Ajou Medical Journal
Vol. 1, No. 2, 1996

Intraoperative Cytologic Examination of CNS Glioma

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The cytologic findings of 18 cases of CNS glioma were reviewed to evaluate the accuracy and the usefulness of intraoperative cytologic examination in central nervous system lesions. Crush preparations were prepared from little tissue fragments followed by hematoxylin-eosin staining. The accuracy of the cytologic examination to detect tumors in this study was 94.4%(17/18) and differentiation of low and high grade glioma was possible in 16 out of 17 cases. The detailed cytologic features are described. The cytologic examination of intracranial tumor in crush preparation is a very useful procedure to have rapid and reliable diagnosis, and to provide valuable information for therapeutic management as well as for further histologic study.

Key Word: Central Nervous System, Glioma, Cytology, Crush preparation

INTRODUCTION

Intraoperative neurosurgical tissue examination is the first step to provide useful information for intraoperative decision making, however it has some limitations. The diminutive nature of many biopsy specimens, particularly those obtained by stereotactic neurosurgical procedures, emphasizes the importance of combining the cytologic smear method with conventional frozen section interpretation. The cytologic features of commonly encountered gliomas in crush preparations are described in this paper, and the advantage of the intraoperative cytologic examination for intracranial tumors are stressed.

MATERIALS AND METHOD

We selected 18 cases of intracranial gliomas from which fresh tissues were obtained for intraoperative diagnosis, and the diagnoses were confirmed by histologic examination. The cases of gliomas in this study consisted of 3 cases of pilocytic astrocytoma, 1 case of protoplasmic astrocytoma, 1 case of anaplastic astrocytoma, 5 cases of glioblastoma, 2 cases of oligodendroglioma, 2 cases of ependymoma and 4 cases of mixed glioma.

The fresh tissues to be examined were incised at the surface of a glass slide and a part of the samples was taken while the remainder was saved for cryostat or permanent sections. Using the second slide on top of the first held at right angle with surfaces parallel, the tissue to be smeared was crushed and drawn along the length of the first one. The smeared slide was immediately fixed in 95% alcohol for two minutes, followed by rapid hematoxylin-eosin stain. They were interpreted concurrently with the frozen section or reviewed with permanent histologic section.

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RESULTS

Correlation of the results obtained by cytological and histological examination

Out of total 18 gliomas with which both histological and cytological results could be compared, 17 cases(94%) showed accordance, and only one case was misdiagnosed as non-neoplastic gliosis by cytologic examination. The case consisted of a small amount of oligodendrogliomatous component in the nonneoplastic glial tissue. When we divided the cases into high and low grade glioma, the sensitivity was 83.3% and the specificity was 100%(Table 1). Among the high grade

glioma cases, one anaplastic astrocytoma was considered to be glioma of intermediate grade by cytologic examination. It showed mild to moderate degree of cellular pleomorphism, hypercellularity, and vascular proliferation with no mitotic figures at the time of intraoperative diagnosis. However, a few mitotic figures were detected by the careful review of the cytological slides.

Table 1. Comparison between crush cytologic diagnoses and histologic diagnoses according to grade

Crush cytologic diagnosis	Histologic diagnosis		Total
	High grade	Low grade	
High grade	6	0	6
Low grade	1	10	11
Total	7	10	17

Cytologic findings of gliomas

Astrocytic tumors

The cytologic findings of astrocytic tumor depending on the grade of glioma are summarized in Table 2.

i) Pilocytic astrocytoma (Fig. 1): This tumor was characterized by bipolar astrocytic cells with cytoplasmic extensions. The background was finely fibrillar with somewhat increased vascularity and occasional endothelial proliferation. Although uniformity and blandness of nuclei were particularly evident, mild nuclear pleomorphism was occasionally observed in longstanding tumors. Cellular elongation was present as fine hair-like bipolar process, and Rosenthal fibers were also visible.

ii) Astrocytoma, grade II (Fig. 2): This tumor had cytologic variability due to its histologic subtypes. It had cytoplasmic processes. Although some cells were naked, others had pink fibrillated cytoplasm. The nuclei were coarser and more irregular than those of normal astrocytes. Neither mitosis nor necrosis was present.

