# Primary cerebral neuroblastoma: a case treated with adjuvant chemotherapy and radiotherapy

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**SUMMARY: Yarış N, Yavuz MN, Reis A, Yavuz AA, Ökten A. Primary cerebral neuroblastoma: a case treated with adjuvant chemotherapy and radiotherapy. Turk J Pediatr 2004; 46: 182-185.**

**Neuroblastoma is the most common extracranial solid tumor of childhood. A wide variety of tumor locations and clinical presentations have been described. However, neuroblastoma is rarely located in the central nervous system, except in the case of esthesioneuroblastoma. We report a child with primary central nervous system (CNS) neuroblastoma who admitted to the hospital in coma. The tumor could be partially removed in our patient. After surgery, we treated the patient successfully with combined radiotherapy and eight courses of cisplatin-based chemotherapy. Our patient was followed-up for 34 months without any evidence of relapse.**

**We recommend that CNS neuroblastoma be treated according to the same principles used in medulloblastoma.**

*Key words: neuroblastoma, brain, childhood.*

Neuroblastoma is the most common extracranial solid tumor of childhood and accounts for 8%-10% of all pediatric cancer. It is derived from primordial neural crest cells. It may arise from anywhere a sympathetic nervous system structure is present. Therefore, a wide variety of tumor locations and clinical presentations have been described[1]. However, neuroblastomas, with exception of esthesioneuroblastoma, are rarely located in the central nervous system (CNS)[2]. Primary CNS neuroblastoma is thought to be derived from second stage of neuronal cytogenesis. Further differentiation of primitive neuroepithelial cells to neuroblast form the cellular origin for neuroblastoma[3]. Here, we report a child with primary CNS neuroblastoma. We aimed to discuss the clinical features and therapy of this rare neoplasm.

## Case Report

A five-year-old girl was admitted to the hospital in coma. During the previous month she had headache and vomiting. Neurological examination revealed diffuse hypereflexia, bilateral Babinski sign, and bilateral papilledema. She was unresponsive to verbal and painful stimuli. There were no localizing findings. Laboratory findings were unremarkable. Computed tomography demonstrated a large frontoparietal mass (Fig. 1). The clinical and radiological dignosis was supratentorial glial tumor. A craniotomy was performed and the tumor was partially removed, on the day of admission. Histopathologically the tumor was quite cellular and composed of small round cells with hyperchromatic nuclei, inconspicuous nucleolus, and scanty cytoplasm. The cells frequently formed Homer-Wright rosettes. Frequent mitoses and capillary networks were observed. Fibrous stroma was limited to the blood vessel walls. No definite glial elements were found. Scattered focal necrosis and hemorrhage were observed (Fig. 2). Immunohistochemical staining showed a strong positivity for neurone-specific enolase and synaptophysin (Fig. 3). The cells were negative for glial fibrillary acidic protein. Histological diagnosis was neuroblastoma of the brain. Other possible sites for the primary lesion were investigated since CNS metastasis might occur in stage IV neuroblastoma. Chest X-ray, ultrasonography and computed tomography of abdomen and bone scan failed to show any

evidence of a primary lesion. Examination of bone marrow showed no evidence of metastatic disease. The postoperative level of urinary vanillylmandelic acid excretion was within normal levels. Cytological examination of cerebrospinal fluid showed no neoplastic cells. Magnetic resonance imaging of whole spinal axis was normal. She received radiotherapy consisting of 30 Gy in 1.8 Gy fractions to the whole brain and 25 Gy boost to the initial tumor bed. Concomitantly, she received eight courses of chemotherapy with a combination of cisplatin (100 mg/m$^2$/day) and VP-16 (120 mg/m$^2$/day, for three day) every four weeks. Follow-up computed tomography at six months showed significant shrinkage of the tumor. Thirty-four months postoperatively she is alive without any evidence of tumor recurrence.

