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Immunohistochemical Examination of Meningioma

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Abstract Immunohistochemical characteristics were examined in 76 cases of primary meningioma, 10 cases of recurrent meningioma, 3 cases of hemangiopericytoma and 2 cases of meningeal sarcoma. Six antibodies, those against epithelial membrane antigen, vimentin, cytokeratin, S-100 protein, neuron-specific enolase and alpha-1-antitrypsin, were used.

In primary meningioma, positivity rates were about 80% for epithelial membrane antigen, over 90% for vimentin, S-100 protein and alpha-1-antitrypsin, and 80-90% for neuron-specific enolase. Cytokeratin was negative in all cases. In recurrent meningioma, positivity rates for viementin were slightly lower in comparison with primary meningioma. The main staining patterns of epithelial membrane antigen, vimentin, S-100 protein and alpha-1-antitrypsin were diffuse and that of neuron-specific enolase was focal. In hemagiopericytoma and meningeal sarcoma, epithelial membrane antigen and cytokeratin were negative and the other antigens were positive.

Positivity for epithelial membrane antigen is thus of some use in distinguishing meningioma from hemagiopericytma or meningeal sarcoma. However vimentin, S-100 protein, neuron-spcific enolase and alpha-1-antitrypsin are not specific.

Key Words: Meningioma, Hemangiopericytyoma, Immunohistochemistry, Epithelial membrane antigen, Vimentin

Introduction

Meningioma is derived from arachnoid cells and shows both epithelial and mesodermal properties[1]. In fact, epithelial membrane antigen, vimentin, cytokeratin, S-100 protein, neuron-specific enolase and alpha-1-antitrypsin have all been reported to be positive in case of meningioma[2,3,4,5,6,7,8,9,10,11,12]. However the positivity rates for these antigens differ among authors. We therefore performed immunohistochemical examination of meningioma using antibodies against these antigens to clarify more concretely the percentages of cells positive for the antigens and their distribution. In addition, a few cases of hemangiopericytoma and meningeal sarcoma were also examined and compared with meningioma to characterize any differences in staining patterns.

Materials and methods

Among cases of meningioma which we had experienced since 1972, 76 cases of primary meningioma, 10 cases of recurrent meningioma, 3 cases of hemagiopericytoma and 2 cases of meningeal sarcoma were selected for immunohistochemical examination. Three cases of primary meningioma and 1 case of recurrent menin-

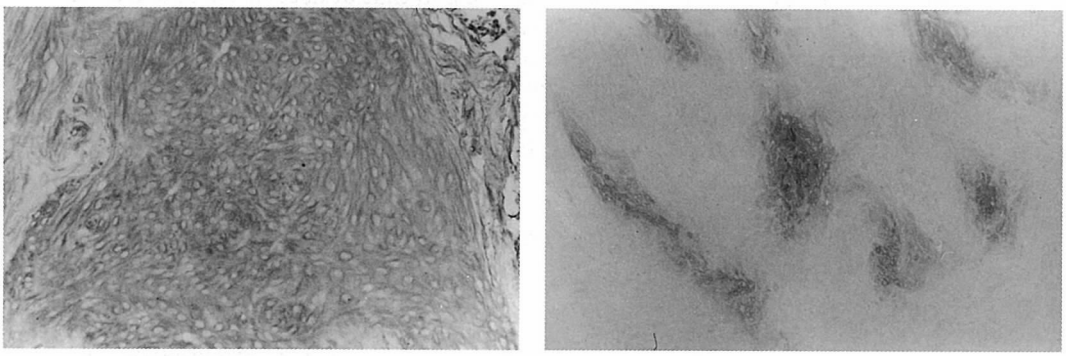
gioma were malignant meningioma. In multiple recurrent cases the latest recurrence was selected to eliminate any redundancy. Recurrence after apparent partial removal and different operations for multiple meningioma were omitted. The age of patients ranged from 16 to 76 years (mean: 51 years) and the male/female ratio was 22/69.

As primary antibodies, those against epithelial membrane antigen (EMA, Dako), vimentin (VM, Dako), cytokeratin (CK, Dako), S-100 protein (SP, Dako), neuron-specific enolase (NSE, Dako), alpha-1-antitrypsin (AT, Dako) were used. From paraffin-embedded specimens 6-μm -thick sections were obtained. Each slice was placed on a glass slide coated with 0.1% poly-L lysine (Sigma). Using the biotin-streptavidin (Biogenex Laboratories, San Ramon, CA) method for the mouse monoclonal antibodies (those against EMA, CK and VM) and the peroxidase-antiperoxidase (Dako) method for rabbit polyclonal antibodies (those against SP, NSE and AT), immunohistocyhemical staining was performed with diaminobenzidine coloration. Primary antibodies were used after dilutions of × 50 for anti-EMA, × 10 for anti-VM and × 100 for the others. The reaction temperature and time for anti-EMA were 4 ℃ and 24 h, respectively, whereas those for the other antibodies were room temperature and 1 h. Treatment using Protease type X XIV (Sigma) for 5 min. was added before blocking of non-specific peroxidase for anti-EMA staining of formalin -fixed specimens.

