Comparative Study of Frozen Section Diagnoses with Histopathology

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ABSTRACT

The correlation of intraoperative frozen section diagnosis with final diagnosis on permanent section is an integral part of quality assurance in surgical pathology. The present study was a retrospective analysis of 404 cases of frozen section biopsy, reported in the BPKMCH pathological department between January 2003 to December 2007. The frozen section diagnoses were correlated with the final histological diagnosis to assess the accuracy of the technique. The number and type of discrepancies were compared the indication, causes for the discrepancies and deferrals were analyzed in order to decrease the avoidable errors and improve on the frozen section diagnosis. The overall accuracy over 5 years was 94.6% with false positive rate of 1.5%, false negative rate of 3.9% and 3.9% of deferred diagnosis. The achieved results in the present study were comparable with the published results. The discrepancies were mainly due to the interpretation error, sampling error, technical artifacts and partly due to lack of interdepartmental communication. Frozen section diagnosis is very useful and highly accurate procedure. Gross inspection, sampling by pathologist, frozen complemented with cytological and histological review and intimal cooperation with surgeon can avoid certain limitations and provide rapid, reliable, cost effective information necessary for optimum patient care.

Keywords: frozen section, histopathology.

INTRODUCTION

Frozen section (FS) technique was first introduced by the eminent pathologist, William H. Welch, from Johns Hopkins Hospital in 1891. By the early and mid 1920s, the technique became popular and was used for intraoperative consultation in everyday practice. However, the technical quality of most frozen sections during these early years was suboptimal. The preparation of frozen section was made easier in the 1950s and 1960s by the development of the modern cryostat, a cabinet cooled to -20 to -30 degree Celsius and enclosing a microtome blade.^{1, 2, 3, 4}

The main purpose of frozen section is to provide rapid diagnosis to guide intra or perioperative patient management. The indications of frozen section are identification of tissue and unknown pathological processes, evaluation of margins, identification of

Correspondence : Dr.Srijana Shrestha (Khadka) Srijana 21849@yahoo.com, 9841298794 lymph node metastasis, confirmation of presence of representative samples for paraffin section diagnosis and to determine the nature of a lesion that may require ancillary test.^{5,6}

It should not be used to merely to satisfy a surgeon's curiosity, to compensate for inadequate preoperative evaluation, or a mechanism to communicate information more quickly to the patient or patient's family.^{5,7}

A college of American Pathologist (CAP) sponsored review of over 90,000 FS at 461 institutions showed a concordance rate of 98.52%. The study reasons that the main causes for the discrepancies were either misinterpretation of the original frozen section (31.8%), absence of diagnostic tissue in the frozen material but present in the unsampled tissue or in the corresponding permanent section (31.4%).⁸

BP Koirala Memorial Cancer Hospital (BPKMCH) is the only referral centre in Nepal where frozen section

facility is available. The present study reviewed 404 cases of frozen section biopsy done in between 2003 to 2007 to assess the accuracy, indication, discrepancies and causes for deferral.

MATERIALS & METHODS

It was a retrospective analysis of 404 cases of frozen section biopsy, reported in the BPKMCH pathological department between January 2003 to December 2007. All the datas were retrived from the bound report book and the register maintained in the reporting room. The frozen section diagnoses were correlated with the final histological diagnosis to assess the accuracy of the technique. The number and type of discrepancies were compared the cause for deferred diagnosis and the discrepancies were analyzed and compared with the other studies.

Frozen sections were cut on a Shandon cryostat machine and evaluated in Hematoxylin and Eosin (H&E) stain. Subsequently, for the permanent section, specimens were fixed in 10% formalin, grossed and adequate representative sections were taken according to the standard guidelines. The sections were then evaluated in H&E stain.

RESULTS

The overall accuracy over 5 years was 94.6% with false positive rate of 1.5%, false negative rate of 3.9% and 3.9% of deferred diagnosis. The causes for false positive diagnosis were due to interpretation error and the unavoidable freezing artifact. Sampling error was the main reason for the false negative diagnosis. In 3.9% of cases, diagnosis was deferred to permanent section mainly due to lack of adequate clinical information and inadequate material.

