Use of Intraoperative Squash Smear in Diagnosis of Central Nervous System Tumors with its Histopathological Correlation

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Abstract

Introduction: Squash smear preparation is a simple and rapid methodology for fairly accurate intraoperative diagnosis of CNS space occupying lesions. It has emerged as an important indispensible intraoperative diagnostic aid guiding the neurosurgeon and helping in better management of patients. The current study was undertaken to study CNS tumors by squash cytology and correlating them with histological diagnosis.

Aims: To evaluate the accuracy and utility of intraoperative squash smear cytology in the evaluation of CNS tumors.

Materials and Methods: A retrospective study was conducted in the Department of Pathology in a tertiary care hospital from November 2019 to November 2020. A total of 74 consecutive cases were included. Squash smears were prepared from the intraoperative samples and biopsy samples were processed regularly. Hematoxylin and eosin staining was done and squash smear cytology results were correlated with the final histopathological diagnosis.

Results: Out of the 74 cases studied, histopathological diagnosis was compatible with the cytological diagnosis in 56 cases, pertaining to 75.67% accuracy. Remaining 18 cases showed partial discrepancy as in tumor grading or complete discrepancy.

Conclusion: This study shows a high degree of cytohistological correlation. With clinicoradiological correlation, squash smear cytology could be the preferred method for intraoperative diagnosis of CNS tumors.

***Keywords**: CNS, CNS SOLs, Intraoperative cytology, Squash cytology*

Introduction

The incidence of central nervous system (CNS) tumors varies from 10-17 per lakh persons per year for intracranial and 1-2 per lakh persons per year for intraspinal tumors. The knowledge of location and size of CNS tumors along with their histological type and grade are important for patient management. Squash smear preparation is a simple and rapid methodology for fairly accurate intraoperative diagnosis of CNS space occupying lesions.[1] First introduced in 1930, central nervous system squash cytology (CSC) has now been established as a method of intraoperative diagnosis of CNS tumors. The soft consistency of CNS tissue is best suited for squash cytology.[2] It has emerged as an important indispensible intraoperative diagnostic aid guiding the neurosurgeon and helping in better management of patients. However, definitive diagnosis is still confirmed by histopathological examination.[3] The current study was undertaken to study CNS tumors by squash cytology and correlating them with histological diagnosis.

Materials and Methods

This was a retrospective study conducted in the Department of Pathology in a tertiary care hospital from November 2019 to November 2020. A total of 74 consecutive cases (including benign and malignant lesion of the brain and spinal cord) were included. Biopsy specimens of all intracranial lesions were collected intraoperatively and squash smears were prepared for each case as soon as received. Sample for squash smear cytology was sent in normal saline and for biopsy it was sent in formalin. For each case, as many as possible smears were prepared. All were fixed immediately in methanol and stained with hematoxylin and eosin stain. Remaining material was kept for making more smears in cases of discrepancy or loss or damage to preparation. Samples inadequate were excluded from the study. Tumors were classified according to the WHO classification and were graded intraoperatively if possible. Squash smear cytology results were correlated with the final histopathological diagnosis. The complete correlation was considered when cytology preparation was found identical to the final histopathological diagnosis. Partial correlation was considered when there ±1 grade of deviation in tumor grading or diagnosis of the cell line of origin was registered. When the intraoperative diagnosis was not confirmed, the cases were labeled as discrepancy. Data collected were statistically analyzed and compared between the intraoperative squash smear cytology to that of final histopathological diagnosis.

Ethical Considerations

All procedures performed were in accordance with the ethical standards of the institution.

