

Primary Intramedullary Neuroblastoma in Adult

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= Abstract = **Primary neuroblastoma in the central nervous system(CNS) is unusual tumor in adult, and primary intramedullary neuroblastoma is extremely rare. The authors report a case of 36-year-old woman presenting with pain in the right anterior chest wall and weakness of the right lower extremity. An upper thoracic intraspinal mass was revealed on magnetic resonance image. On operation, the demarcation plane of the tumor was good and enabled a total removal of the subpially located intramedullary mass. Histopathological examination revealed neuroblastoma. After surgery with whole spinal irradiation, the patient was followed up for one year. There was no evidence of local recurrence radiologically and clinically. However fifteen months after the surgery, multiple metastases to the breast, lung, liver and brain occurred.**

Key Words: *Primary neuroblastoma, Central nervous system, Intramedullary mass, Metastases, Spinal cord, Adult*

INTRODUCTION

Although there is a considerable controversy between primitive neuroectodermal tumor and primary neuroblastoma, primary neuroblastoma in CNS is considered as a subtype of embryonal CNS tumors (Rubinstein 1985).

Primary cerebral neuroblastomas have been documented by several authors (Balakrishnan et al. 1974; Benett and Rubinstein 1984; Henriquez et al. 1973; Rubinstein 1985), but primary intramedullary neuroblastoma of the spinal cord is sel-

dom described. And there is no report on its clinical course or management. We describe here a case of primary intramedullary neuroblastoma.

CASE REPORT

A 36-year-old woman complained of lancinating pain of 5 months duration in the right shoulder and chest. She also experienced vague dysesthetic coldness in the left lower extremity. In addition, she noted a progressive loss of strength in the right lower extremity. The pain was episodic and paroxysmal and was radiating to the ulnar side of the forearm. Motor examinations showed a mild weakness and spasticity in the right lower extremity. Deep tendon reflexes were hyperactive in the right leg. Babinski sign was positive, and

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abdominal skin reflex was absent in the right side. There were no evidence involving the dorsal column and spinothalamic tract in sensory examination except the pain. There were no abnormal findings in electrophysiological studies and lumbar cerebrospinal fluid analysis including cytological examination.

Neuroimaging: Plain films of the T-spine, shoulder, and thorax were normal. On MRI (2.0T: GoldStar, Korea), an ovoid mass of 1.5×2.5cm at T-1 (TR: 500 msec, TE: 30 msec), T-2 (TR: 2500 msec, TE: 90 msec) weighted sagittal images demonstrated the rim of peripheral high-signal intensity and the central portion of low-signal intensity on T₁-weighted image and a somewhat high-signal intensity on T₂-weighted image (Fig. 1A, B) in the upper thoracic intraspinal area. The mass was homogeneously enhanced by gadolinium diethylene-triamine-pentaacetic acid (Gd-DTPA) (Fig. 1C) and looked as mainly located in the right side of the cord on T₁-weighted image (Fig. 1D). It was impossible to identify whether it was an extramedullary tumor which was densely adherent to the cord or an intramedullary tumor.

Operation: A total laminectomy was performed from C7 to T2. When the dura mater was opened, the spinal cord bulged in the right lateral portion, with an area of lightly brownish discoloration on the ventro-lateral portion of the right dorsal root entry zone. A longitudinal incision of the pia mater at the site of the discoloration disclosed a soft suckable intramedullary mass without capsulation. The mass extended to the postero-medial portion. The tumor was relatively well-demarcated, and was totally removed microsurgically using ultrasonic aspiration.

Pathologic examination: The biopsy revealed an undifferentiated tumor consisting of small dark cells defined by round to oval hyperchromatic nuclei and scanty cytoplasm (Fig. 2). Variable sized islands of small round cells were found, and a few number of relatively well-defined Homer-Wright rosettes were scattered, showing their fine fibrillary cytoplasmic processes in the centers (Fig. 3). On immunohistochemical staining, they disclosed a moderate positivity for neuron specific enolase. The tumor cells were totally negative for glial fibrillary acidic protein. Electron microscopic exam-

ination revealed abundant membrane-bound dense core granules compatible with neurosecretory granules (Fig. 4). Other cytoplasmic organelles included microtubules, glycogen particles, SERs, swollen mitochondria and pinocytotic vesicles. The nuclei were round to ovoid, with chromatin clumpings and inconspicuous nucleoli. The cytoplasm was relatively scanty, showing scalloping borders with stellate cell processes. However, synaptic vesicles were not demonstrated.

