Case Report

Secretory Meningioma with Elevated Serum Carcinoembryonic Antigen

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A 57-year old woman is diagnosed with a cavernous sinus meningioma, which is accompanied by an elevated serum carcinoembryonic antigen (CEA). The pathological findings revealed a secretory meningioma containing numerous pseudopsammoma bodies that tested strongly periodic acid-Schiff positive. Secretory meningioma is a rare histological variant that is characterized by a unique epithelial differentiation of meningothelial cells resulting in the production of hyaline inclusions. Although the increased preoperative serum CEA level is not a confirmative tool for secretory meningioma, it appears to be a useful marker for post-treatment follow-up or for detecting a tumor recurrence.

KEY WORDS : Brain tumor · Carcinoembryonic antigen · Pseudopsammoma body · Secretory meningioma Skull base.

Introduction

Meningiomas are histologically diverse, and there are at least 14 variants of this meningothelial tumor. Among them, secretory meningioma represents a rare subtype that is clinically, histologically, and immunohistochemically characteristic. Secretory meningioma is characterized by a unique intra- and extracellular eosinophilic hyaline inclu-sions[1-11]. Bright[10] gave the first description of these charac-teristic structures in 1831. However, the descriptive term "glassy hyaline inclusions" was introduced by Cushing and Eisenhardt[4] a century later. Following the publication of a report by Kepes in 1961, these inclusions were also referred to as "pseudopsammoma bodies". The term "secretory meningioma" was proposed by Alguacil-Garcia et al.[1] in 1986 after the unique secretory features of these meningiomas were established. Currently, secretory meningioma is believed to be a tumor as a result of an epithelial glandular differentiation of meningothelial cells[1,5-11]. We present a case of secretory meningioma at the skull base, which was accompanied by an elevation in the serum carcinoembryonic antigen (CEA) levels.

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Case Report

A 57 year-old female presented with a 4-month history of left facial paresthesia. The patient had previously been treated for hypertension. A neurological examination indicated that the left trigeminal nerve function was normal and the other results were unremarkable. The laboratory tests and systemic evaluations were also normal.

Magnetic resonance imaging (MRI) revealed a $3 \times 3.5 \times 3$ cm-sized, well-circumscribed mass at left parasellar area, which was isointense to the brain cortex on the T1-weighted images and irregularly hyperintense on the T2-weighted images. The tumor was homogeneously enhanced by contrast agent. The tumor originated from the cavernous sinus and extended to the lower pontine level along the clivus. The mass was compressing the brainstem and the left temporal lobe, and was associated with minimal edema in the adjacent temporal lobe. The left internal carotid artery was encased by this mass(Fig. 1). The left internal and external carotid angiograms demonstrated a tumor blush from the branches of the meningohypophyseal trunk, the deep temporal artery and the middle meningeal artery.

A left fronto-temporal craniotomy was performed under general anesthesia. A tumor capsule was exposed after retracting the frontal and temporal lobes. The tumor tissue was so friable that it could be easily aspirated by suction. Parts of the tumor at the posterior fossa and in the cavernous

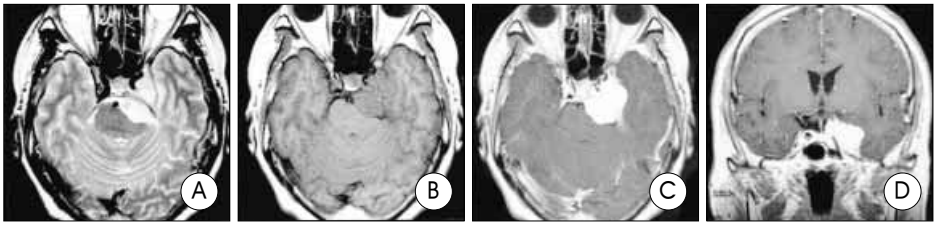

Fig. 1. Preoperative magnetic resonance images. A: T2-weighted axial image reveals a hyperintense mass at the left cavernous sinus. This mass is compressing the brainstem and the left temporal lobe. It is associated with a minimal edema in the adjacent temporal lobe. B: T1-weighted axial image reveals a mass that is isointense to the brain cortex. C, D: Gadolinium-enhanced, the T1-weighted axial and the coronal images demonstrate a well-circumscribed, homogeneous mass with intense enhancement. The tumor is encasing the left internal carotid artery.

sinus were left. Hematoxylin-eosin staining indicated several eosinophilic hyaline inclusions (pseudopsammoma bodies). Intracellular periodic acid-Schiff (PAS)-positive globules were identified on the PAS stain (Fig. 2). Immunohistochemical examinations revealed CEA expression.

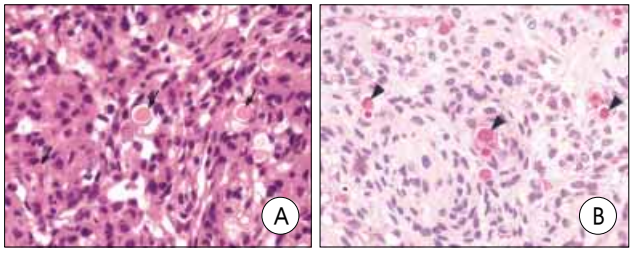

Fig. 2. Microphotographs of the secretory meningioma. A: Several eosinophilic hyaline inclusions (pseudopsammoma bodies) (arrows) are found (H & E, ×400). B: Intracellular periodic acid-Schiff-positive globules (arrow heads) are found (PAS, × 400).

