Clinical Features and Prognostic Risk Factors of Choroid Plexus Tumors in Children

Wen-Jian-Long Zhou1, Xi Wang1, Jia-Yi Peng1, Shun-Chang Ma2, Dai-Nan Zhang1, Xiu-Dong Guan3, Jin-Fu Diao1,4, Jian-Xing Niu4, Chun-De Li1, Wang Jia1,3

1Department of Neurosurgery, Beijing TianTan Hospital, Capital Medical University, Beijing 100050, China
2Department of Neurosurgery, Beijing Fuxing Hospital, Capital Medical University, Beijing 100050, China
3Department of Neurosurgery, Beijing Neurosurgical Institute, Capital Medical University, Beijing 100050, China
4Department of Neurosurgery, Beijing Armed Police General Hospital, Beijing 100000, China

Abstract

Background: Decision-making concerning the treatment of choroid plexus tumor (CPT) in pediatric patients remains a topic of considerable debate. The aim of this work was to describe clinical features and prognostic risk factors of CPT in the pediatric population and to provide theoretical opinions regarding clinical decisions for CPT.

Methods: The data of 96 patients with CPT and younger than 14 years were retrospectively analyzed. Clinical characteristics such as pathological type of CPTs, rate and severity of hydrocephalus, treatment and outcome, and recurrence were investigated. For categorical variables, the Pearson’s Chi-square test was performed. The Mann–Whitney U-test was used for comparisons between nonnormally distributed parameters. Log-rank test was used for progression-free survival (PFS).

Results: The study included 70 choroid plexus papilloma (CPP) cases, 17 atypical choroid plexus papilloma (aCPP) cases, and 9 choroid plexus carcinoma (CPC) cases. Compared with patients with CPP or aCPP, patients with CPC had a shorter disease course (median: CPP, 4 months; aCPP, 2 months; CPC, 1 month; \( H: 23.5, P < 0.001 \)), higher rate of acute hydrocephalus (CPP, 27.1%; aCPP, 52.9%; CPC, 77.8%; \( \chi^2 = 10.9, P < 0.05 \)), and lower incidence of cure rate (CPP, 85.7%; aCPP, 70.5%; CPC, 33.3%; \( \chi^2 = 13.5, P < 0.05 \)). The severity of hydrocephalus with tumor in the lateral or third ventricle was significantly higher than that with tumors in the fourth ventricle (severe hydrocephalus: lateral ventricle, 51.7%; third ventricle, 47.0%; fourth ventricle, 11.1%; \( \chi^2 = 26.0, P < 0.001 \)). Patients with gross total surgical resection had no better PFS than those with partial resection because of the use of adjuvant therapy in the latter (\( \chi^2 = 4.0, P > 0.05 \)). Patients with CPC experienced shorter time for recurrence than those with CPP or aCPP (\( \chi^2 = 40.1, P < 0.0001 \)).

Conclusions: Our results indicated that CPP in the fourth ventricle could trigger serious clinical symptoms at an early stage, requiring early intervention. Adjuvant treatment might be necessary for patients with partially resected CPP, aCPP, and CPC to achieve a favorable outcome.

Key words: Atypical Choroid Plexus Papilloma; Choroid Plexus Carcinoma; Choroid Plexus Papilloma; Pediatric Patients

Introduction

Choroid plexus cells are neuroepithelial cells that line the intraventricular papillae and secrete cerebrospinal fluid (CSF).1,2 Choroid plexus tumors (CPTs) are rare intracranial tumors that account for 2–5% of all pediatric brain cancers, to date, seldom reported.2 According to the histological classification of the World Health Organization (WHO), CPTs can be divided into choroid plexus papilloma (CPP), atypical choroid plexus papilloma (aCPP), and choroid plexus carcinoma (CPC).3 CPTs usually occur in children younger than 2 years, with about 10–20% of cases found in patients younger than 1 year.4 The WHO classification of 2007 first mentioned aCPP, which carried at least a 5-fold increase in the risk of 5-year recurrence compared with CPP. The grade of
histological classification was considered an important factor in the prognosis of CPTs, also influencing clinicians’ decisions regarding adjuvant radiotherapy or chemotherapy after surgery. One of the most important predictors of survival for CPT patients is total resection of the tumor. In this regard, it has been demonstrated that patients with CPC experienced a worse outcome with greater possibility of metastasis (range 25–70%), although some papers have documented long-term survival. The event-free survival (EFS) rate was 92% for CPP, 83% for aCPP, and 28% for CPC according to previously published research. More than 80% of the neoplasms in children arise in supratentorial and especially in lateral ventricles, whereas the cerebellopontine angle (CPA) and fourth ventricle are more common sites in adults; the CPA and the third ventricle are rare locations.

Although numerous studies of CPTs have been published, available clinical data describing therapy and prognosis of CPTs in children are limited. To further investigate the clinical features of CPT in the pediatric population, we retrospectively analyzed the relevant data collected in our institute.

**Methods**

**Ethical approval**

All procedures involving humans were carried out in accordance with the ethical standards of the 2013 Declaration of Helsinki and were approved by the Institutional Review Board of Beijing Tiantan Hospital, Capital Medical University. Informed written consent was obtained from all patients before their enrollment in this study.

**Patients**

This was a retrospective study involving 96 patients, younger than 14 years, and diagnosed with CPT, who underwent surgery between January 1, 2011, and December 31, 2016. Patients were selected from the Department of Neurosurgery of Beijing Tiantan Hospital.

We reviewed the clinical, histopathological, and operative reports, as well as outpatient records of the patients obtained from the hospital information system. All surgical procedures were performed by the senior doctors. All operations were performed via the classical standard approaches. The extent of resection was defined as gross total, subtotal, and partial excision according to the postoperative magnetic resonance imaging (MRI) and the operation records. Gross total resection is defined as 95% tumor extent removed by surgery, subtotal resection is defined as 75% tumor removal, and partial resection as <75% removal. Abnormal accumulation of CSF in the ventricles was regarded as characteristic of hydrocephalus.

Patients were included in the study if: (1) patients younger than 14 years received surgery as the primary treatment; (2) preoperative, postoperative, and follow-up data were fully evaluated; (3) complete medical records were available, including full medical history, accurate laboratory test results, and pre- and post-surgical MRI of the head; and (4) all patients were histologically diagnosed with CPT. Patients were excluded from the study if: (1) patients had received any previous medical intervention, including radiotherapy or medical treatment; (2) medical data of patients were incomplete; and (3) patients died for unrelated reasons during the follow-up.