Postoperative course: Immediately after the operation, the lancinating pain disappeared and there was no additional neurological deficit. On preirradiation follow-up MRI, there was no enhancing lesion in the operation site, and the bulged spinal cord returned to almost normal. Whole spine radiotherapy and booster irradiation to the lesion was performed with a total dosage of 4500 rad. One year after surgery and radiotherapy, there was no evidence of recurrence on MRI (Fig. 5A, B) and previous weakness in the right leg had much improved. The patient reached a normal functional status without any further neurological deficits and pain. However, three months later, multiple metastases to the breast, lung, liver and brain (Fig. 6A, B) were found radiologically. Aspiration cytology of the breast and liver masses revealed same nature of tumor found in the spinal cord.

DISCUSSION

Primary cerebral neuroblastomas have been documented by several authors, including their biological behaviour (Benett and Rubinstein 1984; Berger et al. 1988; Horten and Rubinstein 1976; Louis et al. 1990). However primary intramedullary neuroblastoma of the spinal cord is extremely rare. Only four cases of intramedullary neuroblastoma are reported (Balakrishnan et al. 1974; Rubinstein 1985; Russel and Rubinstein 1989). And two of four cases occurred in childhood. Even for these cases, clinical manifestation, radiological finding or histological characteristics are not sufficient.

Since this tumor is such a rare tumor in the spinal cord one has to speculate on its tumorigenesis. There is little information about postnatal

