endocrine glands function may be also accidentally disturbed. In addition, it is characterized by myxedema appearance, the significantly increased blood cholesterol concentrations and an enlarged heart. Elevation of plasma thyrotropin level has important differentiating role in primary hypothyroidism. Primary hypothyroidism had "super reaction" in TSH stimulation test, while pituitary hypofunction may have no response and hypothalamic

hypofunction may show a delayed response. (3)Chronic adrenocortical hypofunction. This disorder has typical cutaneous and mucosal pigmentation, no sexual organ atrophy or manifestations of hypothyroidism, obvious signs of sodium loss, no response to adrenocorticotropic hormone. As for secondary adrenocortical hypofunction, intravenous infusion of corticotropin hormone for 3-5 days may cause gradual increase of steroid excretion. (4)Autoimmune poly-endocrine syndrome. The patient suffered from clinical signs caused by primary multiple endocrine gland hypofunction, rather than pituitary hypofunction. Adrenocorticotropic hormone and thyrotropic hormone have no response in stimulation test, while pituitary hypofunction often has delayed response. (5) Chronic wasting diseases usually have features of weakness, weight loss, sexual dysfunction and low level of urinary 17-ketone sterol. In some serious cases, secondary pituitary insufficiency may be also observed, but the symptoms can be gradually alleviated after the nutrition condition improvement. Obviously, this patient did not agree with the above features. Cardiac arrhythmia is one of the main performances of this patient. After hormone replacement therapy, her heart rate increased, and the symptoms improved significantly. Long-term chronic arrhythmia is frequently found in primary heart disease or autonomic cell dysfunction caused by degenerative changes. But, systematic disease outside the heart should be excluded. Through active treatment for primary disease, arrhythmia can be alleviated or corrected in most cases, thus the implantation of permanent cardiac pacemaker may be avoided.

(Translator: YANG Zhongsu)

成人腺垂体功能减退症 1 例

1 病例摘要

患者女性，68 岁，退休工人，主因“反复发作头晕，乏力，呕吐 6 年，胸闷，胸痛 1 年”，于 2010 年 2 月 24 日入我院心血管内科治疗。患者 6 年前无明显诱因出现头晕，乏力。曾于宣武医院就诊过程中突发晕厥，意识丧失，当时测血压 62/?mmHg，心率慢（具体不详），持续 1～2 min 意识自行恢复，查头颅 CT 和心电图未见明显异常，住院对症治疗好转出院。此后患者间断纳差，头晕伴恶心，呕吐，无视物旋转，与体位无关，多于冬季出现，持续数天，自行好转，反复发作。1 年前开始出现活动时胸闷，胸痛，每次持续 3～5 min，休息后缓解，于宣武医院诊断“冠心病，心绞痛”，口服曲美他嗪（商品名：万爽力）等药物治疗，胸闷、胸痛偶发。10 d 前患者再次出现头晕，头晕时不伴视物旋转及耳鸣，伴呕吐，平均每日呕吐 4～5 次，均为胃内容物。29 h 前患者步行 100 米后再次出现胸闷，胸痛，伴肩部放散及出汗，休息 3～5 min 后缓解。为求进一步诊治至我院心血管内科门诊，心电图示“窦性心动过缓”，以“心律失常”入院。发病以来自诉血压低，心率慢，怕冷，体弱，饮食及睡眠差，大便正常，体重近 10 年来下降约 10 余斤。

既往史：患颈椎病和慢性浅表性胃炎 30 年，血脂异常 1 年。否认高血压，糖尿病及慢性肾脏病史。47 年前行腰椎间盘突出手术治疗。近 2 个月发现低钠血症。否认外伤及输血史。个人史：生于北京，久居北京，适龄结婚，曾行剖宫产术，无术后大出血病史，育有 1 女，体健。52 岁绝经。否认吸烟及饮酒史。家族史：母亲患高血压及冠心病，妹妹因“心律失常”置入永久型起搏器治疗，弟弟患冠心病曾经行过冠脉支架置入术。

体格检查：体温 36.2℃，脉搏 50 次/min，呼吸 12 次/min，血压 120/80mmHg（1mmHg=0.133kPa）。神志清楚，发育正常，营养中等，自主体位，查体合作，皮肤颜色浅，皮温正常，无色素沉着，皮肤干燥，眉毛稀疏，乳晕色浅，腋毛阴毛脱落，全身浅表淋巴结未触及肿大，颈静脉无怒张，双肺呼吸音清，心界不大，心率 50 次/min，律齐，无杂音，腹软，未触及包块，四肢无水肿。