The postoperative course was uneventful and the preoperative symptoms of facial paresthesia disappeared. Gamma Knife radiosurgery was performed for the residual tumor at the 8th day after surgery before the occurrence of the postoperative artifact. The serum CEA level was measured after confirming the pathological diagnosis, and it was found to be elevated to 4.63ng/ml (normal level; 0-3ng/ml) due to the residual tumor. The patient was examined with a periodic brain MRI and measurements of the serum CEA level, and no recurrence or any specific symptoms has been noted for approximately 27 months after the operation.

Discussion

Secretory meningiomas are a rare histological subtype of these benign intracranial tumors and represent approximately 3% of meningioma cases[1-3,5-11]. This tumor is characterized by a unique epithelial differentiation of meningothelial cells with the glandular lumina containing the PAS-positive secretory globules. Pseudopsammoma bodies, in contrast to the laminated psammoma bodies, neither become calcified nor contain reticulin or collagen fibers. An examination of the hyaline inclusions by electron microscopy revealed that they were housed in both the intracellular and intercellular lumina lined with microvilli[1,5-11]. Furthermore, the ultrastructural resemblance of the hyaline inclusion was observed with the inclusions described in cases of mammary, gastric, and hepatocellular carcinomas, and mesothelioma[1,5-7,9]. These observations suggest the secretory differentiation of the involved meningothelial cells. Other meningiomas can show focal secretory differentiation. However, if these find-ings are diffusely found in the whole area of the tumor tissue, it should be diagnosed as a secretory meningioma. Currently, it is widely accepted that secretory meningiomas develop as a result of an epithelial glandular differentiation of meningothelial cells. This unique epithelial features represent the broad spectrum of the differentiation properties found in meningiomas[1,5-11].

In a study of epithelium-derived tumors, antibodies to cytokeratins (KL1), CEA, and epithelial membrane antigen (EMA), as well as epithelial tumor antigens such as carbohydrate antigen(CA) 19-9 have been widely used. Therefore, the presence of these antigens in both hyaline inclusions and the cells harboring the hyaline inclusion has been interpreted as additional proof of the epithelial differentiation of secretory meningiomas[1,2,5-11].

Secretory meningiomas had been reported as a single case report until Probst-Cousin et al.[10] reported 31 cases. While the female-to-male ratio of usual meningiomas is 3:2, there was striking female predominance among their secretory meningioma cases, which was almost 9:1. The patients age ranged from 30 to 83 years, with a mean age of 59.2 years. Most of the tumors were located at the sphenoid ridge and on the frontal convexity. Secretory meningiomas are more often accompanied by a massive peritumoral edema than other meningiomas of a similar location or size. Eighty-four percent of tumors presented with a slight to marked peritumoral edema. The prognosis of this tumor is more favorable than other meningiomas and recurrences were not observed in their cases.

Brain edema is usually associated with malignant, aggressive, and fast-growing intraparenchymatous tumors. The reason for the higher incidence of severe brain edema in this extracerebral, generally benign and usually a slow-growing tumor, is still unclear. However, numerous explanatory hypotheses have been proposed[1,2,6,9,10]. The location of the tumor is regarded as a factor that is correlated with the production of edema, with both the sphenoid ridge and the frontal region being the areas principally involved. In those areas, the tumor mass can easily occlude major cerebral veins or the dural sinuses evoking venous stasis as well as secondary fluid extravasation into the interstitial brain space[10]. Several authors have observed an unusual pericytic proliferation in secretory meningiomas. They insisted that the increased proliferation of pericytes would impair the vascular integrity or cause a partial breakdown in the blood-brain barrier of the underlying brain[1,6]. The hydrodynamic theory suggests that the increased permeability of meningioma vessels allows the passage of plasma fluid and proteins from the intravascular compartment into the interstitial space of the tumor[10]. Components of the pseudopsammoma bodies have also been hypothesized as being a cause of cerebral edema formation[9]. However, there is no hypothesis that can explain the cause of the higher incidence of peritumoral edema in secretory meningioma. The peritumoral edema development is most likely multifactorial and further studies are needed to clarify this issue.

Secretory meningiomas are usually isointense on the T1-weighted images and hyperintense on the T2-weighted images. These MR signal characteristics may be correlated not only to the presence of moderate to abundant pseudopsammoma bodies, but also to a meningothelial growth pattern of this subtype[9].

Elevated serum CEA levels are frequently associated with a variety of epithelial malignancies and cerebral metastases. They are rarely elevated in primary cerebral tumors. However, several instances of a serum CEA elevation in association with meningioma have been reported, and many of them were the secretory subtype. Furthermore, several cases where the serum CEA levels returned to normal following a meningioma resection have been reported. Because the serum CEA level is elevated in other types of tumors, such as atypical meningioma, the preoperative serum CEA level is not a confirmative tool for secretory meningioma, but can be effective for follow-up after treatment[1,2,8-11].

Buhl et al.[3] insisted that, in female patients with frontally located suspected meningiomas and peritumoral edema, the preoperative evaluation should include measuring the serum CEA level.

In our case, a secretory meningioma was found at the cavernous sinus in a female patient. The peritumoral edema was not that severe because it developed at the skull base region. The histological examination revealed the characteri-stic, intracellular, PAS-positive pseudopsammoma bodies. The preoperative serum CEA level had not been checked and the postoperative serum CEA level was still high as a consequence of residual tumor in the cavernous sinus.

Conclusion

Secretory meningioma represents a rare subtype that is clinically, histologically, and immunohistochemically characteristic. The serum CEA level can be used as an additional marker in the follow-up examinations to rule out a possible recurrence of the tumor, and to evaluate the treatment outcome in addition to the magnetic resonance imaging follow-up.

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