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# Comparison Study of Clinical Presentation and Surgical Outcome between Children and Adults with Craniopharyngioma: A 22-Year Single-Center Experience in Southern Taiwan

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#### Abstract

**Background:** The differences in clinical presentation and surgical outcome between children and adults with craniopharyngioma have not been well-described and there are few data available for Asian population. The aim of this study is to investigate the differences between paediatric and adult patients with craniopharyngioma at a single medical centre in southern Taiwan.

**Methods:** The clinical records of 40 patients with craniopharyngioma who were all surgically treated at Kaohsiung Medical University Hospital from January 1990 to December 2012 were reviewed. The patients were divided into two groups based on age: children ( $\leq$  20 years) and adults (>20 years). MRI and CT images were obtained pre- and post-operatively. Histopathological examination diagnosed tumors. Statistical analyses were performed to compare the differences in the two groups.

**Results:** Among the patients, 17 were children and 23 were adults. The children group demonstrated more diagnoses of large or giant tumors (p<0.001), a higher rate of tumors with both solid and cystic composition (p=0.027) as well as adamantinomatous type tumors (p=0.020). The children group also had a higher surgical complication rate of diabetes insipidus (p=0.023).

**Conclusions:** There are significant differences between children and adults with craniopharyngioma with regard to tumor size, histopathology type of tumor and hormone-related surgical complications. These findings are useful for improving the strategies for managing patients with craniopharyngioma.

Keywords: Clinical presentation; Surgical outcome; Craniopharyngioma

# Introduction

Craniopharyngiomas are tumors that are histologically benign in appearance and are generally believed to originate from remnants of Rathke's pouch [1,2]. A histological resemblance has been noted between adamantinomatous craniopharyngiomas and some odontogenic tumors [3]. This similarity has been explained by their common embryonic origin [3]. Based on epithelium pattern, there are two major histological types of craniopharyngiomas: adamantinomatous and papillary types [4]. Some tumors are mixed type. Craniopharyngiomas in nearly all children and about two-thirds of adults are adamantinomatous type [4]. Craniopharyngiomas are typically located in the infundibulo hypophyseal axis in the sella and suprasellar region, but may grow in any direction. Although regarded as benign, they tend to invade into the hypothalamus, pituitary stalk, and optic pathways [1,5]. Because of the close anatomical relationship of the tumors to adjacent cerebrovascular structures, surgical resection of the tumor is risky about visual and endocrine dysfunctions as well as the possibility of a major vascular trunk injury [6]. These tumors can be purely cystic, predominantly cystic, purely solid, predominantly solid, or multi-cystic. One published data showed about half of the tumors were predominantly cystic, while less than 4% of newly diagnosed tumors were purely cystic [7].

Craniopharyngiomas account for 2% to 5% of primary intracranial tumors, 1% to 3% of paediatric brain tumors, and 6% to 9% of primary paediatric central nervous system tumors [1,2,8,9]. Craniopharyngiomas could occur in both paediatric and adult groups, even in individuals aged more than 80 years [10]. In the paediatric group, the incidence

of craniopharyngiomas peaks at age 5-9 years [11]. For adult group, the Danish study found that the peak incidence occurred in individuals aged 40-44 years [12]. Although craniopharyngiomas could occur in both paediatric and adult groups, the clinical presentation and surgical outcome may differ. Nielsen et al. claimed that there may be differences about how children and adults react to intracranial tumor growth because children's brains were still developing [13]. Furthermore, there had been a perception that the functional outcome of radical surgery is potentially harmful for children [14]. The aim of this study is to investigate the differences between paediatric and adult patients with craniopharyngioma at a single medical centre in southern Taiwan.

# Methods

# Patients

From January 1990 to December 2012, a total of 40 patients (15 males and 25 females) with craniopharyngiomas were treated surgically at Kaohsiung Medical University Hospital in southern Taiwan. MRI

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and CT images were obtained pre- and post-operatively. The clinical presentations were reviewed on medical charts. Based on ages, the patients were divided into two groups: children (age  $\leq$  20 years) and adults (age>20 year).

