Intraoperative Frozen Section - A Golden Tool for Diagnosis of Surgical Biopsies

Abstract

Background: Intra-operative frozen section plays an important role in the management of surgical patients but yet it must be used prudently to avoid the indiscriminate usage of this technique. As it is subjected to many limitations in comparison to the paraffin embedded sections, this study aims to highlight the important concepts and principles of intraoperative frozen section consultation as well as discussing the limitations of this technique. A comparison with other latest techniques.

Aims and objectives: To evaluate the performance and limitations of frozen sections in the Intraoperative evaluation of thyroid, breast, gastric, ovarian, central nervous system and lower extremities biopsies.

Materials and methods: Retrospective and prospective study of frozen sections done over a period of one and half year were taken. Fine needle aspiration cytology, frozen and biopsy performed for various tumours in thyroid, breast, gastric, ovary, CNS and lower limb were studied. A Comparison for frozen, fine needle aspiration was done which was later confirmed by histopathology. Accuracy of frozen section in our study was 91%.

Results: Out of 21 cases, 19 cases of frozen sections coincided with histopathological diagnosis and 20 cases of fine needle aspiration cytology coincided with histopathological diagnosis.

Conclusion: The role, value, and limitations of frozen section and gross consultation were variable in different sites. Frozen section aided the surgeon to choose the best therapeutic approach and in rapid diagnosis of a pathological process. Confirmed the diagnosis of carcinoma if the fine needle aspiration cytology or core needle biopsies are inconclusive prior to major radical surgery. Also provided an assessment of resection margins in carcinoma. When unexpected disease process was found and required a definite diagnosis to decide what to do next frozen section was helpful.

Keywords: Fine needle aspiration cytology; Histopathology; Frozen section specimens; Squamous cell carcinoma; Parotidectomy; MRI; CT-scan; ultrasound; CAT scan

Abbreviations: FS: Frozen Section; FNAC: Fine Needle Aspiration Cytology; CNS: Central Nervous System, CT: Computed Tomography, MRI: Magnetic Resonance Imaging, NIR: Near Infra Red

Introduction

Frozen section was first performed by Welch in 1891 and developed by Wilson in 1905. Lang apparently first employed the use of freezing to harden tissues in the nineteenth century. De Riemer in 1818 made pioneering effort of using frozen section technique for histopathological diagnosis [1]. It is a tribute to men like Hazard, Stevenson and Dockerty that the procedure was accepted by all [2,3]. Following the introduction of the cryostat in 1960, the intra operative frozen section examination was established as a highly reliable procedure for the rapid histological evaluation of tissue specimens during surgery [4].

Materials and Methods

All Intraoperative frozen sections of breast, thyroid, and gastric, ovarian, central nervous system tumours performed at Asram medical college, Elluru over a period of one and half years from 2013 to 2014 were studied. The gross specimens of tumors were examined, painted, cut into thin slices from abnormal and suspected areas, or from firm lesion. A section was taken placed in a mounting medium, frozen immediately to -20 degrees centigrade inside the cryostat. The attending technologist processed the tissue section by freezing it with frozen aerosol spray. Sectioned in cryostat at 4 to 5 microns thickness. Intra and intercellular water is frozen to produce hard matrix to enable slicing of the tissue. The tissue sections were cut and picked up on glass slide and stained in Hematoxylin and eosin. Microscopic findings were reported to the surgeon in the operating room and were recorded immediately. After completion, remains of the frozen tissue on the block and unfrozen tissue were fixed in 10% neutral formaldehyde solution. Permanent histological sections of the frozen material were obtained and compared with frozen section. FNAC was done by standard disposable 27 gauge needle (0.4-0.7mm). 30-50mm long needles are suitable for superficial, palpable lesions. 27 gauge was useful for cell rich and vascular
tissues like thyroid. FNAC, frozen and histological sections were compared. Accuracy of frozen sections was then determined.

