Craniopharyngioma : A Review of 14 Cases at Siriraj Hospital

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ABSTRACT

Objective: 1) To characterize clinical presentations of craniophryngioma in the hypothalamic- pituitary region 2) To examine both pre-treatment and post-treatment endocrine dysfunction of patients with craniopharyngioma.
Methods: Medical records of patients with craniopharyngiomas from the Endocrine Division, Department of Medicine from 1997 to 2005 (9 years) were retrospectively reviewed. Data were expressed as mean ± SD (range) or percent as appropriate.
Results: There were 14 cases (7 males and 7 females) with histological-proven diagnosis of craniopharyngioma. Their mean age was 32.3 ± 13.0 years (15-56). The major distinguishing feature leading to diagnosis was visual field defects (85.7%), and a quarter of them were blind. Other distinguishing symptoms were headaches (78.6%), and menstrual disorders (28.6%). Pre-operative evaluations of their pituitary function revealed hypogonadotropic hypogonadism (55.6%), diabetes insipidus (DI) (42.9%), secondary adrenal insufficiency (18%) and elevated prolactin levels (36.4%) with a mean level of 36.1 ± 39.2 ng/ml (12-138). All tumors were confirmed by pituitary CT or MRI. Mean tumor size was 3.83 ± 1.3 cm. (2-6), and hydrocephalus was found in 54.5% of all patients. Craniotomy was performed in 13 cases with one transphenoidal surgery. Post-operative endocrine evaluations revealed more frequent hypogonadotropic hypogonadism (90%), both secondary adrenal insufficiency and diabetes insipidus (85.7%). 50% of DI cases were permanent DI. Secondary hypothyroidism was found post-operatively (78%). All cases of elevated serum prolactin levels became normal post-operatively and 44% of all patients had visual field improvement within a follow up period of 2.1 ± 2.3 years (0-7).
Conclusion: Craniopharyngioma is associated with high morbidity pre and post-operation. Visual field tests should be carefully evaluated in all patients with headaches to make early diagnosis in order to improve the treatment outcome.

Keywords: Craniopharyngioma; intracranial tumor; suprasellar tumor

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Craniopharygioma is an epithelial tumour arising along the path of the craniopharyngeal duct. It accounts for 25% of all primary intracranial neoplasms[1] and 5.613% of intracranial tumours in children.[2-4] Their potential subsequent pressure effects on vital structures of the brain predispose the patients to many adverse sequelae depending on their location, size and growth potential.[5-10] Despite their benign histological appearance, their prognosis may often be unfavourable and the optimal therapeutic approach remains controversial.

The objectives of this study were to characterize clinical presentations of patients with craniophryngioma in the hypothalamic-pituitary region presenting to our Division of Endocrinology and Metabolism, Department of Medicine, Siriraj Hospital, Mahidol University during a 9-year period (from July 1997 to August 2005) and to examine both pre-treatment and post-treatment endocrine dysfunction of patients with the disease. We have also analyzed the presenting clinical symptoms and signs, imaging study, hormonal profiles and outcomes of the treatment.

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MATERIALS AND METHODS

Patients

Medical records of 14 patients with histological proof of craniopharyngiomas from the Endocrine Division, Department of Medicine from July 1997 to August 2005 (9 years) were retrospectively reviewed. Their mean age was 32.3 ± 13.0 years, range 15-56 yrs. Data were expressed as mean ± SD (range) or percent as appropriate.

