

Craniopharyngioma : Comparison of Tumor Characteristics Relevant with Initial Symptomatology between Children and Adults

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= Abstract =

두개인두중 : 소아와 성인에서 초기 증상과 연관된 종양의 특징 비교

박동혁 · 박정율 · 김주한 · 정용구 · 이훈갑 · 이기찬 · 서중근

Objectives : The craniopharyngioma is a benign tumor located at least in part in the suprasellar cistern. However, the symptoms and signs from this tumor may be determined not only by the location of the tumor but also by its size and the age of the patient. The objective of our study is to analyze retrospectively the clinical manifestations of craniopharyngiomas with regards to tumor characteristics in children and adults.

Material and Methods : Twenty - three patients(16 adults, 7 children) treated for craniopharyngioma between 1990 and 1999 were studied to demonstrate the relationship of tumor size, growth pattern, and its invasiveness with clinical symptoms. As part of the assessment, 16 adults(M : F=8 : 8, mean age : 43.7 years) and 7 children(M : F=5 : 2, mean age : 10.1 years) underwent magnetic resonance(MR) imaging and computerized tomography(CT) scanning with a three - dimensional volume acquisition sequence.

Results : The three major cardinal signs were defined to increased intracranial pressure, endocrine dysfunction, and visual problems. The tumor size in child group was larger than that in adult group. Also, visual problems, symptoms of increased intracranial pressure and hydrocephalus were more frequently observed in child group. However, endocrine dysfunction and neuropsychological symptoms related with hypothalamic connections to the thalamus, pituitary, frontal lobe, and other cortical areas were more frequent in adult group.

Conclusions : In our series, the tumor size and invasiveness of craniopharyngioma revealed to be relevant with initial symptoms of increased intracranial pressure and visual symptoms which were more frequent in child group. As for the growth pattern, we did not find major difference between adults and children.

KEY WORDS : Craniopharyngioma · Symptom · Invasiveness · Growth pattern.

Introduction

Erdheim in 1904 contributed the first correct histologic interpretation and adequate description of craniopharyngiomas¹⁶⁾. He postulated that these tumors originated from

embryonic squamous cell rests of an incompletely involuted hypophyseal-pharyngeal duct. Since then several authors have noted differences in the histological patterns of adult and childhood craniopharyngiomas¹⁰⁾¹⁴⁾. It is speculated that an embryonic origin for tumors in adults is not required and craniopharyngiomas appearing later in life may arise

from metaplasia of pituitary cells. Since squamous cell rests are rarely found in children, but show increasing frequency in each succeeding decade of life, it was suggested that the craniopharyngioma originates from metaplasia of mature cells of the anterior pituitary rather than from embryonic remnants³. As it has been generally believed that the origin of craniopharyngioma in child is different from that in adult, the symptoms and signs caused by this tumor can be thought to be also different between age groups. The aim of this study is to analyze retrospectively the relationship of the clinical manifestations of craniopharyngiomas, with regards to initial symptoms and signs in children and adults, with tumor characteristics (e.g., location, size and growth pattern of the tumor).

Material and Method

1. Patients characteristics

Twenty-three patients who were treated for craniopharyngioma in our institution were included in this study. Of these, 7 patients were children of age less than 16 years at the time of diagnosis. There were 5 males and 2 females. The mean age in child group was 10.1 years with range between 3 to 14 years. There were 8 males and 8 females in adult group. The mean age in adult group was 43.7 years (range 17 - 79 years).

2. Methods

We defined the the tumor characteristics as location, size, direction of growth, and invasiveness by brain MR images. Initial symptoms and signs were defined as those related to increased intracranial pressure, endocrine dysfunction, and

visual problems. Locations of tumor were described as suprasellar, sellar, and combined⁸. Tumor size were expressed as tumor volume, determined from MR images, and is measured by following formula in which A, B, C represent the three orthogonal planes on MR images² ;

A is the largest diameter on the axial slice with the largest area of tumor. B is the diameter that is 90 to diameter A and is measured at the midpoint of diameter A. Diameter C (vertical diameter) is the largest diameter on the sagittal image with the largest area of tumor (Fig. 1) :

$$V = \frac{A \times B \times C}{2} \text{ (cm}^3\text{)}$$

Direction of tumor expansion included prechiasmatic, subchiasmatic, retrochiasmatic and lateral. Also, we defined the invasive craniopharyngioma as large craniopharyngiomas extending either superiorly into the third ventricle, or inferiorly into the sphenoid sinus and nasopharynx, or anteriorly into frontal fossa, or laterally into the temporal fossa, or posteriorly into the posterior fossa.