**Evaluation criteria for the severity of hydrocephalus**

The Evans index was calculated for the hydrocephalus patients, whereby index score of >0.3 is used to define hydrocephalus. Ventricular/biparietal ratio (V/BP) was used to evaluate the severity of hydrocephalus: (1) normal: V/BP ≤25%; (2) mild hydrocephalus: 26%≤ V/BP ≤40%; (3) moderate hydrocephalus: 41%≤ V/BP ≤60%; and (4) severe hydrocephalus: V/BP ≥61%.

**Statistical analysis**

Data were analyzed using SPSS Statistics (version 17.0, SPSS, IBM Corp., Armonk, NY, USA). Statistical computations and generation of figures were performed by R project (version 3.4.1, https://www.r-project.org/; R Development Core Team, New Zealand). Continuous variables were expressed as median (Q1,Q3), and categorical variables were expressed as number (percent). The Mann–Whitney U-test was used for comparisons between nonnormally distributed parameters. The Kruskal–Wallis test was used for multiple comparisons among nonnormally distributed parameters. Frequencies were analyzed using Pearson’s Chi-square test. The prognostic value of patients was estimated by log-rank (Mantel–Cox) test. Other statistical computations and figure generations were performed by GraphPad Prism (version 6.0, GraphPad Software, Inc., California, USA). All statistical tests were two-sided, and P < 0.05 was considered statistically significant.

**Results**

A total of 96 pediatric patients were identified as having CPTs in our analysis. Patients’ age varied from 4 to 168 months, with a median age of 42 months (19.3, 105). 72.9% (70/96) of cases were diagnosed as CPP and 17.7% (17/96) as aCPP, while 9.4% (9/96) of cases were diagnosed as CPC. Clinical information (e.g. age, gender, pathological type of tumor, size, location, initial manifestation, and resection rate) obtained from medical records is summarized in Table 1.

Patients harboring infratentorial CPP were significantly older than those with supratentorial tumors (median: 120 [72, 168] months vs. 35 [15, 72] months; Z = −3.511, P = 0.000). Moreover, patients could be divided into two groups according to the cutoff age of 60 months (sensitivity = 67.5%, specificity = 84.2%) based on maximization of the Youden index. In our dataset, 34.1% (15/44) of the patients older than 5 years and 8% (4/52) of those younger than 5 years suffered...
According to our data, the clinical features of patients with CPC showed a significant difference when compared with CPP [Table 1]. Patients with CPC exhibited a shorter disease course (CPP: 4 [2.0, 8.0] months; aCPP: 2 [2.0, 3.0] months; CPC: 1 [1.0, 1.5] months; \( P < 0.001 \)), a higher incidence of acute hydrocephalus (CPP: 27.1%, aCPP: 52.9%, CPC: 77.8%; \( \chi^2 = 10.9, P = 0.004 \)), and a lower incidence of cure rates (CPP: 85.7%, aCPP: 70.5%, CPC: 33.3%; \( \chi^2 = 13.5, P = 0.001 \)).

### Hydrocephalus and headache in pediatric patients

First, we evaluated hydrocephalus. According to our data, 88.5% (85/96) of the patients suffered from hydrocephalus before surgery. The clinical characteristics of the patients categorized by the degree of hydrocephalus are shown in Table 2. The demographics and clinical features showed from infratentorial tumor (\( \chi^2 = 8.9, P = 0.003 \)). Headache with nausea or vomiting caused by raised intracranial pressure was the most common primary presenting symptom (55 cases, 57.3%), followed by ataxia (21 cases, 21.9%), and lower extremity weakness (45 cases, 46.9%). Nineteen tumors presented no significant symptoms and were found incidentally.

**Pathological type of choroid plexus tumors in pediatric patients**

According to our data, the clinical features of patients with CPC showed a significant difference when compared with CPP [Table 1]. Patients with CPC exhibited a shorter disease course (CPP: 4 [2.0, 8.0] months; aCPP: 2 [2.0, 3.0] months; CPC: 1 [1.0, 1.5] months; \( P < 0.001 \)), a higher incidence of acute hydrocephalus (CPP: 27.1%, aCPP: 52.9%, CPC: 77.8%; \( \chi^2 = 10.9, P = 0.004 \)), and a lower incidence of cure rates (CPP: 85.7%, aCPP: 70.5%, CPC: 33.3%; \( \chi^2 = 13.5, P = 0.001 \)).

### Table 1: Baseline demographics and characteristics categorized by pathological type of CPTs

| Characteristics                  | Total (n = 96) | CPP (n = 70) | aCPP (n = 17) | CPC (n = 9) | Statistics | P     |
|----------------------------------|---------------|--------------|---------------|-------------|------------|-------|
| Male, n (%)                      | 63 (65.6)     | 43 (61.4)    | 12 (70.5)     | 8 (88.9)    | 2.9*       | 0.236 |
| Age (months), median (Q1, Q3)    | 42.0 (19.3, 105.0) | 48.5 (20.0, 120.0) | 39.0 (11.5, 70.5) | 30.0 (20.0, 96.0) | 2.3†       | 0.314 |
| Course of disease (months), median (Q1, Q3) | 3.0 (2.0, 6.0) | 4.0 (2.0, 8.0) | 2.0 (2.0, 3.0) | 1.0 (1.0, 1.5) | 23.5†      | 0.000 |
| Volume of the tumor (cm³), median (Q1, Q3) | 11.6 (6.8, 19.9) | 12.6 (7.1, 22.2) | 10.5 (4.7, 22.0) | 7.6 (5.2, 9.0) | 3.4*       | 0.180 |

**Location**

| Supra-tentorial, n (%)          | 77 (80.2)     | 57 (81.4)    | 13 (76.5)     | 7 (77.8)    | 0.2*       | 0.883 |
| Lateral ventricle, n (%)        | 58 (60.4)     | 42 (60.0)    | 11 (64.7)     | 5 (55.6)    | 15.8*      | 0.015 |
| Third ventricle, n (%)          | 17 (17.7)     | 15 (21.4)    | 1 (5.9)       | 1 (11.1)    |            |      |
| Forth ventricle, n (%)          | 18 (18.8)     | 13 (18.6)    | 4 (23.5)      | 1 (11.1)    |            |      |

