Journal of Korean Medical Science
Vol. 11, No. 4, 369-372 Aug. 1996

Secretory Meningioma

- A Case Report with Histopathological, Immunohistochemical and Ultrastructural Analysis -

Hwa Sook Jeong, M.D., Geon Kook Lee, M.D.

Department of Pathology, Chungbuk National University, College of medicine, Cheongju, Korea

Secretory meningioma have been described as a distinct variant of meningioma based on their histologic, immunohistochemical and ultrastructural features of epithelial and secretory differentiation of meningothelial cells with accumulation of secretory material in the form of hyaline inclusion. Secretory meningioma is also a benign tumor having similar biological behaviour to that of typical meningiomas: hence, it is important for it to be recognized and diagnosed correctly to avoid unnecessary radiation and chemotherapy. Here we present a case of secretory meningioma with typical morphologic features. The patient was a 56-year-old woman with bilateral visual disturbance. A well-circumscribed mass was present in the left frontal lobe of cerebrum with surrounding edema. The tumor was composed of whorls of meningothelial cells and abundant intra- and extracellular eosinophilic hyaline inclusions which showed immunoreactivity for epithelial membrane antigen(EMA) and carcinoembryonic antigen(CEA). Ultrastructural features also supported epithelial and secretory differentiation of tumor cells.

Key Words : *Secretory meningioma, Hyaline inclusion, EMA, CEA*

INTRODUCTION

Secretory meningioma was first named by Alguacil-Garcia et al.(Alguacil-Garcia et al., 1986) and published in a new WHO classification of brain tumors(Kleihues et al., 1993). Meningiomas generally exhibit a wide range of histologic patterns. The broad spectrum of differentiation reflect the pluripotency of the arachnoid cap cells, which are the presumed cell of origin for meningiomas. Among these is a type of meningioma with intracytoplasmic inclusion, which was described as "hyaline inclusion"(Cushing and Eisenhardt, 1938) and "Pseudopsammoma body"(Kepes, 1961). This particular subtype of meningioma, having characteristic hyaline inclusion, which has been termed the secretory variant, shows overt epithelial and secretory differentiation of the meningothelial cell. It is reported that this tumor is frequently associated with severe cerebral edema and a rarely increased serum carcinoembryonic antigen(Alguacil-Garcia et al., 1986 ; Louis et al., 1991). This variety of meningioma is rare and can be mistaken for primary or secondary intracranial tumors. We present a case of secretory meningioma with characteristic light microscopic, immunohistochemical and ultrastructural examination.

Address for correspondence : *Geon Kook Lee, M.D., Department of Pathology, Chungbuk National University College of Medicine, San 48, Gaesin-dong, Cheongju-si, Chungbuk 361-763, Korea.*
Tel : (0431) 69-6276, FAX : (0431) 69-6269

• This work is partly supported by Chungbuk National University Hospital Research Grant(1995).

CASE REPORT

A 56-year-old woman presented with visual disturbance for two months. Fundoscopic examination

revealed bilateral papilledema. She was transferred to Chungbuk National University Hospital for further evaluation. Past medical and family history was not contributory. Brain CT scan and magnetic resonance imaging showed a well defined mass in left frontal lobe which measured 3.5 cm in the largest diameter, and was contrast-enhanced, attached to the inner table of the skull, and assocaited with marked edema of surrounding cerebral cortex(Fig. 1). The serum level of carcinoembryonic antigen(CEA) was not checked. No other tumor-associated symptoms and signs were noted and all other laboratory investigations were within normal limits. Craniotomy and complete removal of the mass were performed.

The excised mass measured 3.5×3.5×2 cm and a flap of meninx was attached to a portion of the mass. The external surface was smooth, and the cut surface was gray white, lobulated and solid. Neither necrosis nor hemorrhage was observed. The tumor was composed of whorls of meningothelial cells virtually identical to those observed in conventional meningothelial meningiomas. Characteristically, there were numerous eosinophilic hyaline inclusions in both the cytoplasm of tumor cells and the small lumina lined by flattened tumor cells. The inclusions varied in shape, size, and number in parts. The larger inclusions, which appeared to be located in the extracellular space and surrounded by a cluster of meningothelial cells, were also present. The inclusion-containing cells formed sheets or nests. The nuclei were eccentric with abundant cytoplasm. There were no mitosis, necrosis or nuclear atypism(Fig. 2). The eosinophilic hyaline inclusions and tumor cells were strongly Periodic acid-Schiff positive and diastase resistant, stained yellow with van Gieson stain and blue or red-brown with Masson's trichrome stain. A remarkable proliferation and crowding of small dark pericytic cells were noted in small branching vessels and occasional medium-sized ones(Fig. 3). True psammoma bodies were seldom seen.

