**Primitive Neuroectodermal Tumor arising from the Thalamus of an Adult**

---Case Report---

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**Abstract**

Primitive neuroectodermal tumors are very rare, malignant tumors of the cerebrum of young individuals, predominantly composed of undifferentiated cells, with differentiation along either neuronal or glial lines. Primary cystic tumors of the thalamus are also very rare and have been reported only in children. The case described here is the first report of a cystic tumor arising from the thalamus of an adult and containing pathologic features of a primitive neuroectodermal tumor. According to the literature, and in our clinical experience as well, primitive neuroectodermal tumors tend to diffusely disseminate into the subarachnoid space, which presents several diagnostic and therapeutic problems.

**Key words:** adult, primitive neuroectodermal tumor, thalamus, therapy

**Introduction**

Recently, reports concerning primitive neuroectodermal tumor (PNET) have increased, in both the clinical and pathologic literature. Since the first description of the clinical course and pathology of PNET by Hart and Earle, several articles about these tumors have been published. They are characterized as malignant tumors of the cerebrum of young individuals, predominantly composed of undifferentiated cells, with differentiation along either neuronal or glial lines.

Primary tumors of the thalamus are also relatively rare, accounting for about 1% of all cerebral tumors, and they present several diagnostic and therapeutic problems. Cystic thalamic tumors have been reported only in children. In this paper we will describe the first reported adult case of a cystic thalamic tumor having pathologic features of PNET and discuss some of the clinico-pathologic problems we encountered.

**Case Report**

A 31-year-old male presented to our clinic with headaches of 2 months' duration. He was slightly disoriented and had mild left hemiparesis and hypesthesia and severe papilledema. Computerized tomography (CT) revealed a cystic, high-density mass in the right thalamus and bilaterally dilated lateral ventricles (Fig. 1). On January 16, 1982, a bilateral ventriculo-peritoneal shunt was performed and an Ommaya reservoir was introduced into the cyst. Approximately 5 ml of fluid, having the consistency of tomato juice, was removed. Histologically, only cell debris was detectable. The patient received radiation therapy (total dose, 6,000 rads), following which Neocarzinostatin (NCS), a proteinaceous anticancer antibiotic, was injected through the Ommaya reservoir into the cyst (total dose, 2,700 μg). The thalamic cyst decreased in size (Fig. 2), but clinically the patient steadily declined, and mental confusion developed. In January of 1983 he developed urinary incontinence. A CT scan showed subarachnoid enhancement, indicating tumor dissemination (Fig. 3). The patient died on February 11, 1983, 15 months after the onset of illness. The
autopsy revealed extensive metastasis within the central nervous system, and significant pathologic findings were restricted to the central nervous system.

**Pathology:** The primary thalamic lesion was gray in color and had small foci of obvious necrosis and hemorrhage. The tumor was well demarcated from the surrounding brain tissue. There were numerous metastatic gray nodules on the surfaces of the cerebrum, brain stem, and cerebellum, extending into the spinal subarachnoid space.

Microscopically, the central portion of the primary lesion was necrotic, with degenerative tumor cells and hyalinized vessels that resulted from radiation and chemotherapy administration into the tumor cyst. In the region surrounding the central necrosis, connective tissue had proliferated and formed septae between clusters of highly cellular tumor cells that showed a tendency to differentiate to astrocytes (Fig. 4). There were scattered calcifications within the necrotic lesion. In the metastatic region of the right caudate nucleus, the tumor was composed of abundant neoplastic cells that were very primitive in appearance. These cells were small and round- or oval-shaped, with dense, hyperchromatic, irregular nuclei and scanty cytoplasm. Bizarre giant cells and mitotic cells were sparsely intermingled. The majority of these tumor cells were undifferentiated and did not react characteristically to any stains (phosphotungstic acid hematoxylin [PTAH], Masson's trichrome, Bodian's, and immunoperoxidase stains for glial fibrillary acidic protein [GFAP] and neuron-specific enolase). However, a small number of tumor cells had differentiated to astrocytes (Fig. 5) and oligodendroglial cells (Fig. 6). Delicate fibrillary structures positive to PTAH and GFAP stains were evidently astrocytic differentiation products. Metastatic nodules contained foci of tumor cells in the process of differentiating to ependymal cells (Fig. 7). A few large tumor cells apparently had differentiated to neuronal cells. These bipolar cells had abundant cytoplasm with long processes and nuclei containing a prominent nucleolus. These processes were partly argentaffin-positive with Bodian impregnation (Fig. 8).

![Fig. 1](image1.png) Precontrast CT scan revealed a high-density cystic mass with calcification in the right thalamic region.

![Fig. 2](image2.png) Precontrast CT scan after radiation therapy and chemotherapy revealed that the mass had decreased in size. The effect of the mass on surrounding brain tissue had disappeared.

![Fig. 3](image3.png) Enhanced CT scan revealed diffuse enhancement in the subarachnoid space.

