Visual Presentation and Factors Affecting Visual Outcome in Children with Craniopharyngioma in East Coast States of Peninsular Malaysia: A Five-year Review

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Abstract

Purpose
To describe the visual presentation and factors affecting visual outcome in pediatric patients treated for craniopharyngioma at a referral center in the East Coast states of Peninsular Malaysia.

Methodology
A retrospective review of medical records of children aged 17 years and below who had been treated for craniopharyngioma in Hospital Universiti Sains Malaysia from January 2014 to December 2018. The data collected included age, gender, presenting symptoms and duration, visual acuity, visual fields, color vision, light brightness, relative afferent pupillary defects, fundus examination and cranial nerves examination. The best corrected visual acuity during presentation, and after a one-year post-operative period, was documented. Records on investigations, surgical procedures, therapeutic modalities and recurrences were also reviewed.

Results
A total of 11 pediatric patients (22 eyes) were recruited. Fifty percent presented with optic atrophy. The mean duration of the onset of symptoms before consultation was 22.3 (24.5) months. A final best corrected visual acuity of 6/12 (20/40) or better was observed in 50% of the patients. There was a statistically significant association between presenting visual acuity, optic nerve function and visual field defects, and the final visual outcome.

Conclusions
Visual presentations in our study were fairly similar to previous reported studies. One-third presented late with permanent visual loss. Almost half had significant visual impairment after one-year post-operative period. Significant associations were observed between presenting visual acuity, duration of symptoms, impairment of optic nerve function tests, and visual field defects during presentation, and final visual acuity at one year after treatment.

Introduction
Craniopharyngioma is a rare intracranial tumor. It is a benign epithelial tumor originating from the remnants of Rathke's pouch, and it is localized in either the sellar or parasellar regions [1]. The systemic sequelae and visual prognosis are strongly related to the tumor's close proximity to surrounding vital structures. The anterior visual pathway is among the most common anatomical structure being compressed by the tumor, leading to a classical visual presentation of bitemporal hemianopia, inferior quadrantanopia and optic nerve atrophy.

The incidence rate for Western countries is estimated at 0.13 per 100,000 people annually [2]. In contrast, the annual rate for Asian countries is even higher with an estimated 0.24 to 0.53 incidents per 100,000 [3-5]. Reports on final visual outcome for patients with pediatric craniopharyngioma have been published in Europe, the Middle East and the United States [6-10].

Based on a PubMed search, the only data available on visual outcomes for Asian children with craniopharyngioma was from Korea [11-12]. This study aims to describe the visual presentation and factors affecting visual outcome for pediatric patients with craniopharyngioma in the East Coast states of Peninsular Malaysia.
Malaysia, and to discuss the existing literature.

**Materials And Methods**

A retrospective survey was performed on pediatric patients (age 17 years old or younger) with craniopharyngioma who were treated at Hospital Universiti Sains Malaysia in Kelantan, Malaysia, from January 2014 to December 2018, and who received a follow-up for at least one year after treatment. This study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the Research and Ethical Committee, School of Medical Sciences, Universiti Sains Malaysia. Hospital Universiti Sains Malaysia is the leading referral center for the East Coast states of Malaysia for pediatric neurology and ophthalmology services.

All children diagnosed with craniopharyngioma, based on clinical, radiological and histopathological examination, were included in this study. Those with pre-existing ocular problems such as amblyopia, other causes of optic neuropathy and infiltrative diseases, were excluded.

The data collected included age, gender, presenting symptoms and duration, visual acuity, visual fields, color vision, light brightness, relative afferent pupillary defect, fundus examination and cranial nerves examination. The best corrected visual acuity during presentation, and after a one-year post-operative period, was documented.

Visual fields were tested using confrontational test or by using the Humphrey visual field test. Visual fields were described as bitemporal hemianopia, homonymous hemianopia, quadrantanopia, unilateral temporal field defect, scotoma or normal fields. Records on investigations, surgical procedures, therapeutic modalities and recurrences were also reviewed.

