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Utility of Intraoperative Frozen Section in Diagnosis of Meningiomas

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***Abstract**:*
***Background:** Meningiomas are the most common primary neoplasms of the central nervous system, attached to the internal surface of dura matter and constitutes 24- 30% of all intracranial tumours.*
***Aims and Objectives:**The study was undertaken to study the epidemiological occurrence of meningiomas and to ascertain the validity and reliability of frozen sections in intraoperative diagnosis of meningiomas and compare it with subsequent histopathological diagnosis.*
***Material and Methods:**A prospective study was done in 31 case who underwent excision surgery at Department of Neurosurgery. Intraoperative frozen section study of the specimens were done.One portion of tissue was kept for FFPE section and final histopathological examination was done. Previous frozen section findings were compared with subsequent histopathology typing and grading.*
***Results:**The most common site was found to be cerebellopontine angle. Out of total 31 cases 28 case were confirmed by histology as meningioma. Total 25 cases which was diagnosed as meningioma in frozen section confirmed by subsequent histopathological examination. According to the histological subtype fibrous(32%) followed by meningothelial meningioma(28%) was found to be most common.Correlation of frozen section analysis was done with final histology. Sensitivity and specificity was found to be 89% & 33% respectively.PPV - 93 % NPV 25% Diagnostic accuracy 89.28% , p <0.05(statistically significant).*
***Conclusions:** Frozen section is a rapid, simple, inexpensive method for detection of Central nervous system tumours. The confirmed histological analysis of meningiomas showed a good correlation with frozen section . Hence we conclude that frozen section is a less expensive, simple, fast and reliable method for diagnosis of various CNS meningioma.*

***Keywords**: Cns tumour, Intraoperative , Grade.*

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I. Introduction

Meningiomas are the most common primary neoplasm of the central nervous system attached to the internal surface of dura matter and constitutes 24- 30% of all intracranial tumors.[1]Meningiomas are mostly benign tumours with atypical and anaplastic meningiomas constituting the higher grade i.e Grade II and Grade III respectively. Frozen section provides an intraoperative consultation for brain tumour assessment thereby providing information during surgery. It is also well established that there is an error rate associated with the interpretation of frozen sections due to a variety of factors including tumor heterogeneity, surgeon operator error pathologist interpretation error and technical artifacts i.e. cautery crush or freeze artifacts. [2,3]

The study was undertaken to study the epidemiological occurrence of meningiomas and to ascertain the validity and reliability of frozen sections in intraoperative diagnosis of meningiomas and correlate with subsequent histopathological diagnosis and to ascertain the subtyping and grading of meningiomas with respect to current WHO classification of tumours of central nervous system.

II. Materials and Method

The study was conducted in the Department of Pathology in association with Department of Neurosurgery at our hospital from June 2017 to March 2019.Patients presenting with symptoms of headache and seizure and diagnosed radiologically as intracranial space occupying lesions and also underwent subsequent

excision at Neurosurgery Department were taken. Those who have diagnosed as meningioma in frozen sections were only taken as subjects. Patients who were diagnosed with CNS neoplasm other than meningioma were excluded from the study.

The study was performed after obtaining the approval from Ethical Committee, and a total of 31 cases were selected.The specimens were sent to the Department of Pathology for further examination. Imprint smears were taken from the fresh specimens and frozen sections examination was done. May–Grunwald–Giemsa and Papanicolaou staining were performed on touch imprint smears and Rapid Hematoxylin and Eosin staining (H &E) was done in frozen sections and provisional diagnosis was given. Final histopathological examination was done with excision biopsies specimen by formalin fixation and paraffin embedding and H&E staining. The histological subtyping and grading were done according to recent WHO classification of central nervous system to reach a confirmed diagnosis and prediction of accuracy of frozen section analysis. Due to tumour heterogeneity and inadequacy in tissue sampling, there is difficulty in assessing grades and subtypes of meningiomas. Besides the evidence of brain invasion is not always apparent in frozen sections. Due to these, often there is a downgrade of histological types seen in frozen section

