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# Symptomatic Subependymoma

## — A Case Report —

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***Subependymoma is a rare, slow-growing, benign noninvasive tumor of the central nervous system that may be located in the fourth ventricle, the septum pellucidum, the third and the lateral ventricles, the aqueduct, and the proximal spinal cord. Symptoms, if any, usually result either from direct compression of the brain stem or from acute hydrocephalus due to occlusion of the foramen of Monro or aqueduct of Sylvius. In this report, we describe a case of subependymoma of the lateral ventricle with headache in a young female patient. This is the first reported case subependymoma in Korea that was documented along with Magnetic resonance image.***

**Key words:** *subependymoma, lateral ventricle, MR image*

## INTRODUCTION

**Subependymoma** is a rare, benign neoplasm originating most frequently from the subependymal region of the fourth ventricle, and is considered to be benign and slow-growing tumor, with relatively sharp demarcation from the adjacent brain tissue (Clarenbach et al., 1979). It was first reported by Scheinker (1945). Since then various nomenclatures were introduced; subependymoma (Scheinker, 1945), subependymal astrocytoma (French and Bucy, 1948) or subependymal glomerate astrocytoma (Boykin et al., 1954; Godwin, 1959), subependymal mixed glioma (Chason, 1956). The majority of subpendymomas are small, asymptomatic and found incidentally at autopsy often in elderly men (Scheithauer, 1978). Scheithauer (1978) found that the mean age at the time of diagnosis of patients with symptom-producing tumors (39 years) is lower than that of patients without symptoms (59 years). More than 75% of these tumors occurin the fourth ventricle or its recess (Hehman et al., 1968). In this report, we report a symptomatic subependymoma arising in the left lateral ventricle in a 26-year-old female.

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## CASE REPORT

This 26-year-old female was admitted due to headache for 14 months. The headache occurred especially left occipital area and paroxysmal in nature. She suffered from this headache once or twice per one to months. And also she suffered from nausea and vomiting. On the admission, the mentality was clear and alert. The orientation and verbal communication were intact. The extraocular muscle movement showed full range of movement and there was no facial palsy. And there were no evidence of pathologic reflexes. Other neurologic examinations were within normal limits. A precontrast computerized tomograph demonstrated isodense mass density with multiple, small low densities at the body of left lateral ventricle and mild contrast enhancement on postcontrast scan. Magnetic resonance imaging (MRI) revealed hyposignal intensity mass (relative to normal white matter) with multiple small high signal intensities at the body of the left lateral ventricle on T1 weighted (short TR/short TE) image, and hyperintense signal on proton density (long TR/short TE), and more hyperintense signal on T2 weighted (long TR/long TE) image (Fig. 1 and 2). On operation, the tumor was

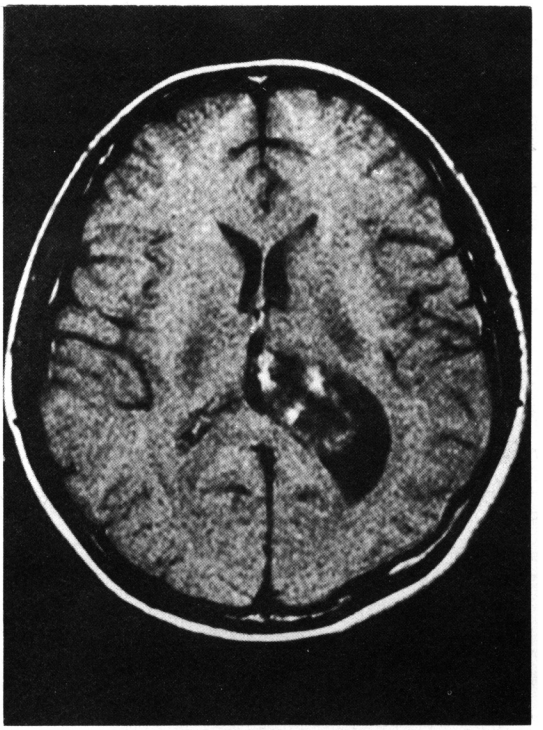

**Fig. 1.** T1-weighted image reveals hypointense signal intensity mass with multiple small high singal intensities at body of the left lateral ventricle.