Symptoms and signs related to increased intracranial pressure included headache, vomiting, papilledema. Symptoms and signs related to the endocrine dysfunction were described into hormonal dysfunction (e.g., growth failure, diabetes insipidus, delayed puberty, sexual problems). Neuropsychological problems (e.g., personality change, mentation deficit) were also described. Visual problems included decreased visual acuity, visual field defect and eye ball motion defect.

These signs and symptoms were analyzed retrospectively with regards to tumor characteristics in both child and adult group.



Fig.1. A is the largest diameter on the slice with the largest area of tumor. B is the diameter that is 90° to diameter A and is measured at the midpoint of diameter A. Diameter C (vertical diameter) is the largest diameter on the sagittal image with the largest area of tumor.

Results

The tumor characteristics, initial symptoms and signs in adult and child group are listed in (Table 1, 2) Five (71%) of 7 patients in child group had headache and vomiting. Whereas, eleven (69%) of 16 patients in adult group had these symptoms. The hydrocephalus was seen in two (29%) of 7 patients in child group, and as disease progressed, 3

patients also developed in child group. However, only one (6%) of 16 patients in adult group developed the hydrocephalus in whom ventriculo-peritoneal (VP) shunt was necessary. Visual problems as mentioned above were noted in six (86%) patients in child group, and ten (62%) of 16 patients in adult group. Four (57%) of 7 patients showed papilledema in child group, and two (13%) of 16 patients in adult group. One patient developed total blindness as disease progressed. Interestingly, two (29%) of 7 patients in

Table 1. Tumor characteristics, initial symptoms and signs in adult group

Patient	Tumor	Tumor	Growth	Visual	Headache	Hydro-	General	Psychologic/hormonal	
Sex/age(y)	location	volume, cm ³	direction	problems	Vomiting	cephalus	weakness	problems	
1	M/34	Suprasellar	12.2	Subchiasmatic	+	+	-	-	-/+
2	M/44	Supra + Intrasellar	60	Prechiasmatic	+	+	-	-	-/-
3	M/79	Suprasellar	55.2	Prechiasmatic + Lateral	-	+	-	+	-/?
4	M/67	Suprasellar	29.4	Retrochiasmatic	+	-	-	-	+/+
5	M/56	Suprasellar	21.6	Retrochiasmatic	-	-	-	+	+/+
6	M/64	Suprasellar	23.1	Retrochiasmatic	+	+	-	-	-/+
7	M/32	Suprasellar	56	Retrochiasmatic	+	+	-	-	-/+
8	M/30	Suprasellar	24.5	Retrochiasmatic	-	+	-	-	+/+
9	F/41	Supra + Intrasellar	3.7	Subchiasmatic	+	+	-	-	+/+
10	F/22	Suprasellar	22.2	Retrochiasmatic	-	+	+	+	-/+
11	F/65	Suprasellar	45	Retrochiasmatic	+	-	-	+	-/+
12	F/35	Suprasellar	24.3	Subchiasmatic	+	-	-	-	-/+
13	F/30	Suprasellar	14	Retrochiasmatic	+	+	-	-	-/+
14	F/46	*Intrasellar	6.75	Subchiasmatic	-	+	-	-	-/+
15	F/55	Supra + Intrasellar	28.6	Prechiasmatic	+	-	-	-	-/+
16	F/49	Suprasellar	1.7	Retrochiasmatic	-	+	-	-	-/?

* : Tumor was initially intrasellar, however, when recurred, it occupied both intrasellar and suprasellar region

? : Hormone studies were incomplete

Table 2. Tumor characteristics, initial symptoms and signs in children group

Patient	Tumor	Tumor	Growth	Visual	Headache	Hydro-	Motor	Hormone	
Sex/age(y)	location	volume, cm ³	direction	problems	Vomiting	cephalus	weakness	deficiency	
1	M/7	Suprasellar	46.8	Lateral Prechiasmatic	+	+	-	-	+
2	M/3	Supra + Intrasellar	21	Retrochiasmatic	-	-	+	+	-
3	M/14	Supra + Intrasellar	9	Retrochiasmatic	+	+	-	-	+
4	M/14	Suprasellar	53	Subchiasmatic	+	+	+	+	+
5	M/12	Suprasellar	32	Subchiasmatic	+	+	+	-	+
6	F/8	Suprasellar	90	Retrochiasmatic	+	-	+	-	-
7	F/13	Suprasellar	125.4	Prechiasmatic	+	+	+	-	+

* : Hydrocephalus developed with disease progression

Table 3. Hormonal dysfunction

Child group(n=7)	Adult group(n=16)
GH deficiency : 5	Cortisol deficiency : 7
Cortisol deficiency : 1	Thyroid hormone deficiency : 1
Panhypopituitarism : 1	Sex hormone deficiency : 2(M) 3(F)
Central DI : 1	Panhypopituitarism : 2 Central DI : 4

GH : Growth hormone, DI : Diabetes insipidus
M : male, F : female

child group showed motor weakness, including the hemiparesis, and four (25%) of 16 patients in adult group complained generalized weakness.

