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Original Article

Intraoperative consultation of central nervous system lesions. Frozen section, cytology or both?

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ABSTRACT

Objective: Frozen section is the traditional method of assessing central nervous system (CNS) lesions intraoperatively. Our aim is to determine the diagnostic accuracy of frozen section and/or cytological evaluation of CNS lesions in our center.
Study design: A total of 157 patients with CNS lesions underwent open surgical biopsy or excision in our center during a period of 2 years (2012–2013). All specimens were studied cytologically; of these specimens, 146 cases were also examined by frozen section. Cytology and frozen section slides were studied separately by two general pathologists who were blind to final diagnoses. The final diagnoses were based on permanent sections and IHC studies.
Results: The accuracy rates of frozen section analysis and cytological evaluation were 87% and 86%, respectively. If the two methods were considered together, the accuracy rate improved to about 95%.
Conclusions: Cytological evaluation is an acceptable alternative to frozen section analysis and also a great supplement to the diagnosis of CNS lesions.

1. Introduction

Despite significant improvement in neuroradiologic techniques, treatment planning is mostly based on histopathological diagnosis [1]. Intraoperative pathological consultation helps the neurosurgeon in different ways to choose the appropriate approach in treating CNS lesions. In some situations, the pathologist's role is vital in the ongoing surgical procedure. For example, differentiation of an inflammatory lesion from a tumor, a high grade glial tumor with cystic component from a low grade one with almost the same deceptive radiological findings (because the cyst wall excision is necessary in the former), radiotherapy related necrosis from tumor recurrence, CNS lymphoproliferative disorders from other tumors (since its excision worsens the prognosis) [2], and the diagnosis of high grade glial tumors for intraoperative radiation source placing, are some of the great aids that the pathologist could offer in this field [3]. In addition, the surgeon informed of the inflammatory/infectious nature of the lesion may submit further specimens for different tests such as microbiology cultures, electron microscopic examination, cytogenetic, flow cytometry and etc. [2].

Although frozen sections can demonstrate the architectural characteristics better than cytological studies, it has its own disadvantages, such as freezing artifact, requiring expensive equipments and trained staff.

Thus cytological evaluation has been introduced as an attractive alternative. In comparison to frozen section, the cytological examination is cheaper and faster, does not need experienced technologist for preparing sections, needs only a piece of 1–2 mm^3 tissue for each slide (especially when submitted tissue is tiny such

Abbreviations: CNS, central nervous system; GBM, glioblastoma multiforme; H&E, hematoxylin and eosin.

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as in stereotactic biopsies), will not cause freezing artifact in prepared slides and also in the remaining tissue, and is a better tool to study cytological characteristics of the lesion [4,5].

Our goal is to determine the diagnostic power of frozen section and cytology of CNS lesions in our center.

2. Methods

From March 2012 to March 2014, fresh specimens of 157 patients with CNS lesions, who underwent open surgery in Imam Khomeini Hospital Complex affiliated to Tehran University of Medical Sciences (TUMS), were submitted to our laboratory for intraoperative pathological consultation. Cytological slides (both touch and squash smears) were prepared from all of them and frozen sections were performed in 146 of the cases. Slides were stained with toluidine blue and accelerated H&E methods, and if enough tissue was available, modified Wright staining was also done. Two general pathologists without prior experience in CNS cytology reviewed the slides separately. They were blind to final diagnoses, but were given brief information about clinical impression and radiological findings. In the first step, the cytology and frozen section slides of each case were examined separately and the pathologists recorded their diagnoses. In the next step, If there was any discrepancy between cytological and frozen section diagnoses, the cytology and frozen sections were studied together to render a final diagnosis based on both methods. The glial tumors and meningiomas were graded as high grade or low grade (two-tiered grading system). These data were compared with the final diagnoses which were based on permanent sections and if necessary IHC studies. The diagnoses of each pathologist were subdivided into three groups as follows: (1) the diagnosis and grading of the lesions are correct, (2) the diagnosis is correct but grading is wrong (not including grade I gliomas, vide infra), (3) both diagnosis and grading are wrong.