Most of the meningothelial cells showed evidence of epithelial differentiation. All tumor cells with hyaline inclusions and the inclusions stained strongly positive for EMA and CEA, and weakly positive for cytokeratin and α-1-antichymotrypsin. Only the tumor cells without hyaline inclusion were positive for vimentin. All tumor cells showed no immunoreactivity for S-100 protein, glial fibrillary acidic protein(GFAP), α-fetoprotein, lysozyme, neuron-specific enolase(NSE) and human chorionic gonadotrophin(hCG)(Fig. 4). Ultrastructurally, the tumor cells showed the characteristics of meningothelial cells, including conspicuous interdigitations, well developed desmosomes with scattered whorls of cytoplasmic tonofibril and variable amounts of intermediate filaments. Other intracellular organelles such as scattered profiles of rough endoplasmic reticulum, mitochondria, and clusters of polyribosomes were also observed.

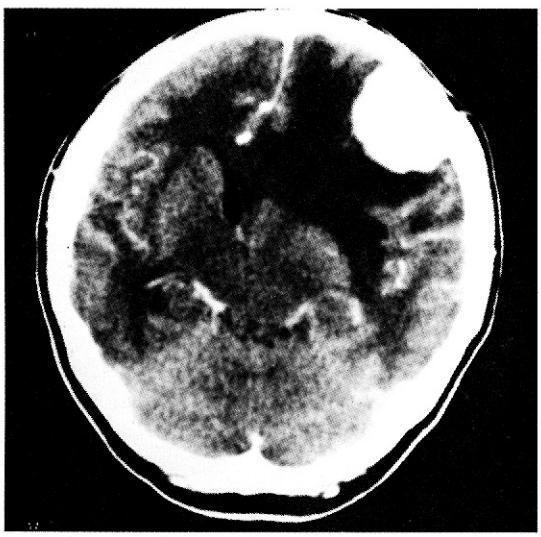

Fig. 1. Brain CT scan. A well-circumscribed mass is present in the left frontal lobe and is attached to the inner table of the skull. Marked edema of surrounding cerebral tissue is associated.

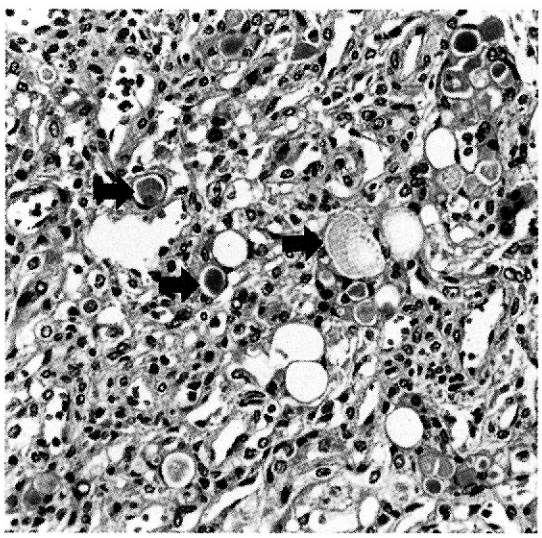

Fig. 2. Many sheets and nests of meningothelial cells possessed abundant rounded eosinophilic hyaline inclusions(arrow).

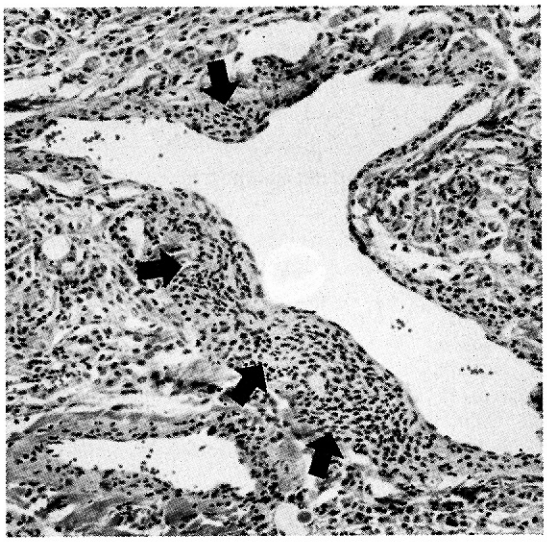

Fig. 3. Proliferation of pericytic(arrow) cells is prominent in and about the wall of small blood vessels.