Table 2. Cytologic findings of astrocytomas according to grade

Cytologic findings	Low grade		High grade	
	Pilocytic	Grade II	Anaplastic	Glioblastoma
Background	fibrillary	fibrillary and/or finely granular	fibrillary and/or finely granular	dirty, necrotic
Cellularity	+	+ +	+ + +	variable
Vascular proliferation	+/−	−	+	+ + +
Perivascular hypercellularity	−	−	+/−	+
Nuclear pleomorphism	+/−	+	+ +	+ + +
Cytoplasm	spindle, bipolar	ill−defined	variable	variable
Mitosis	−	−	+	+
Necrosis	−	−	−	+
Other	Rosenthal fiber			anaplastic giant cells endothelial proliferation

note: −: absence, +: presence by mild degree, + +: presence by moderate degree, + + +: presence by marked degree

Fig. 1. Crush preparation of pilocytic astrocytoma, showing tumor cells with elongated nuclei and bipolar cytoplasmic processes, and Rosenthal fibers(H-E, ×200).

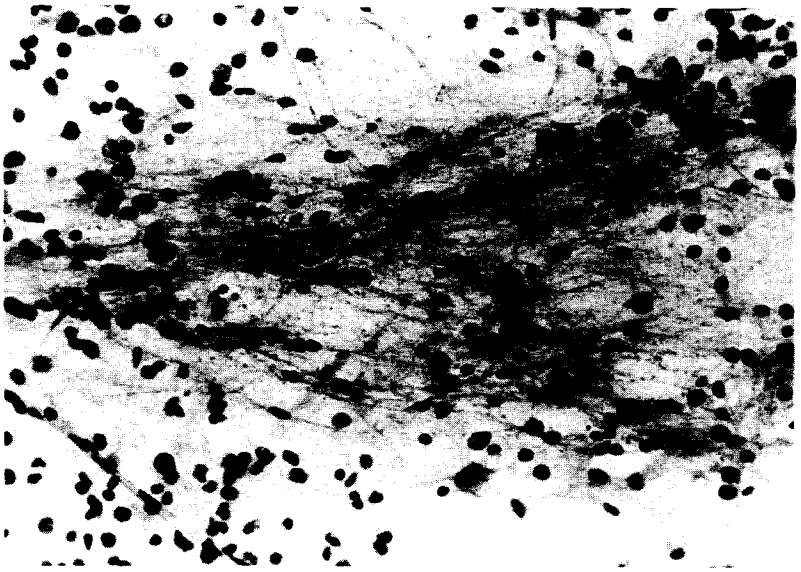

Fig. 2. Grade II astrocytoma, characterized by scattered, slightly pleomorphic astrocytes with increased cellularity in the fibrillary background(H-E, ×200).

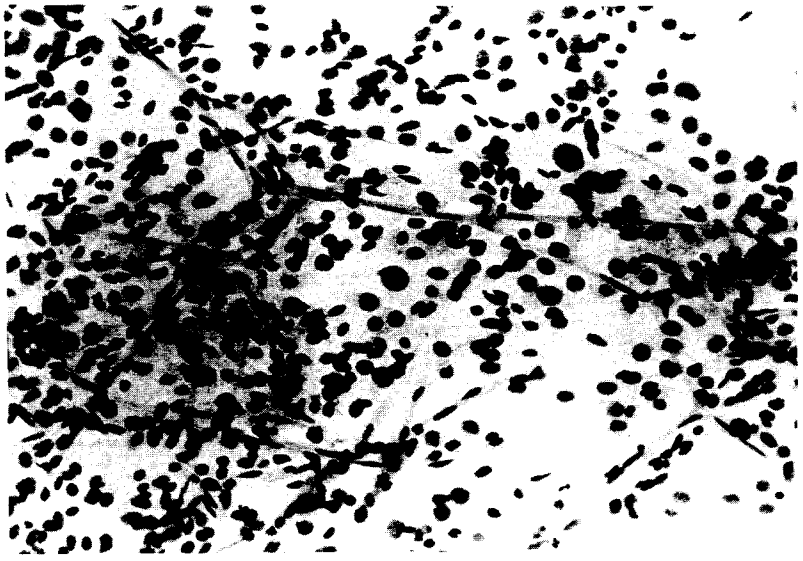

Fig. 3. Anaplastic astrocytoma in crush preparation, revealing highly cellular smear of pleomorphic astrocytes with increased vascularity(H-E, ×200).

