Choroid Plexus Carcinoma in an Infant

Choroid plexus carcinoma is a rare tumor and has a strong tendency to spread along the cerebrospinal fluid pathway. The tumor frequently occurs in infants. Radiation therapy is not indicated in infants and the response of this tumor to chemotherapy is variable. Therefore, surgical removal plays a major role in the management of this tumor, especially in infants. A 2-month-old girl with an acute communicating hydrocephalus was presented. Through the left posterior parietal transcortical approach, a choroid plexus carcinoma which had poor demarcation from the posterior thalamus and the medial wall of the lateral ventricle was subtotally (> 95%) removed. Postoperatively a ventriculoperitoneal shunt was inserted. Chemotherapy was refused. Magnetic resonance imaging taken at 11 months after surgery showed multiple intracranial seeding of the tumor. She was in a bed-ridden state. This case revealed the aggressive behaviour of choroid plexus carcinoma in an infant and the dismal result of subtotal removal alone, though it is rather radical. *(JKMS 1997; 12 : 162~7)*

Key Words : *Choroid plexus carcinoma, Lateral ventricle, Infant, Cerebrospinal fluid seeding*

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INTRODUCTION

Choroid plexus tumor (CPT), first described by Guerard in 1832 (1), is a rare tumor of the central nervous system (CNS), accounting for 0.4~0.6% of CNS tumors in the general population and 1.5~3.9% of those in the pediatric population (2~9). Of those, 20~30% are malignant tumors, choroid plexus carcinomas (CPCs) (10, 11). CPC has a strong tendency to spread along the cerebrospinal fluid (CSF) pathway and frequently occurs in infants, in whom radiation therapy is not feasible. So surgical removal with or without chemotherapy is the treatment in infants. However, subtotal removal without chemotherapy or radiation therapy has a dismal prognosis (12).

A 2-month-old girl with a CPC in the trigone of the left lateral ventricle who presented with an acute communicating hydrocephalus is described. More than 95% of the tumor was removed and chemotherapy was refused. The tumor progressed rapidly with multiple seeding through the CSF pathway, which showed the aggressive behaviour of the tumor.

CASE REPORT

A 2-month-old girl visited our hospital on January 23, 1995, due to irritability and respiratory difficulty. She was the product of a normal full term spontaneous delivery without any perinatal problem. Her birth weight was 2.9 kg. On January 10, she was admitted to a local hospital due to vomiting and diarrhea of 3 days' duration. She was treated for an upper respiratory tract infection or some viral infection. However, there was no symptomatic improvement. Thereafter, new symptoms such as poor oral intake, irritability, rigidity of extremities developed. Then she became lethargic and the respiratory difficulty appeared. On admission to our hospital, she was mildly lethargic and irritable. The body weight was 5.4 kg (25~50 percentile). The pulse rate was 200/minute, respiration rate, 22/minute, blood pressure 105/50 mmHg, and body temperature, 37.3℃. Her lung sound was clear. Her head circumference was 40 cm (> 97 percentile) and the fontanel was tense. Her vomiting was projectile. Light reflex was normal and there was no deficit in sensory and motor systems. Meningeal irritation signs were absent. Laboratory tests showed no abnormalities except low hemoglobin, 8.0 g/dl, low hematocrit, 24.3, and high white blood cell count in the peripheral blood, 18,620/mm^3. Brain computerized tomography (CT) scan revealed a round to ovoid hyperdense, well-enhancing, 3×2×2 cm-sized mass in the trigone of the left lateral ventricle and a marked dilata-