Hormonal dysfunction is listed in (Table 3) Seventy-one percent of child group presented with growth hormone deficiency, but only one (14%) patient showed deficiency of cortisol. Unlike children seven (44%) of 16 patients showed deficiency of cortisol and one (6%) patient presented hypothyroidism. Two (33%) of 8 male patients showed deficiency of sex hormone and one of them presented hypogonadism. All three premenopausal women of 8 female had low level of lutenizing hormone (LH) and follicular stimulating hormone (FSH) except 2 perimenopausal women and 3 postmenopausal women. Two premenopausal women had no menstruation and one postmenopausal woman had early menopause at 32 years old. Two (12.5%) of 16 patients showed panhypopituitarism in adult group. One (14%) of 7 patients presented it in child group, and the boy had no secondary sexual development. Four (25%) of 16 patients developed preoperative or postoperative central diabetes insipidus (DI) in adult group, and one (14%) of 7 patient developed it in child group. Four (25%) of 16 patients in adult group presented neuropsychological symptoms and signs that were disorientation, personality change and memory dysfunction, but one (14%) of 7 children developed irritability like neuropsychological symptoms and signs in adult. Two female patients developed unilateral hearing defect and walking disturbance. A large cystic tumor extended into cerebellopontine angle and foramen magnum was seen in one and a huge cystic suprasellar mass that extended into subfrontal area in the other.

Radiologic evaluation

In child group, the largest tumor size was $7.6 \times 6.6 \times 5\text{cm}$ (volume : 125.4cm^3) and the smallest tumor size was $3 \times 2.5 \times 2.4\text{cm}$ (volume : 9cm^3). The mean volume of tumor in child group was 54cm^3 . In adult group, the largest tumor

size was $6 \times 4 \times 5\text{cm}$ with volume of 60cm^3 . The smallest tumor size was $1.5 \times 1.5 \times 1.5\text{cm}$ with volume of 1.7cm^3 . The mean volume was 26.8cm^3 .

In child group, tumor location in 5 (71%) cases were on suprasellar and 2 (29%) on both supresellar and sellar regions. None of cases in child group showed tumor location limited to sellar area. In adult group, twelve (75%) of 16 tumors were located in suprasellar area and three (19%) cases involved both suprasellar and sellar area. One (6%) case had tumor located within sellar at first operation. However, tumor was located both suprasellar and intrasellar sites after 4 years.

As for the tumor extension, three (43%) of 7 tumors in child group extended into retrochiasmatic area, and two (28.5%) into subchiasmatic area. One case showed prechiasmatic and expanded laterally into temporal fossa, and another case located only prechiasmatic area. In adult group, nine (56%) of 16 tumors into retrochiasmatic area, and four (25%) cases extended into subchiasmatic area. Three (18.7%) cases involved prechiasmatic area. In one case, tumor spreaded into temporal fossa.

As for invasiveness, four (57%) of 7 tumors were shown to be invasive craniopharyngioma in child group. In the contrary, two (12.5%) of 16 tumors in adult group were shown to be invasive craniopharyngioma.

Discussion

Tumor size and volume in child group were greater than that in adult group. The mean volume of tumor in child group was twice as in adult group. Since craniopharyngiomas are slow growing extra-axial tumors, it can be expected that these become quite large before they cause symptoms, especially in children. In the majority of cases the time interval between onset of symptoms and diagnosis of tumor ranged from 1 - 2 years. Invasive craniopharyngiomas in child group were observed more frequently than in adult group. All except one patient with invasive craniopharyngioma had symptoms and signs of increased intracranial pressure and visual problems. The suprasellar area was the most commonly involved location and retrochiasmatic expansion was the most common type of growth. However, there was no definite difference in location and pattern of growth in paragangliomas between children and adults in our series.

Several authors reported that headache was common complaint in patients with retrochiasmatic tumors whereas

hydrocephalus, and visual problems were more common complaint in patients with prechiasmatic tumors³⁾⁹⁾¹⁶⁾. In our series, headache and vomiting in child group were more common than in adult group and it was correlated with size of tumor. Visual problems were more frequently observed in children than adults although they were not correlated to mass location on both groups. It is generally believed that visual deficits may result both from direct compression of the optic pathways by the tumor and secondarily from intracranial hypertension⁵⁾¹⁶⁾. According to several authors and from our experience, children often tolerate a high degree of visual loss without complaint, and continue their school works or watch television without arousing the suspicion from parents and teachers³⁾⁵⁾⁹⁾¹⁶⁾. In our series, only three of 6 patients who diagnosed high visual loss by ophthalmologic examination complained their visual discomforts at initial visit.

