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Original Research Article

A prospective study on the relevance of crush or squash cytology of central nervous system lesions, in the present-day surgery

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ABSTRACT

Background: The intra-operative cytology in the evaluation of central nervous system (CNS) lesions is a simple and rapid technique, and a useful tool. There is not much literature available on the value of crush cytology during the operation. The current study was planned to assess the feasibility and efficacy of intra-operative squash cytology as standalone method in the rapid intra-operative diagnosis of intracranial tumor.
Methods: A prospective observational study was carried out in the department of neurology in collaboration with department of pathology, Medanta: The Medicity, Gurugram, for a period of six months from January 2019 to June 2019, on randomly selected 60 patients, aged: 18 years and above. Two to three tissue bits, from different sites of the mass, were taken to prepare squash cytology smear.
Results: Out of 60 patients operated, 54 had neoplastic and 6 had non-neoplastic lesions. Neoplastic benign lesions were observed in 41 patients and neoplastic malignant lesions were diagnosed in 13 patients. There was 17.67% offering a wrong diagnosis on crush cytology. Out of the 13 cases of meningioma, there was a discrepancy in 3 (three) cases.
Conclusions: Crush cytologyis a useful adjunct to the diagnosis in neurosurgical practice. This study suggests and confirms the reliability of squash cytology, but further multicentre studies with larger number of patients may help to decide its use in clinical practice.

Keywords: Crush cytology, Central nervous system tumors, Intra-operative diagnosis

INTRODUCTION

Pigmented lesions of the central nervous system (CNS) are a diverse group of entities that run the gamut from benign to malignant. These lesions may be well circumscribed or diffuse, and their imaging appearances are influenced by the degree of melanin content as well as the presence or absence of hemorrhage. A glioma tumor forms when glial cells grow out of control. Normally, these cells support nerves and help your central nervous system work. Gliomas usually grow in the brain, but can also form in the spinal cord. Gliomas are malignant (cancerous), but some can be very slow growing. Gliosarcoma, on the other hand, is a rare type of glioma. A pituitary tumor forms in the pituitary gland near the brain that can cause changes in hormone levels in the body. A meningioma arises from the meninges- the membranes that surround the brain and spinal cord. Astrocytoma begins in cells called astrocytes that support nerve cells. An accurate diagnosis of intracranial lesions is almost in-disposable for therapeutic and prognostic reasons. Intracranial tumors account for 10-17 per 1,00,000 persons.[1,2]

In developing countries like India, intracranial lesions can result from inflammation/infection to life-threatening malignancies.[3]

The concept of intra-operative cytology in the evaluation of CNS lesions was first started by Eisenhardt and Cushing in1930.[4] Sinceit is a simple and rapid technique, it is a very useful tool in the intraoperative diagnosis of CNS lesions. In a study of 326 cases, Jaiswal et al noted that in 83.7% of cases, there was a concordance between the intraoperative crush cytological diagnosis and the final histopathological diagnosis. They also showed that the accuracy was the most for glioblastomas, meningiomas, and schwannomas and much less in cases of oligodendrogliomas.[5]

Considerable literature is available on the concordance between cytology and histopathology in CNS lesions, but not much literature is available on the value of crush cytology for the operating surgeon during the operation. For example, in many CNS tumors, the surgeon may not be sure if he is within the lesion despite the specialized neuroimaging techniques.

The presenting clinical features of intracranial lesions are usually varied and similar for many diseases, which often results in diagnostic delays. The radiological features may not always be conclusive about etiology of the lesions. The overall inaccuracy of preoperative radiographic diagnosis ranges between 10 and 30%, thus making it impossible for the surgeon to provide the patient with adequate therapy.[6] In many cases, a small tissue fragment analyzed by the crush technique may be invaluable in telling the surgeon if he is within the lesion.

It is widely believed that high resolution and specialized neuroimaging techniques would obviate the need for any intra-operative consultation, but intra-operative consultation still continues to be relevant. Modification and planning of CNS surgeries can be done by the neurosurgeon when he has an intra-operative diagnosis available.[7] This is why the intra-operative squash preparation is a simple and accurate tool which can be of immense help to the surgeon, in diagnosis of intracranial lesions.