Visual acuity was classified as ‘good’ if the best corrected visual acuity was better than or equal to 6/12 (20/40) during presentation or at the one-year post-operative review. Data was analyzed using the Statistical Package for the Social Sciences for Windows version 24 (SPSS Inc., Chicago, IL, USA). Factors affecting the final visual outcome were further analyzed based on the Fisher exact test.

**Results**

Table 1 represents clinical profile of the study population. A total of 11 pediatric patients (22 eyes) with craniopharyngioma were recruited according to the study protocol. A majority of the patients were male (63.6%), ranging in age from 3 to 16 years, with the mean age of 9.5 (4.2) years. The mean duration for the onset of symptoms before consultation was 22.3 (24.5) months, ranging from one month to five years.
TABLE 1: Clinical profile.

M: Male; F: Female; BE: Both eyes; RE: Right eye; LE: Left eye; BOV: Blurring of vision; HM: Hand movement; PL: Perception of light; CF: Counting fingers; NPL: No perception of light; NA: Not available. Color vision based on Ishihara Color chart.

A majority of the patients (63.6%, n = 7) had no visual symptoms during presentation. Four patients (36.4%) presented with visual loss and two patients (18.2%) showed signs of strabismus. Nine eyes (40.9%) presented a best corrected visual acuity worse than 6/15 (20/50), while a final best corrected visual acuity of 6/12 (20/40) or better was observed in 11 patients (50.0%). Optic atrophy was documented in 11 patients (50.0%). Four patients (18.1%) manifested defects in color vision, while seven patients (31.8%) had relative afferent pupillary defects, and two patients (9.1%) exhibited evidence of papilledema on presentation. Eleven eyes (50.0%) had visual field defects. Out of these 11 eyes, the most common visual field defect was temporal hemianopia (22.7%, five eyes). Other visual field defects included central scotoma (9.1%, two eyes), inferior scotoma (4.6%, one eye), and quadrantanopia (9.1%, two eyes). We were unable to perform visual field testing on the remaining five eyes (22.7%) due to lack of cooperation. These are summarized in Table 2.
Table 2: Demographic and clinical data.

| Variables                        | No (%)  |
|----------------------------------|---------|
| Total patient (n)                | 11      |
| Age                              |         |
| Mean (SD), years                 | 9.5 (4.2) |
| Range, years                     | 3–16    |
| Gender                           |         |
| Male                             | 7 (63.6) |
| Female                           | 4 (36.4) |
| Presenting visual acuity*        |         |
| 6/6 - 6/12                       | 13 (59.0) |
| 6/15 - 6/60                      | 3 (13.6)  |
| Worse than 6/60                  | 6 (27.3)  |
| Final visual acuity*             |         |
| 6/6 - 6/12                       | 11 (50.0) |
| 6/15 - 6/60                      | 1 (4.5)   |
| Worse than 6/60                  | 10 (45.5) |
| Visual field defects*            |         |
| Hemianopia                       |         |
| Bilateral                        | 2 (9.1)  |
| Unilateral                       | 3 (13.6) |
| Scotoma                          | 3 (13.6) |
| Quadrantanopia                   | 2 (9.1)  |
| Constricted visual field         | 1 (4.6)  |
| Normal                           | 6 (27.3) |
| Not available                    | 5 (22.7) |

