

Case Report

Left lateral ventricle tumor with distinct choroid plexus carcinoma and sarcomatous components

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Abstract: Choroid plexus tumors are rarely accompanied by other component. Here we report this rare case of a mixed choroid plexus carcinoma (CPC) and sarcoma. The patient was a 61-year-old woman with a well-defined, heterogeneous, peripherally enhancing, 4 × 4 × 3 cm lateral ventricle mass lesion. Histologically, the lesion displayed characteristics of mixed choroid plexus carcinoma and spindle cell sarcoma. The patient underwent gross excision of the mass. Approximately, 50% of the component demonstrated classic morphological and immunohistochemical characteristics of CPC. However, about 50% of the component has tumor cells with architectural, cytological and immunohistochemical features of sarcomata. In addition, these two tissues were intimately interwoven with each other in many areas. The patient subsequently received involved-field radiotherapy with a total dose of 6000 cGy. Follow up of brain imaging at 32 months after surgery showed no evidence of recurrent tumor. This represents, to the best of our knowledge, the first report of a mixed CPC and sarcomatous component's neoplasm.

Keywords: Choroid plexus carcinoma, sarcoma, left lateral ventricle tumor

Introduction

Choroid plexus tumors are considered as uncommon neoplasms derived from choroid plexus epithelium and characterized by papillary and interventricular growth. Within this family of tumors, there are benign and malignant variants, typically classified as choroid plexus papilloma (CPP), atypical choroid plexus papilloma (ACPP) and choroid plexus carcinoma (CPC), respectively [1]. Choroid plexus tumors are rarely accompanied by other components. As things stand, only two cases of choroid plexus tumor coexisting with other different histological type component have been reported, one by Chunyu (with ependymoma components), and the other by Salazar (with chondroma) [2, 3]. We herein report clinical, pathological, cytogenetic findings and therapeutic aspects of CPC with noticeable sarcomatous components in a 61-year-old woman.

Case presentation

A 61-year-old woman presented to the neurosurgery department with 30 years' history of

headache. The headache was progressively worsening for the past 3 years and presented with a 10 days' history of dizziness and vomiting. On physical examination the patient was awake and alert with normal orientation and cognition. Neurological examination revealed no abnormalities and no family history. Magnetic resonance imaging (MRI) of the brain revealed a well-defined, heterogeneous mass in left lateral ventricle that was predominantly hypointense on T1 (**Figure 1A**) and inhomogeneous hyperintense on T2 (**Figure 1B**), and the fluid attenuation inversion recovery (FLAIR) sequence was uniformly hyperintense (**Figure 1C**). After the administration of contrast, the lesion displayed heterogeneous enhancement (**Figure 1D**). The patient underwent a craniotomy of the triangle of the left lateral ventricle, which revealed a well-defined, tough, grayish red and bloody lesion attached to the posterior horn of lateral ventricle walls (4 cm × 3 cm × 3 cm). The lesion was completely resected and post-operative course was uneventful. She received post-operative radiotherapy (1.5 months). There was no evidence of tumor recurrence at the 32 months' follow-up. The long-term follow-up is still in progress.