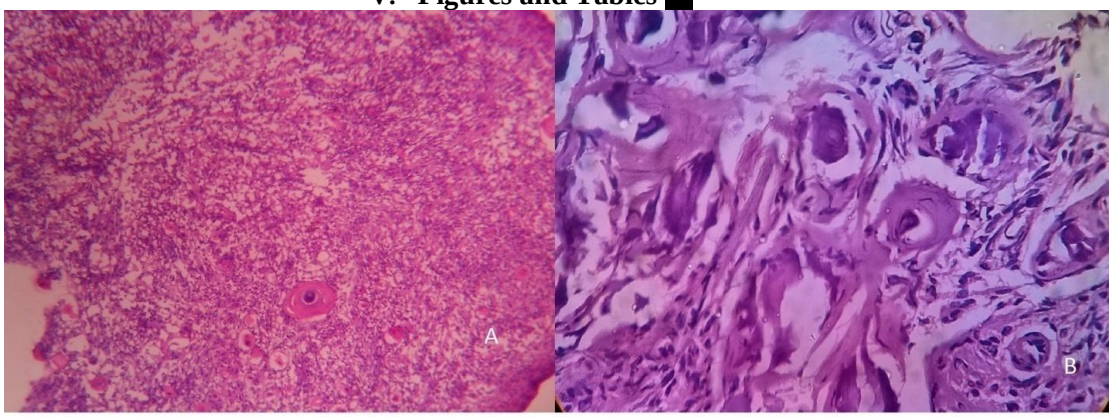
III. Statistical Analysis

All data were copied into Microsoft Excel and contingency charts were prepared for qualitative data. Data were analyzed with the help of SPSS software version20.0(IBM,Armonk,New York,USA),Prism Graph Pad version 5. Matthews correlation coefficient T Test ,Kohen's Kappa (k), Chi square test (x2) were used for the statistical analysis and $P < 0.05$ was considered statistically significant.