辅助检查：（1）血常规：白细胞 2.81×10^9，中性粒细胞 42.7%，嗜酸粒细胞 12.6%，血红蛋白 101 g/L，血小板 118×10^9，血沉 33 mm/h。（2）生化检查：肝功能、肾功能及糖化血红蛋白（HbA1c）均正常；血清钾 4.9 mmol/L、钠 119.7 mmol/L、氯 90.8 mmol/L；凝血 4 项及 D 二聚体正常；超敏 C 反应蛋白 2.28 mg/L，N 端脑钠肽 301.3 pg/ml；乙型肝炎及丙型肝炎抗原、抗体阴性，HIV 及梅毒抗体阴性。（3）尿常规：红细胞 25/μl，尿比重 1.013，余正常。（4）粪便常规及潜血：2 月 28 日及 3 月 6 日粪便潜血阳性，3 月 10 日粪便潜血阴性。（5）血渗透压：246 mosm/L。（6）24 h 尿钠：230.6 mmol/L，尿钾：59.1 mmol/L。血 β2 微球蛋白 1780.8 ng/ml，尿 β2 微球蛋白 131.1 ng/ml。（7）肿瘤 9 项：sFerr357.2～709.7 ng/ml，NSE

17.38～18.85 ng/ml, 余正常。(8) 甲状腺功能: 游离 T3 1.39pg/ml, 游离 T4 0.73pg/ml, 促甲状腺激素 (thyroid-stimulating hormone, TSH) 3.915 pg/ml; 血清皮质醇 8:00 am 36.6 μg/L, 4:00 pm 22.6μg/L, 12 n 39.0 μg/L, 24h 尿游离皮质醇: 36.1 μg/24 h; 促肾上腺皮质激素 (adrenocorticotrophic hormone, ACTH) 8:00 am 3.02pmol/L, 4:00 pm 3.26pmol/L, 12n 2.12pmol/L; 性激素: 雌二醇 7.81pg/ml, 促卵泡激素 (follicle stimulating hormone, FSH) 3.86IU/L, 促黄体生成素 (luteining hormone, LH) 0.8 IU/L, 催乳素 53.88 ng/ml, 孕酮＜0.08 ng/ml, 睾酮 0.46ng/ml; 卧位普食条件下: 肾素活性 0.09ng/ml, 血管紧张素Ⅱ 8.2pg/ml, 醛固酮 0.07ng/ml。(9) 心电图检查示窦性心动过缓, Ⅰ度房室传导阻滞, STV3～4 压低 0.05mV, TⅢ, aVF, V2 低平; 超声心动图: 节段性室壁运动异常, 左心室舒张末期内径 45.7mm, 左心室射血分数 58%。(10) 腹部 B 超: 肝、胆、胰、脾、双肾未见异常; 子宫、附件超声: 绝经期子宫, 附件未见明显肿物, 盆腔未见明显积液。(11) 胃镜: 慢性非萎缩性浅表性胃炎伴糜烂, 幽门螺杆菌检测 (－); 胃窦病理: 小块胃粘膜轻度慢性炎症, 小凹上皮肠化。(12) 颈椎 X 线片: 颈椎病, 颈椎生理弯曲消失, C3 椎体轻度后移。(13) 颈动脉超声: 双颈动脉内膜毛糙。(14) 前庭功能检查: 前庭双温实验正常。(15) 头颅 CT: 轻度老年性脑改变, 空蝶鞍。(16) 垂体磁共振成像 (magnetic resonance imaging, MRI): 鞍内异常信号影, 考虑囊肿可能性大, 空蝶鞍不除外, 垂体极度萎缩。