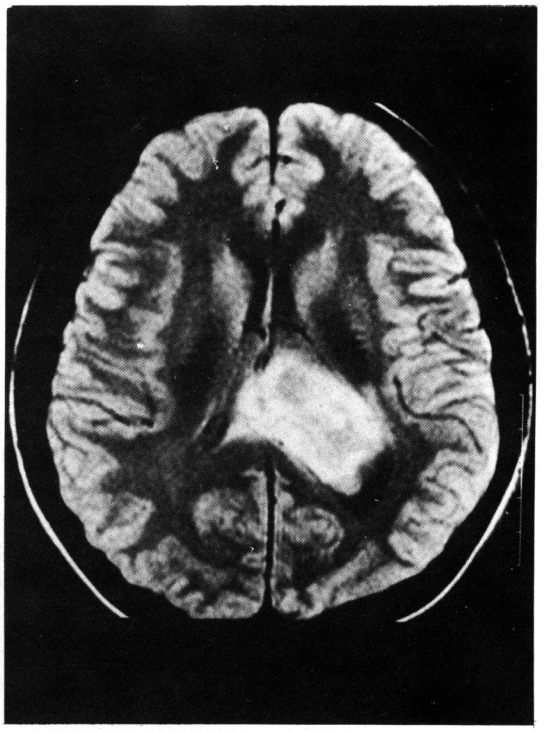

**Fig. 2.** Proton density image shows hyperintense signal mass with dilatation of body of the left lateral ventricle.

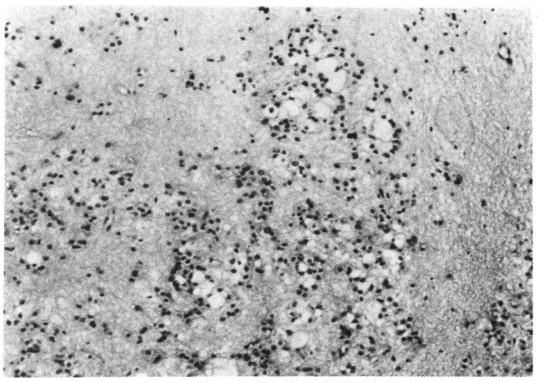

**Fig. 3.** Photomicrograph of the tumor shows clusters of small rounded cells in fibrillary matrix (H-E, ×200).

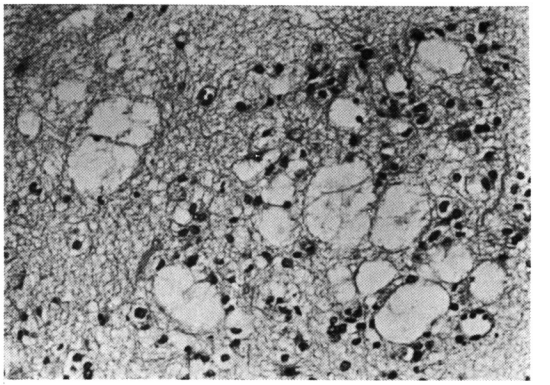

**Fig. 4.** Light micrograph of the tumor reveals microcystic architecture of a highly fibrillated area (H-E, ×400).

a firm, well delineated white to grayish avascular mass. Sharp demarcation from the surrounding normal tissue and attachment to the ventricular wall by a narrow pedicle allowed complete tumor removal. She was well after six months postoperative without evidence of recurrence.