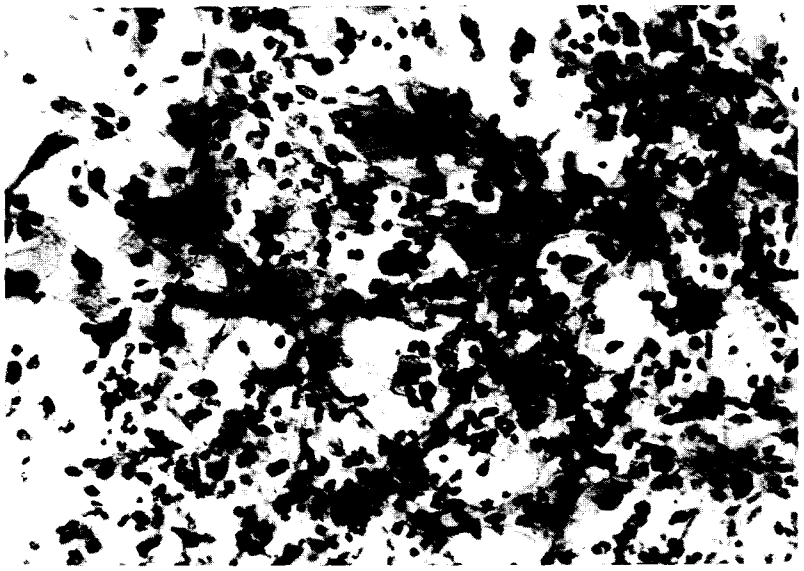

Fig. 4. In the cases of glioblastoma, highly pleomorphic cells including large bizarre cells seen with definite endothelial proliferation in the necrotic background(H-E, ×200).

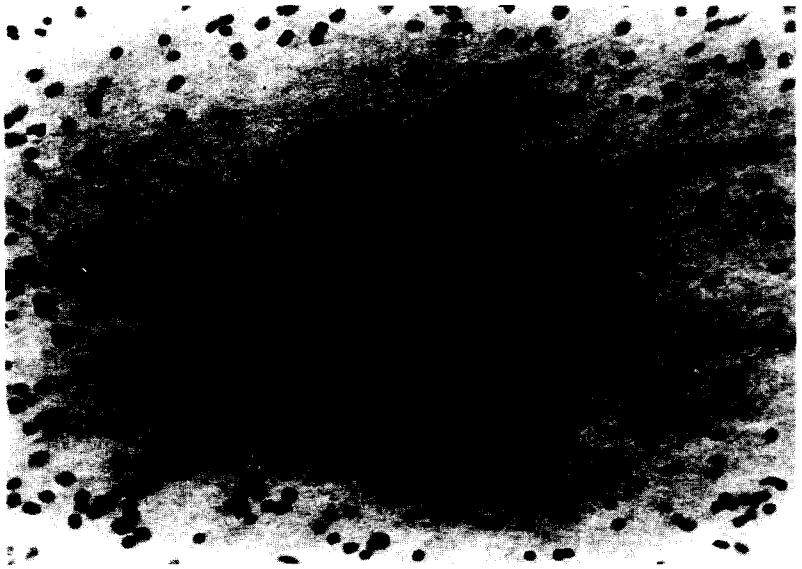

Fig. 5. In the smear preparation of oligodendroglioma, the tumors cells having relatively regular nuclei with small nucleoli and scant cytoplasm, scattered along with capillary proliferation(H-E, ×200).

Fig. 6. Ependymoma characterized by clusters of bipolar cells with abundant cytoplasm and ovoid regular nuclei. The nuclear arrangement of rosette detected(H-E, ×200).

iii) Anaplastic astrocytoma, grade III (Fig. 3): The smears were hypercellular with abundant vascularity. The background was fibrillary or finely granular without necrotic material. The tumor cells showed moderate degree of pleomorphism with size variation and nuclear hyperchromasia. Even though mitotic figures were detected along with atypism, there was no necrotic material. The endothelial proliferation was not obvious in spite of increased vascularity.

iv) Glioblastoma (Fig. 4): The cytologic preparation of the tumor showed variable features. The background was partly fibrillary and partly granular due to necrosis. The cellularity was usually high but low in some cases. Also, the tumor cells had a wide range of nuclear abnormalities, ranging from small cells with somewhat elongated hyperchromatic nuclei and little cytoplasm to large anaplastic cells with large nuclei, prominent nucleoli and abundant cytoplasm. Multinucleated giant cells were observed in some cases. The vascular proliferation was prominent with endothelial hyperplasia with mitotic figures detectable.