In developing countries, frozen section has limited use in routine diagnostic practice because of limited laboratory resources either in terms of human or technical reasons.[8] Nevertheless, often the clinical and therapeutic decisions need to be made before the histological diagnosis is proven conclusive and a trial of more invasive procedures to obtain a biopsy is recommended. In such cases, cytology thus remains the only possible way to provide a rapid and reliable diagnosis even with small samples.

Therefore, the objective of the present study was to assess the efficacy of intra-operative squash cytology as standalone method in the rapid intra-operative diagnosis of intracranial tumor and tumor-like lesions in such settings, where frozen section facility is not available.

METHODS

A prospective randomized observational study was carried out in the department of neurology in collaboration with department of pathology, Medanta: The Medicity, Gurugram, for a period of six months from January 2019 to June 2019. The study was conducted on randomly selected 60 patients, aged: 18 years and above.

Inclusion criteria

All consecutive patients, aged 18 years and above, presented at the department of neurosurgery with clinical features of space occupying lesions in CNS were enrolled in the study.

Exclusion criteria

The patients with history of traumatic concussion injury to head were excluded from the study population.

Informed written consent was obtained and the patients were ensured of confidentiality. The decision to do surgical procedure was made on clinical demand and not for the sake of participation in the study. Ethical approval was obtained from the institutional ethical committee.

The patients were investigated with radio-imaging either with computed tomography (CT) scan (64 slice contrast/non-contrast) or magnetic resonance imaging (MRI) scan (1.5 tesla). Complete blood count, screening for HIV were also done in all the patients. The patients were operated according to the clinical need. The final diagnosis of lesion was established on fulfillment of histological features along-with special stains such as immuno-histochemistry, wherever needed.

As per the Intra-operative procedure that was followed, and in all cases, the mass was cut open and bisected in slices according to size and the surgical biopsy protocol. Two to three tissue bits, from different sites of the mass, were taken to prepare squash cytology smear.

Two squash smears were prepared from the tissue bits taken from the mass before embedding it in 10% formalin. One squash smear was immediately fixed with 95% ethyl alcohol before drying for rapid haematoxylin & eosin (H&E). The slide which was used for crushing was at a right angle to the slide on which the material was placed. The smears were quick- rinsed in water followed by dip in Harris's haematoxylin for one minute, then in acid alcohol (1% hydrochloric acid in 70% alcohol), and in Scott's tap water and counter stained with 0.5% eosin for 30 seconds. The second smear was air dried and kept for Giemsa stain which was done when needed. The time for the procedure was noted, Intra-operative cytology diagnosis was compared with the histology diagnosis and the diagnostic

indices of cytology were calculated. The remaining tissue was processed for routine paraffin section study.

Attempt was made to perform a statistical analysis on our results. However, since this was a descriptive study, no valid statistical analysis could be performed.

RESULTS

Mean age of the participants was 47.63 years, with male to female ratio being: 11/9 (33/27) (Figure 1). Out of 60 patients operated, 54 had neoplastic and 6 had non-neoplastic lesions. Out of 54 patients, neoplastic benign lesions (most common being neurilemmoma, pituitary adenoma and transitional meningioma) were observed in 41 patients and neoplastic malignant lesions were diagnosed in 13 patients. The cytology features of type and grade of lesion were correlated with histological examination and the diagnostic accuracy of intra-operative squash cytology was 83.33%. The percentage of offering a wrong diagnosis on crush cytology was 17.67% (Table 1).

Out of a total of 19 cases of gliomas, reported in this study, based on the clinical and radiological examination, in 3 (three) cases, a wrong diagnosis was offered on crush cytology and was suggestive of a gliosarcoma. The diagnosis of a gliosarcoma was confirmed in all the three cases on histopathological examination.