SD: Standard deviation

Table 3 shows the investigation and treatment profile of pediatric patients with craniopharyngioma. Computed tomography (CT) scans and magnetic resonance imaging (MRI) were performed on all patients. Evidence of suprasellar masses were documented for all patients. A majority of the lesions were cystic (63.6%) and, four patients (56.4%) displayed evidence of mixed cystic and solid lesions. Most of our patients (75%) underwent a total resection of the mass, while one patient (12.5%) had the tumor biopsied.
| No | Humphrey VF | Confrontation test | Imaging (CT scan/MRI) | Histopathology | Surgical intervention | Follow-up (months) | Recurrence |
|----|-------------|--------------------|----------------------|----------------|----------------------|--------------------|------------|
|    | RE          | LE                 | RE                   | LE             | Location             | Extenture           | Characteristics |
| 1  | NA          | Inferior scotoma   | NA                   | Suprasellar    | Preoperative, frontal interhemispheric region | Cystic calcified lobulated | NA          | Refuse intervention | 36  | NA          |
| 2  | NA          | Temporal hemianopia| Temporal hemianopia  | Suprasellar    | Third ventricle, floor of sellar turcica       | Cystic lobulated     | Adamantinomatous | Bilateral craniectomy and tumor excision | 40  | Yes         |
| 3  | NA          | Temporal hemianopia| NA                   | Suprasellar    | Cavernous sinus     | Mixed solid and cystic | Adamantinomatous | Left pterional craniectomy with tumor debulking | 16  | Yes         |
| 4  | Normal      | Normal             | Normal               | Normal         | Suprasellar         | Nil                 | Mixed solid and cystic | Adamantinomatous | Vertex craniectomy with tumor debulking | 0   | No          |
| 5  | Normal      | Normal             | Normal               | Normal         | Suprasellar         | Anterior pons        | Cystic calcified multi-lobulated | NA          | Refuse intervention | 17  | NA          |
| 6  | NA          | Central scotoma    | Central scotoma      | Suprasellar    | Third ventricle      | Cystic              | Adamantinomatous | Ventriculoperitoneal shunt with tumor debulking | 20  | Yes         |
| 7  | NA          | NA                 | Suprasellar          | Anterior commissural, Midbrain, Pons | Cystic calcified lobulated | Adamantinomatous | Left pterional craniectomy with tumor debulking | 24  | Yes         |
| 8  | NA          | Temporal hemianopia| NA                   | Suprasellar    | Pons                 | Cystic calcified     | Adamantinomatous | Right pterional craniectomy with tumor debulking | 24  | Yes         |
| 9  | NA          | Normal             | Normal               | Suprasellar    | Hypothalamic region  | Mixed solid and cystic | Adamantinomatous | Ventriculoperitoneal shunt with endoscopic tumor biopsy | 36  | No          |
| 10 | NA          | Temporal hemianopia| NA                   | Suprasellar    | Optic chiasm, pituitary fossa | Mixed solid and cystic | NA          | Right supraorbital keyhole craniectomy with tumor debulking | 11  | No          |
| 11 | Constricted visual field | Inferior-temporal quadrant-anopia | NA | Suprasellar | Third ventricle, anterior part of midbrain | Cystic calcified | NA          | Left frontal burr hole with endoscopic marsupialization of cyst | 48  | Yes         |

**TABLE 3: Investigations and treatment profile.**

NA: Not available; CT: Computed tomography; MRI: Magnetic resonance imaging; VF: Visual field; LE: Left eye; RE: Right eye.

In Table 4, we analyzed the associations between age, gender, best corrected visual acuity during presentation, duration of symptoms before treatment, impaired optic nerve function tests, visual field defects, tumor size, type of surgery and recurrence with good visual acuities after the one-year post-operative period. The analysis produced evidence of significant associations between best corrected visual acuity during presentation, duration of symptom prior to consultation, impaired optic nerve function tests, visual field defects and good visual acuity after one-year post-operative period (P < 0.05, Fisher exact test).
**TABLE 4: Factors affecting good final visual acuity.**