Hormonal evaluation

Gonadotrophin deficiency was diagnosed on the basis of low or "inappropriately normal" FSH and LH levels combined with serum testosterone or estradiol below the

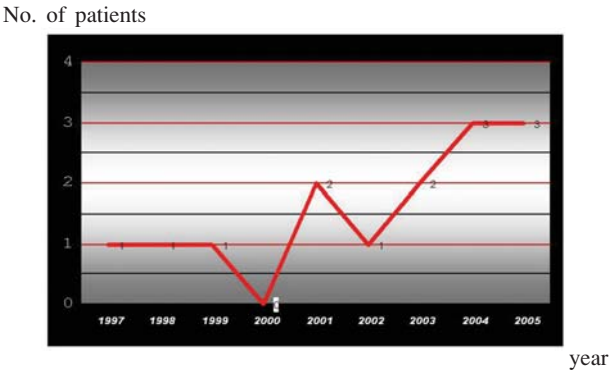


Fig 1. Incidence of patients with diagnosis of craniopharyngioma during July 1997 to August 2005 at Division of Endocrinology and Metabolism, Siriraj Hospital, Mahidol University

reference values associated with oligo-/amenorrhoea. ACTH deficiency was defined by using criteria of peak cortisol level less than 20 μg/dl after provocative testing[11] (Insulin tolerance test) or morning blood cortisol <3 μg/dl[12] especially in patients where provocative testing was not performed. TSH deficiency was defined by low or "inappropriately normal" TSH with thyroid hormone levels below the normal reference values. GH deficiency was defined by GH level <3 μg/dl in adults after provocative testing (Insulin tolerance tests were done in 3 cases). Diabetes insipidus (DI) was diagnosed on the basis of 24-hour urine output >3 litres and urine sp.gr <1.005 or by using water deprivation test (Miller's test was done in 2 cases). Hyperprolactinemia was defined by a level of serum prolactin >25 ng/ml.

Neuroimaging

Imaging studies were available for all 14 patients: computed tomography (CT) scanning for 6; magnetic resonance imaging (MRI) examinations for 6 and CT+MRI scanning for 2. MRI was routinely performed in patients presenting after 2003

Treatment

Patients were classified as 2 modes of surgery: transphenoidal surgery and craniotomy. Gross total removal was defined as the absence of residual tumor in post-operative imaging. Subtotal removal was based on the detection of residual tumor post-operatively and/or on the neurosurgeon's report confirming incomplete excision.

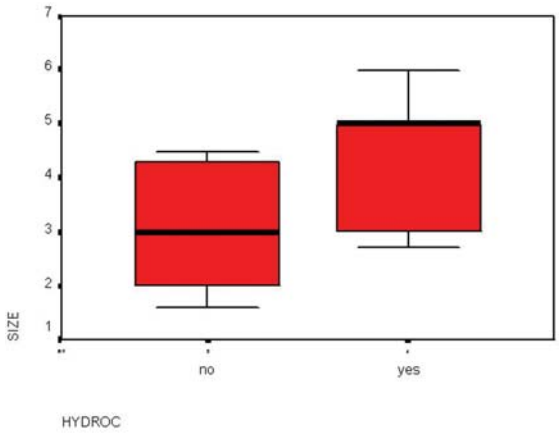


Fig 2. Mean tumor size of the tumor with and without hydrocephalous.

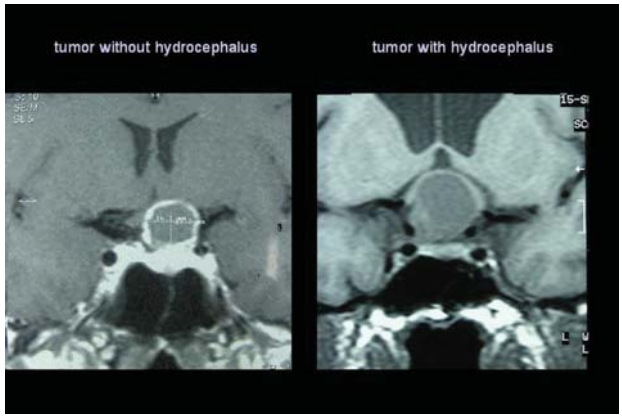


Fig 3. Imaging to compare tumor with and without hydrocephalous.

The decision to perform each type of resection was made by the neurosurgeon during the operation according to the anatomical findings.