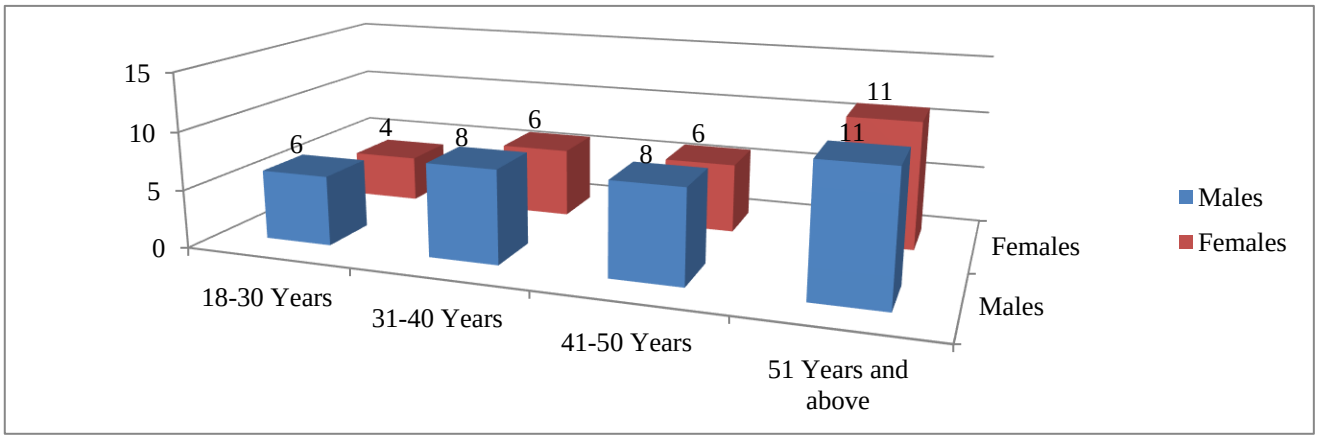

Figure 1: Demographic composition of the participants.

Table 1: Concordance and discordance between the crush cytology and the final histopathology report.

S. no.	Type of neoplastic tumor	Cytology features observed	Concordant	Discordant	Total
1	Glial Neoplasms	Cellular, nuclear pleomorphism, mitotic figures, vascular proliferation	16	3	19
2	Pituitary Adenoma	Sheets of uniform round cells, eosinophilic cytoplasm, vesicular nuclei	6	1	7
3	Meningioma (benign)	Sheets of plump spindle nuclei, whorl pattern, abundant granular cytoplasm	9	2	11
4	Meningioma (malignant)	Plump spindle nuclei, hyper chromatic nuclei, mitoses	4	1	5
5	Astrocytoma	Moderate cellular, irregular clusters, vague papillae, cytoplasmic glial processes	6	0	6
6	Neurilemmoma	Cohesive uniform spindle, ‘twisted rope’ appearance, palisading nuclei or no nucleoli	3	1	4
7	Metastatic tumours	-	1	1	2
	Total		45	9	54

Out of the 13 cases of meningioma, therewas a discrepancy in 3 (three) cases. Two of such cases were of suprasellar mass. The crush cytology showed a mixed cell population with a few spindle cells and scattered squamous cells. The diagnosis offered on crush cytology was a craniopharyngioma. However, the histopathology showed typical features of a meningothelial meningioma, and the diagnosis was revised accordingly.

Seven (7) cases of pituitary tumors were reported. In one case, a wrong diagnosis was offered on crush cytology. In one case, the lesion was reported as a brain abscess based on the clinical and radiological picture. However, the cytology showed extensive areas of necrosis with

fragments of metastatic deposits of a papillary carcinoma. The presence of metastatic deposits was confirmed on histopathology.

Two of the six inflammatory, non-neoplastic lesions (of the type: epidermal cyst), were seen as pearly white slippery membranous which was difficult to smear on squash. Microscopically, smear revealed scanty eosinophilic laminated structure. A wet smear examination was done from the cystic fluid that showed presence of scolex. The case was confirmed as hydatid cyst on histology.

Intra-operative time interval of diagnosis by squash cytology was within 15 minutes in all patients.