# Surgical procedures

Surgical resection was carried out using either the pterional approach (n=35), trans sphenoidal approach (n=4), or transcallosal approach (n=1). The surgical techniques had been previously described in detail [15-17].

## **Radiation therapy**

There were 28 (70%) patients who received radiation therapy after surgery.

# Follow-up

After surgery, the patients received follow-up monthly. The surgical outcome was divided into 3 groups: 1) Good: no post-operative complications; 2) Fair: minor post-operative complications such as prolonged diabetes insipidus or hemiparesis; 3) Poor: major

Characteristics	Total (n=40)	Children (n=17)	Adults (n=23)	p-value
Sex				0.283
Males	15 (37.5%)	8 (47.1%)	7 (30.4%)	
Females	25 (62.5%)	9 (52.9%)	16 (69.6%)	
Age				NA
0-10 yrs	6 (15.0%)	6 (35.3%)	0 (0%)	
11-20 yrs	11 (27.5%)	11 (64.7%)	0 (0%)	
21-30 yrs	9 (22.5%)	0 (0%)	9 (39.2%)	
31-40 yrs	3 (7.5%)	0 (0%)	3 (13.0%)	
41-50 yrs	3 (7.5%)	0 (0%)	3 (13.0%)	
51-60 yrs	5 (12.5%)	0 (0%)	5 (21.8%)	
61-70 yrs	2 (5.0%)	0 (0%)	2 (8.7%)	
>70yrs	1 (2.5%)	0 (0%)	1 (4.3%)	
Clinical presentation				
Visual problem	32 (80%)	13 (76.5%)	19 (82.6%)	0.702
Headache	26 (65.0%)	12 (70.6%)	14 (60.9%)	0.739
Stunted growth	10 (25.0%)	9 (52.9%)	1 (4.3%)	0.001 <sup>*</sup>
Polyuria	9 (22.5%)	5 (29.4%)	4 (17.4%)	0.456
Changes in mentation	6 (15.0%)	2 (11.8%)	4 (17.4%)	1.000
Calcification				
Skull	26 (65.0%)	8 (47.1%)	18 (78.3%)	0.041 <sup>*</sup>
СТ	14 (35.0%)	9 (52.9%)	5 (21.7%)	0.749
Composition				0.074
Solid	5 (12.8%)	1 (5.9%)	4 (18.2%)	0.363
Cystic	13 (32.5%)	3 (17.6%)	10 (43.5%)	0.103
Solid & cystic	22 (55.0%)	13 (76.5%)	9 (39.1%)	0.027*
Size of tumor				<.001 <sup>*</sup>
Small (<2cm)	5 (12.5%)	1 (5.9%)	4 (17.4%)	
Moderate (2-4cm)	16 (40.0%)	3 (17.6%)	13 (56.5%)	
Large (4-6cm)	14 (35.0%)	8 (47.1%)	6 (26.1%)	
Giant (>6cm)	5 (12.5%)	5 (29.4%)	0 (0%)	
Tumor histopathology				0.010 <sup>*</sup>
Adamantinomatous	27 (67.5%)	15 (88.2%)	12 (52.2%)	
Squamous papillary	9 (34.8%)	0 (0%)	9 (34.8%)	
Mixed	4 (10%)	2 (11.8%)	2 (8.7%)	
yrs: Years; NA: Not Assess	ed.			

Data are presented as n (%) by group and were compared using Pearson chisquare or Fisher's exact test.

<sup>\*</sup> Indicates significant difference between children and adults. (P<0.05)

Table 1: Comparison of characteristics between children and adults.

post-operative complications such as permanent diabetes insipidus, hemiplegia or mortality.