Follow-up

There was no fixed protocol for the follow up period. Follow-up imaging was performed based on clinical features and the physician's preference. The mean follow-up period was defined from the first presentation to the last visit. Any recurrence was diagnosed on the basis of radiological appearances (detection of tumor after gross total removal or tumor growth after partial resection) with or without associated signs and symptoms and the time to recurrence was calculated since the date of initial surgery.

Statistical analysis

The evaluations in each case were based on the number of patients with available data. Data were expressed as mean ± SD (range) or percent as appropriate.

RESULTS

Craniopharyngiomas were diagnosed more frequently during the last 5 years as two fold more than the years before as shown in Fig 1.

Clinical presentation

Age, duration of signs and symptoms at presentation, as well as the presenting clinical features of the patients are shown in Table 1. The evaluation of pituitary function at presentation is shown in Table 2. Mean prolactin level in those patients with hyperprolactinemia was 36.1±39.2 ng/ml (range 12-138). Three cases of GH deficiency (21.43%) confirmed by insulin tolerance test were found, but no hypothyroidism was found at preoperative

TABLE 1. Age at presentation, duration of presenting signs and symptoms and presenting clinical features (values are mean ± SD).

● Age-years (range)	32.3±13.0 (15-56)
● Duration of presenting symptom-months	9.2±9.5 (1-36)
● Presenting symptoms	
❍ Visual field defect	85.7%
❍ Blindness	21.4%
❍ Headache	78.6%
❍ Menstrual disorder (women = 7)	28.6%
❍ Nausea and vomiting	18.0%

TABLE 2. Preoperative pituitary evaluation.

● Hypogonadotropic hypogonadism	55.6%
● Diabetes insipidus (DI)	42.9%
● Secondary adrenal insufficiency	18.0%
● Hyperprolactinemia	36.4%

evaluation. Anatomical localization of all tumors was confirmed by pituitary CT or MRI. Findings are shown in Table 3. Preoperative radiological studies demonstrated suprasellar lesion of craniopharyngiomas of 50%, with both intrasellar and suprasellar lesions of 50%. Mean tumor size was 3.8±1.3 cm. (range 2-6). Pituitary imaging showed heterogeneous consistency of the tumor; mixed cystic and solid type, or calcification. We also detected a high percentage of hydrocephalus (54.5%). The mean size of tumors that we found in the hydrocephalus group was 4.4 cm (2.7-6), while those without hydrocephalus had a mean tumor size of 3 cm (1.6-4.5) as shown in Fig 2 and Fig 3.

Treatment

In our series, craniotomy was done in 13 patients and transphenoidal surgery was done in only one. The results of post-operative evaluation of pituitary function are shown in Table 4. In our series, 44% of patients had visual field improvement, 60% of them were patients who had bitemporal hemianopia at presentation. During the follow up period, four of fourteen patients (28.6%) had tumor recurrences with a mean recurrence period of 39 months (range 7-108 months).

Prognosis

The mean follow up period was 2.1 ± 2.3 years (range 0-7). There was no reversal of pre-existing pituitary hormone deficiencies after any surgical intervention. All patients had hormonal replacement therapy during the follow up period. Out of awareness of developing osteoporosis in most of the patients who were hypogonadotropic hypogonadism, we also monitored bone mineral density (BMD), but the data was insufficient to analyze.

During the follow up period, four of fourteen patients (28.6%) had tumor recurrences with a mean recurrence period of 39 months (range 7-108 months). One of them was a patient who had transphenoidal surgery and the others were treated with craniotomy.

DISCUSSION

The effects of craniopharyngioma on the hypothalamopituitary system, visual pathways, and ventricular system predispose patients to multiple clinical manifestations at the time of presentation. In this cross-sectional study, their duration ranged between 1 and 36 months, the delay in the diagnosis probably reflects the tolerance of subtle endocrinological symptoms. The frequent presenting features in our patients were visual field defects (85.7%), headaches (78.6%) and menstrual disorders (28.6%). The clinical findings in our group of patients were nearly the same as in previous studies reported by Petito and others.[5-6, 8-9]

TABLE 3. Imaging features by CT or MRI.