DISCUSSION

The strength of squash/crush cytology is that it is simple, rapid, robust and provides good cellular details. Even very tiny specimens are suitable for smear preparation, which is extremely important in surgical procedure from intracranial lesions which are localized in functionally important areas of brain.[9]

Some studies have found the diagnostic accuracy of squash cytology between 87% to 97% in correlation with histopathology.[10,11] In our study, the overall diagnostic accuracy of squash cytology was 83.33% when compared with histology, as the gold standard, which also correspond to these studies. The reason of slightly lower level of accuracy can be attributed to tissue contamination and possibly poor sample handling.

In the evaluation of CNS lesions, crush cytology has been reported to be an excellent adjunct; they are probably better in the diagnosis of CNS lesions than frozen sections where the cytological detail is not preserved. Cahill and Hidwegi reported that the crushcytology provided a diagnosis in 29 out of the 32 cases.[12] Use of intra-operative cytology can provide diagnostic information when frozen section is equivocal or when frozen-section evaluation could not be done, especially with excessively small sample.[13]

Crush cytology also has its own limitations, as a wrong diagnosis was offered on crush cytology in 3 cases and was suggestive of a gliosarcoma. The diagnosis of a gliosarcoma was confirmed in all the three cases on histopathological examination. High-grade gliomas show a high cellularity with considerable cytological heterogeneity; usually, the cells are close to the blood vessels. Endothelial cell proliferation is seen with glomeruloid bodies, cellular pleomorphism, and necrosis.[14]

Krishnani et al evaluated 365 crush cytologyspecimens of the CNS and reported that discordance between crush cytology and histopathology in the diagnosis of lymphomas was quite high. 9 lymphomas were diagnosed on histopathology. 2 cases were misdiagnosed as high-grade astrocytomas in crush cytology.[15]

Out of the 13 cases of meningioma, therewas a discrepancy in 3 (three) cases. Two of such cases were of suprasellar mass. The crush cytology showed a mixed cell population with a few spindle cells and scattered squamous cells. The diagnosis offered on crush cytology was a craniopharyngioma. However, the histopathology showed typical features of a meningothelial meningioma,and the diagnosis was revised accordingly. A wrong diagnosis was offered on one out of 7 cases of pituitary tumors crush cytology in our study.

In one case, the lesion was reported as a brain abscess based on the clinical and radiological picture. However, the cytology showed extensive areas of necrosis with fragments of metastatic deposits of a papillary carcinoma. Metastasis was confirmed only on histopathology. The difference in interpretation was based on the cell morphology and not the presence or the absence of necrosis. Clearly malignant cells were seen in this case which confirmed the diagnosis.

We misinterpreted one case of meningioma and we could not diagnose one metastatic adenocarcinoma as there was excessive degeneration and necrosis with no obvious cellular yield, suggesting that the type and grade of lesions might be responsible for misdiagnosis.[16,17]

Diagnosis should not be madebased on the background necrosis or the presenceof vascular proliferation both of which may createa confusion. Efforts should be made to identify the cell morphology. It is of paramount importance to the surgeon that a neoplastic and a granulomatous lesion is differentiated, since the extent of surgery is dictated by this diagnosis. Furthermore, care should be taken in evaluating the spindle cells, which can prevent several errors. We found difficult to prepare a good cellular squash smear in case of hydatid cyst because of slippery tissue. In the present study, however, we have shown that using squash cytology as standalone diagnostic procedure, it is possible to achieve consistently high sensitivity and specificity for intra-operative diagnosis of intracranial lesions even in resource-limited settings. The role of pathologists should be to provide sufficient preliminary information for optimal surgery rather than to provide a precise diagnosis and accurate grade for each case.[16]

The limitation of the study is that it restricts us from evaluation of the true value of squash cytology as standalone intra-operative procedure due to limited sample size and absence of decisive statistical conclusions.

CONCLUSION

Crush cytologyis a useful adjunct to the diagnosis in neurosurgical practice. It may be a useful intra-operative technique; preoperative evaluation of the clinical and

radiological findings is also essential in arriving at the correct diagnosis. There seems a feasibility of using the technique as standalone diagnostic technique for better management of patients in settings where frozen section facility is not available. This study suggests and confirms the reliability of squash cytology, but further multicentre studies with larger number of patients may help to decide its use in clinical practice.

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