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Postoperative Total Hypopituitarism Complicated with Refractory Gout: A Case Report

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Abstract

Craniopharyngioma is a benign tumor of sellar epithelial tissue. The tumor is close to the important structures of the brain and is usually surgically removed. The main postoperative complication is impaired pituitary function, resulting in a series of clinical manifestations. Postoperative panpituitarism combined with refractory gout is rare in clinical practice. The report is as follows to provide reference for improving the clinical understanding of the disease.

Keywords: panhypopituitarism, refractory gout, postoperative craniopharyngioma, treatment

1. Introduction

Cranopharyngiomas are tumors formed by partial cystic embryonic malformations in the sellar and parasellar regions, and there are two hypotheses about their embryonic origin: ectodermal residues originating in the Rathke sac and residual embryonic epithelium originating in the anterior and anterior infundibular parts of the pituitary gland (Garre ML & Cama A., 2007), with a total of approximately 0.5 to 2.0 million new cases per year, and despite high survival rates after surgical treatment (approximately 87 to 95 percent) (Müller, HL, 2014), they often affect quality of life due to postoperative complications. Therefore, long-term monitoring of postoperative endocrine indicators is required. Gout is currently the most common cause of inflammatory arthritis worldwide and is due to elevated serum urate and subsequent deposition of monosodium urate crystals in joints and other tissues (Schlesinger, N & Lipsky, PE, 2020). Although gout can be treated with conventional urate-lowering drugs (e.g., allopurinol, febuxostat, etc.), patients with refractory gout are often unable to achieve their treatment goals with these drugs. This case is a patient with total pituitary hypofunction complicated by refractory gout after craniopharyngioma surgery and is reported as follows.

2. Medical History and Physical Examination

The patient, a 28-year-old male, was admitted to the hospital for 2 days mainly due to elevated blood uric acid and pain and fatigue in both lower limbs. The patient found that blood uric acid rose to 651μmol/L during physical examination 7 years ago, no obvious joint swelling and pain, and after a low-purine diet, intermittent oral administration of 2 tablets of sodium bicarbonate for 3/day, no joint swelling and pain attack; 5 years ago, he was hospitalized in our hospital due to joint pain, and checked all biochemical items: alanine aminotransferase 52.3U/L, hypersensitivity C-reactive protein 47.8mg/L, uric acid 706μmol/L, thyroid function three showed FT31.36pg/ml (reference value 2.00–4.40), FT40.84pg/ml (reference value 0.93–1.7), TSH: 0.024μIU/ml (reference value 0.270–4.200), six sex hormones: prolactin 5.81ng/ ml (reference value 4.04–15.20), luteinizing hormone < 0.100mIU/ml (reference value 0.00–8.60), follicle-stimulating hormone < 0.100mIU/ml (reference value 0.00–12–40), estradiol 68.44pg/ml (reference value 25.80–60.70), testosterone 2.27ng/ml (reference value 2.800–8.000), progesterone <0.030ng/ml (reference value 0.000–0.149),

adrenocorticotropic hormone: 16.63pg/ml (reference value 7.2–63.6), cortisol 8.75pg/dl (reference value 6.02–18.4), diagnosed as: 1) gout gouty arthritis acute attack of gouty arthritis 2) total hypopituitarism Secondary hypothyroidism Secondary adrenal insufficiency Secondary hypogonadism Diabetes insipidus After craniopharyngioma surgery, 3) fatty liver damage, given a low-purine diet, sodium bicarbonate alkalinized urine, dexamethasone anti-inflammatory and analgesic and other comprehensive treatment after improvement and discharge; since then, he has been hospitalized in our department for gouty arthritis many times, and the patient has developed pain and fatigue in both lower limbs in the past two days, and was admitted to the hospital for further diagnosis and treatment. In the past 16 years ago, he underwent craniopharyngioma surgery, and currently takes oral administration of levothyroxine sodium tablets 100ug in the morning and 50ug in the evening 50ug 2 times/day, desmopressin acetate tablets 0.025mg 1 time/day, growth and development lag behind peers, allergic to Qingkailing, Shuanghuanglian.

Physical examination: body temperature 36.5°C, pulse 79 times/min, breathing 20 times/min, blood pressure 106/67mmHg, clear consciousness, thyroid gland, clear breathing sounds in both lungs, no dry and wet rales, heart rate 79 times/min, rhythm, no murmur in each valve auscultation area, soft abdomen, no tenderness, no percussion pain in the liver area, no swelling of both lower limbs. Specialty: height 178cm, weight 80kg, BMI 25.2kg/m2, obesity, no beard, no Adam's apple.