## PATHOLOGIC FINDINGS

The resected specimen consisted of gray white solid tumor tissue about 2 cc. After formalin fixation, light microscopic examination revealed unencapsulated hypocellular neoplasm composed of nests of small glial cells. This tumor was separated by broad

of neuroglial fibrils, which imparted a low-power lobularity. The fibrils within and about the cell nests showed positive staining reaction of glial fibrillary acidic protein (GFAP). This GFAP staining reaction was stronger and much intense at the area of less cellular area. This area revealed astrocytic cells without cytoplasmic vacuoles. In area, where microcystic architecture were prominent, the GFAP staining reaction was less intense but positive reaction could be demonstrated. The cells within the island were round, oval or piriform. They contained a prominent vesicular nucleus with a few scattered clumps of chromatin. With the phosphotungstic acid hematoxylin stain some cells did not contain intracytoplasmic granules while other cells were vacuolated. In areas, there were numerous microcystic architectures and perivascular pseudorosettes (Fig. 3 and 4). No mitoses and no giant cells were seen in the tumor cells. There were no proliferative changes or thrombi in any of the blood vessels and tumor cell necrosis.

## DISCUSSION

Subependymoma is tumors of mixed astrocytic and ependymal constituency, in relatively equal proportion (Fu et al., 1974). This subependymoma has been recognized as a distinctive tumor characterized by its intraventricular location and frequent multiplicity, its clear demarcation and lobulation, and its slow-growing and noninvasive behavior (Scheinker, 1945; Boykin et al., 1954; Chason, 1956; Lobato et al., 1980; Ho, 1983). The great majority of subependymomas are found incidentally at autopsy in the fourth ventricle of elderly men (Gandolfi et al., 1981).

The production of symptoms was dependent upon the location of the subependymomas; thus, all tumors involving the septum pellucidum, the foramen of Monro, the aqueduct, or the spinal cord were symptomatic. Usually symptomatic tumors are large, the majority measuring 5cm in their greatest dimension, and are uniformly associated with either localized or generalized hydrocephalus (Scheithauer, 1978). Symptoms were relatively more often caused by supratentorial lesions; 66% of reviewed cases were symptomatic compared to 36% of patients with tumors of the fourth ventricle (Scheithauer, 1978). The symptoms; such as headache, altered consciousness, nausea and vomiting were of little localizing value, although some correlations between other symptoms and tumor site existed. Paresis was most commonly associated with supratentorial tumors, psychiatric and memory disorders with lesions of the septum pellucidum, (French and Bucy, 1948) and the floor of the fourth ventricle and visual disturbances and cranial nerve abnormalities with neoplasms located in the fourth ventricle (Scheithauer, 1978; Gandolfi et al., 1981). Rarely subependymoma presented subarachnoid hemorrhage (Changaris et al., 1981). The symptomatic period was considerably longer in patients with a pure subependymoma (average 38 months, range 2 months to 11 years) than in those with tumors of the mixed subependymoma-ependymoma type (average 7 months, range 2 weeks to 12 months) (Scheithauer, 1978). According to Scheithauer (1978), the mean age of 43 symptomatic patients, of whom 72% were male, was 39 years. 71% of the cases occurred in the fourth to sixth decades. Patients with lateral ventricle lesions averaged 51 years of age. Seven symptomatic cases presented in the first decade; all had transitional tumors of the combined ependymoma-subependymoma type. The mean age of 47 patients with asymptomatic tumors was 59 years. This age shift was most apparent in the seventh to the ninth decades, where all but two of 22 patients were asymptomatic. Male patients were more numerous (87%) than in the symptomatic group of patients.

The location of all 116 tumors found by Scheithauer (1978), 27 were supratentorial, 71 were infratentorial and two were located in the cervico-thoracic region. Among the supratentorial tumors, those originating in the walls of the lateral ventricles exceeded tumors of the septum pellucidum by a ratio of 4:1. Most of these tumors occur in the fourth ventricle (Chason, 1956; Godwin, 1959; Hehman, 1968; Russell and Rubinstein, 1977; Scheithauer, 1978; Lobato, 1986) but they may also arise in the septum pellucidum (French and Bucy, 1948; Hehman, 1968; Russell and Rubinstein, 1977; Scheithauer, 1978), the walls of the third (Lobato et al., 1986) and lateral ventricles (Russell and Rubinstein, 1977; Scheithauer, 1978), the aqueduct (Scheithauer, 1978) and the proximal spinal cord (Boykin et al., 1954).