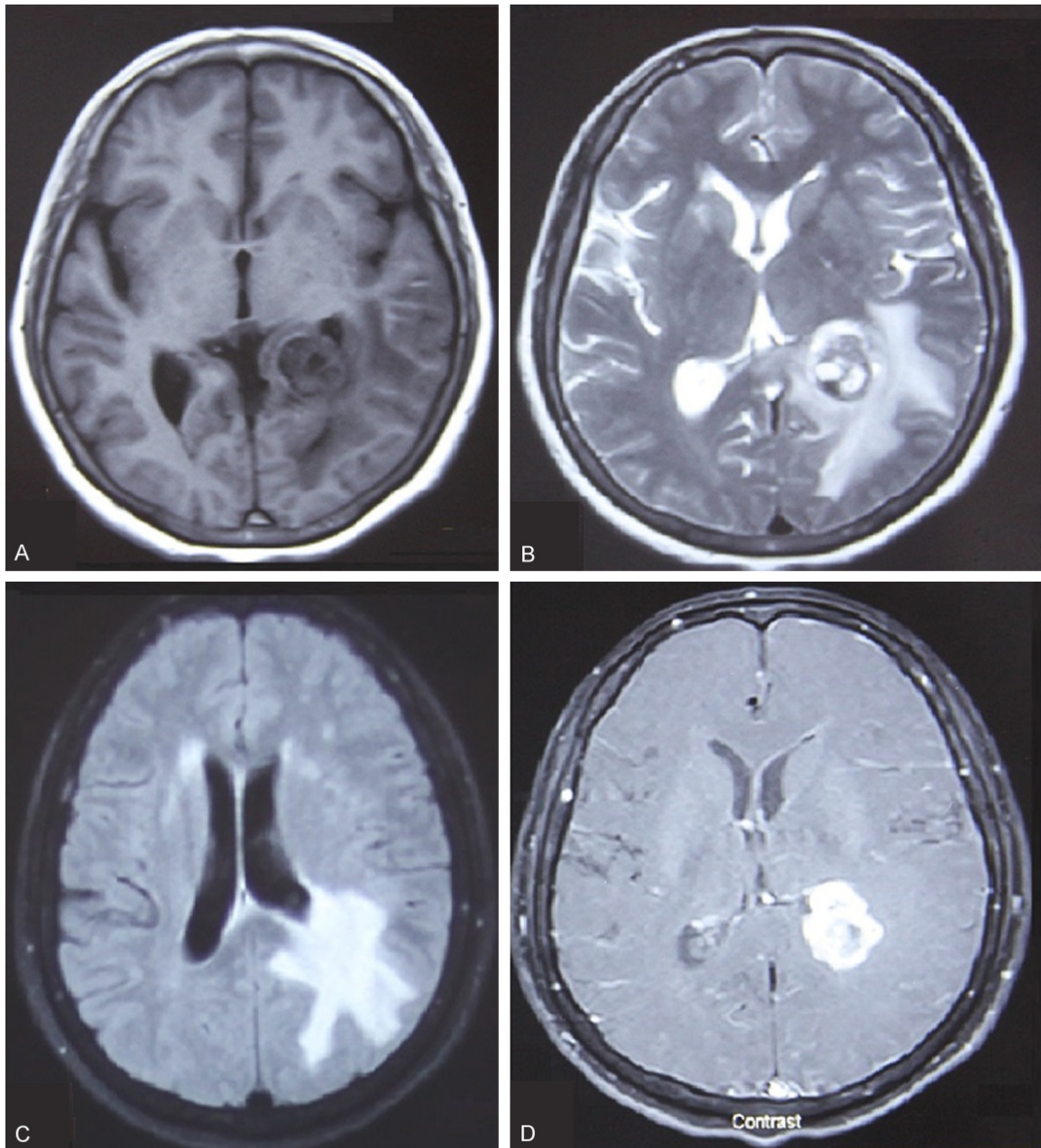


Figure 1. Magnetic resonance image (MRI) revealed a well-defined, heterogeneous mass in the left lateral ventricle. MRI showing a T1-hypo intensity (A), T2-hyper intensity (B), FLAIR-hyper intensity (C) and the heterogeneous enhancement was observed after contrast medium injection (D) (all in axial view).

Pathological examination

Macroscopically, the tumor was an irregular, tough, grayish red and bloody mass that measured 4 × 3 × 3 cm. At sectioning, the mass showed some areas in gray and yellow.