As for the hormonal dysfunction, eighteen patient (78%) showed various types of hormonal dysfunction. Growth hormone deficiency was more common in child group, whereas cortisol deficiency was more frequently observed in adult group. Deficiency of sex hormone was more often observed in adult group with decreased sexual drive in men (50%) and amenorrhea in women (100%). The children with deficiency of sex hormone showed no secondary sexual development. The central diabetes insipidus (DI) was more commonly observed in adult group, and caused longer hospital stay and higher morbidity due to postoperative sepsis and decreased immunity in case. These endocrine changes are believed to be caused by compression of the hypothalamic-hypophysial axis¹⁶⁾. However, difference in the pattern of hormonal deficiency between children and adults in our series did not correlate with tumor growth patterns.

Neuropsychological symptoms and signs such as personality and cognition changes were more evident in adult group. These were commonly seen in adults with tumor mass extended into frontal lobe. Therefore, it is believed that neuropsychological symptoms related with hypothalamic connections to the thalamus, pituitary, frontal lobe, and other cortical areas are more frequent clinical findings in adult group¹⁶⁾. Motor weakness in the form of monoparesis or hemiparesis were observed in two children in our cases. However, no definite motor weakness was seen in adult group.

Although craniopharyngiomas account for a great per-

centage of the intracranial tumors of childhood, they account for only 1 to 3% of intracranial tumors in all ages¹⁴⁾¹⁷⁾. Pathogenesis of craniopharyngioma is explained by two opposing hypotheses. These tumors may arise from ectopic embryonic cell remains of enamel organs. Also, they may represent the residual metaplastic squamous epithelium found in the adenohypophysis and anterior infundibulum¹⁾. Petito et al.¹⁴⁾ reported that the great majority of tumors were located in the suprasellar area (94%) at the time of diagnosis. Only rarely, do these tumors extend into the anterior fossa (5%), middle fossa (2%), or posterior fossa (4%).

However, a study from postmortem examination revealed higher incidence of extension into these fossa has been found (12%)¹⁴⁾. According to Yasargil, the tumor, with its expansive and infiltrative behavior, affects not only the pituitary-hypothalamic axis and visual pathways, but also the frontal lobes, striocapsulothalamic areas, mammillary bodies, and limbic system¹⁷⁾. The three major clinical syndromes associated with craniopharyngioma are related to increased intracranial pressure, endocrine dysfunction, and visual problems¹⁶⁾. Children frequently present with symptoms of increased intracranial pressure (65 - 75%) such as headache and vomiting due to enlarging intracranial mass¹⁶⁾. Visual deficits are commonly well tolerated by children. Only 20 - 30% of them complain of visual problems, usually when almost complete visual loss has already taken place¹³⁾. Endocrine dysfunctions are present in one half of the children, and frequently manifest as short stature and diabetes insipidus. One third of children with craniopharyngioma have growth failure at the time of diagnosis. Delayed puberty is present in one half of the adolescents, and polydipsia and polyuria due to diabetes insipidus in 20% of cases. The hypothalamic-pituitary complex is essential for endocrine, autonomic, and behavioral performance⁴⁾¹⁵⁾. Disturbance of hypothalamic connections to the thalamus, frontal lobes, and other cortical areas have been related to some of the psychological and social problems seen among affected patients⁶⁾⁷⁾¹²⁾. Visual deficits and endocrine dysfunction are the most frequent clinical findings in adults³⁾. Signs of increased intracranial pressure are less common than in children¹⁶⁾. Large subfrontal masses may cause neuropsychological symptoms, mentation deficits and memory loss, as well as incontinence, apathy, and Korsakoff's syndrome¹¹⁾. Large subtemporal masses extending laterally to the sylvian fissure may produce complex psychomotor seizures¹⁶⁾.

Conclusion

The characteristics of craniopharyngiomas in reported and our series, such as the location of tumor, its size, invasiveness and direction of tumor expansion were comparatively similar. However, the symptoms and signs from these tumors, may be determined not only by the location of the tumor but also revealed to be affected by its size and the age of the patient.

In this study, as tumors were more larger and more invasive in child group, the symptoms and signs related to increased intracranial pressure and visual problems were more frequently observed compared with adult group. However, with regards the growth pattern of tumor, there was no distinctive difference between child and adult group. Tumors in children were different from that in adults with respect to endocrine dysfunction resulting from compression of the hypothalamic-hypophyseal axis, but the cause for the difference of endocrine dysfunction between children and adults remains undetermined.

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= 국문 초록 =

목적 :

방법 및 대상 : 1990 ~ 1999년 사이에 23 (남자 : 16, 여자 : 7) 명의 환자를 대상으로 (남자 : 8, 여자 : 8, 평균 나이 : 43.7) 7 (남자 : 5, 여자 : 2, 평균 나이 : 10.1) MRI

CT 3
결과 : 3

결론 :

중심 단어 :