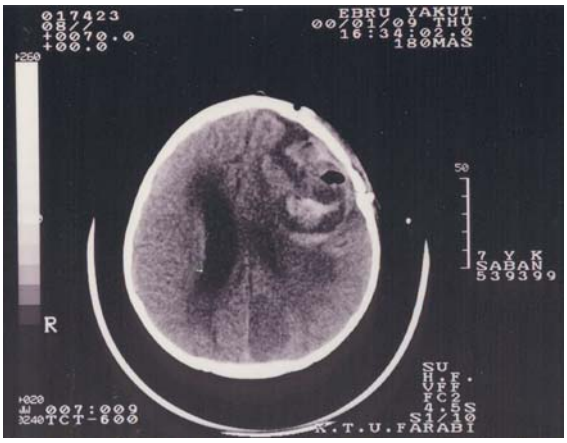


**Fig. 1.** Post-operative computed tomography (CT) scan showing a large tumoral mass in the left fronto-parietal region.

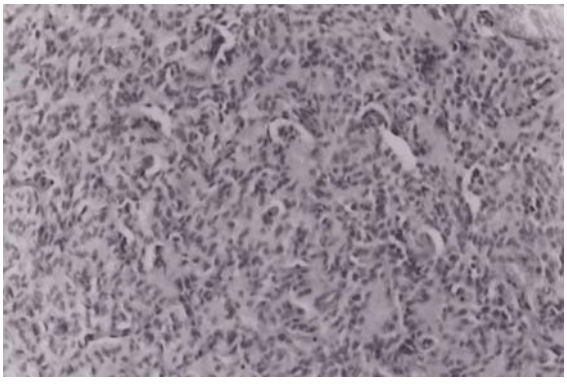

**Fig. 2.** Cerebral neuroblastoma showing collection of small round cells with Homer-Wright rosettes formation (HEx200).

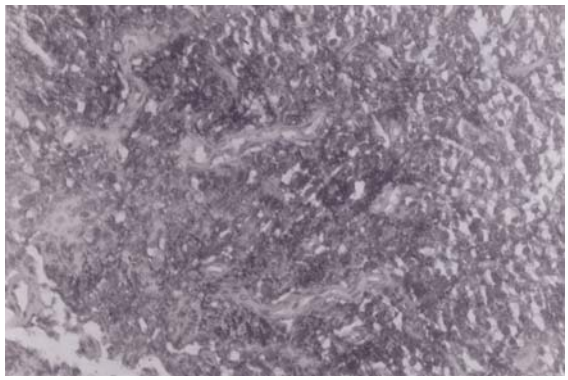

**Fig. 3.** Immunohistochemical staining showed a strong positivity for neurone-specific enolase (x200).

## Discussion

Primary cerebral neuroblastoma is a rare entity. Horten and Rubinstein[4] stated that the incidence of CNS neuroblastoma is approximately one case every decade. It is accepted as a subtype of primitive neuroectodermal tumor (PNET) that shows neuronal differentiation. It was reported that neuroblastoma constituted 6% of whole CNS PNET[5]. PNETs located in the supratentorial region are generally called neuroblastoma[2,5]. The revised WHO classification of pediatric brain tumors used the term PNET with neural cells instead of cerebral neuroblastoma. Some authors prefer to use the term supratentorial PNET instead of cerebral neuroblastoma[2,6].

Primary CNS neuroblastoma mostly occurs in the first decade. Twenty-six percent of cases are under two years of age. Exceptionally, it has been reported in adults. It is located in the cerebral hemisphere with a predilection for parietal and frontal lobes[4,7,8]. The tumor was located in the frontoparietal region in our case as well. She was admitted to our hospital with the symptoms of increased intracranial pressure. Primary CNS neuroblastomas are presented with symptoms and signs of increased intracranial pressure, since the tumor expands rapidly. The tumor is often large but well circumscribed; cysts, focal hemorrhage and necrosis may be present[4,7,8]. We did not obtain an increase in the level of urinary vanillylmandelic acid. The levels of catecholamine metabolites in urine and blood are usually normal in primary cerebral neuroblastoma[4,7,8]. However, there have been some reported cases with a high level of catecholamine in urine and cerebrospinal fluid[9].