Histologically, the tumor consisted of approximately 50% CPC areas (**Figure 2A**) and inter-

laced with a fibrosarcoma component resembling sarcomata (**Figure 2B**). In the tumor area, many small islands of the CPC component were entrapped within sarcomatous areas (**Figure 2C**). These two tissues were closely interwoven in many areas. Histopathological results revealed that CPC areas were of blurring of papillary architecture, layers of neoplastic choroid plexus epithelial cells with pleomorphic nuclei,

Left lateral ventricle tumor

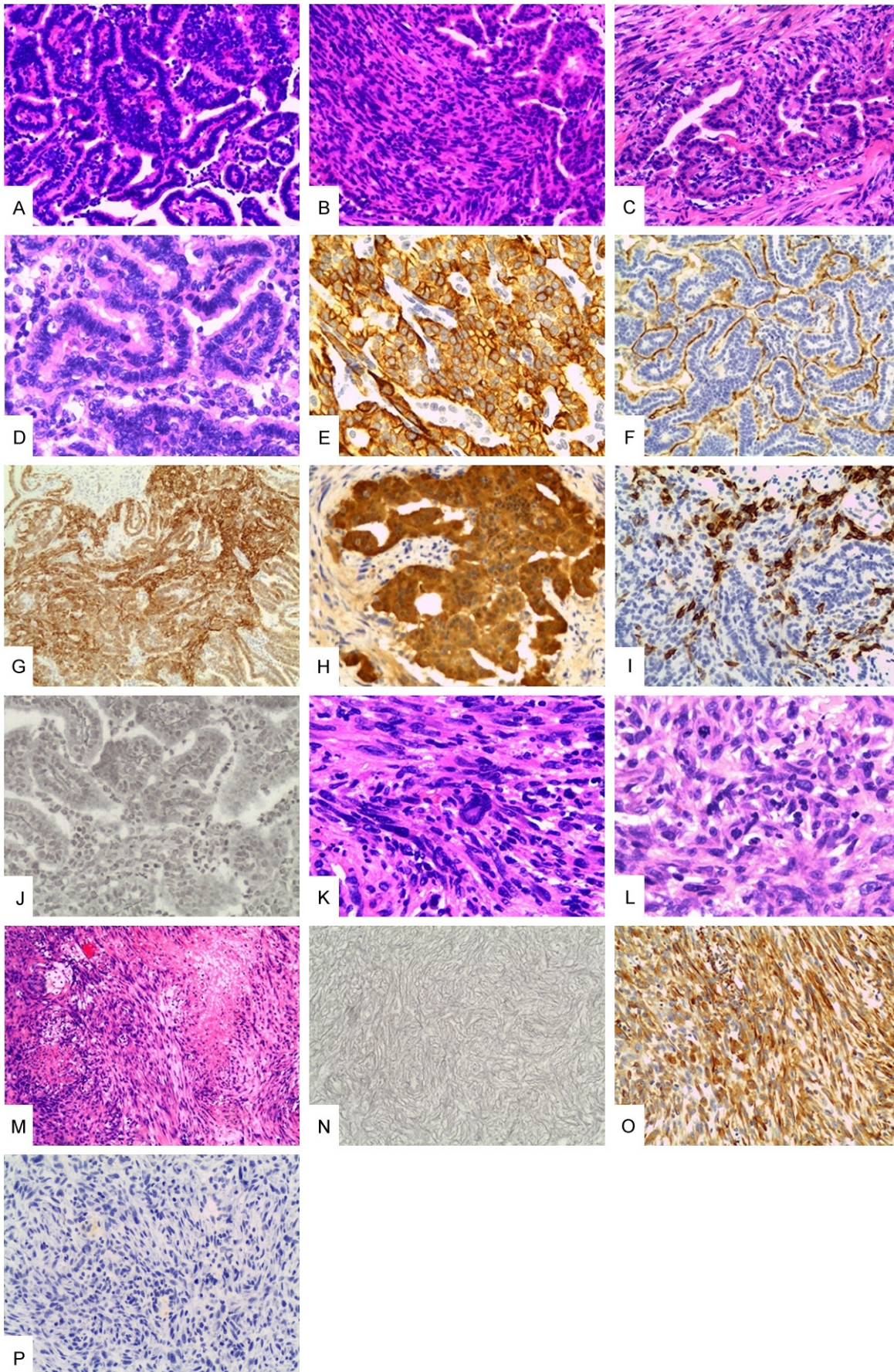


Figure 2. H&E image shows predominantly Choroid plexus carcinoma (CPC) components (A, HE $\times$ 200) with sarcomatous components (B, HE $\times$ 200). CPC areas were entrapped within sarcomatous areas (C, HE $\times$ 200), blurring of papillary architecture, layers of neoplastic choroid plexus epithelial cells with pleomorphic nuclei were found in CPC areas (D, HE $\times$ 400). CPC areas were positive for CK7 (E, $\times$ 200), EMA (F, $\times$ 200), MAP-2 (G, $\times$ 100), S-100 (H, $\times$ 200) and GFAP (I, multifocal positive, $\times$ 200). CPC areas were negative for reticular fibers (J, $\times$ 200). The sarcomatous areas, were composed predominantly of some spindle-shaped cells arranged in short-intersecting fascicles (K, HE $\times$ 200) and in storiform patterns (L, $\times$ 200). Mitoses and necrosis in sarcomatous areas (M, HE $\times$ 100). Sarcomatous areas were strongly positive for reticular fiber staining (N, $\times$ 100). The sarcomatous component cells were strongly positive for vimentin (O, $\times$ 200). The sarcomatous component cells were negative for MAP-2 (P, $\times$ 200).

increased nuclear-to-cytoplasmic ratio and increased mitosis (**Figure 2D**).

Immunohistochemical staining found that the CPC areas were positive for CK7 (**Figure 2E**), EMA (**Figure 2F**), MAP-2 (**Figure 2G**), S-100 (**Figure 2H**) and glial fibrillary acidic protein (GFAP) (multifocal positive, **Figure 2I**) and reticular fiber immunostaining were negative (**Figure 2J**). The CPC areas were negative for TP53, TG, TTF1, CK20, vimentin and Syn. Ki-67 Labelling index was high in tumor cells (15-20%). This part of tissue was considered to be of ectodermal-ependymal origin and was considered as CPC granular cell (WHO III grade).

