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Original Research Article

Intraoperative Squash Cytology of Central Nervous System Lesions: Review of an Eight-Year Experience

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Abstract

Background: Intraoperative squash cytology is a simple and reliable technique for rapid intraoperative diagnosis of neurosurgical specimens. Intraoperative squash cytology is a fairly accurate diagnostic modality which can be used in place of frozen sections. *Aim:* To assess the diagnostic accuracy of the squash preparation and to compare it with the histopathology sections. *Materials and Methods:* This study was conducted over a period of eight 8 years (May 2010 to June 2018) which included 131 patients with CNS lesions. The cytological preparations were stained by the rapid H & E method. The squash interpretation was compared with the paraffin section diagnosis. *Results:* Of the 131 patients, Squash cytology diagnosis was offered in all the cases. With hematoxylin and eosin-stained histopathology sections as the gold standard, the diagnostic accuracy of squash cytology was 95.4% (125/131). Among these cases, gliomas formed the largest group comprising of 50 cases (38.1%). The accuracy of squash cytology in this group was 94% (47/50). *Conclusions:* CNS squash preparations can be used for rapid and reliable intraoperative diagnosis for CNS lesions.

Keywords: Central Nervous System Lesions; Intraoperative Diagnosis; Squash Preparation.

Introduction

Intraoperative central nervous system (CNS) squash cytology has now been established as a method of intraoperative diagnosis of CNS lesions. Some problems like ice crystal artifacts may make morphological interpretation of frozen sectioned tissue difficult and often soft consistency makes it difficult for handling the tissue for frozen section. On the other, the soft consistency of CNS tissue makes it best suitable for squash cytology [1].

With the advent of stereotactic biopsies the squash preparation has an important role to play in CNS lesions. Apart from providing a rapid diagnosis, the small sample size required, can give valuable guidance to the operating neurosurgeon in removing the lesion without causing much damage to the tissue surrounding the intracranial and spinal lesions [2,3].

It is prudent for the upcoming pathologists to be well versed in handling and evaluation of morphological features of various central nervous system (CNS) lesions. The purpose of

this study is to assess the diagnostic accuracy of the squash preparation and to compare it with the histopathology sections.

Materials and Methods

This eight year study was conducted in the department of pathology, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, India. It was four and half year retrospective study from May 2010 to December 2014 and three and half year prospective study from January 2015 to June 2018. The study was done after obtaining approval of the institutional ethical committee. Retrospective data was collected from the Medical records section of the department of pathology. For the prospective analysis, squash smears were prepared from the tissue received. Very tiny fragment of tissue was squashed between two slides to prepare smears as described by Adams et al. [4] and smears were stained using rapid Hematoxylin and Eosin (H and E) stain. The squash slides were examined and reported by senior pathologists. Tissue for histopathological examination and left over tissue after squash preparation were fixed overnight in 10% formalin. After processing, blocks were prepared and 4 mm sections were cut using Leica RM 2035 rotary microtome and stained with Hematoxylin and Eosin. H & E sections were reported by experienced pathologists.

The intraoperative cytological diagnosis offered was based on the rapid H & E staining procedure. The squash cytology diagnosis obtained was compared with the histopathology diagnosis which was the final and gold standard. The grading of the tumors by squash cytology was also attempted to compare with histopathology grading wherever possible. Immunohistochemistry and special stains like PAS and Gomori's silver methenamine stain were done, wherever required. The diagnosis of squash cytology, radiology reports and histopathological diagnosis were compared. The results were analysed using SPSS software version and interpreted.

Results

The patient's age with CNS tumors included in the study ranged from 1–76 years with the mean age being 49.9 years. Ten CNS tumors (12%) were seen in children below 12 years of age. Rest of the tumors were noted in adults. There was a male preponderance with 79 males and 52 female patients. There were 9 intraspinal, 105 supratentorial, and 17 infratentorial tumors. Final histopathology diagnosis is presented in Table 1.