诊疗经过: 入院后血压波动于 120～90/70～60 mmHg, 多数情况下 100/70 mmHg, 反复复查心电图均显示窦性心动过缓, 心率 43～60 次/min。患者间断头晕伴恶心, 进食差, 予持续静脉补钠纠正低钠血症, 最大量每日 12 g 钠, 效果差。频繁恶心, 呕吐。2 月 26 日诉胸闷, 大汗, 心电图较前无明显变化, 测血糖 2.24mmol/L, 予静脉推注 50%葡萄糖溶液 40ml 后, 复测血糖 5.5mmol/L, 症状缓解。3 月 8 日行冠状动脉造影检查示左前降支 (left anterior descending artery, LAD) 近段 50%局限性狭窄, 余正常。结论为冠心病, 单支病变, 累及 LAD。诊断: 成人腺垂体功能减退症; 冠状动脉粥样硬化性心脏病, 心绞痛; 血脂异常; 颈椎病; 慢性浅表性胃炎; 腰椎间盘突出术后。治疗给予 (1) 泼尼松 2.5～5.0mg, 每日 1 次, 口服。(2) 甲状腺激素。甲状腺激素的应用会加速皮质激素的代谢, 加重皮质激素的不足, 故应用泼尼松 1 周后加用左甲状腺素 (商品名: 优甲乐), 50 μg, 每日 1 次, 口服。由于患者仍然心动过缓以及 T3、T4 在低水平, 后加量至 75 μg, 每日 1 次, 口服。(3) 同时给予冠心病的常规治疗。因患者已经 68 岁, 绝经, 未加用性腺激素; 生长激素价格昂贵, 儿童缺乏生长激素, 需补充生长激素, 但在成人常不需要替代治疗。治疗 4 个月后, 我们对患者进行了随访, 患者头晕, 厌食, 恶心, 呕吐, 畏寒, 乏力, 皮肤干燥等症状明显改善, 心绞痛症状消失。查体: 眉毛生长, 乳晕色淡, 腋毛, 阴毛未生长。面色较前红润, 体重增加。血压仍波动于 90～100/60～70 mmHg, 心率增快至 55～60/min, 血钠恢复正常: 137.2mmol/L。治疗后生化检查变化见表 1。

表 1 治疗后生化等检查的变化

项目	治疗前	治疗 4 个月后
白细胞(×10^9)	2.81	9.46
中性粒细胞(%)	42.7	62.7
嗜酸粒细胞(%)	12.6	2.4
血红蛋白(g/L)	101	132
游离 T3(pg/ml)	1.39	1.74
游离 T4(pg/ml)	0.73	1.15
促甲状腺激素(pg/ml)	3.915	0.215
血清皮质醇 8AM(μg/L)	36.6	67.0
血清皮质醇 4PM(μg/L)	22.6	24.6
血清皮质醇 12n(μg/L)	39.0	11.8
肾素(ng/ml)	0.09	0.54
血管紧张素Ⅱ(pg/ml)	8.2	81.9
醛固酮(ng/ml)	0.07	0.03
雌二醇(pg/ml)	7.81	24.49
促卵泡激素(IU/L)	3.86	4.38
促黄体生成素(IU/L)	0.8	1.29
催乳素(ng/ml)	53.88	38.48
孕酮(ng/ml)	＜0.08	0.24
睾酮(ng/ml)	0.46	0.47
促肾上腺皮质激素 8:00am (pmol/L)	3.02	2.33
促肾上腺皮质激素 4:00am(pmol/L)	3.26	＜1.11
促肾上腺皮质激素 12:00am(pmol/L)	2.12	＜1.11

2 临床病例讨论

池洪杰主治医师: 该患者同时具有多种垂体前叶激素分泌不足所引起的征候群, 包括性腺功能减退: 乳晕色淡、毛发稀少、腋毛和阴毛脱落; 甲状腺功能减退: 畏寒, 皮肤干燥、粗糙、苍白、弹性差, 少汗, 食欲不振, 表情迟纯, 心率减慢, 记忆力减退; 肾上腺皮质功能减退: 体力虚弱、易疲劳、厌食、恶心、呕吐、体重减轻、易感染、发作性低血糖、皮肤因 ACTH 分泌减少而色泽变浅、面容苍白、乳晕变浅; 生长激素不足: 肌肉无力、易疲劳、食欲不振、头晕、低血压、低血糖、低血钠、动脉粥样硬化。

ACTH 分泌呈阵发的释放增加, 导致血皮质醇急速升高, 呈一定的昼夜节律, 在觉醒前后数 小时达高峰, 然后整个上午, 下午从高峰渐渐回落, 傍

晚可进一步下降，在入睡后 1～2 h 达最低点。由于 ACTH 血浆半衰期很短，且其分泌呈阵发性，故基础血浆 ACTH 测定常不能作为垂体 ACTH 储备功能的可靠指标。该患者血清 ACTH、皮质醇不同时间的数值均偏低，且节律消失，晨起无高峰。垂体功能低下患者 TSH, T3, T4 在正常或低水平，该患者 TSH 正常，T3、T4 较低。垂体促性腺激素细胞可分别分泌 LH 和 FSH，在妇女月经期间此两种激素分泌有一定的变化。且此两种促性腺激素的分泌是不规则的、脉冲式的、监测有一定的困难，该患者促性腺激素和性激素水平总体低下。经过激素替代治疗，患者症状及辅助检查均有明显改善，符合成人腺垂体功能减退症的诊断。