Histologically, the tumor is always highly cellular consisting of small round cells with hyperchromatic nuclei as with the peripheral counterpart. The presence of Homer-Wright rosettes, ganglionic differentiation and argyrophilic cells process in silver impregnation are the characteristic features of this tumor[4,5,10]. Although we did not perform specific silver impregnation, the immunohistochemical procedures demonstrating neurone-specific enolase and synaptophysin confirmed the neuronal origin. Histologically, three subgroups have been described: classical, desmoplastic and transitional types. The main criteria for distinction were the degree and extent of fibrous connective tissue. In a classical variant, connective tissue is limited and rosette formation is frequent. Desmoplastic variant is characterized by prominent connective tissue stroma. Transitional form is an intermediate form between the classic and desmoplastic variants[4,10]. The histological patterns of the tumor in our case were consistent with the classical variant.

Primary treatment f the CNS neuroblastoma is surgical resection. Although total removal of the tumor is important for survival, generally this is not possible because of the large size of the tumor[4,7,8,11]. There is controversy on the post-operative treatment regimen. Postoperative radiotherapy was applied by most of the authors[4,6-8,11,12]. While some authors recommend spinal radiotherapy in addition to cranial radiotherapy because of the high ratio of the spinal seeding[4,6], others advise spinal radiotherapy only if there is a documented spinal seeding by cerebrospinal cytology and magnetic resonance imaging[8]. Chemotherapy combined with radiotherapy was occasionally used in early series and favorable clinical responses to chemotherapy were obtained[4,6,7]. Berger et al.[8] recommended chemotherapy for those patients whose tumors were resected sub-totally. Recently, various chemotherapy regimens have been used consisting of nitrosoureas, MOPP (nitrogen mustard, vincristine, procarbazine, and prednisolone) and eight-drug regimens in one day. Improvement in survival rates with combined modality has been noted[11,12].

Primary cranial neuroblastoma is a highly malignant neoplasm. There is a high rate of neuroaxis dissemination[4,6-8]. Extracranial metastasis has also been reported[13]. Therefore it can be hypothesized that CNS neuroblastomas behave like medulloblastoma. Medulloblastoma is an undifferentiated form of the primitive neuroectodermal tumor that arises in the cerebellum[2]. We suggest that the same principle used in medulloblastoma must be applied to childhood primary CNS neuroblastoma since they show similar biological behavior. The importance of total resection of the tumor for both CNS neuroblastoma and medulloblastoma has been emphasized in numerous reports[4,6-8,14,15]. It was shown that reduced dose irradiation combined with chemotherapy in standard-risk medulloblastoma seemed to have better or comparable outcome to those treated with standard radiotherapy[14]. In high-risk medulloblastoma (locally invasive disease, limiting resection, overt metastatic disease, age younger than 3 years), chemotherapy made significant improvements in survival compared with radiotherapy alone[15]. In primary CNS neuroblastoma, recurrence rate was reported as high as 40% in a period of 6 months to 7 years. It was reported that the majority of patients had recurrence although they were treated with radiotherapy, and few of them were alive[4,7,8]. These reports support the necessity of the chemotherapy combined with radiotherapy. We gave eight courses of chemotherapy containing cisplatin and VP-16 in addition to radiotherapy. Our patient was followed up for 34 months without any evidence of relapse.

In conclusion, primary CNS neuroblastoma is a rare highly malignant tumor. The appropriate treatment regimen following surgical resection has not been definitely established. We treated our patient successfully with combined radiotherapy and cisplatin-based chemotherapy. We recommend that CNS neuroblastoma be treated according to the same principles used in medulloblastoma.

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