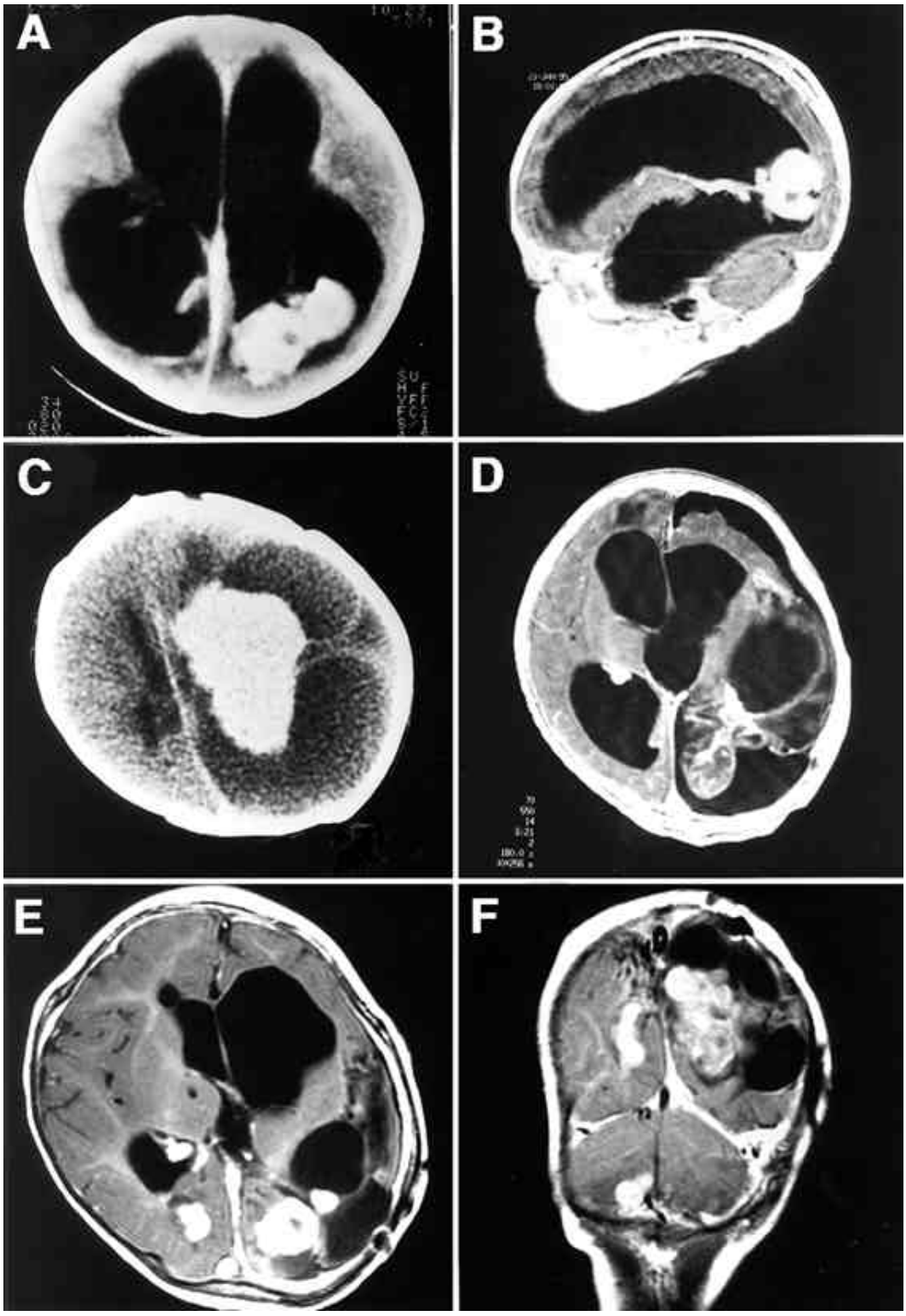

Fig. 1. Enhanced CT at initial presentation showing a round to ovoid hyperdense, well-enhancing, 3×2×2 cm-sized mass in the trigone of the left lateral ventricle and a marked dilatation of all the ventricles (A) ; sagittal T_1 weighted (T_1W) enhanced MRI showing the lobulated mass which has a contact with the posterior wall of the lateral ventricle and the choroid plexus of the trigone (B) ; axial enhanced CT taken at one month after admission showing the markedly enlarged mass (C) ; axial T_1W enhanced MRI after operation showing the residual tumor adjacent to the thalamus (D) ; T_1W enhanced MRI taken at 11 months after surgery revealing multiple seeding of the tumor through the cerebrospinal fluid pathway (E and F).