Results

In twenty one cases of Frozen, fine needle aspiration and histopathology results were also studied. Nineteen cases of frozen section coincided with histopathological diagnosis (Table 1). Twenty cases of FNAC coincided with histopathology diagnosis (Table 2). Two cases of frozen differed from histopathology diagnosis. One was an ovarian tumor and another was of breast lesion. These were benign cyst of ovary in frozen which was immature teratoma in histopathology and benign lesion of the breast in frozen which was ductal carcinoma in situ in histopathology. The accuracy rate of frozen in our study was 91%. The sensitivity of frozen section in our study was 90%. All the cases of FNAC coincided with frozen section diagnosis except for one case (Table 3). The case was ductal carcinoma in situ of breast which was given as benign lesion in FNAC.

Table 1: Nineteen cases of frozen section coincided with histopathological diagnosis.

<table>
<thead>
<tr>
<th>Frozen Section</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell carcinoma</td>
<td>Deposit of moderately differentiated squamous cell carcinoma</td>
</tr>
<tr>
<td>Benign</td>
<td>Chronic gastritis</td>
</tr>
<tr>
<td>Benign</td>
<td>Chronic mastitis</td>
</tr>
<tr>
<td>Benign</td>
<td>Adenocarcinoma stomach, adenomatous hyperplasia</td>
</tr>
<tr>
<td>Follicular adenoma</td>
<td>Follicular neoplasm of undetermined malignant potential</td>
</tr>
<tr>
<td>Follicular adenoma with cystic degeneration</td>
<td>Hurthle cell adenoma of undetermined malignant potential</td>
</tr>
<tr>
<td>Benign cyst ovary</td>
<td>Immature teratoma</td>
</tr>
<tr>
<td>Papillary carcinoma thyroid</td>
<td>Follicular variant of papillary carcinoma</td>
</tr>
<tr>
<td>Benign</td>
<td>Ductal carcinoma insitu</td>
</tr>
</tbody>
</table>

Table 2: Twenty cases of FNAC coincided with histopathology diagnosis.

<table>
<thead>
<tr>
<th>FNAC</th>
<th>Frozen</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular neoplasm thyroid</td>
<td>Follicular adenoma</td>
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</tr>
<tr>
<td>Fibroadenoma</td>
<td>Benign</td>
<td>Ductal Carcinoma Insitu</td>
</tr>
<tr>
<td>Glioma</td>
<td>High Grade Glioma</td>
<td>Glioblastoma Multiforme</td>
</tr>
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Table 3: FNAC coincided with frozen section diagnosis except for one case.