The positivity rates in tumors were calculated for the various antigens. In positive cases the relative number of positive cells were classified into three grades (3+: over half, 2+: under half, 1+: partly) and the distribution of positive cells was classified grossly into three categories (D: diffuse, F: focal, S: scattered) (Fig. 1).

Results

The gross positivity rates for the various antigens accroding to the tumor histological type are shown in Table 1. In cases of primary meningioma the positivity rates were EMA 80.3%, VM 92.1%, SP 90.8%, NSE 78.9% and AT 92.1%. In cases of recurrent meningioma the



(a) (b)

Fig. 1 Example of staining pattern 3+,D (a) and 2+,F (b).
a: anti-VM, ×200, b: anti-NSE, ×100, counterstained with methyl green.

Table 1 Positivity rates (%) in present cases according to histological type.

	Case	EMA	VM	SP	NSE	AT
Primary m.	76	80.3	92.1	90.8	78.9	92.1
Recurrent m.	10	80.0	70.0	90.0	90.0	100.0
HPC	3	0.0	100.0	33.3	100.0	100.0
Sarcoma	2	0.0	100.0	100.0	100.0	100.0

m: meningioma, HPC: hemagiopericytoma
Data of CK were not shown because of the negative result.

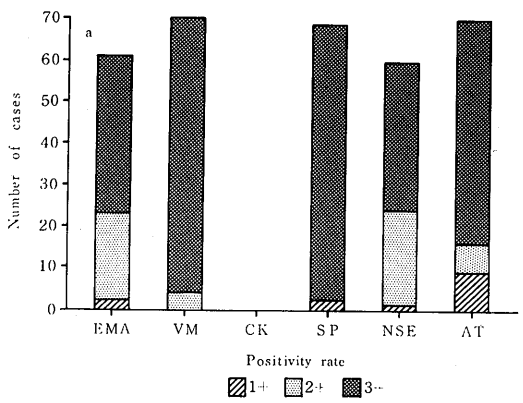
positivity rates were EMA 80.0%, VM 70.0%, SP 90.0% and AT 100%. CK was negative in all cases of meningioma. The positivity rates in primary and recurrent cases were almost the same for each antigen, except for a slightly low value for VM in recurrent meningioma. In cases of hemangiopericytoma and meningeal sarcoma EMA and CK were negative, whereas the positivity rates for VM, NSE and AT were 100%.

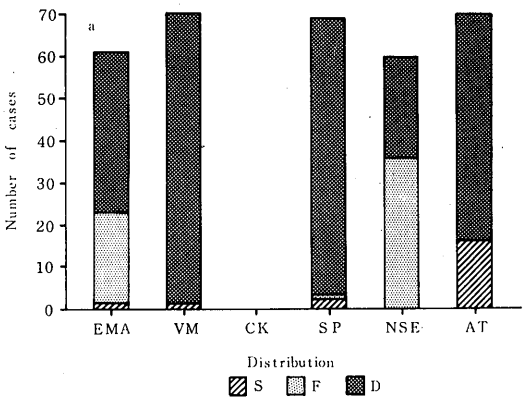
The positive staining pattern for each antigen is shown according to histological type in Fig. 2 and Fig. 3. In meningioma the dominant staining pattern for EMA, VM, SP and AT was 3+,D, whereas that for NSE was characacteristically 3+/2+,F. The pattern was almost the same in primary recurrent meningiomas, except that 2+, F was dominant in recurrent meningioma.

