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Original Research Paper

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INTRA OPERATIVE FROZEN SECTION - REALISTIC EXPECTATIONS IN THE CURRENT SCENARIO- EXPERIENCE WITH 135 CASES IN A TERTIARY CARE CENTRE

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ABSTRACT

Aim: To assess the utility of frozen section in this recent scenario of improved patient care

Methods: In our study we analysed the efficacy of frozen section in 135 cases over a period of one and half years including thyroid, ovary, breast, parotid,lymph node, margin assessment in colon malignancy by comparing it with histopathology, considering the latter as gold standard.

Results: We found the overall accuracy of frozen section to be 85.37% with a sensitivity of 85.3% and specificity of 84.6% in thyroid cases. In case of ovarian tumours frozen section had 90.91%sensitivity and 97.96% specificity for malignant tumours.

Conclusion:Understanding the limitations, frozen section can be used as a reliable intraoperative tool.

KEYWORDS : frozen section, intra operative consultation..

INTRODUCTION

Frozen section is a definitive form of intra operative consultation as it involves the microscopic examination of tissue removed during surgery. Frozen section is highly relevant currently, because of its role in tissue triage, intraoperative diagnosis and thus intraoperative management, finally adding to improved patient care. The active and evolving demand for frozen section not only underscores it as an established parameter of medical practice but also denotes the changes in the clinical questions related to advances in surgical treatment, mostly for tumors in various organ systems.

Materials and methods

We conducted a retrospective study of all cases that were subjected to frozen section over a period of one and half years from june 2011 to December 2013. The cases were sent from department of Surgery and Obstetrics and Gynaecology of MES medical college. All thyroidectomies with solid lesions in any part of thyroid gland as suggested by ultrasonography, suspicious nodules in fine needle aspiration cytology and those thyroid lesions with cervical lymph node enlargement, were sent for frozen section analysis. All cases of ovarian neoplasms undergoing staging laprotomy or laproscopy at the Obstetrics and Gynaecology department were considered for inclusion. Extent of surgery was guided by the results of frozen section. We had a total of 135 cases, of which we had 60 cases of thyroid nodules, 60 cases of ovarian tumors and 15 others which included a parotid tumor, lymphnodes, margin assessment in breast and colonic malignancy, lymphnodes and soft tissue tumors. For thyroid lesions the entire lobe of thyroid with the lesion, was removed and sent for frozen immediately, wrapped in a gauze piece without any fixative in a plastic bottle. If the patient had a lymph node, it was also sent in entire for frozen section analysis. For ovarian tumors, a staging laprotomy was performed and the tumor was removed in entire to take bits from representative areas. The tumor was immediately handed over for frozen section, with all the clinical details of the patient. After thorough gross examination of the specimens, sections were obtained from representative areas. The number of bits which were frozen ranged from 1 to 4 and was decided based on the type and size of the tumor. Sections were taken with the help of a cryostat. Around 7 to 8 µm sections were obtained and stained with hematoxylin and eosin. All the sections were studied microscopically under low and high power by two pathologists. The frozen section diagnosis was conveyed to the surgical team, who then proceeded with the appropriate course of surgery. The average time taken for the entire procedure (sending the sample to obtaining the result) was approximately 20 minutes. Frozen section diagnosis was later compared with the final paraffin section diagnosis (gold standard). We calculated the sensitivity (true positive / true positive +false negative), specificity (true negative / true negative and false positive), positive predictive value (ppv) (true positive / true positive + false positive) and negative predictive value (npv) (true negative / true negative and false negative) of frozen section.

Observations and results

Out of 60 thyroid cases, there were 14 cases of papillary carcinoma of which 11 were diagnosed correctly by frozen. There was one case of follicular carcinoma which was diagnosed wrongly as cellular nodule of colloid goitre. Of the three medullary carcinomas, two could be diagnosed correctly. The two cases of hurthle cell neoplasms and the one case of hashimotos thyroiditis could be diagnosed correctly. There were 15 cases of follicular adenomas and 24 cases of multinodular colloid goiter, of which we could diagnose 14 and 21 cases correctly respectively.

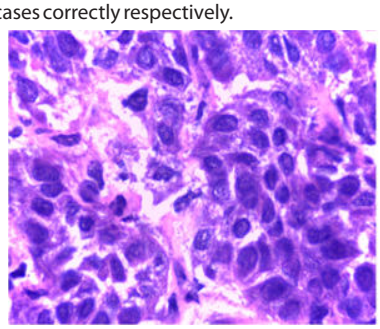

Fig 01 – Frozen section of of papillary carcinoma thyroid showing nuclear grooves and intranuclear inclusions, H&E, 40X.

