Endocrinological Management Influences Rehabilitation Outcome in Patients with Craniopharyngioma

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Craniopharyngioma is a benign intracranial tumor but requires aggressive intervention because of its location and invasiveness. Common clinical manifestations include visual impairment, neurological deficits and endocrinopathy. The most frequent postoperative complications are tumor recurrence, panhypopituitarism and diabetes insipidus (DI). We report a 37-year-old man with craniopharyngioma who came to our department for rehabilitation. He had polyuria and diplopia before the intrasellar tumor had been diagnosed. He had undergone an operation four months before admission to our hospital. Immediately after surgery, he had an infarction in the right internal carotid artery territory, which caused left hemiplegia and impairment of cognitive function. He had a low functional independence measurement (FIM) score (29 out of a full score of 126) when he arrive at our department. Deficiency in thyroid hormone and cortisol, as well as central diabetes insipidus were noted. The patient was given thyroxin, cortisone and desmopressin, and began a rehabilitation program; however, his condition did not significantly improve. A blood sample was drawn and a low serum androgen level was noted. We therefore decided to give him testosterone supplement. FIM score improved from 36 to 44 within 10 days of taking testosterone. This case report illustrates that proper treatment of endocrine disturbance plays a key role in successfully managing patients with craniopharyngioma. **(Mid Taiwan J Med 2006;11:56-61)**

Key words

craniopharyngioma, endocrinopathy, rehabilitation

INTRODUCTION

Craniopharyngiomas, originating from embryonic remnants of Rathke's pouch [1], are regarded as slow-growing benign tumors. The classic description of craniopharyngioma refers to a nonmalignanct cystic, calcified tumor in the suprasellar region. There is a bimodal age distribution in the incidence of craniopharyngiomas, with higher incidence noted in the young (between 5 and 14 years) and old age (between 65 and 74 years) groups [2]. This situation may imply that distinct etiologies exist between these two groups. The overall incidence of craniopharyngiomas is 1.3 per million person years [2].

The location of craniopharyngioma leads to three main clinical manifestations, including optic chiasm compression with visual impairment; neurological signs (mainly headache), which is probably due to the distention of the sella turcica; and hypothalamus-pituitary axis damage with endocrinopathy [3,4].The most common visual deficit is decreased visual acuity and visual field defects. Ocular motor impairment is much less frequently observed [3,4]. Headache, followed by nausea and vomiting, is indicative of increased

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intracranial pressure caused by distention of the sella turcica [4]. Psychological alterations consist of cognitive function impairment and personality changes; however, it is impossible to determine the precise cause for such mental changes [5]. A previous report found that 63 percent of patients with craniopharyngioma have clinical endocrinological symptoms and signs and that 85 percent of them have abnormal serum hormone levels; sexual dysfunction was the most common presentation of endocrinological disorders among those patients [3]. Another study reported that 52 to 87 percent of their patients had endocrinal dysfunction, depending on the tumor type and patients' ages [5].

Optimal management is difficult because craniopharyngioma is always found near critical structures (optic chiasm, circle of Willis, hypothalmus, floor of third ventricle and pituitary gland), [3,4,6,7]. The extent of surgical removal and the role of radiotherapy are controversial arises. Subtotal resection alone is associated with a high recurrence rate [3,7,8], while others support total removal [3,6]. Some studies have revealed better clinical outcome with postoperative radiotherapy [4,7]. Thus, the choices of treatment may depend on the tumor size, the surgical and radiotherapy techniques, and the practitioner's propensity. Taking into account the main clinical disorders, recurrence rate and functional outcome, optimal management is still in the formative stage.

After operations, patients may have endocrinological, ophthalamological, and psychological problems because of the location of craniopharyngioma. Surrounding structures and vessels may be involved because of the invasive nature of some craniopharyngiomas [3]. Leading to cerebral vascular accidents in these patients. All of the above circumstances will affect the normal daily activities and quality of life of the patient. Adequate surgical planning and postoperative medical and rehabilitation programs will improve the functional outcomes.

CASE REPORT

A bedridden 37-year-old man with left hemiplegia and impaired cognitive function was transferred to our department from the department of neurosurgery. He had had decreased visual acuity, general weakness and polyuria for one month before he visited a medical center, at which time a final diagnosis of craniopharyngioma had been made. He underwent a craniotomy to remove the tumor in that medical center. However, an infarction in the right internal carotid artery territory had occurred during his treatment course. The infarction led to brain edema and a subsequent mass effect. A craniectomy and resection of the infarcted brain were performed 2 days later. Four months after the operation, he was transferred to the neurosurgery department of our hospital where he was managed for one week, before being transferred to our physical medicine and rehabilitation department.