**Initial manifestation**

| Hydrocephalus, n (%)            | 85 (88.5)     | 62 (88.6)    | 14 (82.4)     | 9 (100.0)   | 1.8*       | 0.405 |
| Acute hydrocephalus, n (%)      | 35 (36.4)     | 19 (27.1)    | 9 (52.9)      | 7 (77.8)    | 10.9*      | 0.004 |
| Headache, n (%)                 | 55 (57.3)     | 40 (57.1)    | 10 (58.8)     | 5 (55.6)    | 0.0*       | 0.986 |
| Vomiting, n (%)                 | 50 (52.1)     | 35 (50.0)    | 10 (58.8)     | 5 (55.6)    | 0.5*       | 0.789 |
| Ataxia, n (%)                   | 21 (21.9)     | 13 (18.6)    | 7 (41.2)      | 1 (11.1)    | 4.8*       | 0.092 |
| Limb weakness, n (%)            | 45 (46.9)     | 29 (41.4)    | 12 (70.5)     | 4 (44.4)    | 4.7*       | 0.096 |
| Total resection, n (%)          | 85 (88.5)     | 62 (88.6)    | 15 (88.2)     | 8 (88.9)    | 0.0*       | 0.999 |
| Cure, n (%)                     | 75 (78.1)     | 60 (85.7)    | 12 (70.5)     | 3 (33.3)    | 13.5*      | 0.001 |

**V-P shunt**

| Pre-operation, n (%)            | 35 (36.4)     | 28 (40.0)    | 4 (23.5)      | 3 (33.3)    | 4.3*       | 0.364 |
| Post-operation, n (%)           | 5 (5.2)       | 5 (7.1)      | 0             | 0           |           |      |

*\( \chi^2 \) value; †H value. CPP: Choroid plexus papilloma; aCPP: Atypical choroid plexus papilloma; CPC: Choroid plexus carcinoma; CPTs: Choroid plexus tumors; V-P: Ventricular-peritoneal.

### Figure 1: ROC curve of CPT patients for identifying location of tumor with age and hydrocephalus with tumor size. (a) ROC curve for identifying location of tumor with age. The estimated area under the ROC curve was calculated as 0.783 (95% CI = 0.674–0.891, \( P < 0.001 \)). The best cutoff of age was 61.5 months based on maximization of the Youden index with sensitivity 67.5% and specificity 84.2%. This cutoff was rounded to 60 for use in subsequent analyses. (b) ROC curve for identifying hydrocephalus with tumor size. The estimated area under the ROC curve of tumor volume was calculated as 0.682 (95% CI = 0.475–0.886, \( P = 0.044 \)). The best cutoff was 2.1 cm based on maximization of the Youden index with sensitivity 67.5% and specificity 84.2%. This cutoff was rounded to 2 cm for use in subsequent analyses. The estimated area under the ROC curve of tumor volume was calculated as 0.682 (95% CI = 0.468–0.897, \( P = 0.042 \)). The best cutoff was 2.90 cm based on maximization of the Youden index with sensitivity 91.4% and specificity 58.3%. This cutoff was rounded to 3 cm³ for use in subsequent analyses. ROC: Receiver-operating characteristic; CPT: Choroid plexus tumor; CI: Confidence interval.
a significant difference on comparing the degrees of hydrocephalus when considered in terms of location of tumor and pre- or post-operative ventriculoperitoneal (V-P) shunt ($P < 0.05$).

On using the receiver-operating characteristic (ROC) curve for identifying hydrocephalus with tumor size, the best cutoff of maximum diameter of tumor was 2 cm (sensitivity 90.5%, specificity 58.3%) and that of tumor volume was 3000 mm$^3$ (sensitivity 94.1%, specificity 58.3%) based on the maximization of the Youden index divided into small and large groups [Figure 1b]: 58.3% (7/12) of patients with tumor smaller than 2 cm and 92.9% (78/84) of those with tumor larger than 2 cm had hydrocephalus ($\chi^2 = 12.3, P = 0.004$); 50% (6/12) of patients with tumor smaller than 3000 mm$^3$ and 94.0% (79/84) of those with tumor larger than 3000 mm$^3$ had hydrocephalus ($\chi^2 = 12.3, P = 0.004$).

When the relationship between the location and hydrocephalus was compared, the patients with tumor in the lateral ventricle or the third ventricle suffered higher rates of severe hydrocephalus than those with tumor in the fourth ventricle (lateral ventricle: 51.7%, 30/58; third ventricle: 47%, 8/17; fourth ventricle: 11.1%, 2/18; $\chi^2 = 26, P = 0.002$). By contrast, the patients with tumor in the fourth ventricle experienced a higher incidence of acute hydrocephalus compared with the lateral or third ventricle (fourth ventricle: 72.2%, 13/18; lateral ventricle: 20.7%, 12/58; third ventricle: 56.2%, 9/16; $\chi^2 = 18.8, P = 0.000$).

The incidence of headache in patients with tumor in the third ventricle (76.5%, 13/17) or fourth ventricle (77.8%, 14/18) was significantly higher than that in patients with tumor in the lateral ventricle (46.6%, 27/58) ($\chi^2 = 9.1, P = 0.028$). The records are summarized in Table 3.

### Ventriclepoperitoneal shunt pre- or post-operatively

Of the 96 patients in our study, 35 (36.4%) patients underwent V-P shunt pre-operatively and 5 (5.2%) post-operatively, while 56 (58.3%) patients received no treatment before surgery. All patients in our study improved with surgical treatment. There was no significant difference in the cure rate of hydrocephalus among pre-operation or post-operation V-P shunt and no V-P shunt patients (pre-operation V-P shunt:

### Table 2: Baseline demographics and characteristics categorized by the degree of hydrocephalus

| Characteristics               | Total (n = 96) | None (n = 11) | Mild (n = 9) | Moderate (n = 36) | Severe (n = 40) | Statistics | P     |
|-------------------------------|---------------|---------------|-------------|-------------------|---------------|------------|-------|
| Male, n (%)                   | 63 (65.6)     | 5 (45.5)      | 5 (55.6)    | 26 (72.2)         | 27 (67.5)     | 3.1*       | 0.370 |
| Age (months), median (Q1, Q3) | 42.0 (19.3, 105.0) | 71.0 (61.0, 156.0) | 72.0 (31.5, 150.0) | 40.5 (15.0, 83.0) | 35.5 (16.0, 120.0) | 6.1†       | 0.107 |
| Course of disease (months), median (Q1, Q3) | 3.0 (2.0, 6.0) | 4.0 (2.0, 5.0) | 2.0 (2.0, 4.5) | 3.0 (2.0, 5.0) | 4.0 (2.0, 8.0) | 2.8‡       | 0.428 |
| Location                      |               |               |             |                   |               |            |       |
| Supratentorial, n (%)          | 77 (80.2)     | 11 (100.0)    | 4 (44.4)    | 24 (66.7)         | 38 (97.5)     | 19.6*      | 0.000 |
| Lateral ventricle, n (%)       | 58 (60.4)     | 9 (81.8)      | 4 (44.4)    | 15 (41.7)         | 30 (75.0)     | 26.0*      | 0.002 |
| Third ventricle, n (%)         | 17 (17.7)     | 1 (9.1)       | 0           | 8 (22.2)          | 8 (20.0)      |            |       |
| Forth ventricle, n (%)         | 18 (18.8)     | 0             | 5 (55.6)    | 11 (30.5)         | 2 (0.05)      |            |       |
| Initial manifestation          |               |               |             |                   |               |            |       |
| Headache, n (%)               | 55 (57.3)     | 3 (27.3)      | 7 (77.8)    | 21 (58.3)         | 24 (60.0)     | 5.7*       | 0.125 |
| Vomiting, n (%)                | 50 (52.1)     | 4 (36.4)      | 4 (44.4)    | 20 (55.6)         | 22 (55.0)     | 1.6*       | 0.657 |
| Ataxia, n (%)                  | 21 (21.9)     | 3 (27.3)      | 2 (22.2)    | 10 (27.8)         | 6 (15.0)      | 2.0*       | 0.567 |
| Limb weakness, n (%)           | 45 (46.9)     | 5 (45.4)      | 3 (33.3)    | 17 (47.2)         | 20 (50.0)     | 0.8*       | 0.842 |
| Total resection, n (%)         | 85 (88.5)     | 10 (90.9)     | 9 (100.0)   | 31 (86.1)         | 35 (87.5)     | 1.5*       | 0.687 |
| Cure after surgery, n (%)      | 75 (78.1)     | 9 (81.8)      | 7 (77.8)    | 29 (80.6)         | 30 (75.0)     | 0.4*       | 0.932 |
| V-P shunt                     |               |               |             |                   |               |            |       |
| Pre-operation, n (%)           | 35 (36.4)     | 0             | 1 (11.1)    | 17 (47.2)         | 17 (42.5)     | 14.5*      | 0.024 |
| Post-operation, n (%)          | 5 (5.2)       | 0             | 0           | 2 (5.6)           | 3 (7.5)       |            |       |

*χ² value; †H value. CPP: Choroid plexus papilloma; aCPP: Atypical choroid plexus papilloma; CPC: Choroid plexus carcinoma; V-P: Ventricular-peritoneal.

### Table 3: Hydrocephalus and headache in patients categorized by the location of tumor

| Characteristics               | Lateral ventricle (n = 58) | Third ventricle (n = 17) | Fourth ventricle (n = 18) | Other locations (n = 3) | χ²   | P   |
|-------------------------------|-----------------------------|--------------------------|---------------------------|-------------------------|------|-----|
| Degree of hydrocephalus       |                             |                          |                           |                         |      |     |
| None, n (%)                   | 9 (15.5)                    | 1 (5.9)                  | 0                         | 1 (33.3)                | 26.0 | 0.002 |
| Mild, n (%)                   | 4 (6.9)                     | 0                        | 5 (27.8)                  | 0                       |      |     |
| Moderate, n (%)               | 15 (25.9)                   | 8 (47.0)                 | 11 (61.1)                 | 2 (66.7)                |      |     |
| Severe, n (%)                 | 30 (51.7)                   | 8 (47.0)                 | 2 (11.1)                  | 0                       |      |     |
| Acute hydrocephalus, n (%)    | 12 (20.7)                   | 9 (52.9)                 | 13 (72.2)                 | 1 (33.3)                | 18.8 | 0.000 |
| Headache, n (%)               | 27 (46.6)                   | 13 (76.5)                | 14 (77.8)                 | 1 (33.3)                | 9.1  | 0.028 |
28/35; post-operation V-P shunt: 4/5; no V-P shunt: 43/56; \( \chi^2 = 0.1, P = 0.932 \).

**Treatment and outcome**

All of the patients in our study received surgical therapy as primary treatment. Eighty-five patients underwent gross total surgical resection and 11 underwent partial resection. Among the 11 patients with partial resection, eight cases were diagnosed as CPP, two as aCPP, and one as CPC. Adjuvant therapy was mostly used for aCPP, CPC, and CPP including partial resection. Adjuvant therapy and patient outcomes are shown in Supplemental Table 1. All (8/8) CPP patients with partial resection, 70.6% (12/17) of aCPP patients, and 77.8% (7/9) of CPC patients received adjuvant therapy such as chemotherapy or radiotherapy. One aCPP case and one CPC case with partial resection underwent chemotherapy after Gamma Knife. Postoperative complications, such as cerebellar mutism and ataxia, were most common in patients with tumor in the fourth ventricle as shown in Supplemental Table 2.

**Recurrence**

Eighty-two of the 96 patients we treated in our study were followed up regularly after surgery. The median follow-up time was 12 months (range 2–53 months). Among these 82 patients, 18 (22.0%) suffered recurrence with 5 (out of 59) CPPs, 8 (out of 16) aCPPs, and 5 (out of 7) CPCs. Patient’s age, gender, presence of hydrocephalus, location of tumors, tumor size, extent of resection, and use of radiotherapy or chemotherapy were recorded and analyzed by Cox regression [Table 4]. We found the pathological type of CPP to be statistically significant using Cox regression (risk ratio: 3.688, \( P < 0.05 \)). No patients died during follow-up. The EFS showed a significant difference between pathological type of CPP and recurrence \( [\chi^2 = 40.1, P < 0.0001; \text{Figure 2a}], \) patients diagnosed with CPC having a higher rate of recurrence. The EFS for CPT patients with complete resection showed no better prognoses than the patients with partial resection \( [\chi^2 = 2.4, P = 0.122; \text{Figure 2b}], \) We also failed to find any significant difference between the patients with supratentorial tumor and those with infratentorial tumor \( [\chi^2 = 0.4, P = 0.528; \text{Figure 2c}]. \)

**Metastasis**

In the majority (7 of 9) of CPC cases, the Ki-67 (MIB-1) proliferation index with median value was 6% (range 4–15%). Two patients, however, experienced metastatic progression. Case 1 was a 36-month-old boy who suffered a tumor within the right ventricle, which upon neuropathological examination was diagnosed as CPC [Supplemental Figure 1]. He underwent complete removal of the tumor. The Ki-67 proliferation index was 8%. The patient underwent chemotherapy after surgery according to the HIT-SKK protocol.[14] He was diagnosed with recurrence and metastatic spread and was treated in accordance with the CPT-SIOP-2000 protocol 6 months after initial surgery.[1] The patient was stable at 2-year follow-up [Figure 3a]. Case 2 was a 60-month-old boy diagnosed with fourth ventricle CPC with metastasis to the spinal canal before surgery. After V-P shunt, gross total resection of the neoplasm in the skull was achieved. The child underwent regular Gamma Knife treatment for the tumor in the spinal canal and subsequently received chemotherapy. At 30-month follow-up, the patient had an ideal prognosis [Figure 3b].

