



STUDY OF THE ROLE OF FROZEN SECTION EVALUATION IN PATIENTS WITH BREAST LESIONS

Pathology

Dr.Dhananjay Prasad

Assistant Professor, Department of Pathology, RIMS, Raipur, CG, India-492006.

Dr.Vijay Tote*

Associate Professor, Department of Pathology, GMC, Nagpur, Maharashtra, INDIA-440003. *Corresponding author

Dr Brajendra kumar

Professor and Dean, Department of Medicine, RIMS, Raipur, CG, India-492006.

ABSTRACT

Frozen section is an invaluable intra-operative tool for evaluation of breast lumps. The aim of this study was to calculate the overall accuracy, false positivity, false negativity for frozen section of breast lumps, to analyze the causes of discrepancies, and compare the data with that of published literature on frozen section of breast lumps. 300 frozen sections comprising 286 breast lumps, 10 axillary nodes and 4 lumpectomy margins received for frozen section were analyzed. Pathology reports and slides (of both frozen and paraffin sections) were reviewed. The values were calculated using paraffin slides as the gold standard. The 286 lumps received for primary diagnosis comprised 206 malignant and 80 benign lesions. The false negativity rate was 0.42%, false positive rate 0%, deferral rate 0.84%, overall accuracy rate was 99.57%. The false negative diagnosis was an error of interpretation. False negativity rate for axillary nodes was 20% and accuracy was 80%. Accuracy for margins was 100%. Frozen section has a role despite the raging popularity of aspiration cytology in the following settings: (1) Difficult cytology (2) Evaluation of lumpectomy margins. (3) Intra-operative nodal status.

KEYWORDS

Frozen section, breast, accuracy, utility, Diagnosis.

INTRODUCTION

Frozen section procedure is a pathology laboratory procedure to perform rapid microscopic analysis of specimen. It is used most often in oncological surgery. The technical name for this procedure is cryosection. The frozen section procedure as practiced today in medical Laboratories is based on the description by Dr. Louis B. Wilson in 1905. In breast pathology, frozen section allows the surgeons to take an immediate therapeutic decision, possibly sparing the patient a second operation and reducing hospitalization costs. More recently, Fine Needle Aspiration Cytology (FNAC) has diminished the demand for frozen section evaluation of breast lumps. Yet in certain situations, particularly when FNAC fails, the need for frozen section persists.

MATERIAL AND METHOD

We did an analysis of frozen section on 300 breast lesions, 10 axillary nodes, 4 lumpectomy margins together comprising of 11 percent of the total 2250 frozen sections performed. On receipt in the laboratory, the breast specimen of the lymph nodes were examined grossly. The size of the breast lesions, their shape, circumscription, colours, consistency and presence of necrotic, haemorrhagic or cystic areas were noted. Each node was bisected and the abnormal looking hemi-section was processed for frozen section. To evaluate the margins of a lumpectomy specimen, the closest margin(s) were selected, inked and frozen. The most respective tissue slice measuring about 1cm x 1cm x 0.3 cm was processed in an open door cryostat at a temperature of -23°C. Section measuring 5µm in thickness were cut and toluidine blue staining and rapid hematoxylin and eosin staining were performed. After the frozen section diagnosis was rendered, the frozen tissue was thawed to room temperature and fixed in formalin overnight for further paraffin processing. The unfrozen remaining tissue was also transferred to formalin for paraffin embedding. The H & E stained actual frozen section slides on which the diagnosis was rendered and the subsequent paraffin embedded tissue sections were together evaluated with an emphasis on studying the paraffin processed sections of the tissue actually frozen. The lesions were classified as fibrocystic disease, fibroadenoma, inflammatory lesions and malignancies, the latter were further subclassified wherever possible on comparing the frozen section diagnoses with paraffin section diagnoses, it was found that there were no false positives, 0.42% false negative results and the rate of deferral was 0.84% [2 cases]. The accuracy for benign lesions was 98.73%, for malignant lesions it was 100%, and the overall accuracy was 99.57%. Both the deferred diagnoses were labeled as fibrocystic disease with epithelial proliferation. A single false negative

diagnosis occurred due to an error of interpretation, wherein an infiltrating lobular carcinoma was mistaken for fibroadenomatoid hyperplasia on frozen section. Minor modifications of the frozen diagnosis were necessary in four cases. However, these modifications subsequent to paraffin section had no bearing whatsoever on the further management of the patient. The margins of four lumpectomy specimens were received for frozen section evaluation. All 4 were negative on frozen section and confirmed on paraffin section [accuracy 100%]. Samples of ten axillary lymph nodes, one each from 10 patients, were received for frozen section. On frozen section only 2 out of these 10 nodes were positive for metastasis whereas on paraffin processing, 2 additional nodes showed metastasis and 6 remained negative. Thus, metastatic deposits in 2 nodes were missed on frozen; the false negativity rate was 20%, false positivity rate was 0%, and the overall accuracy was 80%.