Results

The study was a retrospective study of 74 CNS space occupying lesions during 1 year period, which included 37 males and 37 females. The age ranged from 1 to 88 years. Cytological and histological diagnoses are summarized in Table 1. Out of the 74 cases studied, histopathological diagnosis was compatible with the cytological diagnosis in 56 cases, pertaining to 75.67% accuracy. Remaining 18 cases showed partial discrepancy as in tumor grading or complete discrepancy as depicted in Tables 2. The cases with the same diagnosis and grade on cytology and histopathology were considered as complete correlation. The cases where intraoperative cytological diagnosis did not correlate with the histological examination were categorized as discrepant cases. Accuracy of squash smear cytology of present study is compared with accuracy found in other studies in table 3. Accuracy of diagnosis by squash cytology was found to be 100% in cases of gliomas, astrocytomas, myxopapillary ependymoma, choroid plexus papilloma and carcinoma, schwannoma, solitary fibrous tumors and sarcomas. Less accuracy was found in cases of ependymoma, oligodendroglioma and medulloblastoma. Glioblastomas showed least accuracy in diagnosis.

Table 1: Histological and cytological diagnosis and correlation of all the cases studied in our study

Tumors	Total histological diagnosis	Total cytological diagnosis	Correct cytological diagnosis	Misdiagnosed cases on squash cytology	Accuracy (%)
Glioma	2	6	2	4	100
Astrocytoma (Fibrillary/ Diffuse)	7	11	7	4	100
Gemistocytic astrocytoma	1	0	0	0	0
Glioblastoma	15	6	6	0	40
Oligodendroglioma	3	2	2	0	66.67

Cont... **Table 1: Histological and cytological diagnosis and correlation of all the cases studied in our study**

Pilocytic Astrocytoma	2	3	2	1	100
Pleomorphic Xanthoastrocytoma	1	0	0	0	0
Myxopapillary ependymoma	1	1	1	0	100
Ependymoma	5	4	4	0	80
Choroid Plexus Papilloma	1	1	1	1	100
Choroid Plexus Carcinoma	1	1	1	1	100
Central Neurocytoma	0	1	0	1	0
Medulloblastoma	3	2	2	0	66.67
Schwannoma	10	10	10	0	100
Neurofibroma	1	0	0	0	0
Meningioma	11	12	11	1	100
Solitary Fibrous Tumor	1	1	1	0	100
Liposarcoma	0	1	0	1	0
Myxoid Chondrosarcoma	1	1	1	0	100
Germ cell tumor	0	1	0	1	0
Craniopharyngioma	2	2	2	0	100
Pituitary adenoma	2	2	2	0	100
Inadequate/ Reactive/ Inflammation/ Infective	1	5	1	4	100

Table 2: Discrepant cases (cytology vs. histology)

Cytological diagnosis	Histopathological diagnosis
Fibroblastic meningioma	Glioblastoma grade IV
Central neurocytoma grade II	Glioblastoma- small cell type Grade IV
Anaplastic glioma	Subependymal giant cell astrocytoma
Atypical meningioma	Meningothelial meningioma
Astrocytoma, Fibrillary astrocytoma II	Glioblastoma grade IV, Pleomorphic Xanthoastrocytoma, Oligodendroglioma grade II
Liposarcoma	Ancient schwannoma
Meningioma grade I	Atypical meningioma grade II, Fibroblastic meningioma grade I, Angiomatous meningioma grade I

***Cont...* Table 2: Discrepant cases (cytology vs. histology)**

P/o Infective etiology/ Tuberculosis	Pilocytic astrocytoma, Glioma grade III
Pilocytic astrocytoma	Fibrillary astrocytoma, Ependymoma grade II
Inflammation	Glioblastoma grade IV
Schwannoma	Neurofibroma
Glioma grade III	Glioblastoma grade IV

Table 3: Diagnostic accuracy of smear cytology in various studies

Study	No. of cases	Accuracy (%)
Present study	74	75.67
Seema A et al[1]	222	83.78
Savita et al[2]	50	87.5-100
Arpita J et al[3]	150	94.67
Swagatika S et al[4]	63	93.44
Arpita J et al[5]	150	94
Rupanita B et al[6]	158	81.11
Manish A et al[7]	48	95
Padmanaban G et al[8]	75	90.67
Shrestha R et al[9]	36	77.8