**Discussion**

CPTs are neoplasms derived from the choroid plexus epithelium, usually located in the ventricles.[13] Available clinical data describing therapy and prognosis of CPTs in children have been limited thus far. We emphasize that patients with tumor in the fourth ventricle had mild hydrocephalus with a higher rate of headache. V-P shunting was recommended to avoid acute cerebellar tonsillar hernia before surgery, whereas there was no need for V-P shunting until acute hydrocephalus occurred after surgery. For CPCs and CPPs with partial resection, adjuvant treatment after surgical resection offers the best chance for long-term survival. Complete resection of the tumor is still the best choice for patients with CPPs, considering the side effects of radiochemotherapy. The findings of our study are consistent with those of previous reports.[1,3,6,16,17]

From our study, of 96 patients, 85 (88.5%) experienced hydrocephalus before surgery and more than half (55/96, 57.3%) experienced headache as the chief complaint. Clearly, therefore, headache is an issue that requires scrutiny. In our study, we found that the incidence of headache in patients with tumor in the fourth ventricle was significantly higher in comparison with the lateral ventricle, while we failed to find any differences between headache and severity of hydrocephalus. Moreover, the age of onset in patients with tumor in the lateral ventricle was significantly earlier than in those with tumor in the fourth ventricle. We also found that more patients with tumor in the fourth ventricle suffered headache at the early stage of hydrocephalus, whereas more patients with tumor in the lateral ventricle suffered headache at the late stage of hydrocephalus.

We found that the degree of hydrocephalus in patients with tumor located in the lateral or third ventricle was significantly higher than in those with tumors located in the

| Variable                  | \( P \)   | RR    | 95% CI          |
|---------------------------|----------|-------|-----------------|
| Age                       | 0.460    | 0.546 | 0.013–13.070    |
| Gender                    | 0.195    | 1.676 | 1.050–1.988     |
| Presence of hydrocephalus | 0.791    | 0.070 | 0.015–0.412     |
| Location of tumors        | 0.724    | 0.125 | 0.036–0.940     |
| Tumor size                | 0.342    | 0.903 | 0.108–4.639     |
| Extent of resection       | 0.074    | 3.197 | 1.104–7.285     |
| Adjuvant therapy          | 0.325    | 0.968 | 0.378–5.896     |
| Pathological type         | 0.024*   | 3.688 | 1.118–11.450    |

\*\( P<0.05 \). RR: Relative risk; CI: Confidence interval; CPP: Choroid plexus papilloma.
fourth ventricle, while the incidence of acute hydrocephalus was much higher in the fourth ventricle (72.2%). There are several possible reasons to explain these findings. First, as the space of the lateral ventricle is larger than that of the fourth ventricle, patients have sufficient time to adapt to the symptoms caused by hydrocephalus. Moreover, because of the anatomical features, a tumor derived from the fourth ventricle would block the patient’s CSF circulation within a short time, so that headache caused by hydrocephalus would occur in the short term. Second, patients with tumor in the fourth ventricle tended to be much younger than others. Because of their limited ability of expression, they would seldom speak out promptly if they suffered headache, thus delaying the early diagnosis of the disease.

Although numerous studies describing an evaluation of endoscopic third ventriculostomy (ETV) and CSF shunts have been published, decision-making regarding ETV or CSF shunts still remains a topic of considerable debate.\cite{18-22} Advocates for the insertion of a V-P shunt doubt the positive effect of ETV in treating hydrocephalus and cite ETV’s unknown effects on the development of nervous system and quality of life, while supporters of ETV cite high success rates and the potential to avoid the risks of shunt placement.\cite{23} Previously published studies made evidence-based recommendations regarding the choice of V-P shunt or ETV for treating pediatric hydrocephalus while assuming that both surgical techniques shared equivalent outcomes.\cite{18,20,22-24} In the present study, according to the postoperative Karnofsky performance scale score for patients to obtain a prognosis, there was no significant difference between V-P shunt before surgery, surgery alone without V-P shunt, and V-P shunt after surgery with regard to patient outcomes. Therefore, when choosing appropriate timing for V-P shunt in children with CPT, the following should be taken into consideration. (1) If the symptoms are acceptable and the patient can tolerate the surgery, V-P shunt before surgery should be avoided. (2) Preoperative V-P shunting...
is recommended if acute cerebellar tonsillar hernia has occurred. (3) There is no need for V-P shunting after surgery until acute hydrocephalus has occurred.

If a CPT is highly suspected in children, favorable treatment should be applied in timely fashion to prevent chronic hydrocephalus. Compression of the brain tissue by chronic hydrocephalus for a long period may affect the healthy development of the brain and the long-term prognosis of patients. This scenario, however, seldom appears in patients with tumor in the fourth ventricle with early symptoms of hydrocephalus.

As a benign tumor, if a CPP is totally resected, the expected outcome is successful without the need of adjuvant treatment.[13] The present work reports a high rate of total resection (88.5%, 85/96) with excellent outcomes as expected, which is in line with previously reported data.[1,30]

In our study, CPP patients with partial resection, aCPP patients, and CPC patients received adjuvant treatment after surgery. The strategy of therapy depended on both the patient’s age and the residual after surgery. Among eight CPPs with partial resection, five were diagnosed as lateral ventricle papilloma and three as third ventricle papilloma. Tumor adherence to the wall of the ventricle was discovered, which necessitated subtotal excision. All of these patients received Gamma Knife as adjuvant treatment and achieved favorable outcomes as expected. Their outcomes showed no significant difference with CPP patients undergoing total resection. For tumor adhering tightly to the surrounding normal tissue, adjuvant treatment such as Gamma Knife or chemotherapy followed by partial resection could also achieve a good outcome. Of course, complete removal of the CPT by surgical resection is still the first choice for the treatment of CPP, especially after taking the side effects of radio-chemotherapy into consideration.