● Mean tumor size - cm.	3.83±1.3 (2-6)
● Hydrocephalus	54.5%
● Location	
❍ Suprasellar	50.0%
❍ Both intrasellar & suprasellar	50.0%

TABLE 4. Postoperative evaluation of pituitary function.

● Hypogonadotropic hypogonadism	90.0%
● Secondary adrenal insufficiency	85.7%
● Secondary hypothyroidism	78.6%
● Permanent diabetes insipidus (DI)	50.0%

A number of our patients who had preoperative evaluation of their pituitary function were diagnosed as hormone deficiency. Our report presents the results of pretreatment and post-treatment endocrine evaluations in 14 patients with craniopharyngioma in an attempt to provide further information about endocrine disturbances effected by this neoplasm. The most frequent preoperative hormonal deficit in our patients was gonadotropin secretion. Twenty-five percent of premenopausal women complained of primary or secondary amenorrhea and 57% of males also showed clinical symptoms of hypogonadism. Diabetes insipidus and ACTH deficiency were found in 42.9% and 18% respectively and one third of the patients had elevated prolactin level. GH deficiency was found in 21.43%, but no hypothyroidism was found at preoperative evaluation. The etiology of endocrine dysfunction in patients with craniopharyngioma remains debatable according to their site of origin. These tumors could interfere with the secretion of hypothalamic hormones. Moreover, the tumor could directly affect the synthesis and secretion of pituitary hormones by invading and destroying pituitary tissue.

Preoperative radiological studies demonstrated suprasellar lesions of craniopharyngiomas of 50%, both intrasellar and suprasellar lesions of 50/%. Pituitary imaging showed heterogeneous consistency of the tumor; mixed cystic and solid type, or calcification. As a large number of patients were evaluated by MRI at their presentation; an imaging modality in which calcification cannot be easily detected, therefore the frequency of this feature was not assessed in our study. We also detected a high percentage of hydrocephalus (54.5%). The mean size of tumors that we found in the hydrocephalus group was 4.4 cm (2.7-6) while those without hydrocephalus group were 3 cm (1.6-4.5). We suggest that hydrocephalus may be associated with large tumor size.

The treatment of craniopharyngiomas poses a surgical challenge because they are often large and adhere to vital neurovascular structure which does not allow a clear line of cleavage making complete resection difficult. As surgery in craniopharyngiomas is a destructive surgery, we found more frequent of pituitary dysfunction in the post-operative period. Impaired gonadotropin secretion remained the most common hormonal deficit in our series which was more than those of ACTH, thyrotropin secretion and also vasopressin. Half of the patients who developed diabetes insipidus in the post-operative period eventually turned out to have permanent diabetes insipidus (DI).

CONCLUSION

Our results suggest that craniopharyngioma is associated with high morbidity pre and post operation. Endocrine abnormalities induced by craniopharyngiomas may be irreversible. Surgical treatments usually cause pituitary function impairment. Visual field defect was the main presenting symptom and should be carefully evaluated in all patients with headaches to make early diagnosis in order to improve the treatment outcomes.

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บทคัดย่อ

ผู้ป่วยที่มีเนื้องอกในสมองเครนิโอฟาริงค์จิโอมา 14 รายที่โรงพยาบาลศิริราช

ธวัชชัย พีรพัฒน์ดิษฐ์ พ.บ., พรศรี ชัยวิจิตรมาลากุล พ.บ., ระวีวรรณ เลิศวัฒนารักษ์ พ.บ., สุนันทา ชอบทางศิลป์ พ.บ., ณัฐเชษฐ์ เปล่งวิทยา พ.บ., สุทิน ศรีอัษฎาพร พ.บ., วรรณี นิธิยานันท์ พ.บ., สาธิต วรรณแสง พ.บ.

