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Diagnostic Accuracy of Squash Cytology for Rapid Intraoperative Diagnosis in Tumors of Nervous System

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Abstract:*Introduction: Tumors of the nervous system constitute less than 2% of the cancers globally. They are the second most common form of cancer in children and seventeenth most common in adults. However the morbidity and mortality due to tumors of the nervous system is high. Hence prompt and correct diagnosis is essential for early intervention. In the era of stereotactic biopsies where the amount of tissue is very small, accurate diagnosis is imperative and it can be achieved with squash cytology which is a simple, non-invasive, cost effective and rapid technique. Aim of the study: The aim of the study was to assess the diagnostic accuracy of Squash cytology for rapid Intraoperative diagnosis in tumors of nervous system by comparing histopathology. Materials and methods: This was a prospective study conducted in department of Pathology in a tertiary care teaching medical college hospital for a period of two years. The study subjects were 50 consecutive patients operated for tumors of nervous system in department of neurosurgery. During surgery, small bits of tissue measuring 1-2mm^2 were removed and sent in a gauge moistened with saline for squash cytology. The squash smears were correlated with histopathology. Results: The overall diagnostic accuracy of squash cytology in the present study was 82%.Conclusion: Squash cytology in tumors of the nervous system provides an efficient means of pathological assessment which in experienced hands of a neuropathologist will provide high degree of diagnostic accuracy.*

Key words: *Squash cytology, Tumors of nervous system, CNS tumors, Intra operative diagnosis, neurosurgery*

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I. Introduction:

Tumors of the nervous system constitute less than 2% of the cancers globally [1]. They are the second most common form of cancer in children [2] and seventeenth most common in adults.However the symptoms associated with the tumors range from headache to crippling paresis culminating in death. The time gap between the point of detection of nervous tumors to the point at which it becomes incurable is very narrow. According to the SEER statistics, the tumors of the nervous system has increased in the past decade. This is in part attributed to the improved diagnostic modalities and date reporting and monitoring [3].

Advances in neuroimaging permit early and exact localisation of tumors. The stereotactic brain biopsies permit accurate sampling of multiple areas. Hence exact diagnosis and accurate grading is possible in nervous system tumors [4]. The methods for intra operative diagnosis of nervous tumors are squash cytology, cryostat sections and imprint cytology. Among the methods, squash cytology is the most effective, rapid and reliable method for rapid intraoperative diagnosis [5, 6]. The main advantages of squash cytology are that it is quick, easy to prepare the slides and no need of specialised equipment like cryostat used for frozen sections. The cellular and nuclear details are well preserved.

Despite the advantages, squash cytology has limitations. It cannot be performed on calcified tissues. The amount of pressure exerted when making the smear is crucial as too much pressure can cause crush

artefacts which can pose difficulties in diagnosis and grading tumors especially astrocytoma [7]. The purpose of the present study was to assess the diagnostic accuracy of Squash cytology in detecting nervous tumors by correlating with histopathology which is the golden standard.

Aim:

The aim of the study was to assess the diagnostic accuracy of Squash cytology for rapid Intraoperative diagnosis in tumors of nervous system by comparing histopathology

Objectives:

- To assess the diagnostic accuracy of squash cytology in tumors of nervous system by correlating with histopathology.
- To assess the utility of squash cytology in predicting the grade of astrocytomas
- To determine the diagnostic limitations of squash cytology

II. Materials And Methods:

This was a prospective study conducted in department of Pathology in a tertiary care teaching medical college hospital for a period of two years. The study was done with approval of the institutional review board. The study subjects were 50 consecutive patients operated for tumors of nervous system in department of neurosurgery. During surgery, upon opening the lesion, small bits of tissue measuring 1-2mm^2 were removed and sent in a gauge moistened with saline for squash cytology. The tissue was placed at the end of a clean glass slide and smeared by compressing the tissue with another slide. Care was taken to ensure uniform thickness of the smear. The smear obtained was fixed in isopropyl alcohol for 5 minutes and stained with rapid hematoxylin eosin staining. The whole procedure of fixation and staining took around 12-14minutes. The smears were reported and graded by the neuropathologist. After surgery, the remaining tissue was sent for histopathology in 10% formalin. 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 compared with histopathology grading. The results were analysed using SPSS software and interpreted.