Out of the 60 patients with ovarian neoplasm, frozen section diagnosis showed that 43 (71.7%) tumors were benign, 11(18.3%) were malignant and six (10%) were borderline. Final histopathological diagnosis showed that 45 (75%) tumors were benign, 11 (18.3%) were malignant and four (6.7%) were borderline. Among the 60 cases, 49 (81%) were surface epithelial tumors, 6 (10%) were germ cell tumors, 2 (3.3%) were metastatic, 2 (3.3%) were endometriotic cysts and one case was a sex cord stromal tumor.

Out of the 49 cases of surface epithelial tumors 36 were benign (22 serous and 14 mucinous), 4 were borderline tumors (1 serous and 3 mucinous) and 9 were malignant (7 serous and 2 mucinous). There were 6 germ cell tumors which included 5 teratomas and one case of

struma ovary. One of the metastatic tumor was a krukenberg tumor with primary in the stomach and the other case was metastasis from a colonic malignancy. The only sex cord stromal tumour found in this study was a fibrothecoma.

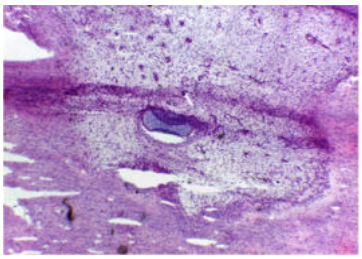

Fig 02 - Frozen section of the case of teratoma showing immature cartilage H&E, 10 X.

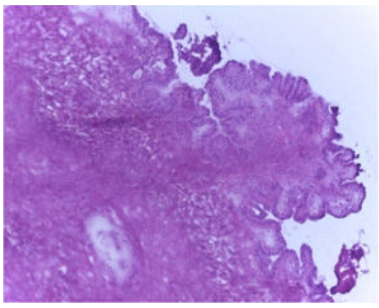

Fig 03 - Frozen section of the case of borderline cystic serous neoplasm. H&E, 10 X.

Among the other cases, there were 3 lymphnodes of which one showed metastasis from papillary carcinoma thyroid, margin assessment for colonic malignancy and breast surgery, parotid tumors, soft tissue tumors, and a case of paraganglioma. All these could be diagnosed correctly except one case of chronic sialadenitis which was over diagnosed as pleomorphic adenoma.

Accuracy of frozen section

Overall accuracy of frozen section in diagnosis of thyroid lesions was found to be 85%.the sensitivity was 87.7%, specificity was 80.95%, positive predictive value was 89.87% and negative predictive value was 81.48%.

The overall accuracy of frozen section diagnosis of ovarian masses was 93.3% in the present study. In the present series we found that in case of benign tumors, frozen section had 95.5% sensitivity, 100% specificity, 100% positive predictive value (ppv) and 88.24% negative predictive value (npv). Frozen section had 90.91% sensitivity, 97.96% specificity, 90.91% positive predictive value and 97.96% negative predictive value for malignant tumors. Thus frozen section had high sensitivity, specificity and predictive values in the prediction of benign and malignant neoplasms of the ovary in the present study. However, frozen section had low sensitivity (75%) and ppv (50%) for borderline tumors.

DISCUSSION

Intraoperative histological assessment of lesions in various organ systems helps clinicians to select an appropriate surgical procedure for patients, avoiding both under and over-treatment. But, frozen section has its own limitations. First and for most is sampling errors. A thorough gross examination and sampling of a wide range of tissues is our best defense against sampling errors. This is often limited by the fact that fresh unfixed samples are flabby and difficult to handle. This is particularly true in case of cystic ovarian tumors as teratoma and mucinous tumors, where the specimen is slimy and even holding the specimen is difficult. This makes identification of solid areas difficult, which results in missing a borderline lesion or even invasion in malignant tumors. Another difficulty that we faced was in cellular neoplasms as follicular neoplasms of thyroid showed bulging of the tumor out of the capsule which made demarcation of the capsule difficult. This makes finding out of capsular invasion difficult in fresh samples mainly and in fixed samples also to some extent.

Next limitation is time; which puts the pressure of grossing,embedding the tissue, freezing the tissue, sectioning and retrieving the tissue, staining and cover slipping the slide, and microscopically interpret the section in a period of 20 minutes in uncomplicated specimens.

There is no place in a surgical pathology practice that challenges our diagnostic skills more than the frozen section room. Under the limitation of time, using the most basic morphologic techniques and knowledge, we are faced with many diagnostic challenges. In routine surgical pathology, we can take our own time, study our slides, and order up a variety of special stains and studies to guide us to the correct diagnosis. The accuracy of frozen section diagnosis can be affected by various factors including sampling errors, quality of frozen section and experience of pathologist.