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วัตถุประสงค์ : 1. เพื่อทราบลักษณะนำทางคลินิกของผู้ป่วยที่มีเนื้องอกในสมองเครนิโอฟาริงค์จิโอมาที่อยู่บริเวณเหนือต่อมใต้สมอง 2. เพื่อพิจารณาตรวจสอบความผิดปกติทางต่อมไร้ท่อในผู้ป่วยที่มีเนื้องอกในสมองเครนิโอฟาริงค์จิโอมาทั้งภาวะก่อนรับการรักษาและหลังการรักษา

วิธีการ: ทบทวนและวิเคราะห์รายงานผู้ป่วยที่มีเนื้องอกในสมองเครนิโอฟาริงค์จิโอมาที่อยู่ในความดูแลรักษาของสาขาวิชาต่อมไร้ท่อ ภาควิชาอายุรศาสตร์ ระหว่าง พ.ศ. 2540-2548 (รวม 9 ปี) โดยเสนอข้อมูลในแบบค่าเฉลี่ย ± ค่าเบี่ยงเบนมาตรฐาน (พิสัย) หรือในแบบร้อยละ แล้วแต่ความเหมาะสม

ผลการศึกษา : ผู้ป่วยที่มีเนื้องอกในสมองเครนิโอฟาริงค์จิโอมาที่มีรายงานยืนยันการวินิจฉัยโดยเนื้อเยื่อจากการผ่าตัดจำนวน 14 รายงาน เป็นชาย 7 คนและหญิง 7 คน อายุเฉลี่ย 32.3 ± 13.0 ปี (15-56) อาการสำคัญที่นำไปสู่การวินิจฉัยคือลานสายตาที่ผิดปกติ (85.7%) และหนึ่งในสี่จะมีตามองไม่เห็น อาการอื่นได้แก่ ปวดศีรษะ (78.6%) ประจำเดือนผิดปกติ (28.6%) ผลการประเมินหน้าที่ของต่อมใต้สมองก่อนผ่าตัดพบฮัยโปโกนาโดโทรปิคฮัยโปโกนาดิสมด์ (55.6%) เบาจืด (42.9%) ต่อมหมวกไตบกพร่องทุติยภูมิ (18%) และระดับโปรแลคตินสูงผิดปกติเฉลี่ย 36.1 ± 39.2 ng/ml (12-138) (36.4%) ขนาดของเนื้องอกเฉลี่ย 3.83 ± 1.3 ซม. (2-6) ตรวจยืนยันทุกรายโดยคอมพิวเตอร์ (ซีทีหรือเอ็มอาร์ไอ) พบฮัยโดรเซฟาลัส 54.5% รักษาโดยการผ่าตัดเครนิโอโตมี่ 13 รายและทรานสฟีนอยด์หนึ่งราย ตรวจสอบความผิดปกติทางต่อมไร้ท่อหลังผ่าตัด พบฮัยโปโกนาโดโทรปิคฮัยโปโกนาดิสมด์ (90%) ต่อมหมวกไตบกพร่องทุติยภูมิร่วมกับเบาจืด (85.7%) โดยครึ่งหนึ่งของผู้ป่วยเบาจืดเป็นแบบถาวร พบผู้ป่วยฮัยโปธัยรอยด์ทุติยภูมิ (78%) ลานสายตาดีขึ้น (44%)ในเวลาเฉลี่ยหลังผ่าตัด 2.1 ± 2.3 ปี (0-7) ระดับโปรแลคตินที่สูงกลับสู่ปกติทุกรายหลังผ่าตัด

สรุป : เนื้องอกในสมองเครนิโอฟาริงค์จิโอมาทำให้เกิดภาวะทุพพลภาพได้มากทั้งก่อนและหลังการผ่าตัด หากหวังให้ผลการรักษาดีขึ้น การตรวจลานสายตาอย่างถูกต้องในผู้ป่วยที่มีอาการปวดศีรษะทุกรายจะช่วยการวินิจฉัยโรคนี้ได้ตั้งแต่ระยะแรก ๆ