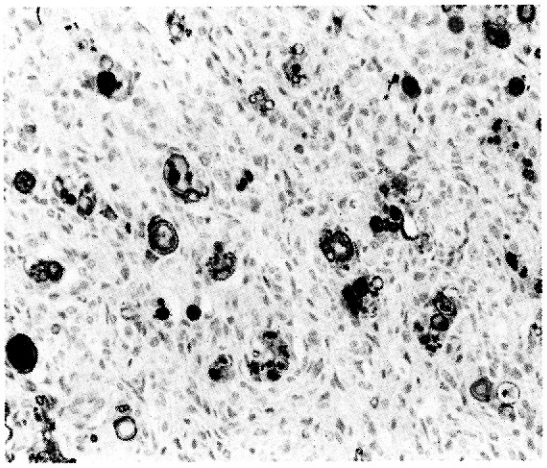

Fig. 4. Only meningothelial cells around hyaline inclusion and hyaline inclusions stained strongly positive for CEA.

Some nuclei of the tumor cells exhibited empty vacuoles, while in some cells cytoplasmic material was incarcerated into the nucleus. The inclusions varied in size from 2 to 15 μm and were either single or multiple. The inclusions varied in shape and density from cell to cell and in parts. Some of the inclusions were composed of granular material containing the more electron-dense core and scattered clusters of small vacuoles, which were located peripherally and showed a honeycombed appearance. Numerous finger-shaped projections resembling numerous microvilli were present in the inner luminal membranes(Fig. 5).

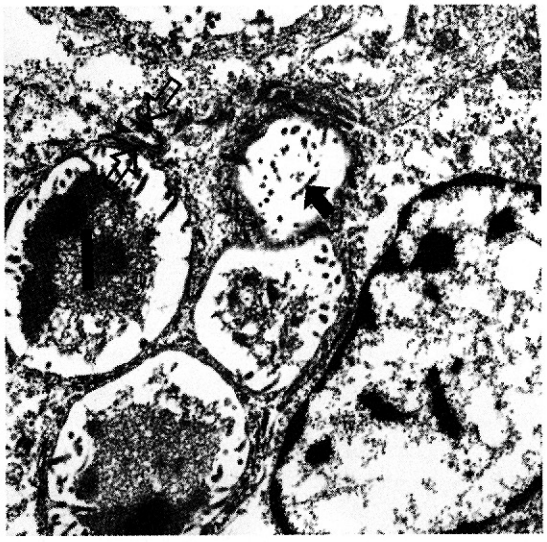

Fig. 5. Inclusions(I) are surrounded by luminal membrane showing numerous microvilli(arrow) and composed of finely granular material showing a more dense core with a cluster of small vacuoles. The tumor cells have numerous well-developed desmosomes(open arrow) and interdigitations.

DISCUSSION

Meningiomas are generally considered to be of mesenchymal origin arising from the arachnoid membrane, in particular from the arachnoid cap cells of the arachnoid granulations. Features indicative of epithelial differentiation in meningiomas have been well described in the literature(Font and Croxatto, 1980; Kock and Teglbjaerg, 1981; Budka, 1982). It is possible that meningiomas showing focal secretory differentiation with only occasional inclusions may occur. However, only those with abundant hyaline inclusions indicating a marked tendency to epithelial and secretory differentiation should be considered as secretory meningioma. Meningiomas with evidence of epithelial and secretory differentiation have been reported in 1.2-9.3% of cases, and the designation of these tumor as "secretory" variants has been made(Kepes, 1961; Font and Croxatto, 1980; Schelper et al., 1984; Alguacil-Garcia et al., 1986).

Hyaline inclusion of meningiomas showed a clear-cut staining pattern for secretory component similar to that of inclusion bodies in the metastatic carcinoma. The very same reactivity for secretory component, was re-