3. Auxiliary Inspection

(1) Hospitalization Test Indicators: Three types of infection: leukocytes: 13.69×109/L, red blood cells 5.97×1012/L, hemoglobin: 163.00g/L, hematocrit: 50.7%, percentage of neutrophils: 75.70%, absolute value of neutrophils: 10.36×109/L, procalcitonin: 0.170ng/m1; Emergency biochemistry: intra-valley aminotransferase 54.30 U/L, total bilirubin: 45.66 μmol/L, direct bilirubin: 14.60umol/L, creatinine: 114umol/L, potassium: 3.40mmol, sodium: 158.0mmo1/L; Glycated hemoglobin: 5.4%; Blood lipids: triglycerides: 2.06mmol/L, high-density lipoprotein sterol: 0.63mmol/L, apolipoprotein A1: 0.80g/L, blood calcium: 2.0 mmol/L, phosphorus: 0.64mmol/L; Blood osmolality: 318mosm/kg*H (reference value 600–1000); Urine osmolality: 601.00mosm/kg*H (reference value 600–1000); Pituitary-related examinations: thyroid function: free triiodothyronine: 1.32pg/ml (reference value 2.00–4.40), free thyroxine: 0.93ng/d1 (reference value 0.93–1.7), thyroid-stimulating microsin 0.018uIU/mL (reference value 0.270–4.200), cortisol: 2.090ug/dl (reference value 6.02–18.4), adrenocorticotropic hormone: 7.16pg/ ml (reference values 7.2-63.6); Six sex hormones: prolactin 5.67ng/ml (reference value 4.04–15.20), luteinizing hormone <0.300mIU/ml (reference value 0.00–8.60), follicle-stimulating hormone<0.300mIU/ml (reference value 0.00–12.40), estradiol 61.02pg/ml (reference value 25.80–60.70), testosterone 3.130ng/ml (reference value 2.800–8.000), progesterone <0.050ng/ml (reference value 0.000–0.149), no abnormalities in coagulation routine.

(2) The changes in the level of pituitary-related hormones in this patient in recent years are as follows (Tables 1, 2, 3)

Table 1.

	reference value	2016-06	2019-09	2020-08	2021-04	2021-06
FT3 (pg/ml)	2.00–4.40	1.36	1.22	1.14	1.60	1.32
FT4 (ng/d1)	0.93–1.70	0.84	0.623	0.68	0.71	0.93
TSH (μIU/ml)	0.270–4.200	0.024	2.77	1.35	0.026	0.018

Table 2.

	reference value	2016-06	2019-09	2020-08	2021-04	2021-06
PRL (pg/ml)	4.04–15.20	5.81	5.25	5.32	5.89	5.67
LH (mIU/ml)	0.00–8.60	<0.100	2.84	<0.300	<0.300	<0.300
FSH (mIU/ml)	0.00–12.40	<0.100	1.53	<0.300	<0.300	<0.300
Estradiol (pg/ml)	25.80–60.70	68.44	<5.00	60.90	60.00	61.02
Test (ng/ml)	2.800–8.000	2.27	0.138	4.450	3.240	3.130
PRG (ng/ml)	0.000–0.149	<0.030	<0.050	<0.050	<0.050	<0.050

Table 3.

	reference value	2016-06	2019-09	2020-08	2021-04	2021-06
COR (pg/ml)	6.02–18.4	8.75	3.80	5.54	3.20	2.09
ACTH (ng/d1)	7.2–63.6	16.63	16.02	17.99	16.76	7.16

4. Diagnosis and Treatment

Post-admission diagnosis: 1) Gout, gouty arthritis, acute attack of gouty arthritis 2) Hypopituitarism, secondary hypothyroidism, secondary adrenal insufficiency, secondary hypogonadism, diabetes insipidus, postoperative craniopharyngioma, 3) fatty liver damage; the treatment instructs patients to eat a low-purine diet, drink more water, reduce activity, topical Voltaren ointment, oral colchicine, hormone replacement, sodium bicarbonate alkalinization urine, anti-inflammatory and analgesic, uric acid lowering, liver protection and other comprehensive treatment. After the patient's condition improved, he was discharged from the hospital, and the patient was instructed to take medication regularly, regular outpatient review, and out-of-hospital medication: prednisone 1.25mg 1 time/day, desmopressin acetate tablets 0.025mg 2 times/day, testosterone undecanoate injection 0.25mg every 4 weeks, levothyroxine sodium tablets 100ug in the morning and 50ug in the evening 2 times/day, febuxostat 40mg 1 time/day, colchicine 0.5mg 2 times/day (gradually reduced, discontinued after 2 months).