III. Results:

In the present study, 50 cases of tumors of nervous system were included. The most common tumor was astrocytoma followed by meningioma. The age group in our study ranged from 6 to 70 years with the mean age of 40 years [Table1]. The maximum incidence of tumors occurred between 41 to 50 years. Pediatrictumors in the study included 2 cases of hemangioblastoma, 2 cases of medulloblastoma, 1 case of pleomorphic xantho astrocytoma and 1 case of small cell variant of glioblastomamultiformae. In astrocytomas, grade 2 tumors occurred in all age groups, grade 3 tumors were common in 4th decade and grade 4 tumors were common in 5th decade. Among meningiomas, the most common in 5th decade followed by 3rd decade. In the present study, astrocytomas were more common in men and meningiomas were more common in women.

Among 50 tumors of the nervous system, 44 were Central nervous system tumors and 6 were in the peripheral nervous system. The most common site in the central nervous system was the middle cranial fossa. The overall diagnostic accuracy of squash cytology in the present study was 82% [Table2]. 9 cases were misinterpreted in squash cytology [Table3].

There were a total of 16 cases of astrocytoma. The most common was grade 4 astrocytoma (n=9) followed by diffuse astrocytoma grade 2 (n=5). There were 2 cases of grade 3 astrocytoma. Among 16 cases, 2 cases were misdiagnosed. Out of 14 cases of astrocytoma diagnosed with squash cytology, exact grading was possible only in 11 cases. 3 cases were incorrectly graded. Hence when predicting the grade of astrocytoma the diagnostic accuracy dropped from 87.5% to 68.8%. 100% diagnostic accuracy was achieved in medulloblastoma, ependymoma and primary central nervous system lymphoma.

IV. Discussion:

Squash cytology is one of the methods employed for rapid intraoperative diagnosis in neuropathology. The main aim of stereotactic biopsy is to obtain enough tissue so that further diagnosis is established with histopathology. Similarly when an unexpected lesion is expected during neurosurgery, squash cytology helps the surgeon to modify the plan of management.

The most common tumor in our study was astrocytoma [8] [Figures 1-4] followed by meningioma. The most common tumor in astrocytoma was glioblastoma (grade 4) which reflects the Indian and global statistics [9, 10]. The diagnostic accuracy of squash cytology was 82% in our study. Other studies have shown diagnostic accuracy ranging from 80 to 97% [Table 4]. This highlights the diagnostic accuracy of squash cytology in detecting tumors of the nervous system.

Among Astrocytomas, the most common tumor was glioblastoma. Glioblastoma revealed extensive nuclear pleomorphism and atypia. Patchy areas of necrosis and endovascular proliferation were evident [Figure4]. 2 cases had diagnostic difficulties. One case was a small cell variant of glioblastoma in a 6 years old male child. This case was misinterpreted as medulloblastoma as the tumor cells were closely packed,

monotonous with scanty cytoplasm. However in histopathology, the tumor revealed necrosis and endovascular proliferation characteristic of glioblastoma. In one study, small cell variant was misdiagnosed as anaplastic oligodendroglioma [19]. In another study, medulloblastoma was misinterpreted as small cell variant of glioblastoma [20]. Similarly, one case of grade 2 astrocytoma was misinterpreted as reactive gliosis as the representative area was not sampled during squash cytology. Grading of astrocytoma posed diagnostic difficulty. The diagnostic accuracy dropped from 87.5% (n=14/16) to 68.8% (n=11/16). In fact, it was accepted by other studies that it is inappropriate to grade astrocytomas by squash cytology as astrocytomas vary in grade from one area to another within a single tumor [21].

One case of neurofibroma was reported as schwannoma as the elongated wavy nucleus of neurofibroma was wrongly interpreted as cellular areas of schwannoma [Figure5]. Similarly 1 case of meningioma was misdiagnosed as schwannoma as the fibrous areas were mimicking as cellular areas of schwannoma [21]. 1 case of fibrous astrocytoma was again missed as fibrous areas were mistaken for neurofibroma. Many studies reported diagnostic difficulties in squash cytology of oligodendroglioma as the classic perinuclear halo seen in histopathology was absent in squash cytology [15, 22]. 1 case of hemangioblastoma was misinterpreted as medulloblastoma as hemangioblastomas were difficult to smear and we had limited experience with hemangioblastoma. Other case was reported correctly as it had the characteristic population of cells showing plump lipidized stromal cells admixed with fusiform endothelial cells [23].

2 cases of metastatic adenocarcinomatous deposits [Figure6] were missed in squash cytology as one case had sampling error and hence reported as reactive gliosis. Other case was reported as grade 3 astrocytoma due to high cellularity which is a common misinterpretation [6,15,16].