tion of all the ventricles (Fig. 1A). On brain magnetic resonance imaging (MRI), the mass was lobulated, of iso signal intensity on T_1 weighted images (WIs) and of iso to low signal intensity on T_2 WIs. After gadolinium infusion, the mass was enhanced homogeneously (Fig. 1B). Though the mass had a contact with the posterior wall of the lateral ventricle, it also had a connection with the choroid plexus of the trigone, which was enlarged, on sagittal images. On the third hospital day (HD 3), she became drowsy and showed Cheyne-Stokes respiration. Emergency external ventricular drainage (EVD) was performed. The opening pressure was 33 cmH_2O. Because of the infection through the EVD catheter, removal of the mass was postponed until HD 33. On CT scans taken on HD 31, the mass was markedly enlarged (Fig. 1C) though the neurological state of the patient was static. Preoperative diagnosis was CPT. The rapid growth of the mass suggested the malignant nature of the tumor. On February 27, through the left posterior parietal transcortical approach, more than 95% of the tumor was removed. The surface of the tumor was not cauliflower-shaped but smooth. The tumor was grayish purple, moderately vascular and slightly hard. The report of the frozen tissue biopsy was 'primitive neuroectodermal tumor / ependymoblastoma'. The tumor had poor demarcation planes from the posterior aspect of the thalamus and the medial wall of the lateral ventricle. A small part of the tumor adjacent to the thalamus was left (Fig. 1D). No additional neurological deficit was found after surgery.

On histopathological examination, the tumor had both papillary and solid areas. The branching papillary structures were composed of several layers of stratified atypical epithelial cells surrounding a thin fibrovascular core (Fig. 2A) which was confirmed by the Masson trichrome staining. However, most of the neoplasm was less differentiated and of solid growth pattern (Fig. 2B). The neoplastic cells were moderately pleomorphic with vesicular nuclei and prominent nucleoli. In the solid areas, there were scattered hemorrhage and necrosis. An average of 1 mitosis per 10 high power fields was found. The tumor showed invasion into the adjacent stromal and neuroglial tissue particularly in solid portions (Fig. 3). Mucin stains were negative. Immunohistochemical examination demonstrated that the tumor cells were reactive for neuron specific enolase, proliferating cell nuclear antigen (PCNA), pancytokeratin and Cathepsin D, but not reactive for transferrin and carbonic anhydrase II. PCNA and cathepsin D were positive in 15% and 10% of the tumor cells, respectively. In PCNA staining, the tumor cells were more reactive in solid areas than in papillary areas (Fig. 4). The tumor was diagnosed as a choroid plexus carcinoma.

Because of the dependency on the EVD, a ventriculoperitoneal shunt (VPS) was inserted on postoperative day 22. At 3 and 5 months after the tumor surgery, VPS was revised due to infection. Chemotherapy was refused. MRI taken at 11 months after surgery revealed a multifocal intracranial spread of the tumor via CSF pathway