cently demonstrated in intracytoplasmic lumina and inclusion bodies of gastric(Syre et al, 1981) and mammary carcinoma cells(Syre and Sehn, 1981). Ultrastructural studies demonstrated intracellular or extracellular lumina with prominent microvilli surrounding hyaline inclusion both meningiomas and carcinomas(Kepes JJ, 1975 ; Font and Croxatto, 1980 ; Syre and Sehn, 1981). Also, light microscopically similar cytoplasmic hyaline inclusions have been reported in carcinomas of the breast, lung, colon and liver(Dekker and Krause, 1973 ; An et al., 1983). Although these tumor types are biologically very different, morphological and immunohistochemical features of intracellular hyaline bodies are that similar as to suggest a similar pathogenesis of these structures in both tumor types. The strongly positivity for CEA and EMA in cells forming intracellular lumina and duct-like structures support the epithelial secretory nature of these cells. The ultrastructural features also indicated that the inclusion-forming cells are secretory. The intra- and intercellular lumina lined by microvilli, accumulation of secretory material, tonofilaments, and desmosomes are all features usually associated with epithelial and secretory differentiation(Battifora H., 1975; An et al., 1983). Although we could not demonstrate immunoreactivity for secretory component in the present case, multiple evidences suggested that the hyaline inclusions of this case are of the same nature of that of the previously reported, and the ultrastructural feature of this case also supported epithelial secretory differentiation of the tumor cells. As the previously reported cases, prominent pericytic proliferation about or in small or medium-sized blood vessels was noted in this case(Alguacil-Garcia et al., 1986). However, its pathologic or clinical significance has not been emphasized.

Secretory meningioma has been known to be associated with more severe cerebral edema and elevated serum level of CEA(Alguacil-Garcia et al., 1986; Louis et al., 1991). In this case severe surrounding cerebral edema was noted but serum level of CEA was not assayed. However, the intense positive reaction for CEA in tissue sections would support the speculation that serum CEA might be elevated. Raised serum level of CEA is more common in metastatic than in primary intracranial tumors(Miyake et al., 1979).

The histologic features of secretory meningioma are characteristic. However, due to the rarity and unusual nature of this lesion, secretory meningioma can present diagnostic difficulties to the pathologist unfamiliar with its characteristic features. Because the biological and clinical behaviour are similar to other types of meningioma, it is important that it is recognized and diagnosed correctly to avoid unnecessary treatment.

REFERENCES

Alguacil-Garcia A, Pettigrew NM, Sima AAF. *Secretory meningioma : a distinct subtype of meningioma. Am J Surg Pathol 1986 ; 10 : 102-11.*

An T, Ghatak N, Kastner R, Kay S, Lee HM. *Hyaline globules and intracellular lumina in a hepatocellular carcinoma. Am J Clin Pathol 1983 ; 79 : 392-6.*

Battifora H. *Intracytoplasmic lumina in breast carcinoma. Arch Pathol Lab Med 1975 ; 99 : 614-7.*

Budka H. *Hyaline inclusions in meningiomas. Acta Neuropathol 1982 ; 56 : 294-8.*

Cushing H, Eisenhardt L. *The meningiomas : Their classification, regional behavior, life history and surgical end results. New York : Hafner Publishing Company, 1938 ; 175.*

Dekker A, Krause JR. *Hyaline globules in human neoplasmas. Arch Pathol Lab Med 1973 ; 95 : 178-81.*

Font RL, Croxatto JO. *Intracellular inclusions in meningothelial meningioma. J Neuropathol Exp Neurol 1980 ; 39 : 575-83.*

Kepes J. *Observations on the formation of psammoma bodies and pseudopsammoma bodies in meningiomas. J Neuropathol Exp Neurol 1961 ; 20 : 255-62.*

Kepes JJ. *The fine structure of hyaline inclusions in meningiomas. J Neuropathol Exp Neurol 1975 ; 34 : 282-9.*

Kleihues P, Burger PC, Scheithauer BW. *The new WHO classification of brain tumours. Brain Pathol 1993 ; 3 : 255-68.*

Kock KF, Teglbjaerg PS. *Meningiomas with a non-meningotheliomatous component. Acta Neuropathol 1981 ; 55 : 199-203.*

Louis DN, Hamilton AJ, Sobel RA, Ojemann RG. *Pseudopsammomatous meningioma with elevated serum carcinoembryonic antigen a true secretory meningioma. J Neurosurg 1991 ; 74 : 129-32.*

Miyake E, Yamashita M, Kitamura K, Ishigami F. *Carcinoembryonic antigen(CEA) levels in patients with brain tumours. Acta Neurochir 1979 ; 46 : 53-7.*

Schelper RL, Beck DW, Boarini DJ, Hart NM, Baumbach GL. *Proteins of hyaline inclusions in meningioma. J Neuropathol Exp Neurol 1984 ; 43 : 297.*

Syre G, Fellinger E, Krisch K. *Demonstration of secretory component and immunoglobulins within intracytoplasmic vacuoles in gastric cancer cells. Proc VIIIth Eur Congr Pathol, Helsinki, 1981 ; 61.*

Syre G, Sehn M. *Intracellular storage of Ig A and secretory component in carcinomas of the female breast. Virchows Arch A 1981 ; 393 : 315-20.*