Mazindol Administration Improved Hyperphagia After Surgery for Craniopharyngioma

—Case Report—

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Abstract

A 54-year-old man presented with visual disturbance and polydipsia. Magnetic resonance imaging disclosed a cystic mass which extended from the intrasellar to the suprasellar region. Bifrontal craniotomy was performed and the tumor was totally removed. Histological findings confirmed the diagnosis of craniopharyngioma. Postoperatively, the patient suffered from transient disorientation. About one month after the operation the patient manifested hyperphagia and he gained 15 kg in one month. Mazindol, a non-amphetaminergic anorectic agent, was administered for 3 weeks. His appetite normalized and his weight fell and stabilized even after mazindol administration was ceased.

Key words: craniopharyngioma, hyperphagia, mazindol

Introduction

Craniopharyngioma can now be totally resected in many cases because of recent microsurgical techniques. Radiotherapy, including gamma knife radiosurgery, provides an alternative to re-operation in cases of incomplete resection. Thus, the prognosis for patients with craniopharyngioma is improving. However, obesity is a problem in about 50% of patients treated for craniopharyngioma, so the quality of life is not necessarily satisfactory. Dieting or physical exercise is usually unsuccessful in such patients. However, no other treatment has been evaluated. We report the use of a non-amphetaminergic anorectic agent to suppress hyperphagia and consequent obesity.

Case Report

A 54-year-old man presented in March 1996 with a one-year history of gradually worsening visual disturbance and polyuria. Head computed tomography disclosed a cystic tumor in the sellar region. The patient was admitted for further evaluation and surgical treatment. On admission, he was fully alert but with bitemporal hemianopsia, panhypopituitarism, and diabetes insipidus. Head magnetic resonance (MR) imaging revealed a cystic tumor which extended from the intrasellar to the suprasellar region and compressed the optic chiasm (Fig. 1). The diagnosis was craniopharyngioma based on these findings.

Surgery was performed in April 1996. The tumor was completely resected through the subfrontal approach. Histological examination confirmed the diagnosis as craniopharyngioma of the papilloma type. The day after the operation, the patient experienced transient psychogenic disorientation. This symptom disappeared on the 14th postoperative day and the patient recovered clear consciousness. Thereafter, the patient did well for some time and he was medicated with cortisol, thyroxine, and desmopressin. Postoperative MR imaging showed no residual tumor (Fig. 2). Slight ventricular dilation was detected, but no signs of hydrocephalus. Thus, no shunt operation was performed.

About one month after the operation, hyperphagia emerged and the patient gained 15 kg in one month. Dieting was attempted but failed because of excessive
Fig. 1 Magnetic resonance images on admission showing a cystic mass extending from the intrasellar to the suprasellar region and compressing the optic chiasm.

Fig. 2 Postoperative magnetic resonance images showing no residual tumor and the pituitary stalk is clearly seen. Mild ventricular dilation is present. The high intensity spots at the foramen of Monro are thought to be internal cerebral veins.

Fig. 3 Graph showing changes in the patient’s weight. Mazindol was administered at 0.5 mg per day for 3 weeks. Just before starting the medication, his weight was 70 kg, 15 kg heavier than his weight on admission. Then, his weight decreased to 60 kg one and a half months after withdrawal of mazindol.

Discussion

There are two types of body weight abnormalities caused by disorders of the central nervous system, hypothalamic obesity and leanness, as seen in Russell syndrome. Hypothalamic obesity is caused by tumors, inflammation, and trauma. Causative tumors include craniopharyngioma, germinoma, hamartoma, and glioma, and inflammation includes sarcoidosis, tuberculosis, and encephalitis. The satiety center and feeding center are located in the hypothalamus. The satiety center is located in the ventromedial hypothalamic nucleus and its function is controlled by blood sugar level or extension of the stomach. The feeding center is located in the lateral hypothalamic area and is activated by free fatty acids. Another mechanism that controls appetite has been identified which is controlled by intracerebral amines. Specifically, activation of α-adrenergic receptors located in the paraventricular nucleus provides food intake, whereas activation of β-adrenergic receptors or dopaminergic receptors located in the lateral hypothalamic area, or serotonin receptors suppresses the appetite. Appetite is controlled by these mechanisms, so if the feeding center becomes dominant to the satiety center due to hypothalamus dysfunction, hyperphagia and obesity will appear.

In our patient, hyperphagia did not manifest either preoperatively or just after the operation, but at one month after the operation. We suspect that the hypothalamus was deformed very slowly by the tumor so the hypothalamic function adjusted to the change. However, the hypothalamus reshaped in a comparatively short time after the tumor was re-
moved and the hypothalamic function was disturbed. Another possible mechanism is dysfunction of the hypothalamus due to dilation of the third ventricle. A shunt operation might improve hyperphagia if this hypothesis was true. However, no classical signs of hydrocephalus were seen in our patient, and we did not perform a shunt operation. There may be other reasons for hyperphagia.

Mazindol is a non-amphetamine anorectic agent which activates the β-adrenergic receptors in hypothalamus.9) This drug is usually used for the treatment of excessive obesity (body mass index over 35 kg/m²). However, our patient gained weight so abruptly that dieting was not effective and moreover he continued to eat when unsupervised. Thus, we decided to treat him with mazindol. Just after he started taking mazindol, he felt a loss of appetite and his food consumption returned to the previous level. Fortunately, after withdrawal of the medication, hyperphagia did not appear again. However, we do not know the reason. Oral administration of mazindol in healthy male volunteers causes a significant increase in plasma levels of adrenocorticotropic hormone, β-lipotropin, β-endorphin, and growth hormone, but has no effect on plasma levels of prolactin, thyroid-stimulating hormone, luteinizing hormone, or follicle-stimulating hormone.7) Plasma cortisol also increases significantly. No side effects of mazindol associated with changes in the plasma level of anterior pituitary hormones was observed in our patient. Therefore, the quality of life in patients with craniopharyngioma may be improved by treatment of hyperphagia with mazindol.

References


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