The clinical data regarding aCPP are sporadic. Adjuvant treatment can be used as the second-stage therapy after surgical treatment. The good clinical prognosis reported here (5-year overall survival [OS] = 96.2% with pathological review) is consistent with previous work. Wrede et al. found that aCPP with subtotal resection, metastasis, or at relapse could obtain benefits from chemotherapy and radiotherapy.[5,26,27] In our study, 15 (88.2%) of 17 patients diagnosed as aCPP cases underwent complete resection. Two patients with partial removal and 10 with total resection received adjuvant treatment after surgery according to the CPT-SIOP-2000 protocol.[14] One patient with partial tumor resection received chemotherapy as second-stage treatment followed by Gamma Knife after surgery, while the other received only the Gamma Knife. Both improved as expected as did the 10 total resection patients who received adjuvant treatment after surgery. All the aCPP patients had a good outcome (5-year OS = 100%). Postoperative chemotherapy was recommended as the first-line therapy for aCPP patients. Nevertheless, more such cases should be included in future analyses.

As CPC is the highest malignant extent of CPTs, the treatment of CPC remains a challenge. Indeed, total resection of the tumor was always regarded as the most important factor in the clinical outcome of all CPTs. In the present study, perhaps because of involvement of highly experienced surgeons, eight out of nine patients with CPC underwent gross total resection, which was better than results reported previously.[5,27] However, the only patient with incompletely resected CPC underwent chemotherapy after surgery after consideration of the side effects of radiotherapy. The chemotherapy regimen was prescribed according to the CPT-SIOP-2000 protocol. Chemotherapy or radiotherapy after surgical resection has been reported to improve the OS in patients with CPC, which was also apparent in the present study. In light of the side effects in pediatric patients, radiotherapy is not recommended in infants younger than 3 years.

As benign tumors, long-term survival of patients with CPPs is expected[1] although we suspected that tumor size might be related to patients’ prognosis: The larger was the tumor, the more difficult was the surgery, and the greater was the possibility of more residue. However, tumor size turned out not to be a prognostic factor in our study, similar to the results previously reported.[5,17]

First, the relationship between the pathological type of CPPs and prognosis is relatively close, while in CPC, the situation is entirely different. The recurrence of CPC is obviously higher and earlier than in patients with CPP or aCPP. After adjuvant treatment for CPC, we obtained results similar to those previously reported.[28,29] Radiotherapy might be an effective method against recurrence of tumors in older children. Unfortunately, radiotherapy could not be considered the primary option in some cases because of the young age and the residuals to be irradiated. Radiotherapy could not prevent recurrence although radio-chemotherapy contributed to the long-term survival of patients with CPCs.

In the past, we all believed that partial resection of the tumor was an independent risk factor for recurrence,[13] but this was not demonstrated in the present study. Thanks to adjuvant therapy after surgery, we failed to find any difference in recurrence between patients with complete excision and partial excision. Postoperative adjuvant therapy after partial removal of tumor significantly reduced the risk of high recurrence rates. The residuals of tumor after surgery can be controlled effectively by radio-chemotherapy, resulting in outcomes in our study equitable with those of patients with total resection. Adjuvant therapy after surgery can be used as an effective option for patients with incomplete resection of tumors.[6,13] Based on our experience, many patients with tumor in the fourth ventricle experienced complications after surgery such as cerebellar mutism, blurred vision, and ataxia. Many clinicians hesitate to undertake any procedures in these patients. On the one hand, incomplete resection of tumors may result in recurrence. On the other hand, the operation may lead to complications for the patient when pursuing total resection. For the tumor in the fourth
This was a retrospective analysis of a series of intracranial tumor patients undergoing surgical therapy. Our study has some limitations. First, all of the patients in our group were recruited from one hospital, instead of multiple centers, which is a limitation in our study. Second, the sample of the study is limited and cannot be used to analyze the postoperative complications in different phenotypes. At last, the patients in our hospital came from locations across the whole country. For alleviation of symptoms, more patients with acute hydrocephalus received V-P shunt at preperation while waiting for future treatment than in any other clinical centers primarily because of the limited medical resources, which resulted in a higher rate of preoperative V-P shunt in our center.

In conclusion, our results indicated that CPP in the fourth ventricle could trigger serious clinical symptoms at an early stage, requiring early intervention. It is necessary to initiate adjuvant treatment for patients with partially resected CPP, aCPP, and CPC to achieve a favorable outcome.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

Financial support and sponsorship
This work was supported by grants from the National Natural Science Foundation of China (No. 81471229), Natural Science Foundation of Beijing (No. 7142054), and Capital Medical Development Research Foundation (No. 2018-1-1071).