Furthermore, the other part, sarcomatous areas were composed predominantly of some spindle-shaped cells arranged in short-intersecting fascicles (**Figure 2K**) or in storiform patterns (**Figure 2L**). No heterologous component was observed. Mitoses and necrosis (**Figure 2M**) were easily found in sarcomatous component. In order to evaluate the mesenchymal component, histochemical study of reticulum fibers was performed and the results demonstrated a rich network of fibrils in this area (**Figure 2N**). Immunohistochemically, the sarcomatous component cells were strongly positive for vimentin (**Figure 2O**). The TP53, CK, CK7, EMA, MAP-2 (**Figure 2P**) and S-100 immunostaining were negative. Labelling index of Ki-67 was high in tumor cells (15%-20%). This part was considered to be of mesenchymal origin and accounted as sarcomata (WHO III grade).

Fluorescence in situ hybridization (FISH) was performed on patient's tumor tissue, using the techniques previously described [4]. The EGFR gene copy number was determined by FISH using the LSI EGFR (spectrum-orange)/CEP 7 (spectrum-green) probe (Vysis/Abbott Molecular). Dual-color FISH was performed using LSI PTEN/CEP 10 dual color probe (Vysis/Abbott Molecular) for loss of PTEN. Fluorescent

signals were visualized and quantitated under fluorescence microscope. A minimum of 100 non-overlapping intact nuclei were assessed by hybridization. At least 30% or more increase in nuclei numbers is necessary for a signal to be scored as a deletion. Amplification of EGFR was defined as ratio of EGFR signal to CEP7 signal equal to or greater than two. Percentage of the cells showing deletion and amplification was estimated separately and independently for two component parts of this tumor.

FISH results revealed that no amplification of EGFR (**Figure 3A, 3B**) and no loss of PTEN (**Figure 3C, 3D**) in two component parts of this tumor.