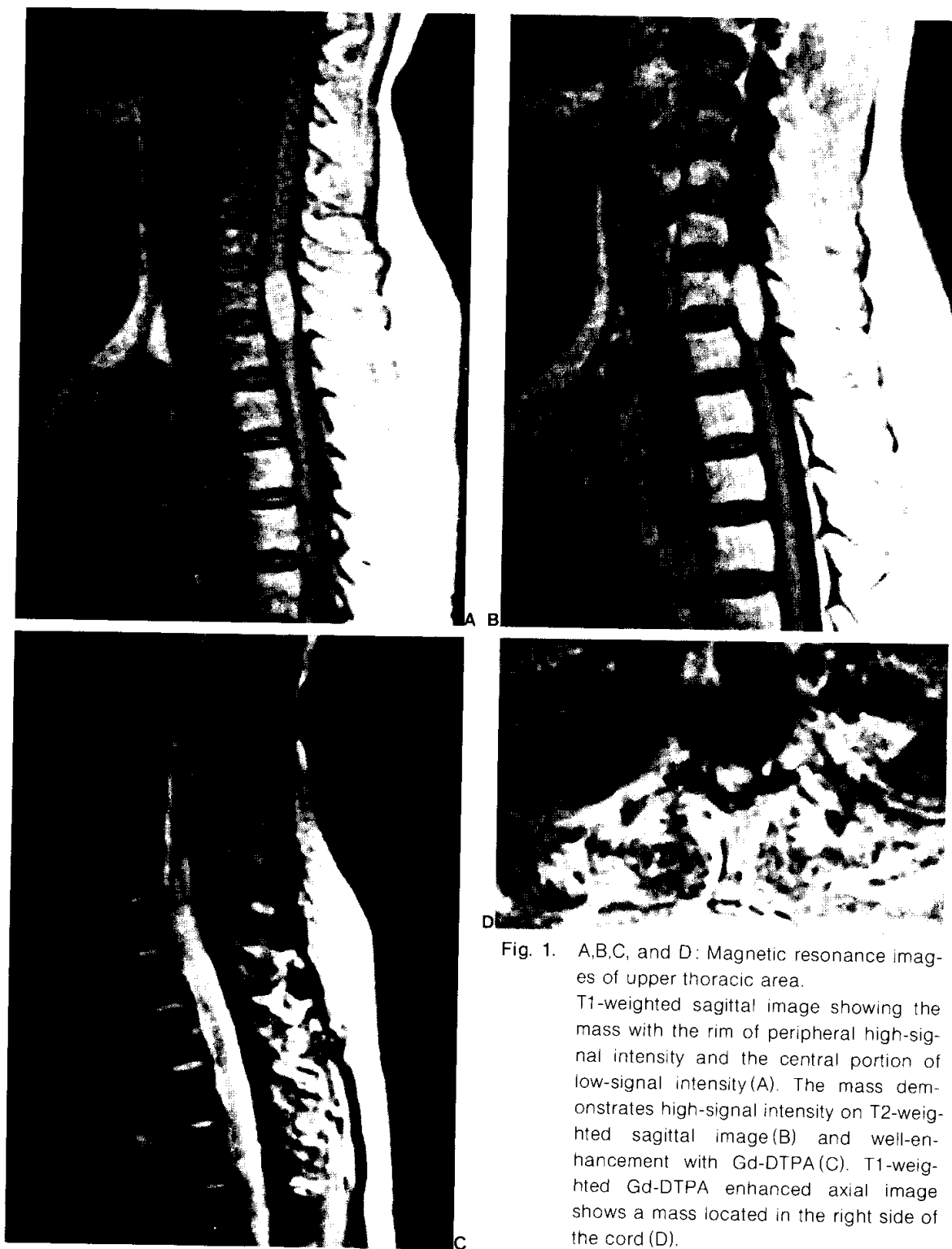


Fig. 1. A,B,C, and D: Magnetic resonance images of upper thoracic area. T1-weighted sagittal image showing the mass with the rim of peripheral high-signal intensity and the central portion of low-signal intensity (A). The mass demonstrates high-signal intensity on T2-weighted sagittal image (B) and well-enhanced with Gd-DTPA (C). T1-weighted Gd-DTPA enhanced axial image shows a mass located in the right side of the cord (D).

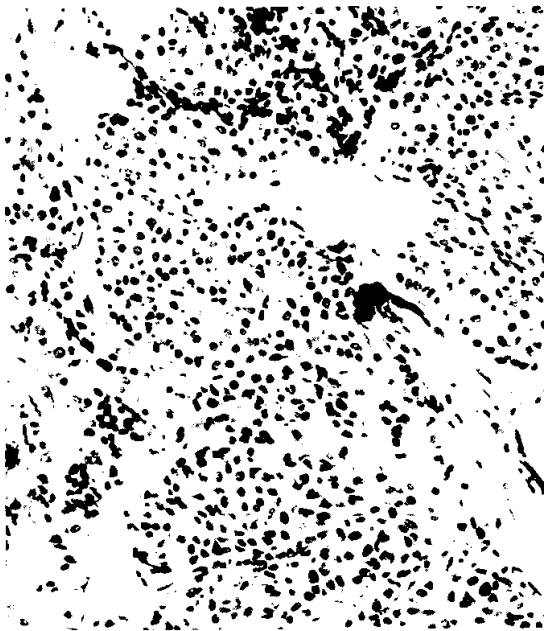


Fig. 2. Highly cellular infiltrates are composed of malignant small round cell tumor showing monotonous round to ovoid dark nuclei and scanty but small amount of fibrillary cytoplasm. They are usually compactly arranged in solid nests separated by thin fibrovascular strands ($\times 100$, H&E).