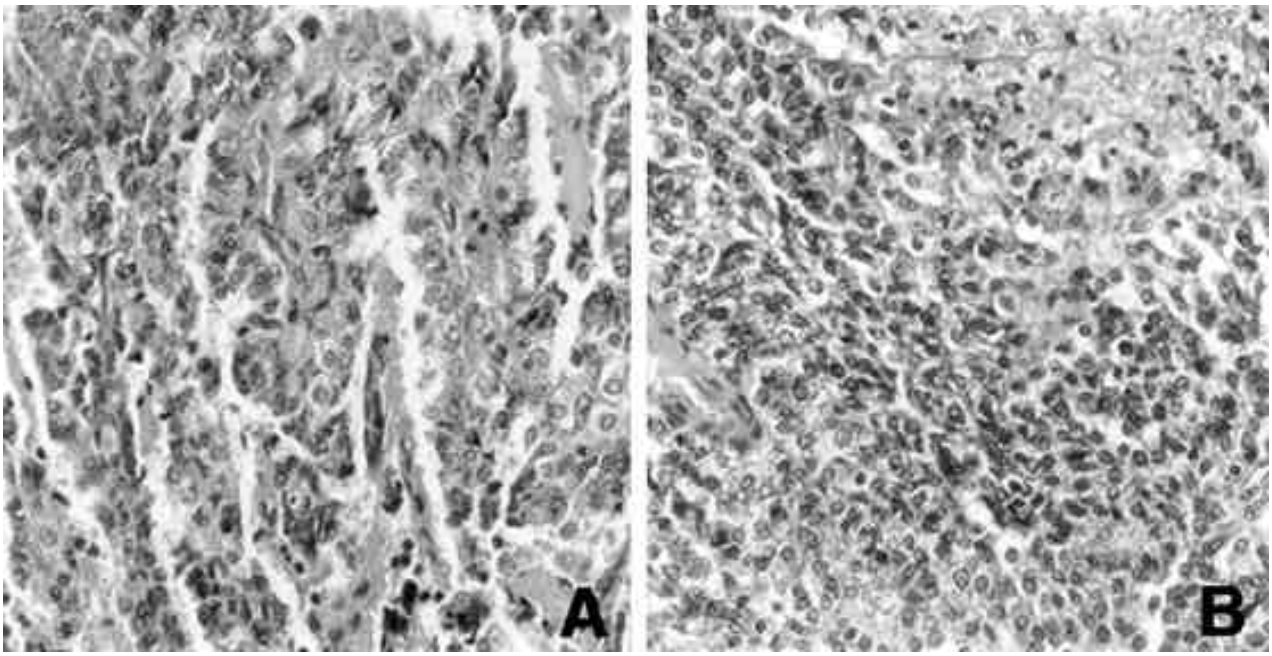

Fig. 2. The neoplastic cells show various degree of differentiation. In A, papillary configuration is evident. In B, the tumor is largely solid and composed of poorly differentiated cells (H & E, original magnification, × 200).

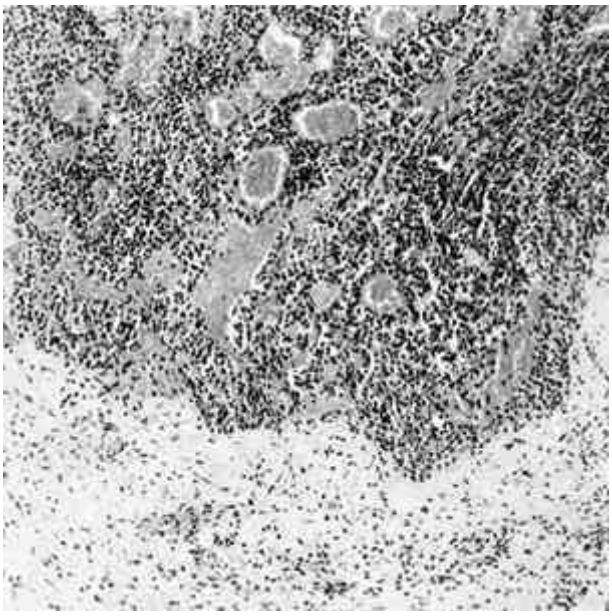

Fig. 3. Adjacent neuroglial tissue is invaded by a solid sheet of poorly differentiated tumor cells(H&E, original magnification, ×100).

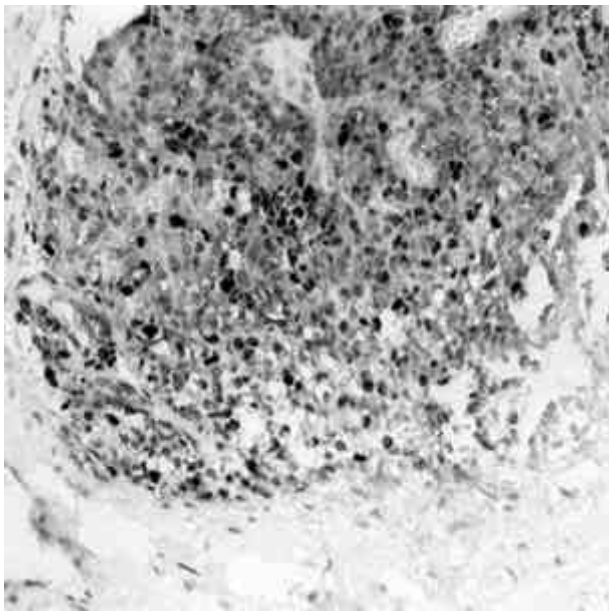

Fig. 4. Invading neoplastic cells express positive reactions to PCNA (original magnification, × 200).

