Craniopharyngioma or its surgery induces diabetes mellitus

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Abstract

A 23-year-old non-diabetic woman presented to our emergency room with progressive headache. She was diagnosed with craniopharyngioma and received tumor resection. Her blood glucose level was within the normal limit before surgery, and she had no family history of diabetes. Three months after the surgery, acute hyperosmolar hyperglycemic state developed. After 4 months of follow-up, her diabetes persisted but improved with oral antidiabetic drugs. This is the third case report of diabetes developing several months after craniopharyngioma tumor resection. The possible mechanisms of cranipharyngioma or its surgery inducing diabetes mellitus are hypothalamic obesity or hypothalamic damage. The degree of hypothalamic damage before the operation is predictive of diabetes development, and blood glucose level monitoring is important for these patients.

INTRODUCTION

It is well established that craniopharyngioma may cause diabetes insipidus. Destruction of the antidiuretic hormone-secreting cells in the hypothalamic nuclei by craniopharyngioma tumor itself or surgical removal both can cause diabetes insipidus (Maghnie *et al.* 2000). However, the correlations between diabetes mellitus and cranipharyngioma has rarely been mentioned. The mechanisms of diabetes are insufficient insulin secretion or peripheral insensitivity to insulin, but the central nervous system also plays a role. Here we introduce a patient who had new-onset diabetes after craniopharyngioma surgery and discuss the possible mechanism.

CASE REPORT

A 23-year-old non-diabetic woman presented to the emergency room with progressive headache for several days. The patient also had nausea and vomiting, but no vision or visual field problem. She had no family history of diabetes mellitus and the body

CASE REPORT

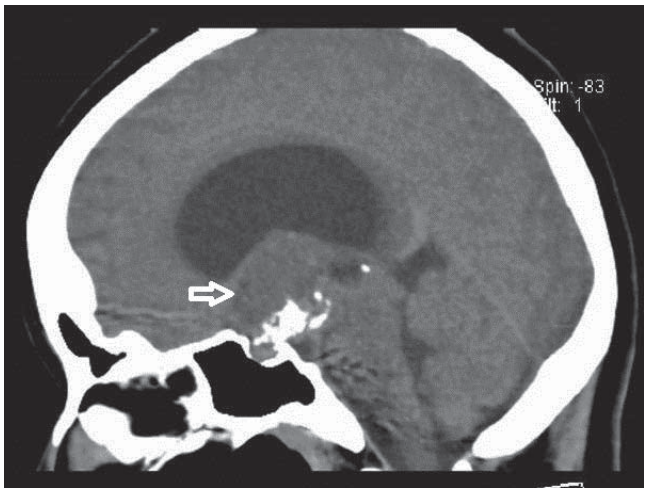

Fig. 1. A 2 × 2 cm third ventricular craniopharyngioma with calcification and cystic components.