In all 131 cases, squash cytology diagnoses were attempted and compared with paraffin sections. In 18 patients, diagnosis of inflammatory disease was given. Among them, 15 had granulomatous inflammation and three had fungal abscesses. In all the cases except for one case, smears were adequate. In one case, squash preparation yielded only necrotic material, with few cells that were diagnosed as infarcted pituitary adenoma in subsequent paraffin sections.

Diagnostic accuracy on cytology was found to be 95.4% (125/131). Of the 131 cases, 50 were gliomas, forming the largest category of tumors (38.1%). The cytological accuracy in this group was 94% (47/50). The lineage of the gliomas was correctly established in 96% (48/50) cases and the grade established in 94% (47/50) cases. Among three cases of gliomas which were incorrectly graded, one grade below the actual grade was reported.

Multiple smears were required in few cases like meningioma, schwannoma, since these tumours were too fibrous for proper spreading. In these cases, simultaneous frozen sections were also studied for

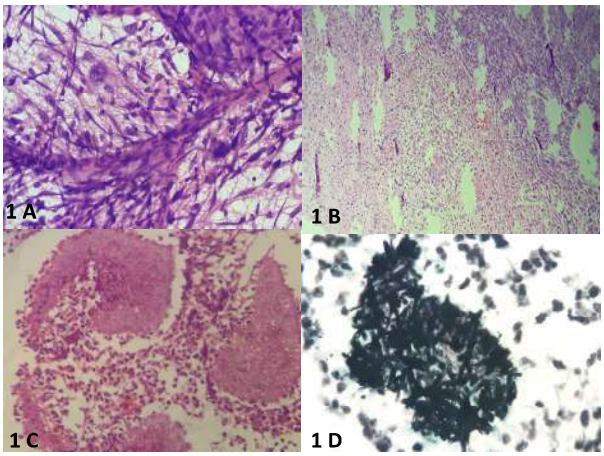
Table 1: Histopathological spectrum of CNS lesions

Histopathological diagnosis	No. of cases	Percent (%)
Diffuse Astrocytoma WHO grade II	15	11.4%
Anaplastic astrocytoma, grade III	7	5.3%
Glioblastoma multiforme	23	17.5%
Oligodendroglioma	5	3.8%
Ependymoma	2	1.5%
Meningioma	19	14.5%
Schwannoma	6	4.5%
Metastatic adenocarcinoma	3	2.2%
Medulloblastoma	2	1.5%
Hemangioblastoma	1	0.76%
Craniopharyngioma	1	0.76%
Pituitary adenoma	6	4.5%
Epidermoid cyst	1	0.76%
PNET	3	2.2%
Central neurocytoma	4	3.05%
Chordoma	3	2.2%
Gemistocytic Glioblastoma	1	0.76%
Choroid Plexus papilloma	1	0.76%
CNS embryonal Tumor NOS	2	2.2%
Neuroenteric cyst	1	0.76%
Hemangioma	1	0.76%
Astroblastoma	1	0.76%
Lymphoma	5	3.8%
Granulomatous Inflammation	15	11.4%
CNS Fungal infections	3	2.2%
Total	131	100%

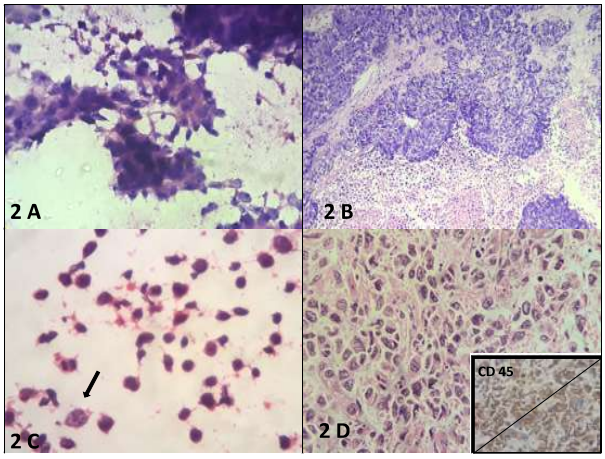
better diagnosis. In one case, metastatic tumour as reported on squash, which on subsequent paraffin section turned out to be anaplastic astrocytoma, grade III.