5. Discussion

Cranopharyngioma is a common congenital sellar tumor, due to the influence of tumor, most patients with craniopharyngioma have different degrees of abnormal hormone secretion before surgery, and different degrees of damage to the hypothalamic-pituitary axis during craniopharyngioma surgery can cause pituitary dysfunction, and the phenomenon of postoperative hormonal abnormalities is more significant. Among them, the incidence of anterior pituitary dysfunction is 43%-67% (Sinha A, Ball S, Jenkins A, et al, 2011), while the incidence of central diabetes insipidus and sodium and water disorders can reach 70%-95% (Pugets, Garnea M, Wray A & et al, 2007), and the mortality rate and disability rate are high. The main hormones released by the pituitary gland are thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), growth hormone (GH), follicle-stimulating hormone (FSH) and luteinizing hormone (LH), prolactin (PRL), melatinizing hormone (MSH) and other hormones (Soren A, CooPer N S & Waugh TR, 2012). The level of endocrine function after surgical treatment of craniopharyngioma determines the quality of life of patients, and under high-quality endocrine replacement therapy, not only can long-term survival, but also some patients can continue to grow and develop, and even preserve fertility, so endocrine replacement therapy after craniopharyngioma surgery is particularly important. The clinical symptoms of Adenohypopituitarism vary greatly and depend on the atrophy of each target gland and hypophylaxis of adenohypophysis. In this case, the diagnosis of total pituitary hypofunction and diabetes insipidus caused by craniopharyngioma after surgery is clear, and long-term hormone replacement plus meridian therapy should be used, and individualized treatment should be used in principle.

The patient was treated with a sufficient course of urate-lowering drugs, blood uric acid was still higher than 360mmol/L and gout attacks more than twice a year, and the diagnosis of refractory gout was clear. The reasons for the patient's refractory gout may be: (1) Patients with hypopituitarism secrete hormones from their own pituitary gland and are in a state of low metabolism, which is easy to cause obesity and the accumulation of uric acid in the body. The hypothalamus can control the center of satiety and hunger and can also control weight by regulating leptin and insulin signaling pathways, and craniopharyngioma masses can cause hypothalamic obesity by causing hypothalamic injury (Zheng Kunjie, Yang Guoqing & Mu Yiming, 2021), which is strongly associated with hyperuricemia and gout. (2) Gout is related to the patient's lifestyle, and the patient has a number of high-risk factors for gout such as male sex, obesity, high-purine diet, and metabolic syndrome. (3) Various studies at home and abroad have shown that hypothyroidism is closely related to the occurrence and development of gout. The decrease of thyroid hormone can directly reduce the glomerular filtration rate, reduce uric acid excretion, and can also regulate leptin levels by affecting body fat content and leptin gene expression to affect renal excretion of uric acid (Ashizawa K, Imaizumi M, Usa T & et al, 2010), so it may change serum uric acid levels, which is a risk factor for gouty arthritis.

For the treatment of refractory gout in the patient, domestic and foreign guidelines and consensus are basically the same, after 2–4 weeks of acute attack control, start urate-lowering drugs, because the patient has taken urate-lowering drugs, the drug should not be stopped during the acute period, the patient's blood uric acid should be reduced while hormone replacement therapy, improve the clinical symptoms of the patient, use a small dose of colchicine or a sufficient course of non-steroidal anti-inflammatory drugs as soon as possible, colchicine and NSAIDs are the first-line drugs in the current acute attack of gout, intolerance to the above drugs, patients with

poor response or contraindications recommend systemic glucocorticoids with the addition of urate-lowering agents (Endocrinology Branch of Chinese Medical Association, 2020). For the initial selection of urate-lowering drugs, the 2016 EULER guideline (Richette P, Doherty M, Pascual E & et al, 2017) recommends the detection of renal uric acid excretion to select urate-lowering drugs and recommends clinical classification according to the two indicators of total renal uric acid excretion and renal uric acid excretion rate at 24 hours. For patients with poor efficacy of non-steroidal anti-inflammatory drugs and low-dose hormone therapy, biological agents such as IL-1 and TNF-α antagonists can be used, but these drugs are expensive and not marketed in China, and the patient's blood uric acid control is acceptable (< 360μmol/L) at the time of discharge, long-term review of the follow-up patient, such as the patient's repeated condition, it is recommended to use biological agents (anakinra, kanarimab and linacept, etc.) for treatment.

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