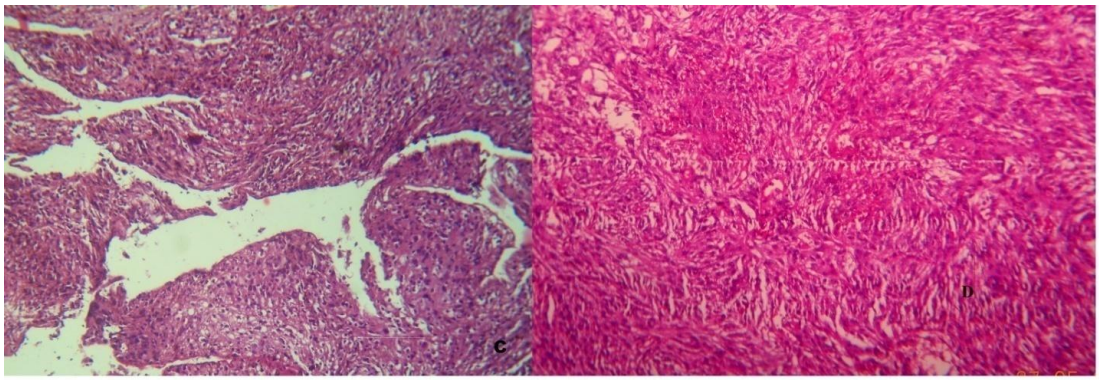
IV. Results

Out of the total 31 patients who formed the study group there were21 females (61 .74%) and 10 (32.25%)males. The age range in was from 1year to 80 years of age at the time of surgery.The mean age (± standard deviation) is 41± 14 .76 years.There was a single patient within 20 years of age, 14 patients within 21 and 40 years of age 13 patients of the age range of 41- 60 years and rest 3 within 61- 80 years. According to the location the most common site of tumour was cerebellopontine angle (9/31) followed by temporal lobe(5/31), olfactory groove (4/31), parasagittal lobe(4/31), sphenoid wing (3/31), orbital lobe(2/31), dorsolumbar spine (2/31), suprasellar region(1/31), parietal lobe(1/31). (**Table 1**)**)** The histological subtype of meningioma was graded according to the WHO classification of central nervous system. The most common histological subtype was fibrous meningioma(9/28), followed by meningoepithelial(8/28), psammomatous(6/28), angiomatous and atypical (2/28) and anaplastic (1/28). According to the tumour grade, there were 25/28 of Grade 1, 2/28 grade 2 and a single case was found to be of grade 3. (**Fig 1,2,3,4,5,6)** Out of total 31 cases of tumour we got 28 cases of meningioma confirmed by histology 2 case were schwannoma 1 case was Malignant peripheral nerve sheath tumour. 25 cases was diagnosed as meningioma in frozen section was subsequently confirmed by histology.So diagnostic accuracy was 89.28%. The correlation with frozen sections and confirmed histopathological diagnosis were analyzed and it was found to have a sensitivity of 89%, specificity of 33%, positive predictive value of 93%, negative predictive value 25%, false positive rate (α) of 67%, false negative rate (β) of 11%, positive likelihood ratio 1.34 and a negative likelihood ratio of 0.32.(**Table 2 &3)**

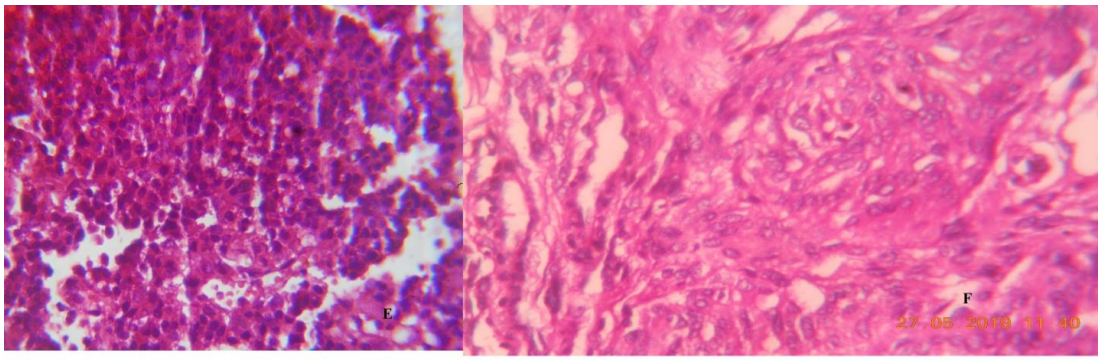
V. Figures and Tables



1.Fig A.Picture showing Psammatomatous merningioma in frozen section (x100)
2.Fig B.Picture showing Psmmamomatous meningioma in histology (x400)



3 .Fig C .Picture showing fibrous meningioma in frozen section(x100)
4. Fig D .Picture showing fibrous meningioma in histology (x100)



5. FIG E :PICTURE showing meningothelial meningioma in frozen section(x400)
6 .FIG F: PICTURE showing meningothelial meningioma in histology (x400)

Table 1: Distribution Of Site Of Total Tumours .

LOCATION	NUMBER
CP ANGLE	9
TEMPORAL LOBE	5
OLFACTORY GROOVE	4
PARIETAL LOBE	1
PARASAGITTAL	4
SPHENOID WING	3
ORBITAL LOBE	2
DL SPINE	2
SUPRACELLAR	1

Table 2: Distribution Of True Positive And True Negative Cases As per Diagnosis From Frozen Section And Histopathological Examination

	HP tested as gold standard		
Frozen Diagnosis	positive	negative	
Positive	25	2	27
Negative	3	1	4
Total	28	3	31

Table 3 : Overall efficacy of Frozen section in diagnosing meningiomas

SENSITIVITY	89%
SPECIFICITY	33%
PPV	93%
NPV	25%
False positive rate (α)	67%
False negative rate (β)	11%
Positive likelihood ratio	1.34
Negative liklihood ratio	0.32