The grade I gliomata included pilocytic astrocytoma, subependymal giant cell astrocytoma and ganglioglioma (one case each). Because the grade I astrocytomas are specific entities and grading is almost always an inseparable component of diagnosis, we did not consider the second category (correct diagnosis but wrong grading) for these cases. In other words, correct diagnosis was equated to both correct diagnosis and correct grading, and vice versa.

Statistical analysis was performed using SPSS version 16.0.1 (SPSS Inc., Chicago, IL, USA). To determine the frequencies and differences between groups, descriptive and comparative statistics including Kappa test were employed, respectively. P values of less than 0.05 were considered as significant and a Kappa of 0.8 was considered as a satisfactory agreement.

2.1. Ethical considerations

Touch/squash preparations and frozen sections were performed on cases with adequate tissue so that the final diagnosis would not be compromised because of this study. Additionally, frozen sections were prepared from specimens that were stored at −80 °C in our tissue/tumor bank after we were completely sure that the final diagnosis had been rendered and the tissue was not needed for patient's diagnosis. If the formalin-fixed specimens were not adequate for definite diagnosis, the frozen tissue of tissue/tumor bank was used for preparation of additional formalin-fixed paraffin-embedded sections.

Patients' identities were treated strictly confidential. We also obtained informed consent from all research participants. This research is approved by the vice-chancellor for research and ethics committee of TUMS.

3. Results

The patients were mostly adults i.e., about 65% of the patients were in the age group of 31–60 years. Fifty-four percent of patients (84 cases) were male. Supratentorium was the most prevalent location of the lesions in this study (84%) followed by sella turcica (24%), infratentorium (19%), and spinal cord (4%).

Meningioma comprised most of the cases (27.4%), which consisted of 74% typical, 21% atypical and 5% anaplastic ones; followed by gliomas (22.4%) (Table 1).

When we considered complete agreement between cytology and definite diagnosis as correct diagnosis, the total accuracy rates were 79.6% and 77.1% for the two pathologists, respectively. These rates raised to 87.2% and 87.5%, respectively, when we ignored the discrepancy in the grading of the lesions. The accuracy rates of frozen section examination were 77.5% and 75.4% for the two pathologists, respectively. These rates raised to 87.4% and 85.2%, respectively, when we ignored the discrepancy in the grading of the lesions. There was no statistical difference between the accuracy rate of cytology and frozen section examination performed by each pathologist ($P = 0.45$ for pathologist #1 and $P = 0.85$ for pathologist #2).

The accuracy rates of examining cytological and frozen section slides together were 88.8% for complete agreement and 95.2% when we overlooked the mistakes in the grading of the lesions. This improvement of accuracy was statistically significant in comparison with both cytology alone or frozen section alone ($P = 0.007$ for pathologist #1 and $P = 0.043$ for pathologist #2).

The agreement between two pathologists was evaluated by Kappa test, which revealed excellent results (Kappa coefficients = 0.8 and 0.81 for cytology and frozen section analyses, respectively).

Because of the excellent agreement between the observers, the sensitivity and specificities of the two pathologists were almost the same. The highest accuracy of 100% was achieved for pituitary adenomas in frozen sections. The lowest sensitivity (65%) belonged to cytological study of metastatic tumors. However, frozen sections and combined evaluation of both cytology and frozen section raised the sensitivity to about 89%. The specificity of about 98% was obtained for cytological and frozen section study of metastatic tumors.

4. Discussion

The cytology and frozen section for intraoperative diagnosis of CNS lesions have been of interest for a long time; however, to the best of our knowledge, only few studies have compared these two methods by general pathologists and there is no report about the interobserver reproducibility of results.

Some studies are in favor of superiority of the intraoperative frozen section examination over cytological examination of CNS lesions [6,7]; however, recent studies have shown no difference between these two methods [8,9]. In our study, there was no statistical difference between the cytology and frozen section examinations ($P = 0.45$ for pathologist #1 and $P = 0.85$ for pathologist #2) and there was an excellent Kappa coefficient of agreement between the two pathologists for both cytology and frozen section confirming a great reproducibility of the results. In accordance with other studies, conducting cytology and frozen section examination simultaneously, improved the diagnostic accuracies significantly [4].

In tumors with high cellularity, imprint cytology slides were superior to squash smears, because of crushing artifact produced during preparation of the latter (Fig. 1).