Table 1. Frozen section diagnosis in 404 cases			
Accuracy (%)	366(94.3%)		
False positive (%)	6 (1.5%)		
False negative (%)	16 (3.9%)		
Deferred (%)	16(3.9%)		
Typing /grading error (%)	18 (4.5%)		

The most common indication encountered were verification of type of neoplasm (360/404), assessment of margin (120/404) and for nodal status (93/404).

Out of 404 cases, 278(68.8%) cases turned out to be malignant in final diagnosis. The common sites sent for frozen section is tabulated in table 2.

Tabl	e 2. Organs s	ubm	nitted for froze	n sections a	nd
the	distribution	of	malignancies	diagnosed	in
para	ffin section				

Organ submitted	No. of cases	No. of malignancy
Breast	94	67
Nervous system	68	40
Gastrointestinal tract	59	53
Thyroid	20	8
Female genital tract	48	31
Urinary bladder& male genital tract	6	4
Skin	27	22
Hepatobiliary	22	15
Lung and mediastinum	11	7
Lymph node	15	9
Soft tissue &Bone	8	6
Retroperitoneum	12	9
Others	14	7
Total	404	278 (68.8%)

Among 94 breast cases, invasive ductal carcinoma(58)was the most common followed by, mucinous carcinoma(3), lobular carcinoma², malignant phylloides tumor², non Hodgkin lymphoma¹ and mixed tumor¹. The remaining (27) cases were benign.

Gastrointestinal tract (GIT) comprised of 59 cases where 33 cases were squamous cell carcinoma from oral cavity, 5 from omentum, 4 from pancrease and 4 from salivary gland and remaining 13 from small and large bowel.

Sixty eight cases of nervous system included gliomas of WHO grade 1 to 4, metastasis, meningioma, neurofibroma, craniopharyngioma and medulloblastoma. Typing of lesion and grading of gliomas was common source of error in brain biopsy.

Out of 48 cases of female genital tract, 36 were from ovary, 4 from cervix and 8 from uterus. Prostate (2), Penis (2) and bladder (2) were classified under one category.

There were 4 cases of papillary carcinoma, 2 cases of follicular carcinoma and 1 anaplastic carcinoma of thyroid.

Non Hodgkin Lymphoma was the most common lesion in retroperitonium followed by ganglioneuroma, spindle cell tumor and germ cell tumor.

Each case of thymoma and Hodgkin Lymphoma from mediastinum were included with lung lesions and correctly assessed in frozen section.

Among 27 cases of skin biopsy,18 were from scalp and face and the remaining from extremities. Squamous cell carcinoma(12) was the most common followed by Basal cell carcinoma(6),metastasis(4), Malignant melanoma(1) and remaining (4) were benign lesion.

The frozen and permanent diagnoses of false positive and false negative cases are compared in table 3 and 4.

Table 3. Comparison of frozen and final diagnosis infalse positive cases				
Site	Frozen diagnosis	Final Diagnosis		
Breast	Apocrine carcinoma	Apocrine metaplasia		
Ovary	Granulosa cell tumor	Mature teratoma		
Ovary	Malignant lesion	Tuberculosis		
Brain	Glioma	Neurocysticercosis		
Brain	Meningioma	Gliosis		
Thyroid	Papillary carcinoma	Nodular goiter		

Table 4. Comparision of frozen and final diagnosis infalse negative cases

Site (No. of cases)	Frozen diagnosis	Final diagnosis
Breast (1)	Ductal hyperplasia	Ductal carcinoma
Breast (3)	Benign	Ductal carcinoma
Ovary (4)	Benign	Mucinous cyst adenocarcinoma
GIT (2)	Inflammatory	Adenocarcinoma
Brain(3)	Gliosis	Glioma
Lymph node (2)	Reactive	Malignant
Thyroid (1)	Multinodular goitre	Follicular carcinoma