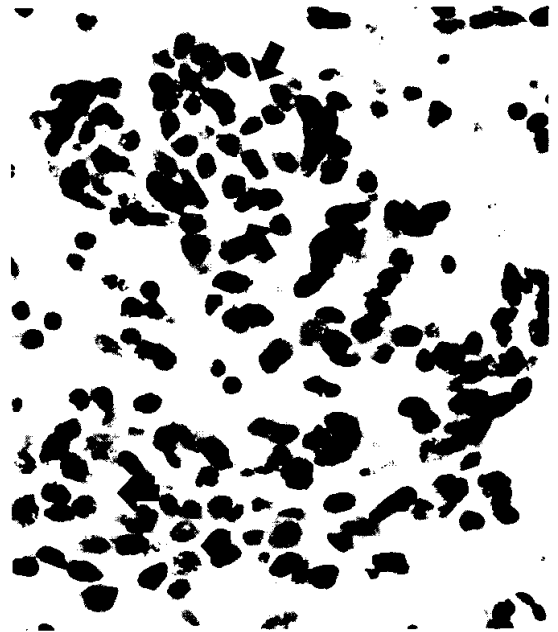


Fig. 3. The small round tumor cells revealed occasional rosette formation with centrally located eosinophilic fibrillary cytoplasmic process and nuclear rimming, which demonstrates neuroblastic differentiation ($\times 200$, H&E).

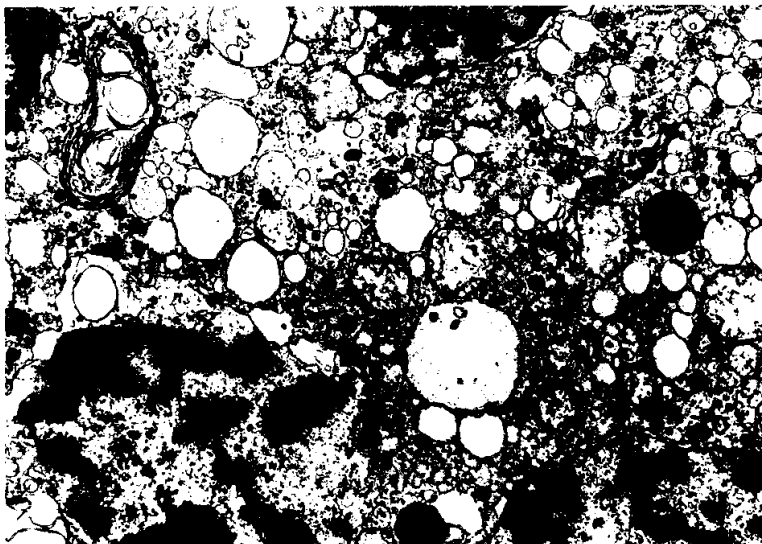


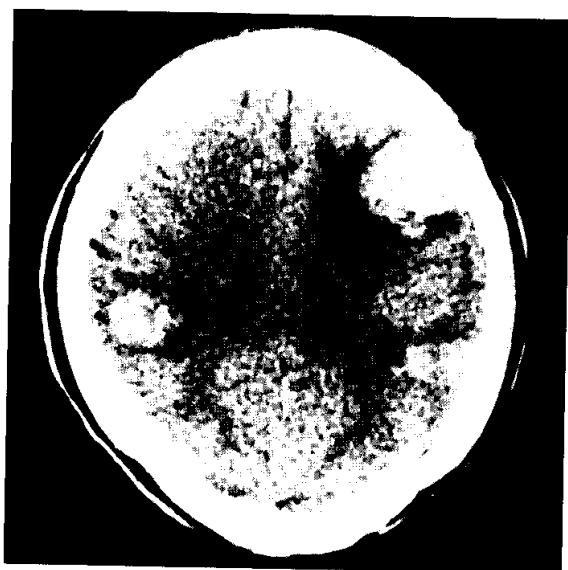
Fig. 4. Ultrastructurally, the tumor cells contain membrane-bound dense core neurosecretory granules in the cytoplasm.