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Ogiwara H, Dipatri AJ Jr, Alden TD, Bowman RM, Tomita T. Choroid plexus tumors in pediatric patients. Br J Neurosurg 2012;26:32-7. doi: 10.1080/02688697.2011.601820.
2. Saider C, Sub IH, Murphy ES. Choroid plexus tumors. Adult CNS Radiation Oncology. Berlin: Springer; 2018.
3. Chhabda S, Carney O, D’Arco F, Jacques TS, Mankad K. The 2016 World Health Organization classification of tumours of the central nervous system: What the paediatric neuroradiologist needs to know. Quant Imaging Med Surg 2016;6:486-9. doi: 10.21037/qims.2016.10.01.
4. Zaky W, Finlay JL. Pediatric choroid plexus carcinoma: Biologically and clinically in need of new perspectives. Pediatr Blood Cancer 2018;65:e27031. doi: 10.1002/pbc.27031.
5. Shi YZ, Chen MZ, Huang W, Guo LL, Chen X, Kong D, et al. Atypical choroid plexus papilloma: Clinicopathological and neuroradiological features. Acta Radiol 2017;58:983-90. doi: 10.1177/0284185116676651.
6. Siegfried A, Morin S, Munzer C, Delisie MB, Gambart M, Puget S, et al. A French retrospective study on clinical outcome in 102 choroid plexus tumors in children. J Neurooncol 2017;135:151-60. doi: 10.1007/s11060-017-2561-2.
7. Almamy A, Schwerk C, Schroten H, Ishikawa H, Asif AR, Reuss B. Interactions of antisera to different chlamydia and Chlamyphila species with the ribosomal protein RPS27a correlate with impaired protein synthesis in a human choroid plexus papilloma cell line. Innol Res 2017;65:1110-23. doi: 10.1007/s11060-017-8952-9.
8. Tena-Suck ML, Salinas-Lara C, Rembao-Bojorquez D, Castillejos M. Clinicopathologic and immunohistochemical study of choroid plexus tumors: Single-institution experience in Mexican population. J Neurooncol 2010;98:357-65. doi: 10.1007/s11060-009-0808-5.
9. Guo A, Suresh V, Liu X, Guo F. Clinicopathological features and microsurgical outcomes for giant pediatric intracranial tumor in 60 consecutive cases. Childs Nerv Syst 2017;33:447-55. doi: 10.1007/s00381-017-3341-1.
10. Morshed RA, Lau D, Sun PP, Ostling LR. Spinal drop metastasis from a benign fourth ventricular choroid plexus papilloma in a pediatric patient. Case report. J Neurosurg Pediatr 2017;20:471-9. doi: 10.3171/2017.5.PEDS17130.
11. Kazy W, Finlay JL. Handbook of Brain Tumor Chemotherapy, Molecular Therapeutics, and Immunotherapy, 2nd ed. Cambridge: Academic Press; 2018. p. 639-50.
12. Tubbs RS, Shoja MM, Aggarwal A, Gupta T, Loukas M, Sahni D, et al. Choroid plexus of the fourth ventricle: Review and anatomic study highlighting anatomical variations. J Clin Neurosci 2016;26:79-83. doi: 10.1016/j.jocn.2015.10.006.
13. Yeamans CL, Gutierrez-Quintana R, Haley A, Lamn CG. Magnetic resonance imaging and clinical findings associated with choroid plexus spinal cord “Drop” metastases. J Am Anim Hosp Assoc 2017;53:265-9. doi: 10.5326/JAAHA-MS-6479.
14. Timmermann B, Kortmann RD, Kühl J, Rutkowski S, Dieckmann K, Meisner C, et al. Role of radiotherapy in anaplastic ependymoma in children under age of 3 years: Results of the prospective German brain tumor trials HHT-SKK 87 and 92. Radiother Oncol 2005;77:278-85. doi: 10.1016/j.radonc.2005.10.016.
15. Lafay-Cousin L, Keene D, Carret AS, Fryer C, Brossard J, Crooks B, et al. Choroid plexus tumors in children less than 36 months: The Canadian pediatric Brain Tumor Consortium (CPBTC) experience. Childs Nerv Syst 2011;27:259-64. doi: 10.1007/s00381-010-1269-9.
16. Thomas C, Ruland V, Kordes U, Hartung S, Capper D, Pietsch T, et al. Pediatric atypical choroid plexus papilloma reconsidered: Increased mitotic activity is prognostic only in older children. Acta Neuropathol 2015;129:925-7. doi: 10.1007/s00401-015-1434-z.
17. Bahar M, Hashem H, Tekautz T, Worley S, Tang A, de Blank P, et al. Choroid plexus tumors in adult and pediatric populations: The Cleveland Clinic and University Hospitals experience. J Neurooncol 2017;132:427-32. doi: 10.1007/s11060-017-2384-1.
18. Di Rocco C, Massimi L, Tamburrini G. Shunts vs. endoscopic third ventriculostomy in infants: Are there different types and/or rates of complications? A review. Childs Nerv Syst 2006;22:1573-89. doi: 10.1007/s00381-010-1269-9.
19. Drake JM, Kulkarni AV, Kestle J. Endoscopic third ventriculostomy versus ventriculoperitoneal shunt in pediatric patients: A decision analysis. Childs Nerv Syst 2009;25:467-72. doi: 10.1007/s00381-008-0761-y.
20. Kulkarni AV, Drake JM, Kestle JR, Mallucci CL, Sgouros G, Constantini S, et al. Endoscopic third ventriculostomy vs cerebrospinal fluid shunt in the treatment of hydrocephalus in children: A propensity score-adjusted analysis. Neurosurgery 2010;67:588-93. doi: 10.1227/01.NEU.0000373199.79462.21.
21. El-Ghandour NM. Endoscopic third ventriculostomy versus ventriculoperitoneal shunt in the treatment of obstructive hydrocephalus due to posterior fossa tumors in children. Childs Nerv Syst 2011;27:117-26. doi: 10.1007/s00381-010-1263-2.
22. Jernigan SC, Berry JG, Graham DA, Goumnerova L. The comparative effectiveness of ventricular shunt placement versus endoscopic third ventriculostomy for initial treatment of hydrocephalus in infants. J Neurosurg Pediatr 2014;13:295-300. doi: 10.3171/2013.11. PEDS13138.
23. Kulkarni AV, Hui S, Shams I, Donnelly R. Quality of life in obstructive hydrocephalus: Endoscopic third ventriculostomy compared to...
24. Tuli S, Alshail E, Drake J. Third ventriculostomy versus cerebrospinal fluid shunt as a first procedure in pediatric hydrocephalus. Pediatr Neurosurg 1999;30:11-5. doi: 10.1159/000028753.

25. Muscatello LV, Avallone G, Serra F, Seuberlich T, Mandara MT, Sisó S, et al. Glomeruloid microvascular proliferation, desmoplasia, and high proliferative index as potential indicators of high grade canine choroid plexus tumors. Vet Pathol 2018;55:391-401. doi: 10.1177/0300985817754124.

26. Wrede B, Liu P, Ater J, Wolff JE. Second surgery and the prognosis of choroid plexus carcinoma – Results of a meta-analysis of individual cases. Anticancer Res 2005;25:4429-33.

27. Jeibmann A, Wrede B, Peters O, Wolff JE, Paulus W, Hasselblatt M. Malignant progression in choroid plexus papillomas. J Neurosurg 2007;107:199-202. doi: 10.3171/PED-07/09/199.

28. Rickert CH, Paulus W. Tumors of the choroid plexus. Microsc Res Tech 2001;52:104-11. doi: 10.1002/1097-0029(2001101)52:1<104::AID-JEMT12>3.0.CO;2-3.

29. Safae M, Oh MC, Bloch O, Sun MZ, Kaur G, Auguste KI, et al. Choroid plexus papillomas: Advances in molecular biology and understanding of tumorigenesis. Neuro Oncol 2013;15:255-67. doi: 10.1093/neuono/ntt289.