吴兴利副主任医师：该患者头颅 CT 检查示轻度老年性脑改变，空蝶鞍。垂体 MRI 发现鞍内异常信号影，考虑囊肿可能性大，空蝶鞍不除外，垂体极度萎缩。其病史长达 6 年余，对治疗反应良好，其蝶鞍内占位考虑为囊肿或无功能性腺瘤。任何引起垂体前叶或下丘脑损伤的疾病均可引起垂体前叶功能减退症，包括原发性和继发性。原发性疾病有：（1）垂体及附近组织的良性、恶性肿瘤压迫、破坏腺垂体，腺瘤可分为功能性和无功能性。（2）产后大出血（席汉综合征）及其它血管疾病，如糖尿病性血管病变引起的腺垂体缺血性坏死。产后垂体坏死是本病最常见的原因，腺垂体在妊娠后期增生肥大，当分娩时发生大出血，可以引起低血压，使腺垂体小动脉痉挛，垂体前叶发生缺血性坏死。（3）累及垂体的感染（垂体结核、脑膜炎或脑炎）、手术和创伤、垂体卒中、浸润性病变（包括白血病浸润）等。继发性疾病有：（1）垂体柄损伤，如外伤、垂体或蝶鞍区手术等；（2）下丘脑及其他中枢神经系统病变，如结节病及组织细胞病、药物毒性（长春新碱等）等。本病可分为部分性与完全性二类，前者为非全部垂体前叶激素合成与分泌不足，该患者催乳素水平偏高，为部分性垂体前叶激素合成不足。

杨忠苏副主任医师：原发性内分泌腺体疾病引起的激素水平低下，通常会有垂体前叶合成和分泌的相应的促激素水平的明显升高，如果促激素水平没有升高或降低，特别是多种促激素水平同时受影响时，应当考虑成人腺垂体功能减退症。该患者符合成人腺垂体功能减退症的诊断。该病需要与下列疾病鉴别：（1）神经性厌食。该病有消瘦、闭经，由于焦虑及营养不良可影响垂体功能，出现某些类似垂体功能减退的症状；但其特点多为 20 岁前后的青年女性，有精神受刺激病史，消瘦程度较腺垂体功能减退为重，而腋毛和阴毛往往并不脱落，尿 17-酮类固醇及尿 17-羟皮质类固醇正常或稍减低。（2）原发性甲状腺功能减退症，有时除甲状腺功能不足外，少数情况下其它内分泌腺功能亦可能低下，但是该病黏液性水肿外貌和血胆固醇浓度增高更明显，往往有心脏扩大。血浆中促甲状腺激素在原发性甲状腺功能减退症中升高最具鉴别价值。TSH 兴奋试验时，原发性甲状腺功能减退 TSH 过度反应，腺垂体功能减退可无 TSH 升高反应，而下丘脑性者则呈延迟反应。（3）慢性肾上腺皮质功能减退症，该病有典型的皮肤、粘膜色素沉着，通常无性器官萎缩及甲状腺功能减退的表现，失钠现象比较明显，对促肾上腺皮质激素不起反应，而继发性肾上腺皮质功能减退者，在静脉滴注促皮质素 3～5 d 后，类固醇的排出量逐渐增加。（4）自身免疫性多发性内分泌腺病综合征，患者有多种内分泌腺功能减退的表现，该病是由于多个内分泌腺原发的功能减退，而不是由于垂体功能减退引起。促肾上腺皮质激素及促甲状腺激素兴奋试验，在此征群中，皆无反应，而腺垂体功能减退症，往往有延迟反应。（5）各种慢性消耗性疾病可伴有乏力、消瘦、性功能减退、尿 17-酮类固醇偏低等，严重者甚至可伴有继发的腺垂体功能不足，但是在营养情况好转后症状可逐渐恢复。该患者与上述疾病不符。心律失常是该患者的主要表现之一，经过激素替代治疗后，心率明显提高，症状明显改善。长期的缓慢性心律失常主要见于心脏自身疾病或退行性变导致的自律细胞的功能异常，但是应当排除心脏外全身性疾病引起，通过积极治疗原发性疾病，多数心律失常能够改善或纠正，从而避免置入永久性心脏起搏器。

（参加讨论医师：池洪杰，吴兴利，杨中苏）

（杨中苏整理）

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