(Fig. 1E and F). Further treatment on the tumor was refused again. At 16 months after surgery (19 months of age), the patient was bed-ridden with intermittent clusters of simple partial motor seizures (about 2 clusters a month) in spite of medication of antiepileptic drugs. Her development was markedly delayed. She was unable to control her head and could speak only a few words. The Karnofsky performance scale was 50.

DISCUSSION

CPC is a rare brain tumor and occurs mainly in young children and can sometimes be regarded as a congenital brain tumor (13), as can be this case. Krol et al. (14) reported one case of CPC in a premature infant. It tends to occur in the lateral ventricle in young children, while in the fourth ventricle in adults (15). Until 1995, 72 pediatric cases and 16 adult cases were described in the literature (16).

It is difficult to differentiate CPC from choroid plexus papilloma (CPP) by clinical symptoms and signs. For the diagnosis of CPC, the histological criteria promoted by Lewis (17) or Russell and Rubinstein (18) should be met. These include 1) transition from normal to abnormal choroid plexus ; 2) cellular (or nuclear) atypia ; 3) invasion into adjacent neural tissue. The tumor shows loss of normal papillary architecture, cellular immaturity and neoplastic invasion into the connective tissue stroma. The first criterion helps confirm the lesion as originating from the choroid plexus. This is important to rule out the metastatic lesion in adults. However, it is less important in children. The cellular atypia includes pleomorphism, cellular anaplasia, variations in chromatin content, glandular and acinar structure, solid sheets of anaplastic cells, necrosis and mitotic figures. Frequently the third criterion may not be applicable since tissue adjacent to the tumor is not included in the sample. CPP can invade the adjacent brain. However, CPP does not show cellular atypia (12, 18). In the present case, the invasion into the brain parenchyma and the evident cellular atypia support the diagnosis of CPC. The young age of the patient almost excluded the possibility of a metastatic tumor and the fibrovascular nature of the papillary core was not compatible with papillary ependymoma.

According to Coates et al. (19), local parenchymal invasion of CPC induce significant peritumoral edema with increased signal intensity in the surrounding white matter on T_2 WIs. However, it is frequently impossible to differentiate CPC from CPP by the radiological appearance alone. The presence or absence of the seeding through the subarachnoid space is not helpful in the differentiation of CPC from CPP.

The intraventricular location, lobulated appearance of the mass and connection with the choroid plexus on the initial MRI of the present case seemed typical findings of CPT and the initial presumptive diagnosis was CPP. However, rapid growth of the tumor found on follow-up CT scans of a month's interval favored the diagnosis of CPC rather than CPP. The present case showed an iso

to low signal intensity on T_2 WIs. Usually tumors of high cellularity or with fibrosis are of low signal intensity on T_2 WIs while tumors of low cellularity are of high signal intensity. The CPP is usually of intermediate or increased signal intensity (19). The relative low signal intensity of the mass in the present case may suggest high cellularity.