Discussion

Squash smear preparation was first introduced for rapid intraoperative diagnosis by Eisenhardt and Cushing in 1920. It is now an acceptable method of intraoperative consultation in CNS lesions [1]. The intraoperative diagnosis of CNS tumors by smearing the tissue can provide guidance in modifying the surgical approach by the neurosurgeons. The knowledge of location, clinical presentation, and imaging findings, as well as its correlation with cytological and histological findings is of utmost importance to pathologists. [2] An advantage of CNS cytology, such as squash cytology, is that it can be done on a tiny tissue, and is of great value when the tissue obtained is limited or one does not want to lose it to frozen section but preserve it for paraffin sections. The CSC not only economizes on tissue but also on time. The intraoperative diagnosis with it can be obtained in as early as 10 minutes [1].

Accuracy of cytological diagnosis depends on the good cytological preparation and staining of the smear. Smearing of the tissue with ease depends on the consistency of the tumor. The soft and friable tissues in the CNS tumors are easy to smear and thus provide good cellular details. This is especially exhibited in gliomas, medulloblastomas, pituitary adenomas, most of the meningiomas, and metastatic tumors. Many tumors such as nerve sheath tumors, epidermoid cysts, and some meningiomas, especially the fibroblastic type, are relatively tough to smear. [5] Although smears provide good cytological details, a few diagnostic difficulties were encountered due to misrepresentation of the tumor tissue.

The present study revealed an accuracy of 75.67% that was comparable with some other studies. The diagnostic errors were encountered mostly with glioblastoma as well as astrocytomas and typing of meningiomas. There were 18 discrepant cases in our study.

Five glioblastomas were misinterpreted as fibroblastic meningioma, central neurocytoma, fibrillary astrocytoma, grade III glioma and inflammatory changes. Small cell type glioblastoma was misdiagnosed as central neurocytoma due to misinterpretation of morphology of small cells. One subependymal giant cell astrocytoma was misdiagnosed as anaplastic glioma. Squash smear showed many atypical cells and atypical mitoses which were later on H & E diagnosed as cells of giant cell astrocytoma. One neurofibroma was misinterpreted as schwannoma. Typing of meningiomas was found especially difficult with squash smear cytology in four cases. One ancient schwannoma was misdiagnosed as liposarcoma pertaining to spindle cell morphology. One ependymoma was misdiagnosed as pilocytic astrocytoma and oligodendroglioma was misdiagnosed as fibrillary astrocytoma. Cases of pilocytic astrocytoma and glioma grade III could not be diagnosed correctly by squash smear and were given the diagnoses of infective and tuberculosis due to lack of tumor tissue in squash and coagulative necrosis of tumor respectively.

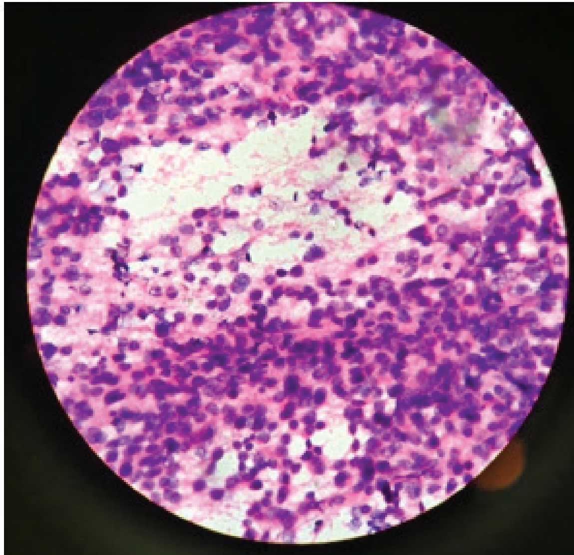

Figure 1:

Squash smear cytology, H&E, 40x

Anaplastic glioma III

Glioblastoma multiforme IV

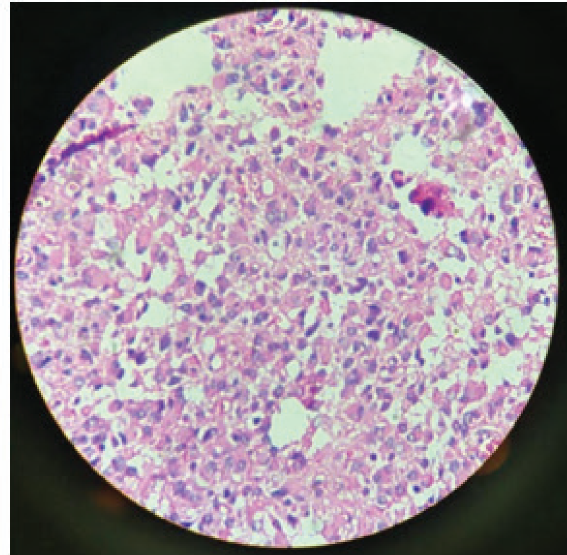

Figure 2:

Histology, H&E, 40x

Subepithelial giant cell astrocytoma

Gemistocytic astrocytoma

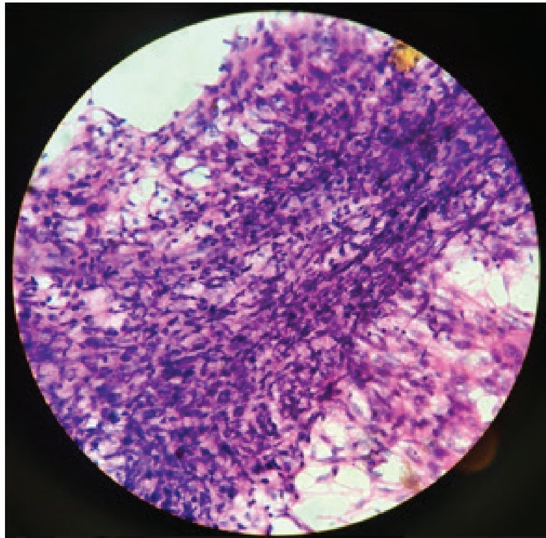

Figure 3:

Squash smear cytology, H&E, 40x

Liposarcoma

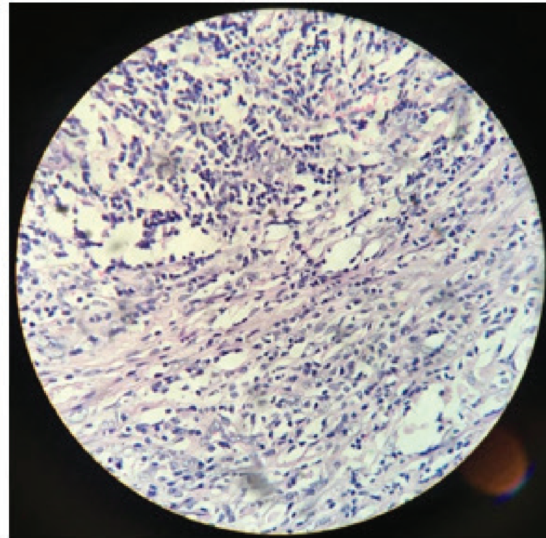

Figure 4:

Histology, H&E, 40x

Ancient schwannoma

Conclusion

This study shows a high degree of cytohistological correlation. With better radio imaging and stereotactic biopsies, the percentage of cytohistological correlation can improve and increase further. Some cases and typing of tumors will always require histopathological study and/or immunohistochemical markers for definitive diagnosis, but for most of the lesions, cytology of the CNS tumors performed intraoperatively fulfills all the determinants of an excellent diagnostic modality. Cytology provides reliable intraoperative guidance. With clinicoradiological correlation, squash smear cytology could be the preferred method for intraoperative diagnosis of CNS tumors.

Source of Funding: Self.

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