Tables:

Table1: Age distribution of the tumors of the nervous system

S.No	Age group	Tumors of nervous system
1	0-10 years	5
2	11-20 years	1
3	21-30 years	7
4	31-40 years	8
5	41-50 years	16
6	51-60 years	10
7	>60 years	3
Total number of cases		50

Table2: Correlation of squash cytology with histopathology in tumors of the nervous system

S.No	Tumors of the nervous system	Total number of cases	Correlation with histopathology		Diagnostic accuracy
			Correlation	No Correlation	
1	Astrocytoma	16	14	2	87.5%
2	Meningioma	15	13	2	86.7%
3	Neurofibroma/Schwannoma	6	5	1	83.3%
4	Oligodendroglioma	2	1	1	50%
5	Medulloblastoma	2	2	0	100%
6	Ependymoma	1	1	0	100%
7	Hemangioblastoma	2	1	1	50%
8	CNS lymphoma	2	2	0	100%
9	Metastatic deposits	4	2	2	50%
Total number of cases		50	41	9	82%

Table3: Cases misinterpreted in squash cytology

S.No	Squash cytology	Histopathology
1	Medulloblastoma	Small cell variant of glioblastoma
2	Reactive gliosis	Diffuse astrocytoma grade 2
3	Schwannoma	Neurofibroma
4	Schwannoma	Meningioma
5	Neurofibroma	Fibrous astrocytoma
6	Diffuse astrocytoma grade 2	Oligodendroglioma
7	Medulloblastoma	Hemangioblastoma
8	Reactive gliosis	Metastatic carcinomatous deposits
9	Grade 3 astrocytoma	Metastatic carcinoma deposits

Table4: Comparison of diagnostic accuracy of squash cytology with published studies

Study place	Study year	Sample size	Diagnostic accuracy	Reference
Brazil	2001	650	97.3%	11
Uttar Pradesh, India	2010	334	94.9%	12
Rajasthan, India	2012	150	94%	13
Maharashtra, India	2016	50	92%	14
Tamilnadu, India	2016	75	90.67%	15
Nepal	2014	60	88%	16
Gujarat, India	2006	278	87.76%	17
Present study	2014	50	82%	-
Odisha, India	2015	63	80.33%	18

Figures:

Figure1: Squash cytology of Grade 2 astrocytoma showing cells with delicate processes and eosinophilic cytoplasm in a fibrillary background

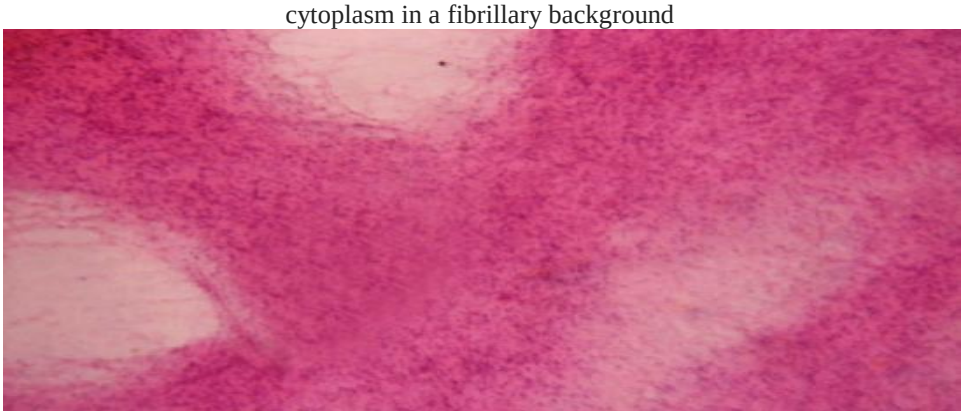


Figure2: Squash cytology of Grade 3 astrocytoma showing increased cellularity and high nuclear cytoplasmic ratio

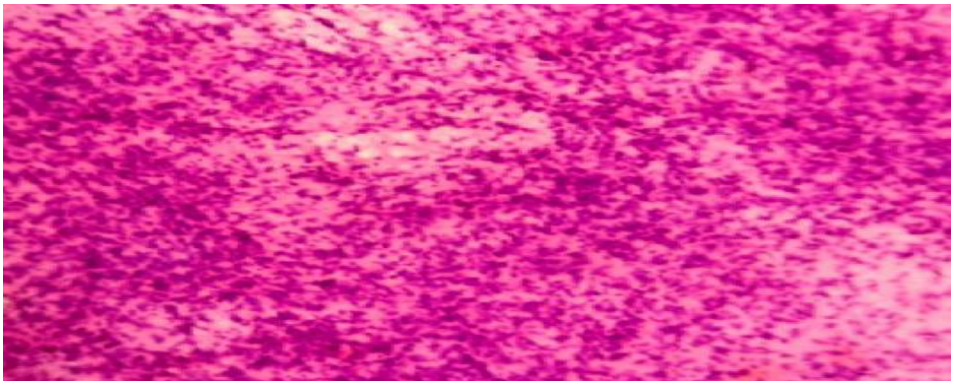


Figure3: Glioblastoma in squash cytology showing pleomorphic astrocytes and endothelial proliferation (arrow)