Oligodendroglioma (Fig. 5)

The smear showed scattered uniform round nuclei with small nucleoli and little or no visible cytoplasm. The background was more fibrillary on smear than one would expect examining the histologic sections alone. Perinuclear halos were not apparent in cytologic preparation. Microgemistocytic cells with an eccentric glassy or finely fibrillary cytoplasm were seen occasionally.

Ependymoma (Fig. 6)

With cytologic preparation, this tumor showed a monolayer composed of sheets and clusters of polygonal or columnar cells, showing regular dark ovoid nuclei along with dispersed cells. The tumor cells had both glial and epithelial features. There was a tendency of perivascular arrangement. In the case of myxopapillary ependymoma, myxoid material was interspersed among the tumor cell nests and the vessels.

DISCUSSION

Histologic typing is essential for therapeutic management of intracranial tumors, even though their sizes and locations are also important. Especially, intraoperative neurosurgical tissue examination is not only the first step to provide useful information for intraoperative decision making, but also is necessary for optimal sampling and preparation of tissue for further procedures such as electron microscopy, immunohistochemistry, microbiologic culture, and so on. There are also many cases where to obtain the tissue samples through open craniotomy is difficult or is not necessary because the tumor is deeply-seated or unresectable. In order to solve these problems, rapid, easy, and safe stereotactic biopsies has been developed in recent years[1~3]. However, the procedure has some limitations in that the small size of obtainable tissue makes their evaluation difficult, and softened or necrotic areas are easily sheared which are unsuitable for embedding and histologic procedures.

Cytologic examination by crush preparation of tissue samples of brain tumors is not a new technique. It has been used by Eisenhardt and Cushing[4], and others[5~9], and the diagnostic procedure has been recognized gradually as a useful adjunct to the histologic diagnosis of intracranial tumors because of its rapid processing and little artifact compared to frozen section. With the widespread use of stereotactic biopsies in recent years, cytologic procedure has become a routine and invaluable procedure for rapid and accurate intraoperative diagnosis[10~19]. This method can be done fast with small amount of the specimens obtained from stereotactic biopsy, and makes artifact considerably less than frozen section, greatly increasing the diagnostic accuracy.

Even though the significance is limited due to a small number of cases included in this study, the accuracy of the cytologic examination to detect tumors in the present study was 94.4%(17/18), and differentiation between low and high grade glioma was possible in 16 out of 17 cases. Other authors have also reported highly positive correlation between the cytologic examination and histology in 79% to 95%[7,10~12,20,21]. The cytologic diagnosis by crush preparation is accurate enough to be a helpful tool by itself for rapid intraoperative decision-making.

Differentiation between the low and the high grade was possible by the criteria used for histologic diagnosis proposed by WHO classification[22]. Low grade glioma has features of slight pleomorphic nuclei without mitosis, endothelial proliferation, or necrosis. Among the high grade gliomas, glioblastoma showed definite nuclear pleomorphism, mitosis, endothelial proliferation, and/or necrosis. Anaplastic astrocytoma

(grade III) did not have necrosis and had less degree of other parameters. Though usual astrocytic tumors revealed an occasional fibrillary cytoplasmic process, pilocytic astrocytoma was characterized by elongated nuclei, bipolar cytoplasmic processes, and Rosenthal fibers. In the cases of oligodendroglioma, regular round nuclei with small nucleoli and capillary proliferation were characteristic. Ependymomas had both glial and epithelial features with a tendency of perivascular arrangement.

The intraoperative cytologic examination, however, has some limitations. These limitations are mainly due to small amount of tissue obtainable by stereotactic biopsy technique. The minute amount of specimen may not represent all the characteristics of the regional variation expected in a given tumor; specimen might be taken from the totally necrotic or hemorrhagic area of the tumor. In the latter case, immediate further sampling is required, and the accuracy of diagnosis and grading can be increased by assessing more cellular regions predominated by neoplastic cells. To ease the limitation, the radiologic correlation becomes important. Without consideration of radiologic image study, it is not right and rather dangerous to make diagnosis based on solely cytologic or histologic findings with a small specimen.

In summary, the cytologic examination of intracranial tumor in crush preparation is a very useful procedure for rapid and reliable diagnosis and provides valuable information for therapeutic management, especially when it is supplemented with radiologic imaging. It also help us saving more specimen for permanent section and further specific studies.

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