| Variables                              | Frequency, n (%) | Final visual acuity (6/12 or Better), n (%) | p-value |
|----------------------------------------|------------------|---------------------------------------------|---------|
| Age of diagnosis (years)               |                  |                                             |         |
| Less than six years old                | 6 (27.3)         | 5 (22.7)                                    | 0.074   |
| Six years old and older                | 16 (72.7)        | 6 (27.3)                                    |         |
| Gender                                 |                  |                                             | 0.33    |
| Male                                   | 14 (63.6)        | 6 (27.3)                                    |         |
| Female                                 | 8 (36.4)         | 5 (22.7)                                    |         |
| VA presentation*                       |                  |                                             | 0.04    |
| 6/6-6/12                               | 13 (59.1)        | 9 (40.9)                                    |         |
| Worse than 6/15                        | 9 (40.9)         | 2 (9.1)                                     |         |
| Duration of symptoms prior to consultation |              |                                             | 0.012   |
| Less than 12 months                    | 14 (63.6)        | 4 (18.2)                                    |         |
| 12 months and longer                   | 8 (36.4)         | 7 (31.8)                                    |         |
| Optic nerve function*                  |                  |                                             | 0.04    |
| Impaired                               | 9 (40.9)         | 2 (9.1)                                     |         |
| Normal                                 | 13 (59.1)        | 9 (40.9)                                    |         |
| Visual field*                          |                  |                                             | 0.012   |
| Impaired                               | 14 (63.6)        | 4 (18.2)                                    |         |
| Normal                                 | 8 (36.4)         | 7 (31.8)                                    |         |
| Imaging findings                       |                  |                                             | 0.11    |
| Tumor size (by greatest dimension)     |                  |                                             |         |
| 4 cm and greater                       | 12 (54.5)        | 9 (69.2)                                    |         |
| Less than 4 cm                         | 10 (45.5)        | 4 (30.8)                                    |         |
| Treatment                              |                  |                                             | 1       |
| Total resection                        | 16 (72.7)        | 8 (39.4)                                    |         |
| Partial resection/biopsy               | 2 (9.1)          | 1 (4.5)                                     |         |
| Refused surgery                        | 4 (18.2)         | 2 (9.1)                                     |         |
| Recurrence                             |                  |                                             | 0.135   |
| Yes                                    | 6 (54.5)         | 4 (18.2)                                    |         |
| No                                     | 3 (27.3)         | 5 (22.7)                                    |         |
| Missing                                | 2 (18.2)         | 2 (9.1)                                     |         |

*Based on 22 eyes; p-value < 0.05 is statistically significant, Fisher Exact Test.

VA: Visual acuity

**Discussion**

Improved visual outcome is the main concern for ophthalmologists and neurosurgeons managing pediatric craniopharyngioma. Table 5 summarizes published reports on visual presentation and outcome in patients with pediatric craniopharyngioma from Asian countries, the United Kingdom, Spain, Israel, and France, as
well as those included in our study [6, 8-13].