DISCUSSION

Breast carcinoma is the second most common malignant tumor among rural Indian women after carcinoma cervix whereas in urban Indian women, breast carcinoma overcomes the incidence of carcinoma cervix. Frozen section is useful for obtaining diagnosis of a breast lump, axillary nodes, and lumpectomy margins. FNAC is a simple, cheap technique, which is utilized much more frequently in the evaluation of breast lumps, and axillary nodes; yet the need for frozen section evaluation is felt in the following situations: 1. The aspirate is scanty or acellular due to desmoplastic reaction or due to extensive necrosis. 2. The tumor is of low cytologic grade. 3. The lesion is either a lobular carcinoma or a lymphoma, and the distinction between the two is difficult but therapeutically important. 4. Evaluation of lumpectomy margins. In the present study, 51% of frozen sections on breast lumps were requested despite earlier FNAC evaluation. One-fourth of the FNACs were suspicious for malignancy for which tissue diagnosis was advised. Although clinically radial scars are non palpable small lesions detected incidentally, microscopically they can be mistaken for malignant lesions especially when the spindle cell and inflammatory component is conspicuous and scarring is less. Papillomas, both solitary and multiple, may undergo infarction and extensive sclerosis; this in turn can produce frightening distortion and patterns which can lead to an over diagnosis of carcinoma. However, blandness of epithelial proliferation is an important feature to recognize. The confident distinction between a papilloma and a papillary carcinoma on frozen section is difficult and according to some should not be attempted till paraffin section is ready. The present study did not reveal any false positive diagnosis on frozen section. The malignant lesions

which are commonly under diagnosed as benign. The single false negative entity in the present study was an infiltrating lobular carcinoma on paraffin sections. Amongst the 16 cases (including present study) in publications comprising lobular carcinoma, 5 false negatives were finally diagnosed as lobular carcinomas (5 out of 16 = 31.5%), and out of the total 40 false negatives enlisted, 19 were intraductal carcinomas. Thus, invasive lobular carcinoma and intraductal carcinoma are the two most frequently underdiagnosed lesions on frozen section. The presence of intracytoplasmic lumina within the proliferating cells and their pagetoid growth pattern within the involved ducts favors a diagnosis of lobular neoplasia. Intraductal carcinoma is an intraductal proliferation of monotonous cells, with hyperchromatic, round or oval nuclei forming regular spaces, rigid geometric configuration and no swirls or streaming. The incidence of false negativity on frozen tissues increases with diminishing size of the lesion, due to artifactual distortion on freezing, and the apprehension about lack of adequate tissue for paraffin section. Hence the Association of Directors of Anatomic Surgical Pathology recommends that lesions less than 1cm should not be frozen. In the present study, there were 10 requests for axillary node sampling. There were no false positive diagnoses. The false negativity rate was 20% [2 cases] which is unacceptably high due to microscopic metastasis. Step sectioning at frozen, and assessment of entire node including adipose tissue, trisection of the node and immunohistochemistry at frozen for detection of micrometastasis have all been recommended to improve the diagnostic accuracy of frozen section. Literature published on axillary node analysis by frozen has shown accuracy rates of 92.08%, 95.58%, 96.29% and false negativity rates of 8%, 4.5%, 3.8% respectively in studies comprising 88, 68, 54 cases respectively.

CONCLUSION

Despite increasing popularity and undisputed utility of FNAC, there will be situations where frozen section still stands out as the method of choice for rapid diagnosis. Only in those few conditions where frozen section fails to provide a conclusive diagnosis, will the final paraffin section be needed to accurately arrive at a definitive diagnosis. A judicious selection of one or more of these modalities is required in every patient presenting with a suspicious breast lump.

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