VI. Discussion

The role of frozen section interpretation for central nervous system tumours by the pathologist is mainly to corroborate with clinico-radiological features so as to assist the neurosurgeon while doing the surgical procedure. [4] This helps the surgeon to decide upon the appropriate surgery and further follow up and management of the patients.[5,6] The craniotomy specimen will help in reaching a definitive diagnosis after performing cytological examinations coupled with frozen sections.This will help in initiating proper intraoperative procedure as well as adjuvant chemotherapy if needed. The limitation in this aspect is the amount of the tissue sampled. Depending upon the detailed clinical profile, radiological investigations, proper cytological evaluation of the tissue sample an algorithm of differential diagnosis is reached at and finally a rapid evaluation and a confirmed diagnosis according to the features in frozen section is given. For this a correlation of touch imprint preparation and frozen sections are of extreme help. [7] The main focus of our study was assessment of meningiomas whether accurate grading and subtyping is possible by frozen section during the surgical procedure as in the study done by RA Prayson. [8] The subtyping was based on the recent WHO classification .[9]

Among the total 31 patients analysed, median age was found to be 42 years and there was female preponderance. Cerebellopontine angle was the most common site seen. The most common subtype found was fibrous followed by meningoepithelial quite corroborating according to the WHO classification. Among the 25 cases of frozen section confirmed by subsequent histology grading of tumour also can be done easily on frozen section .One case of atypical meningiona (grade 2) was found anaplastic (grade 3) on permanent sections. One grade 1 tumour was found to be grade 2 on histology . In all other case grading done in frozen sections more or less confirmed with histological section grading a high sensitivity level of 89% and a positive predictive value of 93% whereas a low specificity of 33% and a negative predictive value of 35%. Hence frozen section was found to be a highly sensitive procedure with a low specificity.

Friable nature of the frozen section and freezing artefacts due formation of ice crystals were the most common limitations faced in the procedure resulting in anisonucleosis and nuclear hyperchromasia. Besides these, thicker sections and loss of sections were among the other limitations. Fibroblastic meningioma due to their fibrous nature and lesser friability yielded better quality sections. [10]

As we compare our study done by Tofte et al , the sensitivity and positive predictive value were > 90%, found to be corroborative. WHO grade 1 tumours were found to be the most common histological variety.[11]On literature survey studies have reported the discrepancies in reporting frozen section with ovegrading or undergrading of the tumours. Several lesions were found to be the close mimickers like Schwannoma, sarcoma, paraganglioma amongst others. Evaluation of the age,site of lesion, clinico radiological correlation, a proper diagnosis is sought for. [12,13,14,15] If we consider differentiating meningioma from other entities the confirmed diagnosis can be made at most of the times with accurate mention of site of lesion from the neuroimaging. [16]With a very small biopsy following a stereotactic surgery it is extremely difficult to distinguish Spindle cell sarcoma its variants schwannomas, malignant peripheral nerve sheath tumours with meningiomas in frozen sections. As meningiomas and schwannomas share the site of origin and show benign spindled cell appearance in a collagenous stroma and perivascular whorling . differentiation is done based on alternate hypocellular, hypercellular areas, Verrucay bodies favoring Schwannomas whereas uniform nuclear arrangement and presence of psammoma bodies favor meningiomas. In specimens where there is presence of crush artifact making diagnosis bit more difficult, a provisional diagnosis of benign spindle cell neoplasm is made to avoid over interpretation. Sarcomas also fall in the group of mimickers, but the spindle shaped cells with cytological atypia and presence of increased mitotic figures favors a sarcomatous differentiation.[17] However in spite of all these limitations our study results of frozen section diagnosis and permanent histopathological diagnosis were quite corroborating with each other and henceforth provided as an useful tool regarding patient treatment during surgery. [7] Depending upon the pathologist's evaluation of the detailed clinicopathological findings consultation with the neurosurgeon and quality reporting the frozen section still remains the mainstay for intraoperative consultation of Cns neoplasms.

VII. Conclusion

Frozen section serves as an useful tool in providing an insight as an adjunct to intraoperative procedure in neurosurgery. Our study showed a high sensitivity of frozen section procedures in subtyping and grading of meningiomas. Majority of the cases were intracranial Grade I tumours with a female preponderance. Hence we conclude that frozen section is a less expensive, simple, fast and reliable method for diagnosis of various Cns meningiomas.

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