The patient was somnolent at the time he came to our department. He was unable to follow orders properly. When he was awake, he could only sit with support for a short period of time. He could recognize his wife, but interacted with her inconsistently. Neurological examination revealed left hemiplegia, left hemianesthesia, left hemineglect, dysphagia and dysarthria, all of which are substantial signs of right cerebral hemispheric stroke. Clinical evaluation revealed that motor function of his left limbs was at Brunnstrom stage 2 [9] without contracture. Muscle power of his right limbs was grade 4. We evaluated his functional status by functional independence measurement (FIM) [10,11],which is a disability evaluation instrument composed of 18 items arranged in 6 categories of self care, sphincter control, mobility, locomotion, communication and social cognition; every item was assessed on a seven point scale, ranging from total assist (score = 1) to complete independence(score = 7). His FIM score was 29 out of a total score of 126 at the time of transferal to our department (self care: 7, sphincter control: 2, mobility: 3, locomotion: 2, communication: 8, social cognition: 7). The patient was enrolled in a rehabilitation program, which included passive range of motion exercises, postural training,

therapeutic exercises, swallowing training, cognitive training and verbal production training. Endocrinopathies were noted soon after he was transferred to our ward. The combination of diabetes insipidus, hyperprolactinemia and hypopituitarism indicated his endocrinopathy was due to hypothalamic damage. The patient was given hormone replacements, including cortisone (25 mg BID), thyroxine (0.1 mg QD) and desmopressin (0.1 mcg/dose BID).

Two weeks after he was transferred to our ward, he was able to tolerate sitting in a wheelchair for a short period of time. Although he had been taking cortisone 25mg twice daily, he was still weak in general. After 3 weeks in our department, his cortisol level was 0.89 μg/dL in the morning and 4.19 μg/dL in the evening. During that time, episodic low arterial blood pressure was noted (around 90/70 mmHg). According to his clinical symptoms and signs, we increased the dose of cortisone and then finally replaced it with prednisolone for aggressive control. Acceptable arterial blood pressure (around 120/80 mmHg) was maintained after the prednisolone doses (10 mg in the morning and 5mg in the afternoon) had been adjusted, although he was still weak in general. Furthermore, we checked his testosterone level because he displayed clinical characteristics of femininity, such as loss of beard and body hair and decreased muscle mass. Low testosterone level (testosterone: < 0.2 ng/mL, normal range: 2.8 to 1.5 ng/mL) was noted 4weeks after being admitted to our department. After consultation with an endocrinologist, we started him on testosterone.

His general condition gradually improved within days after injection of testosterone enanthate (250 mg, IM). In light of this improvement, he was given testosterone (250 mg, IM) every 2 weeks. Although his condition still fluctuated, he subjectively became more energetic and active. We arranged for a more aggressive rehabilitation program for him. After six weeks in our department, his FIM score had improved to 36 (self care: 8, sphincter control: 4, mobility: 4, locomotion: 2, communication: 10, social cognition: 8). Thereafter, he continued to participate in the comprehensive rehabilitation program. Ten days later, just before discharge, his FIM score had further improved to 44 (self care: 12, sphincter control: 4, mobility: 6, locomotion: 4, communication: 10, social cognition: 8).

DISCUSSION

Craniopharyngioma requires aggressive management because of its location and invasiveness [7]. Several critical and important structures from which diverse imperative functions are derived may be involved in craniopharyngiomas, such as the optic chiasm, hypothalamus, pituitary gland, frontal lobe, third ventricle and circuit of limbic system. Indeed, the tumor itself and the strategy of treatment influence the functional outcomes of patients with intracanial tumors. Invasion of craniopharyngioma to surrounding structures will result in various complications. Endocrinological manifestations are diverse and variable, ranging from diabetes insipidus to panhypopituitarism [3,4]. The most common manifestation are sexual dysfunction preoperatively and diabetes insipidus postoperatively [3,4,7]. Involvement of the optic nerve is frequent; however, the occurrence rate of permanent blindness can be decreased with close attention [3]. If the hypothalamus is involved, vegetative function impairment, autonomic nerve system disturbance, as well as endocrine or emotional problems may occur [12].