Computerized tomographic characteristics of the subependymoma are well limited tumors, with attenuation values close to those of the surrounding brain parenchyma and showing no enhancement after contrast medium administration (Vaquero et al., 1983). But Lobato et al. reported that in precontrast studies the tumor was isodense with the brain in 18 cases (85%), lucent in 2 (9.5%), and hyperdense in 1 (4.7%) (Lobato et al., 1986). And Lobato et al. also reported that after intravenous contrast injection, 16 (84%) of 19 tumors showed discrete enhancement, either homogeneous or nonhomogeneous. Ring-like en-

hancement occurred in 1 case (Lobato et al., 1986). But others stated that subependymoma showed minimal or no enhancement on the postcontrast CT study (Swartz et al., 1982; Vaquero et al., 1983). On magnetic resonance image (MRI) scan, Spoto et al. (1990) noted that solid ependymoma and subependymomas demonstrated iso-to hypointense signal on T1 weighted image and hyperintense signal on proton density and T2 weighted images. Foci of signal heterogeneity within solid neoplasm represented methemoglobin, hemosiderin, necrosis and encased native vessels or tumor vascularity (Spoto et al., 1990). And also they described that the subependymomas could not be distinguished from ependymomas by signgal-intensity differences, consistency or location. The multiplanar imaging capability of MRI was valuable in assessing the location and routes of extension of ependymomas and subependymomas. Compared to Spoto et al. (1990), our case revealed hypointense signal on T1 weighted image and hyperintense singal on porton density. And also it revealed foci of scattered small high signal heterogeneity within isosignal mass, which is thought to be hemorrhage or tumor necrosis on radiologic view points.

The histogenesis of subependymoma is still uncertain. The subependymal cell plate is composed of three layers. First, the ventricle is lined by a continous layer of ependymal cells, beneath which is a layer of glial fibers and still deeper layer of subependymal glial cells. There is no basement membrane separating the layers of ependyma and subependymal glial cells, but long processes of ependymal cells may project from their basalpoles into the underlying neuropiles (Hehman et al., 1968, Fu et al., 1974). During embryonic development, the subependymal layer contains undifferentiated, mitotically active cells, which play an important role in the formation of the cerebral cortex (Fu et al., 1974). These undifferentiated cells may persist into adult life and retain their mitotic proliferative activity (Rubinstein, 1972; Fu et al., 1974). So, these tumors seemed to originate from clusters of small fibrillary astrocytes (layer three) found in the normal subependymal cell plate. Thus Boykin et al. (1954) referred to them as subependymal glomerate astrocytomas. And subependymal glial cells may be a major cellular element in the neoplastic and reactive conditions of the ventricular wall (Boykin et al., 1954; Rubinstein, 1972). Rubinstein and Russell and Rubinstein considered subependymoma to be a variant of ependymoma because of its frequent occurrence within a typical ependymoma, and because of the similarity of its cells to ependymal cells, with blephaloplasts seen on PTAH stain (Rubinstein, 1972; Russell and Rubinstein, 1977). Also Zulch and Wechsler (1968) regard subependymoma as an ependymoma in a state of pressure atrophy and sclerosis. Minor differences do exist between the subependymoma and ependymoma, such as: 1) the presence of more frequent and extensive cytoplasmic degeneration within the subependymomatous area 2) the presence of more astrocytes in the subependymoma 3) the fact that the ependymal cells in the subependymoma contain much more abundant glial filaments. So they consider that subependymoma is more likely to be a variant of ependymoma, rather than a pure astrocytoma (Zulch and Wechsler, 1968). But Duffel et al. (1963) who described the astrocytic nature of subependymoma in an electron microscopic study, detected no differences between astrocytoma and subependymoma. Fu et al. (1974) and Azzarelli et al. (1977) reported that, using the recent elelctron microscopic and tissue cluture, studies support the original interpretation of Scheinker (1945). That is, subependymomas are of mixed composition and originate from the pluripotential cells of the subependymal layer (Scheinker, 1945; Zulch and Wechsler 1968; Rubinstein, 1972; Fu et al., 1974; Russell and Rubinstein, 1977; Azzarelli et al., 1977). In recent years, results of tissue culture, ultrastructural and immunohistochemical studies have demonstrated that subependymoma is composed of ependymal cells, astrocytes, and transitional cells (Fu et al., 1974; Azzarelli, 1977) and that its cytoarchitecture is like that in human subependymal layer (Fu et al., 1974; Azzarelli, 1977).