The radiological diagnosis correlated well with the final histopathological diagnosis in cases like meningioma, pituitary adenoma, craniopharyngioma and some cases of glioblastoma multiforme. In most of the cases of cerebral lesions, the radiological findings were nonspecific and differential diagnoses were offered. However, the final diagnosis on histopathological evaluation was also one of the differential diagnoses offered on radiological evaluation.

Morphological features of some squash smears are shown in Figure 1 and 2.



1 A- Glioblastoma with prominent endothelial proliferation. (H and E, ×400).1 B- Glioblastoma with necrosis (H and E, ×400).1 C- Fungal elements surrounded by inflammatory cells. (H and E, ×400).1 D- - Septate fungal elements.(GMS, ×400).



2 A- Metastatic tumour cells arranged in cohesive clusters. (H and E, ×400).2 B- Metastatic tumour cells arranged in sheets with adjacent necrosis (H and E, ×400). 2 C- Non Hodgkins lymphoma, discrete large cell. (H and E, ×400). 2 D- Non Hodgkins lymphoma, (H and E, ×400). Inset - Tumour cells showing membrane positivity for CD45.

Discussion

The soft and friable nature of the CNS tumors makes it possible to prepare intraoperative squash smears which can be stained with quick stains and also provide good cellular details. Thus, the diagnosis on intraoperative squash preparations can provide guidance to neurosurgeons to modify the surgical approach. Clinical presentation, exact location and provisional diagnosis on imaging studies can help the pathologist in making reasonably accurate diagnosis. Good cytological preparation and well stained smears are critical for accurate cytological diagnosis. The ease of squash preparation depends on the consistency of the tumours. This attribute can be seen in tumours like gliomas, medulloblastomas, and metastatic tumors. However, many tumors which have more fibrous stroma are difficult to smear, namely tumors of neural origin and some meningiomas [3,5].

In our study, the diagnostic accuracy of the smears was 95.4%. In previously reported studies, the cytomorphological accuracy of diagnosis has varied from 80% to 95% [2,3,6–12]. Cases misdiagnosed on cytology but correctly interpreted on paraffin sections are depicted in Table 2.

Two cases were misdiagnosed as neutrophilic abscess which actually were granulomatous inflammation with caseation, probably of tubercular origin. A case of infarcted pituitary adenoma was misdiagnosed as only necrosis, which could be due to sampling error. Another case was misinterpretaed as metastatic deposits which later turned out to be anaplastic astrocytoma. Two other cases were reported as granulomatous lesions which actually had fungal elements that were demonstrated on paraffin sections using Grocott-Gomori's methenamine silver and PAS special stains.

WHO Grading was misinterpreted in three cases as diffuse astrocytoma WHO grade II which were correctly reported as anaplastic astrocytoma and anaplastic oligoastrocytoma. The reason

Table 2: Cases misdiagnosed on cytology but correctly interpreted on paraffin sections

Cytology	Paraffin section diagnosis
Neutrophilic abscess (2 cases)	Caseating granulomatous inflammation
Metastatic tumour	Anaplastic astrocytoma WHO grade III
Granulomatous inflammation (2 cases)	Fungal abscess
Necrosis only	Infarcted pituitary adenoma

behind misinterpretation of WHO grade could be attributed to regional variation of tissue in squash preparation.

The discrepancies observed between the squash preparations and the paraffin sections are comparable with previous studies. Authors of previous studies have cited sampling error as the cause for discrepancies in differentiating specific inflammatory lesions. It is a known fact that astrocytomas may have different grades in different areas within the tumour that can lead to faulty grading of gliomas [13,14].

Conclusion

The soft consistency of the CNS lesions makes it easy to obtain intraoperative samples that are best suitable for CNS squash preparations. It is very affordable compared to Cryostat, especially for developing countries. Squash preparations give fairly accurate and consistent results for diagnosis of CNS lesions intraoperatively. Hence, CNS squash preparations can be used for rapid and reliable intraoperative diagnosis for CNS lesions.

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