Discussion

We described a rare lateral ventricle mixed CPC with significant sarcomatous components in an old woman. The rarity of this case is embodied in the sense that the association of tumors of different histogenesis occurring in one individual discovered at the same time and in the same location in CNS. Although foci of sarcomatous components have been described in ependymomas and gliomas [5-9] and the terms ependymosarcoma and gliosarcoma have been proposed for such composite tumors [8, 10], sarcomatous change occurring in CPC tumors has never been reported. CPC is an uncommon highly aggressive malignant intracranial neoplasms accounting for 15-20% of choroid plexus tumors. In the present case, the components of CPC included blurring of papillary architecture, pleomorphic nuclei and increased mitosis and the sarcomatous component consisted of a reticulum rich, glial fibrillary acidic protein-negative, high mitotic rate spindle cells. The present case was without any history of pre-treatment, including radiotherapy. Therefore, malignant mixed CPC with striking sarcomatous components arising in the lateral ventricle was finally diagnosed.

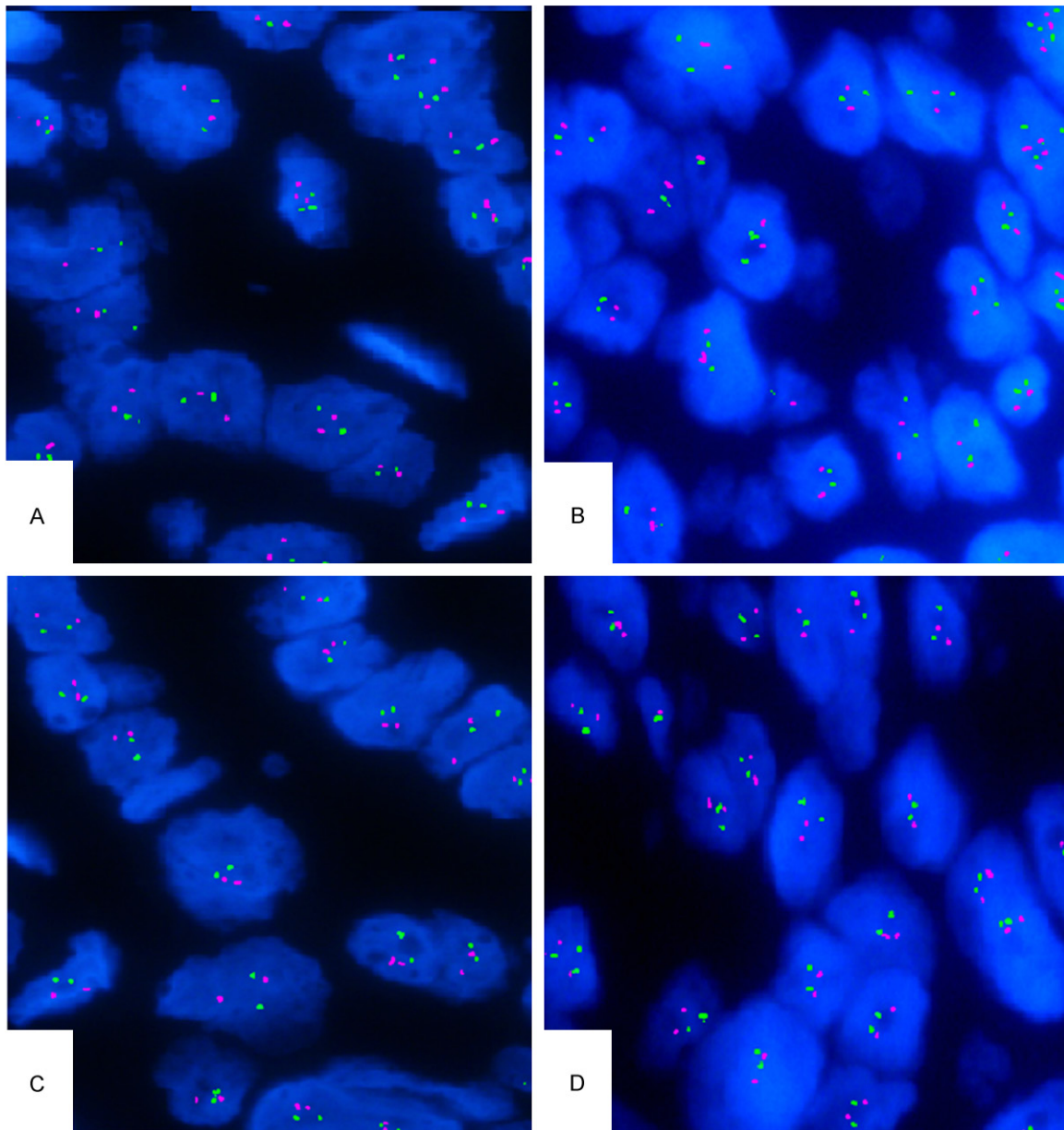


Figure 3. FISH utilizing probes against the chromosome 7 centromere (green) and EGFR gene (red). No EGFR gene amplifications were found in CPC areas (A) and in sarcomatous areas (B); FISH utilizing probes against PTEN (10q23; red) and CEP10 (green) genes. No PTEN gene deletions were found in CPC areas (C) and in sarcomatous areas (D).

It was known that choroid plexus epithelial cells represent a continuation of, and have the same origin as, ventricular ependymal cells, and are thus regarded as modified ependymal cells [11]. The terms ependymosarcoma have been proposed for such composite tumor (mixed ependymomas and sarcomata). It is, therefore, conceivable that a composite tumor (mixed CPC and sarcomata) could emerge. Although the pathogenesis of the development of sarcomatous components in such composite tumor

(ependymosarcoma) has not yet been fully elucidated, it has been proposed to include a “polyclonal hypothesis” and “monoclonal hypothesis” [12]. According to the “polyclonal hypothesis”, the mesenchymal element was thought to develop from vascular smooth muscle cells, fibroblasts or multi-potential stem cells of the peri-vascular spaces [12]. Whereas according to the “monoclonal hypothesis”, the mesenchymal component developed from glial precursors during tumor progression [12]. More