Discussion

Most centers reported an accuracy rate of frozen sections 92% to 98% depending on type of cases studied. A large center like Mayo clinic Rochester, USA reported an overall accuracy of 97.8% on reviewing 24,880 frozen cases in a year [5]. A comparative overall accuracy of 97.56% was noted at general hospital in Malaysia involving 215 frozen section specimens over 4 years duration [6]. Accuracy rate in our study was 91% involving 23 specimens over duration of one and half years. Other reported cases include accuracy rate of 94% in central nervous system lesion [7], 98.4% for tumours of the testis [8] and 91.1% for basal and squamous cell carcinoma of the skin [9]. Accuracy of frozen section in gynecological cases can be as high as 97.5 % [10]. Pinto et al. [11] in studying 243 frozen sections for ovarian tumours noted an accuracy rate of 98.5% for malignant tumours but only 78.6% for borderline tumours. Utilizing frozen section to determine tumour grade is also less sensitive with accuracy of only 88.6% in 260 endometrial cancers studied by Quinlivan JA et al. [12]. Even though the accuracy rate is generally very high, in some surgery especially in the head and neck surgery, determination of the margin clearance may be quite costly and cannot reliably eradicate positive final margin [13]. The accuracy rate in our study for squamous cell carcinoma is 100%, central nervous system tumors is 100%, ovarian tumors is 50%, thyroid tumors is 97% and breast tumors is 50%. At times diagnostic accuracy of frozen section may be much higher than that of fine needle aspiration cytology. In an audit of 31 parotidectomy cases in Singapore, it is noted that 98% of frozen section histology concurred with the final histology in contrast to 66.6% of fine needle aspiration cytology cases [14]. However, in our study we did not encounter any tumours salivary gland. The diagnostic accuracy of fine needle aspiration cytology was slightly higher than frozen section in our study in various tumours. The studies of Rosai J, Ackerman LV accuracy of frozen section in 679 breast specimens diagnosis was 98.5% [15]. Most of the deferred diagnosis and false negative results involved occult/ intraductal/intrabular lesions. In our study diagnostic accuracy for breast specimens was 50%.False negative result in frozen section in our study was that of intraductal/in situ carcinoma of breast.In major published studies of consecutive FS examinations reported in the literature, the breast is always listed as an organ most frequently examined [16]. The relative frequency of breast specimens in these studies ranged from 16% to 62% of all cases [17]. The frequency of performing breast frozen sections is 20% to 30% at MD Anderson in Houston, Texas, USA, where they have average 70 diagnostic frozen sections per day. In our study the frequency of breast specimens is 20% of all the cases. For thyroid lesions, the...
In a study done at university of Michigan Hospitals, Ann Arbor, USA on FS requests of 914 cases, it was noted that 95% were performed for appropriate reasons, including frozen section examination, reaching 89% by Mak AS [22]. The accuracy rate is 97%. Diagnosing difficulty in follicular neoplasm and Hurthle cell neoplasm depends on capsular and vascular invasion which is not possible by FNA and FS [20]. Therefore certain laboratories are reluctant to carry out FS on thyroid lesions, particularly when dealing with follicular neoplasm. In fact, some authors do not support the use of routine FS for thyroid nodules [20]. The accuracy in ovarian specimens in reported studies was 90-97% [21]. Sampling error is the main reason for diagnostic discrepancy. Intraoperative fluorescence imaging provides real-time visualization of signal from fluorescent reporters over a large field of view (FOV) with exceptional sensitivity and resolution [26, 27]. Fluorescence imaging is used during surgery to assess patency of blood vessels and ureters [28]. Near-infrared (NIR) fluorescence (700 to 900nm) is often preferred for deep tissue imaging due to its higher depth of penetration and lower background fluorescence [25, 28]. However, NIR fluorescence is invisible to the human eye, and emitted light levels are typically low for the human eye to see, requiring camera-based detection. Clinical optical imaging systems typically consist of highly sensitive, scientific digital cameras with appropriate illumination source and optical filters for fluorescence detection [26, 29, 30]. Fluorescence image information is acquired via attached computer, processed to reduce background signal and enhance contrast, then displayed on an adjacent digital monitor alongside or overlaying the reference bright field image (Figure 1-12).

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Figure 2: Hurthle cell adenoma on frozen and FNAC X40, X10.

Figure 3: Papillary carcinoma thyroid on H&E stain X100, Frozen section x100.

Figure 4: Papillary carcinoma thyroid on frozen X40, X10.
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Figure 5: Adenocarcinoma stomach on histopathology and frozen.

Figure 6: Immature teratoma H&E X10, X10.

Figure 7: Immature teratoma, glial tissue on H&E X40 frozen section.
Figure 8: Ductal carcinoma \textit{in situ} HPE, H&E x10.

Figure 9: Ductal carcinoma \textit{in situ} on frozen section X10.

Figure 10: Squamous cell carcinoma H&E on FNAc, frozen section X10, X10.
Conclusions

The role, value, and limitations of frozen section and gross consultation are variable in different sites. Frozen section aids the surgeon to choose the best therapeutic approach and in rapid diagnosis of a pathological process. Confirms the diagnosis of carcinoma if the fine needle aspiration cytology or core needle biopsies are inconclusive prior to major radical surgery. Also provides an assessment of resection margins in carcinoma. When unexpected disease process is found and requires a definite diagnosis to decide what to do next frozen section is helpful. Newer techniques like MRI scan, CT scan, optical imaging, intra-operative cytology, and immunohistochemistry techniques are also helpful in diagnosing cancers.

References