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## Statistical analysis

Data for surgical profiles and pathology characteristics were presented as n (%). Differences between children and adults were compared using Pearson chi-square or Fisher's exact test if any cell number was less than 5. All statistical assessments were two-tailed and considered significant at p<0.05. Statistical analyses were performed using SPSS 18.0 statistics software (SPSS Inc, Chicago, IL, USA).

#### Results

A total of 40 patients were enrolled in this study. Among these 40 patients, 17 were children (age  $\leq$  20 years; 8 males and 9 females) and 23 were adults (age >20 years; 7 males and 16 females). The characteristics of these 40 patients are presented in Table 1. At clinical presentation, children had a higher rate of stunted growth than adults (52.9% vs. 4.3%; p=0.001). About calcification, adults had a higher rate of calcification in the skull than children (78.3% vs. 47.1%, p=0.041). Children had a higher rate of having tumors with both solid and cystic composition than adults (76.5% vs. 39.1%, p=0.027). With respect to tumor size, more than 70% of children were diagnosed with large or giant tumors whereas adults were frequently diagnosed with small or moderate tumors (p<0.001). No adult was found having a giant tumor. The tumor histopathology results were significantly different between children and adults (p=0.010). Children had a higher rate of adamantinomatous type tumors than adults (p=0.020, not shown in the table). Nine squamous papillary cases were observed in adults while none in children. Table 2 presents the results of the comparison between children and adults about the surgical procedures, postoperative complications, and follow-up outcome. Children had a higher rate of post-operative temporary diabetes insipidus than adults. (41.2% vs. 8.7%; p=0.023). No significant differences were observed in surgical procedures or hydrocephalus requiring shunt placement between children and adults. The follow-up prognosis for 30 (75%) patients was good, for 6 (15%) fair, and for 4 (10%) poor with late mortality. A total of 28 (70%) patients received radiation therapy after surgery. There were 6 patients (5 children and 1 adult) having tumor recurrence. Table 3 presents the results of comparison of clinical characteristics among different histopathology types in children and adults.

Figure 1 shows 3 examples of H&E staining of adamantinomatous, papillary, and adamantinomatous plus papillary (mixed type) craniopharyngiomas. Figure 2 demonstrates a post-operative complication from a 10-year-old male patient with a giant adamantinomatous craniopharyngioma. In Figure 3, MRI scans reveal a 11-year-old male patient with a giant craniopharyngioma and the total removal of the tumor was performed.

#### Discussion

The differences in clinical presentation and surgical outcome between children and adults with craniopharyngioma have not been well-described and there are few data available for Asian population. The aim of this study is to investigate the differences between paediatric and adult patients with craniopharyngioma at a single medical centre in southern Taiwan. Our study demonstrates some differences such as that children tended to have stunted growth, large or giant tumors with solid and cystic composition, and adamantinomatous type histopathology. Post-operative diabetes insipidus was more often seen in children group. Karavitaki et al. compared the symptoms between 41 children and 78 adults with craniopharyngioma and found that a significantly higher Citation: Chu C, Su Y, Lieu A, Lin C, Kwan A, et al. (2017) Comparison Study of Clinical Presentation and Surgical Outcome between Children and Adults with Craniopharyngioma: A 22-Year Single-Center Experience in Southern Taiwan. J Neurol Disord 5: 350. doi:10.4172/2329-6895.1000350