Immunohistochemical staining can aid in differentiating CPTs from other primary intracranial tumors such as papillary ependymoma and metastatic disease, and be helpful in differentiating between CPP and CPC (5, 20, 21). Transthyretin is the most sensitive immunohistochemical marker for CPTs. However, there is no clear difference in the pattern of staining between CPP and CPC. Though myxopapillary ependymoma of filum terminale and metastatic papillary thyroid carcinoma also show positivity to transthyretin, the reaction is much weaker (20). Immunoreactivity to laminin is different in CPP and CPC. The former has a continuous linear pattern, while the latter shows a less intense, fragmented pattern (22). The reactivity to glial fibrillary acidic protein is variable (3, 5, 18, 22, 23). According to Felix et al. (3) and Paulus and Janisch (23), S-100 protein has a high association with CPP than with CPC and has a prognostic significance. CPTs are also reactive in stainings for cytokeratins and vimentin (24, 25). Intracranial ependymoma does not present reactivity to cytokeratins (22, 25). Though a small number of CPC display positive reactions to carcinoembryonic antigen (CEA), metastatic adenocarcinoma to choroid plexuses should be considered first, when the tumor shows reactivity to CEA, especially in adults (23). Newbould et al. (26) described the immunohistochemical characteristics of CPC. Transthyretin, transferrin, cathepsin D and neuron specific enolase were positive in all the cases and carbonic anhydrase II, S-100 protein, epithelial membrane antigen and vimentin were positive in the majority. CPC arising from the fourth ventricle can be distinguished from medulloblastoma by the staining patterns for transthyretin, carbonic anhydrase II, transferrin, cytokeratins and epithelial membrane antigen. The present case revealed positive reactions to neuron specific enolase, pancytokeratin and cathepsin D, which supports the diagnosis of CPC. The reactions to carbonic anhydrase II and transferrin were negative, which is different from the results of Newbould et al. (26). The immunohistochemical findings in this case were not enough to differentiate CPC from CPP. The differential diagnosis between CPC and CPP was made mainly by findings of hematoxylin and eosin staining. Proliferating cell nuclear antigen (PCNA) could be used to distinguish normal choroid plexus from CPP or CPC in small, diagnostically difficult biopsy specimens (27). In this case, PCNA was positive in 15% of the tumor cells and the tumor cells were more reactive in solid areas than in papillary areas. It might mean that the tumor cells in the solid areas are less differentiated and more proliferative. According to Centeno et al. (27), there was no significant difference between the mean labeling indices of CPPs ($3.1 \pm 4.1\%$) and CPCs ($7.9 \pm 8.6\%$), but some of the CPCs had the highest PCNA labeling indices.

Because the radiation therapy and chemotherapy have limited roles in the management of CPTs, gross total removal is the goal (28) and even in cases of localized recurrence, additional surgical resections should be performed first if the patient's clinical condition permits (12). Sometimes the hypervascularity and poor demarcation from the adjacent brain, especially if the tumor is located at an eloquent area, prohibit the gross total removal. In these cases, removal of the residual tumor after radiation therapy and chemotherapy can be an option because these treatments reduce the vascularity and bulk of the mass so that total resection is feasible without significant risks (29). In the present case, due to poor demarcation from the thalamus, a small part of the mass was left. Radiation therapy was applied by most authors in cases of CPC, even when the tumor was totally removed and there is no evidence of seeding (2, 7, 30). In cases with a residual tumor, some recommended regional radiation therapy (10) while others used craniospinal radiation due to frequent spread through the CSF space as in the present case (28, 30). The present case was too young to be irradiated. Chemotherapy is indicated in young children with a residual CPC after surgical resection and in patients with metastatic spread (10, 28). Cyclophosphamide, vincristine, cisplatin, etoposide, carboplatin, ifosfamide, etc., were used with various results (10, 28, 31). Because the response to chemotherapy is limited, its role is mainly controlling the tumor until radiation therapy is feasible in some cases or it is used as a measure for reduction of vascularity and size before an attempt at total resection of a large tumor (29).

The prognosis of CPC is grave when the tumor is removed subtotally. According to Ellenbogen et al. (12), all patients with subtotal removal died in spite of adjuvant therapy while only 3 of 9 cases with gross total removal had recurrences. The role of total resection of the tumor was emphasized. Ellenbogen et al. (12) and Packer et al. (28) reported 5 year survival rate of 50%. Majority of deaths occurred within 7 months after surgery. Dohrmann and Collias (32) stated that the tumor is more aggressive in children comparing the mean survival of 9 months after diagnosis in children with the mean survival of 3.5 years in adults. In the present case, chemotherapy as a measure to control the tumor until the time of radiation (age more than 3) and reoperation

were all refused. Though only a small part of the tumor was left, it rapidly regrew and spread to multiple sites along the CSF pathway, which showed the aggressive nature of the tumor.

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