| Author (Year) | Our study (2019) | Drimtzias et al. (2014) [6] | Puget et al. (2007) [13] | Mediero et al. (2015) [8] | Lee et al. (2012) [11] | Jung et al. (2010) [12] | Bialer et al. (2012) [9] |
|---------------|------------------|-----------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Country       | Malaysia         | United Kingdom              | France                  | Spain                   | Korea                   | Korea                   | Israel                  |
| Population    |                  |                             |                         |                         |                         |                         |                         |
| Adult         | 0                | 0                           | 0                       | 0                       | 0                       | 0                       | 0                       |
| Children      | 11               | 20                          | 66                      | 10                      | 27                      | 17                      | 20                      |
| Mean age (SD) | 9.5 (4.2)        | 7.3                         | 7.4                     | 5                       | U                       | 12                      | 6.5 (3.9)               |
| Gender, n (%) |                  |                             |                         |                         |                         |                         |                         |
| Male          | 7 (63.6)         | 10 (50.0)                   | 42 (63.6)               | 6 (60.0)                | 15 (55.6)               | 12 (70.6)               | 10 (50.0)               |
| Female        | 4 (36.4)         | 10 (50.0)                   | 24 (36.4)               | 4 (40.0)                | 12 (44.4)               | 5 (16.7)                | 10 (50.0)               |
| Systemic symptoms, n (%) | | | | | | | |
| Headache      | 8 (72.7)         | 14 (70.0)                   | U                       | U                       | 18 (66.7)               | 13 (76.5)               | 6 (55.0)                |
| Nausea/vomiting | 7 (63.6)       | U                           | U                       | U                       | 6 (22.2)                | NS                      | U                       |
| Motor deficit | 2 (18.2)         | U                           | 8 (12.0)                | U                       | 0 (0)                   | U                       |                         |
| Seizure       | 1 (9.1)          | U                           | 3 (4.5)                 | U                       | 0 (0)                   | 1 (9.0)                 |                         |
| Ocular symptoms, n (%) | | | | | | | |
| Visual loss   | 4 (36.4)         | 6 (30.0)                    | 29 (44.0)               | U                       | 12 (44.4)               | 4 (23.5)                | 1 (9.0)                 |
| Color vision defect | 1 (9.1)    | U                           | U                       | U                       | U                       | 0 (0)                   | U                       |
| Diplopia/strabismus | 2 (18.2)  | U                           | U                       | U                       | 4 (14.8)                | 0 (0)                   | 3 (27.0)                |
| VA presentation*, n (%) | | | | | | | |
| 6/6–6/12      | 13 (59.0)        | 19 (47.5)                   | U                       | U                       | 33 (61.1)               | U                       | U                       |
| 6/15–6/60     | 3 (13.6)         | 8 (20)                      | U                       | U                       | 14 (25.9)               | U                       | U                       |
| Worse than 6/60 | 6 (27.3)      | 13 (32.5)                   | U                       | U                       | 7 (13.0)                | U                       | U                       |
| VA final*, n (%) | | | | | | | |
| 6/6–6/12      | 11 (50.0)        | 23 (57.5)                   | U                       | 12 (60)                 | 37 (68.5)               | U                       | U                       |
| 6/15–6/60     | 1 (4.5)          | 4 (10.0)                    | U                       | 3 (15.0)                | 13 (24.1)               | U                       | U                       |
| Worse than 6/60 | 10 (45.5)     | 13 (32.5)                   | U                       | 5 (25.0)                | 4 (7.4)                 | U                       | U                       |
| Fundus examination*, n (%) | | | | | | | |
| Optic atrophy | 11 (50.0)        | 12 (60.0)                   | U                       | 15 (75.0)               | 14 (30.4)               | U                       | 17 (42.5)               |
| Papilledema   | 2 (9.1)          | 6 (30.0)                    | U                       | 0 (0)                   | 10 (21.7)               | U                       | 6 (15.0)                |
| Normal finding | 8 (36.4)        | U                           | U                       | 5 (25.0)                | 22 (47.8)               | U                       | U                       |
| Visual field defect*, n (%) | | | | | | | |
| Bilateral hemianopia | 2 (9.1)    | 5 (35.7)                    | 10 (15.0)               | 2 (20.0)                | 3 (11.1)                | U                       | 4 (26.7)                |
| Unilateral hemianopia | 3 (13.6)  | U                           | 9 (14.0)                | 2 (20.0)                | 3 (11.1)                | U                       | 3 (20.0)                |
| Central scotoma | 3 (13.6)        | U                           | U                       | 0 (0)                   | 2 (7.4)                 | U                       | 0 (0)                   |
The mean age of presentation was 9.5 (4.2) years in our study. In the majority of the studies reviewed, the mean age of presentation was less than 10 years [6,8,9,11-13]. In contrast, Jung et al. reported the mean age was 12 years [12]. There was a male preponderance in our study population, which is also consistent with other pediatric craniopharyngioma studies [8,11-13]. In contrast, Drimtzias et al. and Bialer et al. from the United Kingdom and Israel respectively, reported an equal ratio of males and females [6,9].

The most common symptom reported by our patients was headache (72.7%), which is consistent with findings documented by other studies (ranging from 55 to 76.5%) [6,9,10-11]. However, visual loss or blurring of vision was only noted in one-third of our patients (36.4%, four eyes). This observation is also similar to studies from the United Kingdom (30.0%) and Korea (23.5%) [6,12]. A slightly higher percentage was reported from a second study from Korea (44.4%) and France (44.0%) [11,13]. This observation suggests that these children were not able to express or may not have been aware of visual symptoms during the early stages of the disease.