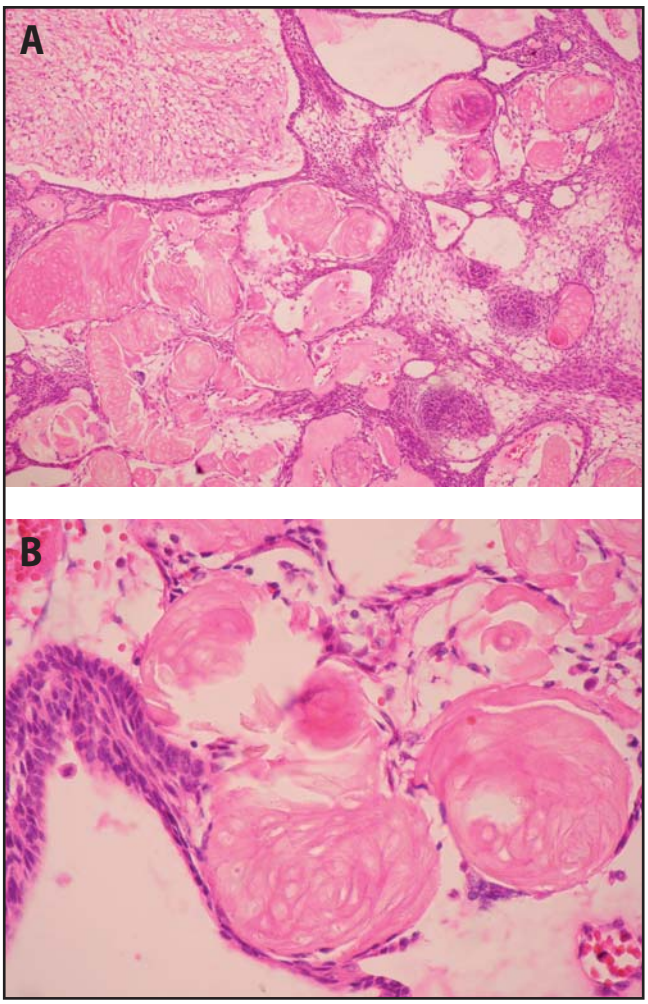

Fig. 2. Pathology. (**A**) The photomicrograph shows an adamantinomatous craniopharyngioma composed of broad strands of bland squamous epithelia and copious compact wet keratin and dystrophic calcification. The tumor invading the peripheral brain tissue was also noted. (100×, H and E stain). (**B**) A higher magnification shows the proliferation of nests of squamous epithelium with prominent peripheral palisades and wet keratin structures. (400×, H and E stain).

mass index (BMI) was 23.0 kg/m^2. The blood glucose level was 102 (70–110) mg/dl. The endocrine profile showed LH 3.21 (2.12–10.89) mIU/mL, FSH 6.21 (3.85–8.78) mIU/mL, ACTH 208.0 (5.0–77.0) pg/mL, cortisol 16.9 (6.2–19.4) µg/dL, TSH 0.55 (0.27–4.20) µIU/mL, and prolactin 27.22 (0.0–20.0) ng/mL. Head computed chromatography showed a 2 × 2 cm craniopharyngioma with hydrocephalus in the third ventricle (Figure 1).

Tumor resection was smoothly performed. Craniopharyngioma arising from the third ventricle with hypothalamic adhesion was found on operation. Diabetes insipidus developed on the second day after the operation and she was kept on desmopressin 20 mcg nasal spray 3 times daily. Cortisone acetate of 25 mg daily before noon and 12.5 mg daily after noon were started for prevention of adrenal insufficiency. The pathology report confirmed craniopharyngioma with calcification and cystic components (Figure 2).

Three months after the surgery, the patient was re-admitted to our emergency department because of general malaise, polydipsia and polyuria for 2 days. She denied increased food intake or cold intolerance. Although the patient denied increased food intake, her body weight increased from 53 kg to 68 kg in 3 months. Her physical activity was reduced after craniopharyngioma surgery. On physical examination, her temperature was 38 °C, blood pressure 115/80 mm/Hg, pulse 105 beats per minute and respiratory rate 16 breaths per minute. Edema was not observed on her face and legs. Skin was normally pigmented and dry. The patient did not have a moon face, buffalo hump, or central obesity. Her chest was symmetrically expanded, and she did not have wheezing, crackles, or rales. The abdomen was soft without tenderness.

The laboratory results revealed glucose levels of above 600mg/dL, osmolarity 383 (278.0–305.0) mOsm/kg H_2O, sodium concentration 168 (133.0–145.0) mEq/L, random urine sodium concentration less than 10 (40.0–220.0) mEq/L, urine osmolarity 252 (300.0–900.0) mOsm/kg H_2O, ketone bodies in blood, trace amount; arterial pH 7.31, P_{CO_2} 46.1 mm/Hg, HCO_3 23.7 mmol/L, BUN 33 (8–20) mg/dl, creatinine 0.9 (0.5–1.3) mg/dL, AST 34 (5–35) U/L, and ALT 21 (10–50) U/L. Endocrine study revealed LH of 1.21 (1.20–12.60) mIU/mL, FSH 1.40 (1.79–5.12) mIU/mL, GH 0.05 (0.00–5.00) ng/mL, ACTH 13.50 (5.0–77.0) pg/mL, cortisol 14.20 (6.2–19.4) µg/dL, TSH 0.71 (0.27–4.20) µIU/mL, free T4 0.59 (0.93–1.70) ng/dL, and prolactin 20.79 (0.0–20.0) ng/mL.

Glucagon test showed insulin and C-peptide level after glucagon 1-mg intravenous injection as follows: before glucagon administration, glucose level was 181 mg/dL, insulin level was 52.0 µIU/mL, and C-peptide level was 13.5 ng/mL; after glucagon injection, glucose level was 224 mg/dL, insulin level was 55.0 µIU/mL, and C-peptide level was 14.2 ng/mL (normal range of C-peptide: fasting 0.0–2.10 ng/mL, 2 hours postpran-

dial 1.10–3.20 ng/mL, and of insulin, 2.60–24.90 μIU/mL). She started anti-diabetic drugs after discharge.