Frozen section has its limitations in detecting malignancy in thyroid lesions; especially in follicular and or hürthle cell lesions. The same applies to the follicular variant of papillary carcinoma. This is because the diagnosis of malignancy depends on finding capsular and or vascular invasion [1,2,3,] . To assure its presence or absence one must evaluate the entire capsule[4], which is time consuming. The interpretation of frozen sections is made more difficult by freezing artifacts that cause cellular distortion, blood vessel distortion and collapse [2,4] . For instance, it is more difficult to see the ground glass appearance of the nuclei in papillary carcinoma of thyroid. In our experience we could find the classical nuclear details that are described for papillary carcinoma thyroid in only few of the frozen sections that were diagnosed correctly. We correlated the pattern of the tumor with cytological and nuclear details in scrape smears which guided us, mostly to the correct diagnosis.

In our centre it takes about 25 minutes to give the diagnosis which is well within the range reported in the literature (15-48 minutes)[4,5,6,] but the more the slices that are made, the more the time is spent. These factors limit the utility of frozen sections in thyroid surgery. For microcarciomas less than 1 cm the limitation was availability of tissue for permanent section, which we overcame by using the same bit as of frozen for permanent section. Since frozen sections were done in planning the extend of the surgery, it needed high specificity.

In the case of ovarian neoplasms, benign lesions are usually managed conservatively and a similar approach may be taken in some patients with borderline tumors or even for a selected few with malignant tumors, who wish to preserve their fertility. However, most patients with borderline or malignant tumors undergo complete pelvic clearance, omentectomy, and appropriate staging procedure. Therefore, intraoperative frozen section should ideally be used to accurately discriminate between benign, borderline and malignant ovarian tumors and also to identify those malignancies of extra ovarian origin[7]. In the present study conducted to examine the role of frozen section in managing ovarian tumors , it was observed that frozen section had high sensitivity, specificity and predictive values in the prediction of benign and malignant neoplasms of the ovary, but had low sensitivity and ppv for borderline tumors. It was also noted that inaccurate diagnosis occurred more commonly with mucinous tumors than other histological types. This is due to the inadequate sampling during the limited time and due to the difficulty in holding the specimens as it was slimy and slippery and will be jam packed with jelly like mucinous material that makes it difficult to identify the solid areas during sampling.

Sampling errors were considered to be the major reason for the diagnostic discrepancy in most studies [8,9].this is particularly true in some groups of tumors, in which there was remarkable heterogeneity of tumors from areas to areas within the same

ovarian mass, such as mucinous tumors and teratomas. A single mucinous ovarian tumor may sometimes contain benign, borderline and malignant components, in contrast with serous tumors [10,11,12]. Frozen section may fail to sample the most severe lesion or frankly malignant area in a limited number of sections intraoperatively [12].this is particularly true in case of follicular carcinoma of thyroid. Morphological complexity of borderline ovarian tumors was found to be the cause for inaccurate diagnosis of such tumors in frozen section[13].

Another probable reason for low ppv for borderline tumors in the present study may be the lesser number of borderline tumors. Ppv and npv are directly related to prevalence of the disease. Number of frozen sections sampled also correlate with the accuracy of the test. In our study one to four frozen section samples were taken based on size and type of tumor. In case of borderline tumors at least two sections were sampled. Wang et al recommended that multiple frozen section samples may help increase the accuracy in the diagnosis and advocated taking one frozen section per each 10 cm diameter of the mass [14].

Other factors that can influence frozen section diagnosis are the quality of sections prepared by this technique that limits the evaluation of cellular details and the experience of pathologists. In all cases the sections were studied and discussed by atleast two pathologists in our centre to make the observation errors to the minimum.

The two benign cases inaccurately over diagnosed by frozen section as borderline did not have critical therapeutic implications in our study since both patients were young and underwent conservative management.

One borderline case in this study, which was over diagnosed as malignant was of a 60 year old who underwent a completion surgery. This kind of over diagnosis may have had serious therapeutic implications for a younger patient because an extensive cytoreductive surgery would have been unnecessary for her.

One malignant tumor which was under diagnosed as borderline was a 54 year old female who underwent a completion surgery considering the age and parity status.

C. Dener et al suggest that intraoperative margin assessment by frozen section is an effective procedure in reducing the need of a second operation for margin control. Furthermore, sufficient margin width (> 2 mm negative margin in our cases) is obtained during the same operation [15].

Conclusions

Understanding its limitations, frozen section can be used in intraoperative diagnosis.

At least in some cases, frozen section is found to be time consuming, waste of money, and confusing to the surgeons as in follicular carcinomas of thyroid and borderline ovarian tumors.

We found the accuracy of frozen section to be more for ovarian tumors than thyroid lesions.

The accuracy was found to be low for borderline ovarian tumors compared to benign and malignant tumors.

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