Hyperprolactinemia was noted early in the course of our patient's disease. He also had polyuria during the time he suffered from decreased visual acuity. These findings indicate that the tumor not only had invaded the optic nerve but also the hypothalamus preoperatively. Different mechanisms have been used to explain hypopituitarism. According to the physiology of the hypothalamus and pituitary gland, at least three explanations can be offered: a) diminished release and/or secretion of hormones from the hypothalamus, b) interrupted hypothalamic hormone delivery to the pituitary gland and c)

decreased numbers of hormone-producing cells in the pituitary gland [13]. The diminished release and/or secretion of hormones from hypothalamus and decrease in hormone-producing cells in pituitary gland itself can be distinguished roughly by the signs of central type DI and hyperprolactinemia. The diminished release and/or secretion of hormones, due to the hypothalamus dysfunction, results in DI and hyperprolactinemia, while decrease in hormone producing cells, due to pituitary gland dysfunction, results in DI without hyperprolactinemia. Hypothalamic hormone delivery can be interfered with by increased perisellar pressure caused by compression of the portal vein of the stalk. The clinical and laboratory presentations of increased perisellar pressure are similar to diminished release and/or secretion of hormones from the hypothalamus [14]. Because the effect of compressive disruption of hormone delivering can be reversible, decompression surgery may solve hypopituitarism [13].

Hypopituitarism (characterizal by decreased cortisol, thyroxine, testosterone levels) affects both the physical and the emotional aspects of a person's life. The clinical presentations of cortisol deficiency include listlessness, weakness, fatigue, dizziness and anorexia. These manifestations occur insidiously, may be overlooked and even misdiagnosed. However, severe hypotension during stress indicates adrenal crises, especially catecholamine-resistant hypotension [15]. The above alterations of cortisol deficiency affect progress during rehabilitation. Our patient's general function did not markedly improve after a period of treatment with cortisone and thyroxine. We therefore doubled the dose of cortisone; however, he was still remained generally weak. This implied that some underlying problems were still unresolved. Further evaluation and laboratory investigation suggested that insufficient testosterone level might be the cause for his lack of significant improvement.

Testosterone is secreted by the interstitial cells of Leydig in the testes in response to the stimulation of luteinizing hormone from the pituitary gland [16]. Testosterone, the main form of endogenous androgen in adult men, produces many rudimentary biological effects. For example, testosterone can affect the body is composition by increasing fat-free body mass, muscle bulk, muscle power and bone density [17]. After initiation of testosterone therapy, our patient became more responsive to external stimuli, more energetic and improved in functional status. The main side effects of androgen replacement are hyperlipidemia, prostatic enlargement, priapism, acne, polycythemia and obstructive sleep apnea; however, the most serious one is Peliosis hepatitis caused by high dose alkylated androgen [18]. The above side effects were not observed in our patient during the treatment course. It has been suggested that the priority in the management of these tumors should be to prolong life with minimal visual and endocrine disturbance [19]; however, the disease course in our patient was complicated by infraction in the right internal carotid artery territory, which caused advanced motor, sensory and high cortical dysfunction in addition to poor visual acuity due to craniopharyngioma invasion of the optic chiasm. His potential relatively low FIM score (29) on admission to our rehabilitation ward was proof that his ability to improve markedly was limited. No obvious functional improvement occurred until testosterone therapy was initiated, which enabled him to participate more actively in the rehabilitation program. After two-weeks of testosterone therapy, his FIM score had improved to 36. More obvious improvement in FIM score from 36 to 44 was noted ten days later.

Different hormones have their own roles in physiologic functions. The clinical observation in our patient re-enforced the importance of testosterone to a healthy man. In conclusion, not only rehabilitation program but also proper managment of endocrine disturbance with interdisciplinary cooperation are key for patients with craniopharyngioma. Underlying problems should be considered, especially when the progress of rehabilitation is stationary. Proper

management, authority consultation and a comprehensive rehabilitation program optimize the functional recovery of our patient.

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內分泌問題之處理影響顱咽瘤患者復健之預後

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顱咽瘤是一種具侵犯性之顱內腫瘤，常有視覺、神經學及內分泌之異常。手術後常有腫瘤復發、全腦下垂體功能低下和尿崩症等問題。病例爲37歲男性，最初主訴複視及多尿，不久便被診斷患有顱咽瘤，並於轉至本院4個月前接受手術，手術後併發右內頸動脈梗塞。轉至本院復健科時左側偏癱伴隨認知功能障礙，功能獨立量表只有29分。檢查顯示其有廣泛內分泌異常，在腎上腺皮質素、甲狀腺素之適當補充下，復健之進步仍有限。但補充睪固酮後，出現長足之進步，功能獨立量表於出院前達到44分。這案例顯示調整內分泌異常爲顱咽瘤病患復健進步之重要角色。（中台灣醫誌 **2006;11:56-61**）

關鍵詞

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