![Fig. 4](image4.png) Abundant connective tissue surrounding clusters of tumor cells. Masson's trichrome stain, × 50.
Discussion

The cystic tumor that arose in the thalamus of a male adult showed features consistent with those of a typical PNET. In 1973, Hart and Earle first outlined the concept that the cell responsible for PNET is the primitive, multipotential cell of the cerebrum. These tumor cells are considered to have some similarities to the cells of the developing fetal cortical plate. There have already been 59 cases of PNET reported, with an average age at diagnosis of 5.6 years. There have been only 5 cases reported of patients over 15 years old, including one adult male 57 years of age. Our patient was 31 years old and his case can thus be regarded as very rare in terms of age.

PNET occurs most often in the cerebral hemisphere and occasionally in the spinal cord. Macroscopically the tumor is well demarcated, is liable to form a cyst, and sometimes is accompanied by hemorrhage. Histologically, it is primarily composed of round- or oval-shaped cells with dense, hyperchromatic nuclei and scanty cytoplasm and characteristically contains foci of differentiation along glial and neuronal lines. The primary lesion in our patient showed degenerative necrosis because of the effects of radiation and administration of an antineoplastic drug into the tumor cyst. The central region of the primary lesion was necrotic and had been replaced by abundant connective tissue and foci of calcification.

In support of a neuroectodermal origin for PNET, Roessmann et al., using antibodies against a neurofilament polypeptide and glial acidic protein, immunohistochemically revealed neuronal and glial differentiation. Markesbery et al. pointed out ultrastructural evidence suggesting that PNET differentiates into neuronal, ependymal, and astrocytic elements. Our case showed a focus of cells that had differentiated into astrocytes, oligodendroglial cells, and ependymal cells; neuronal cells were found in distant metastatic areas.
The contrast CT scan had revealed subarachnoid enhancement, and the autopsy disclosed dissemination extending into the spinal subarachnoid space. Significant autopsy findings were restricted entirely to the central nervous system. Only 13 of the 59 cases reported in the literature were subjected to autopsy, and 12 of the 13 cases had disseminated metastases in the subarachnoid space along the cerebrospinal fluid pathway.\textsuperscript{2,3,6,8} Two cases involved extraneural metastases.\textsuperscript{3,6,8}

PNET is characterized by a fulminating clinical course. All of the previously reported patients had short post-diagnostic survival periods. Among children, survival times were 7.8 months, 7 months, and 18 months, according to Kosnik et al.,\textsuperscript{6} Parker et al.,\textsuperscript{10} and Markesbery et al.,\textsuperscript{31} respectively. The adult patient reported by Bellis et al.,\textsuperscript{3} survived for about 7 months, and our patient lived for 15 months.

Primary tumors of the thalamus are relatively rare and present several diagnostic and therapeutic problems. Glioma occurring in the thalamus represents only about 1\% of all cerebral tumors.\textsuperscript{9} In the literature,\textsuperscript{13} 56\% of 296 reported cases of thalamic tumor were diagnosed by autopsy or at operation; 52\% were diagnosed as glioblastoma multiforme or malignant astrocytoma, and 22\% as low-grade astrocytoma. Only 8 (2.7\%) of the thalamic tumors were cystic, and most of these cystic tumors were reportedly benign astrocytomas in children.\textsuperscript{5,13}

PNET tends to form cysts.\textsuperscript{13} Our research indicates that our case was the first in which a PNET occurred as a cystic thalamic tumor in an adult.

Because of their location, many thalamic tumors are difficult to verify histologically and problematic to treat.\textsuperscript{13} We administered NCS, a proteinaceous anticancer antibiotic, into the cyst through an Omaya reservoir, in conjunction with local radiation therapy. Follow-up CT scans revealed reductions in the tumor size and its mass effect. Kosnik et al.,\textsuperscript{6} have treated PNET with local radiation of 4,000 to 6,000 rads combined with multidrug chemotherapy (methotrexate, vincristine, BCNU, and prednisone). However, because of diffuse tumor dissemination into the subarachnoid space, the results were very poor.

Many of the clinical manifestations of PNET are similar to those of cerebellar medulloblastoma. Histological similarities have also been pointed out, and some have said that PNET is, in effect, cerebellar medulloblastoma.\textsuperscript{1,5,12} It is known that, like PNET, medulloblastoma has a potential for differentiation along several neuroepithelial cell lines, and it can be postulated that PNET and medulloblastoma arise from primitive cerebral germinal cells and from primitive germinal cells of the cerebellar external granular layer, respectively.\textsuperscript{12} However, medulloblastoma has a lower potential for differentiation than does PNET. Both diffusely disseminate into the subarachnoid space,\textsuperscript{9} and preventing such dissemination is important in the treatment of these tumors. Therefore, the therapeutic protocol for both medulloblastoma and PNET should include surgery, radiation of the entire neuroaxis, and chemotherapy.

The new proteinaceous anticancer antibiotic NCS, which we used, also acts as an immunopotentiator, eliciting macrophage accumulation,\textsuperscript{7} and histological study of our patient's tumor showed infiltration by many macrophages in the perivascular region of the tumor. Both intracystic and intrathecal administration of NCS may become the treatment of choice for subarachnoid dissemination of this tumor.

References


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