DISCUSSION

The achieved results in the present study (accuracy of 94.6% with the false positive rate of 1.5%, false negative rate of 3.9% and deferred rate of 3.9%) were comparable with the published results where accuracy ranged from 94% to 98%, with 3 to 4.6% of deferred rate. However, the indication, accuracy and limitations of frozen section vary with different organ that have been discussed and published regularly. ^{9, 10, 11, 12}

In the present study, 23.3% of biopsy for FS was from breast. It was indicated mainly to establish the diagnosis and in few cases, to assess the margin and lymph node metastasis. A case of ductal papilloma with apocrine metaplasia was overdiagnosed as apocrine carcinoma. Two cases of ductal carcinoma were underdiagnosed as hyperplasia. These discrepancies were mainly due to the interpretation error and partly due to lack of interdepartmental communication. A retrospective study have documented the diagnostic errors related to intraoperative consultation can be divided into interpretation error (57%), sampling erro(35%) and lack of interdepartmental communication (9.5%). Interpretation errors may result from artifacts of the freezing procedure and rarity of the lesion or the inexperience on the part of the pathologist.^{13,14,15}

Among 16.8% cases of frozen section from neurosurgical department, two cases of neoplastic lesion were misdiagnosed as benign lesion and one case of glioma was underdiagnosed as reactive gliosis. Sampling error is the main reason for these discrepancies. Typing and grading error was very frequent in neurosurgical biopsies. Freezing artifact, obscuring cytological detail and heterogeneous behavior of gliomas are the causes for discrepancies. Many studies have mentioned about taking multiple bits from different areas of a lesion and using smear/squash cytological technique along with the frozen section to reduce the error. ³



In ovary, one case of mucinous cystadenocarcinoma was underdiagnosed as cystadenoma and a case of mature teratoma was misinterpreted as granulosa cell tumor. Coffey et al. state that the accuracy is lower in mesenchymal and mucinous tumors of ovary. Generous sampling particularly from solid portion of ovarian tumor is required to rule out invasion in mucinous tumor. Using intraoperative cytological techniques including fine needle aspiration biopsy and touch imprint cytology can provide clear nuclear and cytoplasmic details without freezing artifact. ¹⁶



Figure 2. Frozen section.Metastatic Carcinoma

In thyroid, one case of nodular goitre with multiple papillary folds was misinterpreted as papillary carcinoma. Cases of follicular carcinoma were diagnosed as follicular neoplasm and a case of follicular carcinoma was underdiagnosed as multinodular goitre. These discrepancies were again due to lack of inadequate preoperative information and partly due to the artifacts. The limitations mentioned by Hwang et al and Anton RC et al in frozen section evaluation of thyroid are sampling and freezing artifact. Ground glass appearance of the nuclei as an artifact produced during formalin fixation is a diagnostic feature which is not present in frozen section and alcohol fixed smears. Studies have also confirmed that it is as difficult to differentiate benign from malignant follicular lesions at the time of frozen section. Entire capsule must be submitted for the microscopic examination which could be time consuming and less productive at the time of frozen section. Frozen section distorts and collapses blood vessels resulting in a difficult task to locate angioinvasion. Literature have mentioned that the angioinvasion and the capsular invasion are best assessed on permanent histological sections. However, the frozen section evaluation of thyroid and parathyroid lesions remains a highly accurate procedure with a low false positive rate. Gross inspection, complemented by cytological and histological review, provides the surgeons with the rapid, reliable and cost effective information necessary for optimum patient care.^{2, 17}

In other site such as retroperitonium, salivary gland, hepatobiliary, stomach and bowel and pancreas, frozen section was sent for primary diagnosis, margin assessment and nodal metastasis. Benign and malignant lesions were identified correctly in most of the cases, but, typing error was a frequent problem. This was due to loss of architectural pattern and freezing artifact. Many authors believe that determining the presence of malignancy without subtyping or a judicious deferral can be the best option to decrease the discrepancies.¹⁸

CONCLUSION

Frozen section diagnosis is very useful and highly accurate procedure. Gross inspection, sampling by pathologist, frozen complemented with cytological and histological review and intimal cooperation with surgeon, good communication between surgeon and pathologist can avoid certain limitations and provide rapid, reliable, cost effective information necessary for optimum patient care.

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