30. Gupta N. Choroid plexus tumors. In: Gupta N, Banerjee A, Haas-Kogan D, editors. Pediatric CNS Tumors. Pediatric Oncology. Berlin: Springer; 2017. p. 187-98.
小儿脉络丛肿瘤的临床特征及预后危险因素的相关研究

摘要

背景：目前针对小儿脉络丛肿瘤的诊疗决策仍具争议。本研究通过探讨小儿脉络丛肿瘤的临床资料，为小儿脉络丛肿瘤的诊疗决策提供理论基础。

方法：对本中心96例小于14周岁的脉络丛乳头状肿瘤患者的临床资料进行回顾性分析。本研究纳入包括脉络丛乳头状肿瘤患者的病理分型、脑积水的发病率以及严重程度、治疗方式、预后以及复发情况在内的临床资料进行统计分析。皮尔逊卡方检验用于分类数据。曼-惠特尼秩和检验用于非正态分布的数据。时序检验用于无进展生存曲线。

结果：本研究共入组70例脉络丛乳头状瘤患者、17例非典型脉络丛乳头状瘤患者和9例脉络丛乳头状癌患者。脉络丛乳头状癌患者较其他几种类型的患者病程更短(中位数, CPP: 4月; aCPP: 2月; CPC: 1月, H: 23.5, P<0.001), 急性脑积水发病率更高(CPP: 27.1%; aCPP: 52.9%; CPC: 77.8%, χ²=10.9, P<0.05)以及较低的治愈率(CPP: 85.7%; aCPP: 70.5%; CPC: 33.3%, χ²=13.5, P<0.05)。肿瘤位于侧脑室以及三脑室的患者脑积水的严重程度明显高于肿瘤位于四脑室的患者(重度脑积水: 侧脑室, 51.7%; 三脑室, 47.0%; 四脑室, 11.1%, χ²=26.0, P<0.05)。由于术后辅助放化疗的干预，肿瘤大部切除的患者其预后较肿瘤全切的患者没有明显差异(χ²=4.0, P>0.05)。本组研究还发现在脉络丛肿瘤患者中，病理类型是影像预后的一个危险因素(χ²=40.1, P<0.0001)。

结论：本研究的结果显示位于四脑室的脉络丛乳头状肿瘤患者在早期即可出现明显的临床症状，需要早期干预。对于次全切除的脉络丛乳头状肿瘤患者、非典型脉络丛乳头状瘤患者和脉络丛乳头状癌患者，术后辅助治疗可以获得理想的预后。
## Supplemental Table 1: Adjuvant treatments in aCPP, CPC, and partial resection of CPP

| Case number | Age (months) | Extent of resection | Chemotherapy | Radiotherapy | Outcome |
|-------------|--------------|---------------------|--------------|--------------|---------|
| **CPP**     |              |                     |              |              |         |
| 16          | 41           | PR                  | N            | Y            | CoR     |
| 17          | 42           | PR                  | N            | Y            | CoR     |
| 27          | 120          | PR                  | N            | Y            | PaR     |
| 32          | 6            | PR                  | Y            | N            | CoR     |
| 34          | 20           | PR                  | Y            | N            | PaR     |
| 45          | 72           | PR                  | N            | Y            | CoR     |
| 61          | 37           | PR                  | N            | Y            | PaR     |
| 80          | 19           | PR                  | N            | Y            | CoR     |
| **aCPP**    |              |                     |              |              |         |
| 6           | 120          | CR                  | Y            | N            | CoR     |
| 8           | 11           | CR                  | Y            | N            | PaR     |
| 10          | 65           | CR                  | Y            | N            | CoR     |
| 19          | 11           | CR                  | N            | N            | CoR     |
| 20          | 61           | CR                  | N            | N            | PaR     |
| 24          | 21           | CR                  | N            | N            | PaR     |
| 33          | 8            | CR                  | Y            | N            | CoR     |
| 42          | 69           | CR                  | Y            | N            | CoR     |
| 43          | 10           | CR                  | Y            | N            | PaR     |
| 50          | 12           | CR                  | Y            | N            | CoR     |
| 58          | 12           | CR                  | Y            | N            | CoR     |
| 66          | 68           | PR                  | N            | Y            | PaR     |
| 71          | 30           | CR                  | N            | N            | CoR     |
| 88          | 168          | CR                  | Y            | N            | CoR     |
| 89          | 72           | CR                  | Y            | N            | CoR     |
| 92          | 72           | PR                  | Y            | Y            | CoR     |
| 95          | 39           | CR                  | N            | N            | CoR     |
| **CPC**     |              |                     |              |              |         |
| 31          | 39           | CR                  | Y            | N            | CoR     |
| 46          | 84           | CR                  | N            | N            | PaR     |
| 59          | 23           | CR                  | Y            | N            | PaR     |
| 60          | 25           | PR                  | Y            | N            | PaR     |
| 62          | 108          | CR                  | Y            | N            | PaR     |
| 75          | 4            | CR                  | N            | N            | PaR     |
| 79          | 17           | CR                  | Y            | N            | PaR     |
| 93          | 156          | CR                  | Y            | Y            | CoR     |
| 96          | 30           | CR                  | Y            | N            | CoR     |

CPP: Choroid plexus papilloma; aCPP: Atypical choroid plexus papilloma; CPC: Choroid plexus carcinoma; CR: Complete resection; PR: Partial resection; Y: Yes; N: No; CoR: Complete remission; PaR: Partial remission.
Supplemental Table 2: Complications after surgery and outcome with follow-up in CPP patients

| Symptoms               | Total (n = 96) | Lateral ventricle (n = 58) | Third ventricle (n = 17) | Fourth ventricle (n = 18) | Others (n = 3) |
|------------------------|----------------|-----------------------------|--------------------------|---------------------------|---------------|
| Headache               | 21             | 10                          | 6                        | 5                         | 1             |
| Remission              | 18             | 9                           | 4                        | 5                         | 1             |
| Blurred vision         | 8              | 5                           | 2                        | 1                         | –             |
| Remission              | 6              | 3                           | 2                        | 1                         | –             |
| Ataxia                 | 12             | 2                           | 1                        | 9                         | –             |
| Remission              | 9              | 2                           | 1                        | 6                         | –             |
| Cerebellar mutism      | 13             | –                           | –                        | 13                        | –             |
| Remission              | 7              | –                           | –                        | 7                         | –             |
| Tremor                 | 13             | 4                           | 2                        | 7                         | 1             |
| Remission              | 7              | 2                           | 1                        | 4                         | 1             |
| Hoarseness             | 4              | –                           | –                        | 4                         | –             |
| Remission              | 3              | –                           | –                        | 3                         | –             |
| Dysphagia and cough    | 4              | –                           | –                        | 4                         | –             |
| Remission              | 3              | –                           | –                        | 3                         | –             |
| Facial paralysis       | 4              | –                           | –                        | 3                         | 1             |
| Remission              | 3              | –                           | –                        | 2                         | 1             |

–: Not applicable; CPP: Choroid plexus papilloma.

Supplemental Figure 1: Neuropathological examination of the 36-month-old boy diagnosed with CPC. The case was diagnosed as recurrence and metastatic spread after surgical therapy 6 months later. The tumor sample was identified by H and E staining. CPC: Choroid plexus carcinoma. Scale bar = 100 µm.