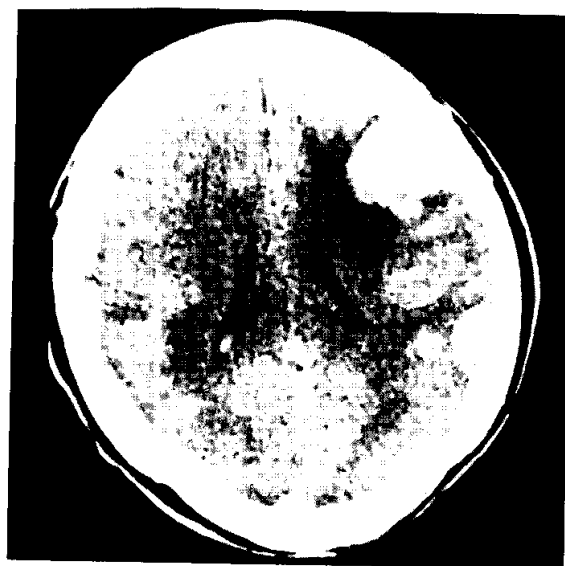
B



Fig. 5. A and B. Follow-up magnetic resonance images, one year after the operation. T1-weighted sagittal image shows absence of high-signal intensity mass (A). T1-weighted Gd-DTPA enhanced axial image shows no longer enhancing mass in the spinal cord (B).



A



B

Fig. 6. A and B. Brain CT showig multiple high density masses in the left frontal, and both parietal areas. Pre-enhancement (A), and post-enhancement (B).

sites of continuing neurogenesis in the spinal cord that might constitute the source of central neuroblastoma in the brain (Rubinstein 1985). However primary intramedullary neuroblastoma could have arisen from cells adjacent to the central canal as in supratentorial germinal matrix around the ventricle.

Although there has been controversy about characteristic MRI findings of cerebral neuroblastoma (Davis et al. 1990; Porter-Grenn et al. 1991), our case showed basically similar MRI features with those of cerebral neuroblastoma. Central low-signal with peripheral high-signal intensity on T1-weighted image and strong Gd-DTPA enhancement seems to be the characteristic finding of intramedullary neuroblastoma. The MRI findings of our case is unusual for ependymoma and astrocytoma of the spinal cord.

Histologically, undifferentiated small round cell tumors always cause differential problems. The diagnosis of neuroblastoma should be confirmed by appropriate means. Some authors (Horten and Rubinstein 1976) proposed the criteria for the histological diagnosis of neuroblastoma: (1) the presence of distinctive neuroblastic (Homer-Wright) rosettes (2) occasional maturation to ganglion cells, and (3) demonstration of argyrophilic cellular processes. Among these Homer-Wright rosettes had been most frequently demonstrated (69%). Positive immunostains for neuron specific enolase and negative for glial fibrillary acidic protein favor the neuroblastoma. The immunoreactivity for neuron specific enolase is an indication of neuronal origin. The tumor cells of neuroblastomas are usually negative for glial fibrillary acidic protein but can show positivity for neuron specific enolase (Russel and Rubinstein 1989).

By electron microscopy, cerebral neuroblastoma has irregular nuclear contours, scanty cytoplasm and numerous fine cytoplasmic processes often arranged in fascicles, and these processes contain dense-core granules, microtubules, and intermediate filaments (Ojeda et al. 1980; Poon et al. 1988; Rubinstein 1985). Above features were found in our case. Synapse-like structures with aggregates of small clear vesicles that are not seen in our case can also be seen particularly in more differentiated tumor. Recognition of neur-

osecretory granules allows the tumor a diagnosis of neuroblastoma. Ultrastructural identification of characteristic neurosecretory granules, cell junctions, and synaptic vesicles, as well as immunoreactivity with the neuron specific enolase, lead to the diagnosis of this unusual tumor (Poon et al. 1988).

The prognosis of cerebral neuroblastoma seems to depend on the site of tumor, the presence of distant metastases, and particularly the age of the patient (Balakrishnan et al. 1974; Benett and Rubinstein 1984; Rubinstein 1985). Histology is less helpful. In general, the 3-year survival and 5-year survival rate are known to be 60 percent and 30 percent, respectively (Benett and Rubinstein 1984; Berger et al. 1988; Rubinstein 1985). Most deaths or fatal recurrences occurred within the first 3 years after operation (Rubinstein 1985). It is not known if spinal cord neuroblastoma bears same prognosis with cerebral neuroblastoma.

