Hypothalamic obesity due to hydrocephalus caused by aqueductal stenosis

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Abstract

A case is presented of 14 year old female with hypothalamic obesity due to hydrocephalus caused by aqueductal stenosis. Evidence of hypothalamic obesity included 1) acute hyperphagia and weight gain, 2) neuroradiology showed hydrocephalus with focal enlargement of the third ventricle, 3) endocrinological studies revealed hyperinsulinaemia and impaired growth hormone (GH) response to arginine, but normal GH response to growth hormone-releasing factor (GRF) and 4) Torkildsen's ventriculo-cisternal shunting resulted in improvement in hyperphagia and obesity.

Hypothalamic obesity is produced by bilateral destruction of ventromedial regions of the hypothalamus.¹ Clinically it results from various organic diseases in the hypothalamus such as tumour, head trauma, inflammatory disease, and leukaemia.² To our knowledge hydrocephalus due to aqueductal stenosis rarely causes this condition. We report the case of a young female with hypothalamic obesity due to hydrocephalus caused by aqueductal stenosis, which was improved by a Torkildsen's shunt.

Case report

A 15 year old female was admitted to the Yokohama City University Hospital for evaluation of obesity. She had suffered from meningiocephalitis at the age of three months and her weight increased after this episode. She did not walk until she was four years old probably because of sequela of meningiocephalitis and being overweight. Her height and weight were 133 cm and 63 Kg at six years of age, and 145 cm and 67 Kg at 13 years; within the next

year she had an acute gain of 28 Kg and weighed 95 Kg at the age of 14. During this period she showed hyperphagia with a calorie intake of approximately 3000 kcal/day.

On admission the patient's height was 147 cm and her weight was 89 Kg (body mass index: 41). She was mentally retarded with an IQ of 57. Her menarche had occurred at the age of seven and her menstruation had been irregular with hyper- and/or poly-menorrhea.

Endocrinological examination showed an impaired GH response to arginine but normal GH response to GRF in the preoperative state, and hyper-insulin response in 100g oral glucose tolerance test (table).

Plain skull radiographs were normal. CT revealed cerebral atrophy and hydrocephalus with focal enlargement of the third ventricle. Metrizamide CT cisternography showed no reflux of the contrast material into the ventricular system and its clearance from the cistern was within normal limits. A metrizamide ventriculography was performed after placement of an Ommaya's reservoir, which showed focal stenosis of the cerebral aqueduct but no evidence of mass lesion in the third ventricle.

After admission, she was placed on 420 kcal per day of semi-starvation treatment for seven weeks. At the end of this treatment her weight dropped 12 kg, but her strong appetite still remained, resulting in hyperphagia (approximately 3000 kcal/day) and weight gain when the semi-starvation treatment was stopped.

She then had a suboccipital craniectomy with a ventriculocisternal shunt (Torkildsen's procedure) using a Pudenz ventricular catheter.

Hyperphagia with strong appetite improved after the operation and her weight fell 6 kg in two weeks. Endocrinological studies one month after the operation revealed subnormal GH response to arginine and normal response to GRF (table). Insulin response to 100g oral

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Received 25 July 1989 and in
final revised form
14 February 1990.

Accepted 5 April 1990

Table Changes of blood sugar, serum insulin (IRI) and growth hormone (GH) in various tests

Time (minutes)	0	15	30	60	90	120	150
At admission (BW 89 kg)							
100 g oral glucose tolerance test							
Blood Sugar (mg/dl)	86		120	167	155	160	
IRI (μ U/ml)	23.3		98.1	207.1	154.5	87.1	
Arginine stimulation	GH (ng/ml)	0.9	1.0	1.0	0.9	4.6	3.0
Levodopa stimulation	GH (ng/ml)	1.1	1.5	1.7	1.3	1.2	
GRF stimulation	GH (ng/ml)	2.3	37	16	5.0	2.4	
After Torkildsen's shunt (BW 68 kg)							
100 g oral glucose tolerance test							
Blood Sugar (mg/dl)	80		117	136	131	125	
IRI (μ U/ml)	13.8		98.0	84.6	137.4	126.7	
Arginine stimulation	GH (ng/ml)	5.1	12	6.7	3.0	2.0	2.2
Levodopa stimulation	GH (ng/ml)	—	—	—	—	—	—
GRF stimulation	GH (ng/ml)	1.3	12	23	9.0	3.2	2.8

glucose improved but still remained high (table).

One year after the operation, her weight remained around 68 kg and she had a normal appetite. Her menstrual cycle returned to normal. Post operative CT scan showed reduction in size of the third ventricle although the size of the lateral ventricle was unchanged.

Discussion

Bray and Gallagher² reported eight cases of hypothalamic obesity and reviewed the literature. They found only one case of this type of obesity associated with hydrocephalus among the 120 cases they checked (including the eight they reported), and this was due to surgical intervention for the treatment of a ruptured cerebral aneurysm. They did not discuss the causal relationship between hydrocephalus and hypothalamic obesity.

Fifteen cases of non-tumoural aqueductal stenosis with obesity have been reported.³⁻⁵ Visual symptoms and endocrinological symptoms such as amenorrhea, polyuria, hypogonadism and dwarfism were associated in many of these cases, and marked enlargement of the third ventricle was noted by CT scan in all cases. Some of the 15 obese patients might have been classified as hypothalamic obesity due to hydrocephalus. However, no evidence was provided in these reports that hydrocephalus due to aqueductal stenosis was the cause of their condition.

Bray and Gallagher² utilised the two criteria for the diagnosis of hypothalamic obesity in their study; 1) pathological evidence of damage involving the hypothalamus and 2) obesity arising from an acute gain in weight following this injury. They also listed hyperphagia, intractable hyperinsulaemia, impaired GH response to its stimuli (insulin induced hypoglycaemia and arginine), and abnormal reproductive function including amenorrhea as the characteristics of hypothalamic obesity. The present case meets all of these criteria. In addition we have other evidence which strengthens the diagnosis of hypothalamic obesity. The patient showed normal GH response to GRF in the preoperative state, although she showed impaired GH response to arginine and levodopa. It is well documented that GH response to arginine, levodopa and GRF are impaired in simple obesity.⁶⁻⁸ In GH release,

GRF acts on the pituitary,⁶ whereas arginine or levodopa acts within the hypothalamus.^{7,8}

In experimental animals, we have recently found that GH response to GRF was normal in ventromedial hypothalamic obesity whereas to arginine or levodopa it was impaired.^{9,10} These results imply that GH release from the pituitary is preserved in hypothalamic obesity. In our case, we observed the exact same phenomenon in GH release in the preoperative state.

Hydrocephalus caused by aqueductal stenosis might have produced the hypothalamic obesity in this patient since hyperphagia and obesity were improved as well as reduction in size of the third ventricle after the shunting operation. The increased appetite after semi-starvation treatment and the enlarged third ventricle suggested ventromedial hypothalamic damage, and this was the reason we decided to perform the operation. After the operation hyperphagia was relieved and her weight declined. We did not measure the pressure of CSF in either the pre- or post-operative state; however, CT scan findings and the clinical course strongly suggested that intraventricular pressure decreased after the operation.

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