DISCUSSION

Till date, there are only 2 case reports with diabetes complicating craniopharyngioma. Chen M *et al.* reported 2 patients, age 39 and 43, who developed hyperosmolar hyperglycemic state several months after crainiopharyngioma resection (Chen *et al.* 2010). Ma XW *et al.* reported a patient, age 41, who was found to have acute diabetic ketoacidosis 3 months after surgery (Ma *et al.* 2010). As for our patient, she was much younger at diabetes onset (age 23), and she had no family history of diabetes mellitus, normal BMI (23 kg/m^2) before surgery. Hyperinsulinemia was also found. Considering her age and very low risk, it is unusual for diabetes or hyperosmolar hyperglycemic state to develop. In another paper surveying morbidity and mortality in patients with cranipharyngioma after surgery followed at 1 hospital in Dublin, United Kingdom (Crowley *et al.* 2010), prevalence rate of diabetes was 11.5% , which is twice higher than the average. Simoneau-Roy *et al.* found that children and adolescents with hypothalamic obesity following craniopharyngioma resection had significantly increased insulin secretion and slightly lower insulin sensitivity compared with a group of age- and BMI-matched controls (Simoneau-Roy *et al.* 2010). Similarly, Trivin *et al.* also found that children with cranipharyngioma of greater hypothalamic involvement before surgery had higher glucose and insulin resistance (Trivin *et al.* 2009). In conclusion, there exists some relationship between cranipharyngioma and diabetes.

In our patient, type 1 diabetes is ruled out because the insulin and C-peptide levels were both high before and after glucagon infusion. She had no family history of type 2 diabetes, was young (23 years of age), and had a normal BMI (23.0 kg/m^2) before tumor resection. Therefore, she had a low risk of type 2 diabetes. The patient took physiologic doses of corticosteroid (cortisone 37.5 mg/day) , hence, steroid-related hyperglycemia was unlikely. The post-operative pituitary function was normal, thus she had no endocrinopathy-related diabetes. Because of the time sequence, craniopharyngioma is the most possible cause of her diabetes.

The mechanism of craniopharyngioma or surgery for cranipharyngioma inducing diabetes is not quite clear. As we have known, obesity is one of the risk for diabetes, and craniopharyngioma patients have a high risk for the development of obesity in children surviving brain tumors (Lustig *et al.* 2003). This patient gained 15 kg after the surgery. Because her craniopharyngioma had hypothalamus involvement, hypothalamic obesity is the possible mechanism. Besides surgery for hypothalamic tumor with suprasellar extension, tumor causing hypothalamus damage, such as pituitary macroadenoma, glioma, meningimoa, also can cause hypothalamic obesity (Hochberg *et al.* 2009). Therefore, it is craniopharyngioma itself, or surgery for craniopharyngioma, that cause hypothalamic obesity, which is a high risk for diabetes mellitus. In one study of obesity after craniopharyngioma surgery, reduced physical activity, rather than increased energy intake was found responsible for the obesity development (Harz *et al.* 2003).

The ventromedial hypothalamus is the region responsible for glucose homeostasis. It monitors blood glucose levels and regulates reactions to hypoglycemia. In animal experiments, puncturing the ventral surface of the brainstem stimulated the adrenergic system and produced transient hyperglycemia, glycosuria, which is known as piqure diabetes, or puncture diabetes (Feldberg *et al.* 1985). In humans, there is also a similar phenomenon. Patients with skull base fracture, intracranial hemorrhage, or surgery near the floor of the third ventricle, which causes hypothalamic damage, were found to have transient hyperglycemia and glycosuria (Braunstein 2003). Children with craniopharyngioma who have greater hypothalamic involvement before surgery are associated with higher insulin resistance index (Trivin *et al.* 2009), this explained some, but not all craniopharyngioma patients having diabetes. Conclusively, tumor compression, or tissue damage during operation, induces diabetes.

In summary, hypothalamic obesity, and hypothalamic damage are 2 of the most possible causes of diabetes in craniopharyngioma patients. The degree of hypothalamic damage before operation is predictive of diabetes development. Therefore, blood glucose follow-up is especially important for these patients. Reduced physical activity, rather than increased food intake contribute to the post-operative obesity. Encouraging post-operative patients to exercise might decrease the risk of diabetes.

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