	Total (n=40)	Children (n=17)	Adults (n=23)	p-value
Surgical procedures				
Surgical approach				
Pterional	35 (84.7%)	15 (88.2%)	20 (87.0%)	1.000
Transsphenoidal	4 (10.0%)	1 (5.9%)	3 (13.0%)	0.624
Transcallosal	1 (2.5%)	1 (5.9%)	0 (0%)	0.425
Treatment types				0.523
Gross total	20 (50.0%)	7 (41.2%)	13 (56.5%)	
Subtotal	20 (50.0%)	10 (58.8%)	10 (43.5%)	
Post-operative complications				
Diabetes insipidus				
Temporary	9 (22.5%)	7 (41.2%)	2 (8.7%)	0.023*
Permanent	2 (5.0%)	2 (11.8%)	0 (0%)	0.174
Chronic subdural				
hematoma	3 (7.5%)	3 (17.6%)	0 (0%)	0.069
Convulsion	5 (12.5%)	2 (11.8%)	3 (13.0%)	1.000
Hemorrhage	1 (2.5%)	1 (5.9%)	0 (0%)	0.425
GI bleeding	1 (2.5%)	0 (0%)	1 (4.3%)	1.000
Hydrocephalus requiring shunt placement				
Hydrocephalus	22 (55.0%)	12 (70.6%)	10 (43.5%)	0.116
V-P shunt	11 (27.5%)	6 (35.3%)	5 (21.7%)	0.477
Follow-up				
Prognosis				0.141
Good	30 (75.0%)	11 (64.7%)	19 (82.6%)	
Fair	6 (15.0%)	3 (17.6%)	3 (13.0%)	
Poor	4 (10.0%)	3 (17.6%)	1 (4.3%)	
Receiving radiation	28 (70.0%)	14 (82.4%)	14 (60.9%)	0.179
Recurrence	6 (15.0%)	5 (29.4%)	1 (4.3%)	0.067
Note: Data are presented as n (%	6) by group a	nd compare	d using Pears	on chi-

<sup>\*</sup> Indicates significant difference between children and adults. (*P*<0.05)

 Table 2: Comparison of the surgical procedures, treatment types, post-operative complications, and follow-up outcomes between children and adults.

proportion of children had headache, nausea/vomiting, cranial nerve palsy, papilloedema, and hydrocephalus [18]. Nielsen et al. compared 39 children with 150 adults and reported that children had a higher frequency of acute symptoms, radiologic evidence of hydrocephalus, and ophthalmoplegia while adults had a higher incidence of visual field reduction [13]. It should be noted that in these 2 studies, the children were aged <15 years and the adults aged  $\geq$  15 years whereas in our study children were aged  $\leq 20$  years and adults aged >20 years because the civil law in Taiwan provides that adults are people over 20 years of age. 5 of 17 patients in children group are between 15-20 years old. We did not find any significant differences in frequency of headache or visual problems at presentation between children and adults. The only significant difference we found at clinical presentation was that a significantly higher percentage of children had stunted growth. Differences in results between the 2 previous studies and ours may be mainly due to racial variations.

Many studies had compared some histopathology characteristics between children and adults with craniopharyngioma about histological type, tumor composition, and tumor size. It has been clearly shown that children rarely have the papillary type tumor. Gautier reported that 61 children had the adamantinomatous type tumors compared with only 3 other children with the papillary type ones [2]. In our study, none of the children had the papillary type tumor. We also found that children more often had tumors with both solid and cystic composition. Sorva et al. reported that adults more often have solid tumors while children more frequently had tumors with calcification [19]. Likewise, Mortini et al. reported that a significantly higher proportion of children had calcified tumors [9]. It has been consistently reported that craniopharyngiomas are larger in children than in adults [19]. Nielsen et al. found that the mean tumor diameter in children was 39.3 mm compared with 26.5 mm in adults [13]. In our study, we found that a significantly higher percentage of children have large or giant tumors. An important finding of our