recent molecular genetic studies have shown that both glial and mesenchymal components share common genetic features in most instances, therefore supporting the monoclonal hypothesis [12-15]. There was no evidence of EGFR amplification or PTEN deletion in the two components of the present case. Unfortunately, no more specific genetic alterations associated with CPC components and sarcomatous components are found at this time which could be of help to understand the real biology of this tumor. More genetic work is needed to explain the origin of the two components of the tumor.

It was also known that CPC has anaplastic features and a high recurrence rate, rapid progression and leptomeningeal seeding and adjuvant treatment should follow for CPC patients after surgery. And the presence of sarcomatous components in this tumor is also a factor that portends a more aggressive behavior. There have been encouraging results from many reports of irradiation treatment in CPCs [16-19]. However, the role of chemotherapy remains speculative in CPCs [17, 20]. And the sarcomatous components in some tumors appear to be resistant to standard chemotherapy [21]. Based on these analyses, the patient underwent radiotherapy who received a dose (6000°C Gy) as adjuvant treatment. Since the patient has remained free of recurrence for 32 months, we believe that this therapy is currently reasonable and appropriate.

Furthermore, it was previously reported [21] that the presence of TP53 mutations resulted in extremely poor survival in CPC. And many studies suggested that p53 negativity is an indicator of good prognosis in many common human tumors [22-24]. Both of the two components were negative for TP53 in the present case, which lead us to think that negative staining for TP53 might be one of the possible underlying factors for good prognosis. A longer follow-up could be of help to understand this new type of tumor.

In summary, primary mixed CPC with sarcomatous components is extremely rare. As a result of the extreme rarity of this disease, further studies are needed to identify important prognostic factors. There are no specific treatment guidelines due to limited number of cases of mixed CPC component and sarcomatous com-

ponents. As for treatment, total excision by surgery, radiotherapy and close follow-up may be an acceptable approach for this disease.

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Disclosure of conflict of interest

None.

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