Among our patients, papilledema during presentation was only observed in two eyes (9.1%), while optic atrophy was documented in 11 eyes (50%). This finding is also consistent with studies reported by Drimtzias et al. (30% papilledema, 60% optic atrophy), Mediero et al. (none had papilledema, 75% showed optic...
atrophy) and Blair et al. (15% papilledema, 42.5% optic atrophy) [6,8-9]. These data indicate that the diagnosis was only confirmed at a later stage, after the disease had progressed.

We found a significant association between presenting best corrected visual acuity and good final visual outcome (p = 0.040). Nine patients (40.9%) presented with visual acuity worse than or equal to 20/15 (6/50) and, of this group, only two patients (9.1%) documented good final visual acuity (6/12 or 20/40, one year after treatment). A similar pattern was reported by Repka et al. [10]. They evaluated preoperative and postoperative visual acuities in 12 children younger than 18 years with craniopharyngioma. They reported that 17% of their patients had visual acuity worse than 20/60 (6/12) in the better eye at the time of diagnosis, and 27% of their patients continued to have visual acuity worse than 20/40 (6/12) in the better eye postoperatively [13]. In contrast, Drimtzias et al. and Lee and Hwang reported a higher percentage of visual acuity at 20/40 (6/12) after one year (57.5%, 68.5% respectively) [6,11].

We observed a significant association between the duration of systemic symptoms before consultation and good final visual acuity at the one-year post-operative period (p = 0.12). Fourteen patients (65.6%) presented less than one year after the onset of systemic symptoms. Four patients (18.2%) had good final visual acuity after one year. We had difficulty finding published data on this issue for comparison.

However, Chen et al. reported a median duration of systemic symptoms of seven months in their patients [14]. Lee and Hwang documented duration of 5.2 ± 6.8 months in children with craniopharyngioma with normal visual field, and 8.9 ± 10.6 months in those with abnormal visual fields [11]. However, no further analysis regarding the final visual outcome was performed by these authors [11,14].

All patients were examined for optic nerve functions during their first consultation, and at each follow-up visit to detect signs of optic neuropathy. The examination included visual acuity tests, afferent pupillary defect assessment, color vision tests, light brightness and visual field assessments. Impairment of the optic nerve functions identified during diagnosis of craniopharyngioma is significantly associated with final visual acuity after treatment (p = 0.040). Nine patients (41%) showed evidence of optic neuropathy, while 15 patients (59%) showed normal optic nerve function during diagnosis. Only two patients (9.1%) who had impaired optic nerve functions displayed good visual acuity a year after treatment.

We also noted a significant association between visual field defects and final visual acuity (p = 0.012). Fourteen eyes (63.6%) had visual field defects in our series. Only four patients (18.2%) had good visual acuity one year after treatment. Our findings agree with Lee and Hwang who reported that patients with normal visual fields at presentation were more likely to have better visual acuity postoperatively [11].

We found no significant association between the size of the tumor and good visual acuity post operation (p = 0.110). Among our patients, 54.5% had tumor that were larger than 4 cm, as measured on CT scans or MRI findings, based on the greatest dimension. Our findings were similar to Wan et al. who also reported 54% of their patients had tumor sizes greater than 4 cm. Interestingly, Wan et al. also found no significant association between tumor size and visual decline [15]. Lee and Hwang supported these findings, noting that there was no significant difference in tumor size with visual field defects [11].

We observed that six patients (54.5%) had tumor recurrences, which is consistent with other studies that reported a recurrence rate of 40.7% to 55% [6,11,13]. However, there was no significant association observed between recurrence of tumors and final visual acuity.

**Conclusions**

Visual presentations in our study were fairly similar to previous reported studies. One-third of our patients presented late with permanent visual loss, and almost half of our patients had significant visual impairment after one-year post-operative period. There were significant associations between presenting visual acuity, duration of symptoms, impairment of optic nerve function tests, and visual field defects during presentation, and final visual acuity at one year after treatment.

**Additional Information**

**Disclosures**

**Human subjects:** Consent for treatment and open access publication was obtained or waived by all participants in this study. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.
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