Variables	Children				Adults		
	Adamantinomatous (n=15)	Mixed (n=2)	p-value	Adamantinomatous (n=12)	Squamous-papillary (n=9)	Mixed(n=2)	p-value
Sex			1.000				0.189
Males	8 (53.3%)	1 (50%)		6 (50%)	1 (12.5%)	2 (100%)	
Females	7 (46.7%)	1 (50%)		6 (50%)	7 (87.5%)	0 (0%)	
Age			1.000				0.561
0-10 yrs	5 (33.3%)	1 (50%)					
11-20 yrs	10(66.7%)	1 (50%)					
21-30 yrs				4 (33.3%)	4 (50%)	1 (50%)	
31-40 yrs				1 (8.3%)	1 (12.5%)	0 (0%)	
41-50 yrs				3 (25.0%)	0 (0%)	0 (0%)	
51-60 yrs				3 (25.0%)	2 (25%)	0 (0%)	
61-70 yrs				0 (0%)	1 (12.5%)	1 (50%)	
>70yrs				1 (8.3%)	0 (0%)	0 (0%)	
Size of tumor (cm)			1.000				0.565
Small (<2)	1 (6.7%)	0 (0%)		3 (25%)	1 (12.5%)	0 (0%)	
Moderate (2-4)	3 (20%)	0 (0%)		5 (41.7%)	6 (75.0%)	1 (50%)	
Large (4-6)	7 (46.7%)	1 (50%)		4 (33.3%)	1 (12.5%)	1 (50%)	
Giant (>6)	4 (26.7%)	1 (50%)		0 (0%)	0 (0%)	0 (0%)	
Follow-up							
Prognosis			0.596				0.069
Good	10 (66.7%)	1 (50%)		9 (75%)	9 (100%)	1 (50%)	
Fair	2 (13.3%)	1 (50%)		3 (25%)	0 (0%)	0 (0%)	
Late mortality	3 (20.0%)	0 (0%)		0 (0%)	0 (0%)	1 (50%)	
Recurrence	4 (26.7%)	1 (50%)	0.515	0 (0%)	1 (12.5%)	0 (0%)	0.456

Note: Data are presented as n (%) by tumor histopathology for children and adults, separately. Difference among tumor histopathology was compared using Fisher's exact test.

No significant association with tumor histopathology was observed in children or adults (P<0.05).

Table 3: Comparison of clinical characteristics among different histopathology types in children and adults.

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**Figure 1:** Examples of immunohistochemical staining. (A) Adamantinomatous craniopharyngioma. Loosely cohesive squamous cells surrounded by peripherally palisading cells. A squamous nodule (wet keratin) (arrowheads) is observed (H&E x100). (B) Papillary craniopharyngioma. Well-differentiated squamous epithelium lining loose connective tissue (H&E x100). (C) Adamantinomatous (A) + Papillary (P) craniopharyngioma (mixed type) (H&E x40).



**Figure 2:** CT scan images showing a post-operative complication from a 10-year-old male patient with a giant adamantinomatous craniopharyngioma. (A) A giant craniopharyngioma. (B) Post-operative suprasellar hemorrhage. (C) Status post total hematoma removal.



Figure 3: MRI images of a representative case from an 11-year-old male patient. (A) A giant craniopharyngioma. (B) Status post total removal of tumor via pterional approach.

study was that children had more frequent post-operative complication of diabetes insipidus than adults. Gautier et al. found that patients with early onset disease (age <10 years) had a significantly higher morbidity rate [2]. Lower awareness of increased intracranial pressure (IICP) might facilitate the brain tumor progression. Some IICP symptoms such as headache and nausea in children group might be considered as non-specific cold or gastrointestinal disturbances. Since children tend to have larger tumors which potentially lead to diabetes insipidus because of mass effect and are more difficult to be totally removed, it would be expected that post-operative morbidity would be greater in children. On the other hand, we did not find any significant difference between children and adults in the frequency of chronic subdural hematoma, convulsion, haemorrhage or gastrointestinal bleeding. Our study has several limitations. It was a retrospective study in design. The sample size was small with 40 patients being included. However, the number of children (n=17) and adults (n=23) was similar with no gender predominance (p=0.283). We defined children as patients aged <20 years but some other studies used different definitions making the further comparison difficult. Larger studies are needed to investigate the differences between children and adults with craniopharyngioma and the age definition of these groups need to be standardized. Also, more studies on Asian population are needed to determine whether there are any racial differences with this disease.

#### Conclusion

There are significant differences between children and adults with craniopharyngioma about tumor size, histopathology type of tumor and hormone-related surgical complications. These findings are useful for improving the strategies for managing patients with craniopharyngioma.

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