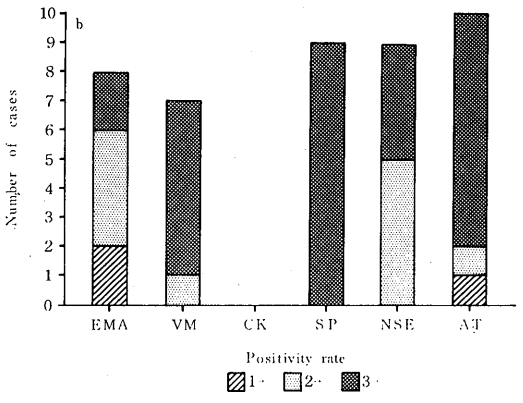
Discussion

The positivity rate of menigioma was high (80-90%) in EMA, VM, SP and NSE (Fig. 2a). The recurrent meningioma showed slightly low positivity rate (70%) of VM compared with primary meningioma (Fig. 2b). The distribution of positive cells was diffuse in VM, SP and AT, and focal in NSE (Fig. 3a). The pattern of EMA was mainly diffuse in primary meningioma and focal in recurrent miningioma (Fig. 3b). The focal staining of NSE was interesting and its cause was not clarified.

EMA, derived from human milk fat globule







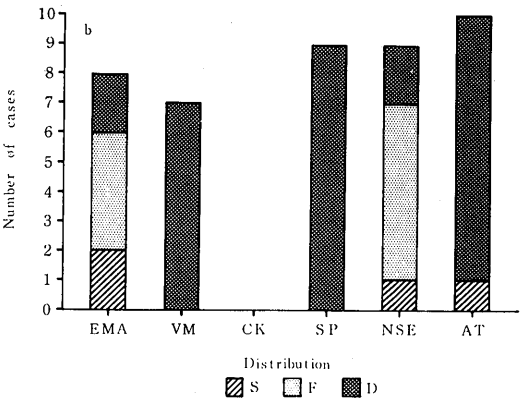


Fig. 2 Positivity rate of various antibodies in meningioma.
a: primary meningioma, b: recurrent meningioma.

Fig. 3 Distribution of positive cells against various antibodies in meningioma.
a: primary meningioma, b: recurrent meningioma.

Table 2 Comparison of positivity rates (%) in meningioma accroding to various authors.

	Case	EMA	VM	CK	SP	NSE	AT
Cras et al.	44	—	—	—	—	75.0	—
Hitchcock et al.	50	—	100.0	46.0	78.0	80.0	—
Jitawi et al.	19	—	—	—	42.1	84.2	—
Mennel et al.	80	—	98.9	8.8	6.3	—	—
Moss	14	78.6	—	21.4	0.0	—	—
Ng et al.	29	89.7	—	—	—	—	—
Sawaya et al.	22	—	—	—	—	—	50.0
Schnitt et al.	22	100.0	—	—	40.9	—	—
Tabuchi et al.	50	—	—	—	38.0	—	—
Kamiryo et al.	86	80.2	89.5	0.0	90.7	80.2	93.0

protein, has been proved to be positive in secretory cells[13,14] and has recently been noted as a marker of meningioma[9,15]. In primary meningioma, mitoses were present in 6.7% (1/15) of EMA positive cases and 3.3% (2/61) of EMA negative cases. These results showed no significant difference and no relation seemed to be present between the malignancy and EMA positivity rate. Both the primary and recurrent specimens in a same patient were available in 6 cases of meningioma and EMA positivity rate was 50% (3/6) in primary specimens. Less EMA positive tendency of cases recurring in the future was suspected, but it was not concluded because of the small number of cases.

VM is positive in cells of mesenchymal origin, SP is calcium-binding protein and positive in glial cells[12] and NSE is one of the glycolytic enzyme and positive in neurons and glial cells. AT is positive in several types of carcinoma and its significance in malignant cells has been explained in terms of protection against cell lytic activity by the host[10]. The highly positive result of AT in both primary and recurrent meningioma proved no relation with malignancy in meningioma. The immunohistochemically various attitude against these various antigens shows the variety of the origin of meningioma.

CK, the marker of epithelial cells , was all negative in meningioma in this study. These are some reports of positive case of meningioma[4,6,7], therefore the difference of the serial number or the manufacture of the antibody might produce the different results.

Comparison with hemangiopericytoma and meningeal sarcoma depicted the difference of EMA staining attitude. EMA was all negative in these cases. Usual sarcomas were reported to be EMA negative, but synovial sarcoma was reported to be EMA positive[13]. On the contrary, EMA was highly positive in meningioma and these results proved the usefulness of EMA in differential diagnosis between these menix related tumors.

Conclusion

Meningioma was highly and diffusely positive for EMA, Vimentin, S-100 protein and alpha -1-antitrypsin and highly and focally positive for NSE, whereas hemangiopericytoma and meningeal sarcoma were negaitve for EMA. Positivity for EMA is thus of some use in distinguishing menigioma from hemangiopericytoma or meningeal sarcoma. However vimentin, S -100 protein, NSE and alpha-1-antitrypsin are not specific.

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