In this report, we discussed a case of symptomatic subependymoma arising from the left lateral ventricle with general clinicopathologic features and histogenesis of the tumor.

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## REFERENCES

Azzarelli B, Rekate HL, Roessmann U: *Subependymoma. A Case report with ultrastructural study. Acta Neuropathol 40:279-282, 1977.*

Boykin FC, Cowen D, Iannucci CAJ, Wolf AJ: *Subependymal glomerate astrocytoma. J Neuropath Exp Neurol 13:30-49, 1954.*

Changaris DG, Powers JM, Perot PL Jr. Hungerford D, Neal GB: *Subependymoma presenting as subarachnoid*

*hemorrhage. J Neurosurg 55:643, 1981.*

Chason JL: *Subependymal mixed gliomas. J Neuropath Exp Neurol 15:461-470, 1956.*

Clarenbach P, Kleihuse P, Metzel E, Dichgans J: *Simultaneous clinical manifestation of subependymoma of the fourth ventricle in identical twins. J Neurosurg 50:655-659, 1979*

Duffel D, Farber L, Chou S, Hartman JF, Nelson E: *Electron microscopic observations on astrocytomas. Am J Pathol 43:539-554, 1963.*

French JD, Bucy PC: *Tumors of the septum pellucidum. J Neurosurg 5:433-449, 1948.*

Fu YS, Chen ATL, Kay S, Young H: *Is subependymoma (subependymal glomerate astrocytoma) an astrocytoma or ependymoma? A comparative ultrastructural and tissue culture study. Cancer 34:1992-2008, 1974.*

Godwin JT: *Subependymal glomerate astrocytoma: report of 2 cases. J Neurosurg 16:385-389, 1959.*

Gondolfi A, Brizzi RE, Tedeschi F, Paini P, Bassi P: *Symptomatic subependymoma of the fourth ventricle. J Neurosurg 55:841-844, 1981.*

Hehman K, Norrell H, Howieson J: *Subependymomas of the septum pellucidum. Report of two cases. J Neurosurg 29:644, 1968.*

Ho KL: *Concurrence of subependymoma and heterotopic leptomeningeal neuroglial tissue. Arch Pathol Lab Med 107: 136-140, 1983.*

Lobato RD, Cabello A, Carmena JJ, de la Fuente M, Muñoz MJ: *Subependymoma of the lateral ventricle. Surg Neurol 15:144-147, 1980.*

Lobato RD, Sarabia M, Castro S, Esparza J, Cordobés F, Portillo JM, Rivas JJ: *Symptomatic subependymoma; Report of four new cases studied with computed tomography and review of the literature. Neurosurg 19:594-598, 1986.*

Rubinstein LJ: *Tumors of the central nervous system. Atlas of tumor pathology, 2nd ser. fasc 6. Washington, D.C., Armed Forces Institute of Pathology, pp 168-118, 1972*

Russell DS, Rubinstein LJ: *Pathology of tumors of the nervous system. London Arnold, 4th ed. pp212-213, 1977.*

Scheinker IM: *Subependymoma: A newly recognized tumor of subependymal deviation. J Neurosurg 2:232-240, 1945.*

Scheithauer BW: *Symptomatic subependymoma. Report of 21 cases with review of the literature. J Neurosurg 49:689-696, 1978.*

Spoto GP, Press GA, Hesselink JR, Solomon M: *Intracranial ependymoma and subependymoma: MR manifestations. AJR 154:837-845, 1990.*

Swartz JD, Zimmerman RA, Bilaniuk LT: *Computed tomography of intracranial ependymomas. Radiology 143:97-101, 1982.*

Vaquero J. Cabezudo JM, Nombela L: CT *scan in subependymomas. Br J Radiol 56:425-427, 1983.*

Zulch KJ, Wechsler W: *Pathology and classification of gliomas. Prog Neurol Surg 2:1-84, 1968*