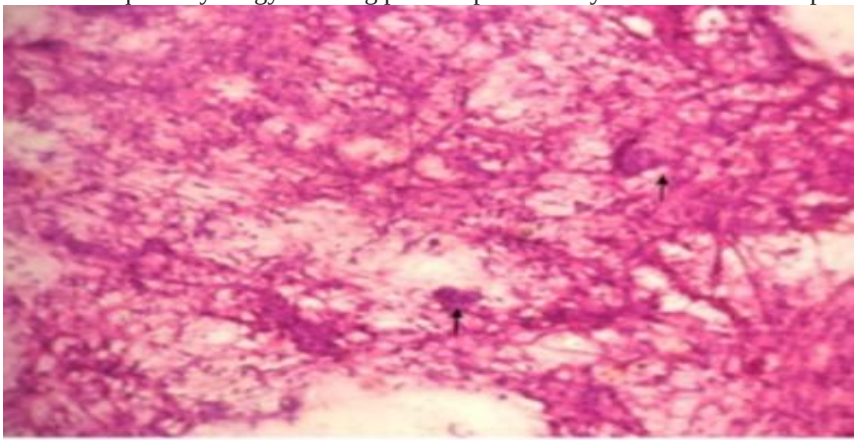


Figure4: Schwannoma in squash cytology showing fascicles of tumor composed of cohesive cellular areas (100x)

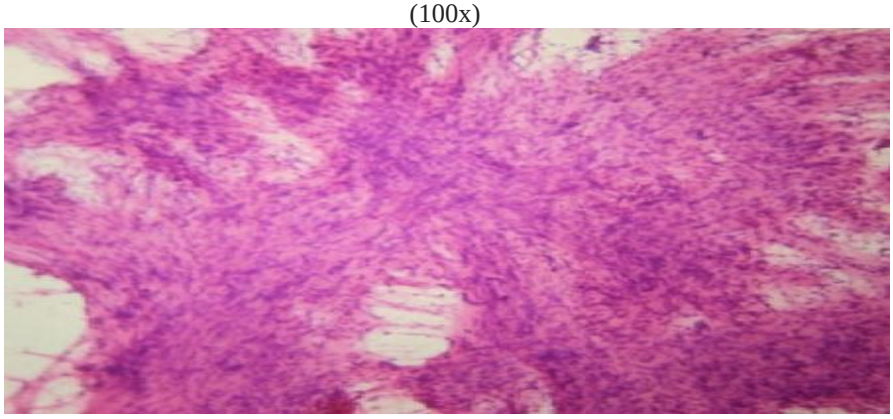
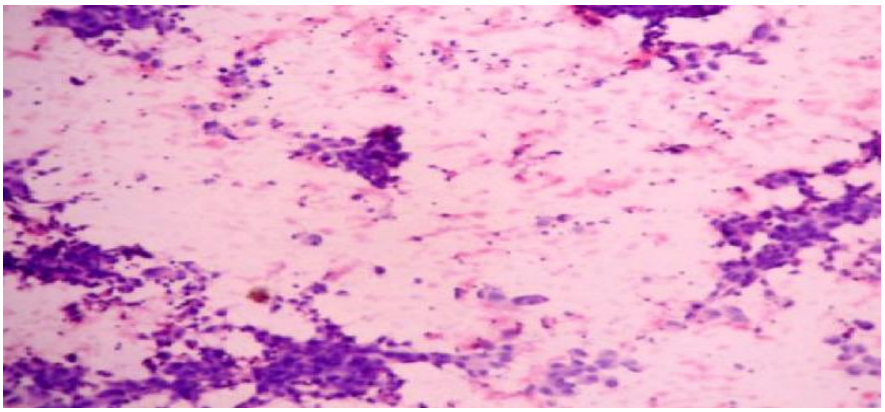


Figure5: Metastatic adenocarcinomatous deposits in squash cytology showing vague glandular pattern of tumor cells



V. Conclusion:

The overall diagnostic accuracy of squash cytology in the present study was 82%. The method is easy, rapid and inexpensive. Details of the cellular morphology are well preserved with squash cytology. Hence Squash cytology in tumors of the nervous system provides an efficient means of pathological assessment which in experienced hands of a neuropathologist will provide high degree of diagnostic accuracy.

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