Local recurrence was frequent in patients who survived after operation in cerebral neuroblastoma (Benett and Rubinstein 1984). Therefore some authors (Berger et al. 1988) recommend radical excision of the tumor whenever possible, followed by irradiation directed to tumor bed with wide margins and adjuvant chemotherapy for patients from whom solid tumors are subtotally removed. Meanwhile others (Bennett and Rubinstein 1984) claimed that postoperative irradiation with or without chemotherapy did not improve the postoperative survival. In addition to local recurrence, a notable development has been metastases via cerebrospinal and extraneural pathways (Balakrishnan et al. 1974; Benett and Rubinstein 1984; Henriquez et al. 1973; Sasaki et al. 1981). Metastases from primary cerebral neuroblastoma are the result of both lymphatic and hematogenous spreads when the tumor extends beyond the dura mater (Henriquez et al. 1973; Sasaki et al. 1981). The high rate of recurrence and protracted clinical course raise the advisability of entire neuraxial radiation after surgery. But, others (Berger et al. 1988) proposed that entire neuraxial irradiation should be reserved for cases showing evidence of tumor dissemination. In our case, there were multiple metastases without local recurrence. No evidence of lymph node enlargement was present.

We managed our case according to the conventional methods, i.e., gross total removal followed by spinal irradiation. This tumor was static for one year after these procedures, only to recur fifteen months after surgery, with multiple metastases including brain. Subsequent chemotherapy and additional irradiation to brain did not alleviate the clinical course. The potential difference between primary spinal and cerebral neuroblastoma should be elucidated in future.

REFERENCES

- Balakrishnan V, Rice MS, Simpson DA: Spinal neuroblastomas. Diagnosis, treatment, and prognosis. *J Neurosurg* 40: 631-638, 1974
- Bennett JP, Rubinstein LJ: The biologic behaviour of primary cerebral neuroblastoma. A reappraisal of the clinical course in a series of 70 cases. *Ann Neurol* 16: 21-27, 1984
- Berger MS, Edwards MSB, Wara WM, Levin VA, Wilson CB: Primary cerebral neuroblastoma. long-term follow-up review and therapeutic guidelines. *J Neurosurg* 59: 418-423, 1988
- Davis PC, Wichman RD, Takei Y, Hoffman JC Jr. : Primary cerebral neuroblastoma. CT and MR findings in 12 cases. *AJNR* 11: 115-120, 1990
- Henriquez AD, Robertson DM, Marshall WJS: Primary neuroblastoma of the central nervous system with spontaneous extracranial metastasis. *J Neurosurg* 38: 26-231, 1973
- Horten BC, Rubinstein LJ: Primary cerebral neuroblastoma. A clinicopathological study of 35 cases. *Brain* 99: 735-756, 1976
- Louis DN, Swearinger B, Linggood RM, Dickersin GR, Kretschmar C, Bahn AK, Healey-Whyte ET: Central nervous system neurocytoma and neuroblastoma in adults-report of eight cases. *J Neurooncol* 9: 231-238, 1990
- Ojeda VJ, Jacobsen PF, Papadimitriou JM: Primary cerebral neuroblastoma. Case report with light microscopy, tissue culture, and electron microscopy study. *Pathology* 12: 269-279, 1980
- Poon TP, Mangiardi JR, Matoso I, Weitzner I Jr. : Third ventricular primary cerebral neuroblastoma. Electron-microscopic and immunohistochemical Study. *Surg Neurol* 30: 237-41, 1988
- Porter-Grenn LM, Silbergleit R, Stern HJ, Patel SC, Mehta B, Sanders WP: Intraventricular primary neuronal neoplasmas. CT, MR and angiographic findings. *J Comput Assist Tomogr* 15: 365-368, 1991
- Robey SS, Olson JL, Brem H, Epstein JI: Posterior fossa neuroblastoma occurring in an elderly man. *Human Pathol* 19: 365-367, 1988
- Rubinstein LJ: Embryonal central neuroepithelial tumors and their differentiating potential. A cytogenetic view of a complex neurooncological problem. *J Neurosurg* 62: 795-805, 1985
- Russel DS, Rubinstein LJ: Pathology of Tumors of the Nervous System. ed 5. Baltimore. Williams and Wilkins, 1989, pp 279-289
- Sakaki S, Mori Y, Motozaki T, Nakagawa K, Matsuoka K: A cerebral neuroblastoma with extracranial metastases. *Surg Neurol* 16: 53-59, 1981