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IMPRINT CYTOLOGY: A RELIABLE ALTERNATIVE TO FROZEN SECTION

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ABSTRACT

Background: There are instances when either we do not perform pre-operative biopsy due to the fear of spread of malignancy, or needle aspiration cytology is inconclusive. During surgical exploration for a benign pathology if surgeons find suspicious lesions, per-operative cytological diagnosis becomes important to rule out malignancy. The frozen section facility is available only at few large volume centres. So there is always a need for an easy and cheap alternative to frozen section that can help surgeons at low volume centres as well.

Aim: Aim of the study was to assess the reliability of imprint cytology in per-operative (immediate) diagnosis of malignancy.

Material and methods: The present study was a prospective analysis of 69 specimens from suspected or diagnosed cancer patients that were sent for per-operative (or urgent) imprint cytology (IC) from July 2012 to Feb. 2014, at surgical oncology unit of our institute. All the specimens were then subjected to paraffin section (PS) and final reports were compared.

Results: Out of 69 specimens 61 were found to be malignant, and five were found to be benign by both IC and PS. In all such situations IC helped us a lot in decision making regarding change in treatment plan further. The sensitivity and specificity of imprint cytology were 96.8 % and 83.3% respectively. The positive predictive value (PPV) of IC was 98.3 %.

Conclusions: The imprint cytology is a cheap and reliable method for per-operative diagnosis of malignancy. It can be used for per-operative confirmation of parathyroid glands before auto-implantation.

Key Words: Frozen section, Imprint cytology, Per-operative cytology, Touch cytology

INTRODUCTION

For past many years it has become a trend to have definitive diagnosis before surgery, as it helps in surgical planning, planning of neo-adjuvant therapy and in patient counselling. This practice has decreased the numbers of surgical explorations. Surgeons feel difficulty in planning out the extent of resection of lesion whenever initial tissue diagnosis is not available. Still there are instances when we do not perform pre-operative biopsy or cytology due to the fear of capsular rupture, needle tract seedling or spread of malignancy. Sometimes fine needle aspiration cytology (FNAC) or needle biopsy is inconclusive and we have to take surgical (excision) biopsy, and then plan the definitive procedure after biopsy report, thus making it a 2 stage procedure. Many times during surgical exploration for a benign pathology if surgeons find suspicious lesions, per-operative cytological diagnosis becomes important to rule out malignancy, as this may change the intra-operative surgical plan further. Since a long time frozen section (FS) and imprint cytology (IC) are considered as two methods of per-operative cytological diagnosis. After popularity of frozen section in practice, pathologists have given up interest towards imprint cytology. The frozen section facility is available only at few centres in India as compared to large number of hospitals and patients. So there is always a need for an easy and cheap alternative to frozen section that can help surgeons at low volume centres as well. The aim of this study was to assess the reliability of imprint cytology in per-operative (immediate) diagnosis of malignancy.

MATERIAL AND METHODS

The present study was a prospective analysis of 69 specimens from suspected or diagnosed cancer patients that were sent for per-operative (or urgent) imprint cytology

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from July 2012 to Feb. 2014, at surgical oncology unit of our institute. In all these situations it was important to confirm (or to rule out) malignancy, as this would make a major difference in treatment plan or extent of resection or in initiating a specific treatment. At our hospital we did not have facility for frozen section. Many times we felt difficulty in decision making where per-operative cytological diagnosis was needed. So we started doing imprint cytology as an alternative to frozen section based on previous literature, along with systematic recording of data.

Slides were either made in operation theatre or fresh adequate tissue samples were taken and wrapped in saline soaked cotton gauss pieces and, sent to pathology laboratory for urgent imprint cytology. The imprint cytology slides were then prepared in pathology lab by standard technique, fixed and stained. The reporting was done by a senior pathologist who was expert in cytological diagnosis of malignancy. All the specimens were then subjected to paraffin section (PS) and final reports were compared.

RESULTS

The results are shown in table 1.

From various surgical explorations (or excision biopsies) suspicious 12 metastatic nodules, six breast lumps, two encapsulated ovarian masses and 14 lymph nodes (including celiac, pelvic or para-aortic lymph nodes) were examined and all found to be positive by IC and PS as well. In all such situations IC helped us a lot in per-operative decision making.

The sensitivity and specificity of imprint cytology were 96.8 % and 83.3% respectively. The positive predictive value (PPV) of IC was 98.3 %. The average time taken in reporting was 23 minutes.

The only false positive result of IC was a specimen of lower uterine fibroid protruding out of cervix with surface erosions. It was giving appearance of defined cervical cancerous mass clinically (including imaging), but showing only dysplasia in cervical biopsy. We did radical hysterectomy and send specimen for imprint cytology to rule out malignancy in cervical mass before pelvic lymph node dissection (PLND). The IC reported it as malignant and we did bilateral PLND. Later on in final PS report it was found to be a uterine fibroid with surface dysplasia, all nodes negative.

Now let me discuss with you the two false negative cases. There was a confirmed case of carcinoma cervix, confined to cervix only in imaging, opened for radical hysterectomy. On exploration there was a significantly large, hard, round right pelvic lymph node (LN), which was sent for imprint cytology. The IC reported it as granulomatous disease and we proceeded to radical hysterectomy. The LN was finally found to harbour metastatic cancer.

The second false negative report was from a per-operative biopsy of stomach suspicious of linitus plastica. Multiple endoscopic biopsies were negative for malignancy, but clinically patient was not improving and CT (computed tomography) scan was constantly showing a diffuse wall thickening. Surgery with per-operative cytology was planned. The tumour was inoperable on exploration, as it was infiltrating into porta and transverse mesocolon. A small full thickness stomach wall biopsy was taken and sent for IC, which was negative for malignancy. We took a large full thickness biopsy and based on clinical judgement closed the abdomen. Finally both showed carcinoma stomach.

In a known case of laryngeal malignancy, 'wide field laryngectomy' surgery was planned. During surgery all four parathyroid glands were isolated and cut. One fourth part of each was sent for confirmation by IC. In the report three were normal parathyroids (auto-implanted) and one was found to be metastatic LN (discarded), which were confirmed by final PS.

The sub typing of malignancy (although it was not a predecided criterion to report) was given in 22 IC reports, but it was changed finally in nine patients. This makes IC unreliable for diagnosis of specific subtype (PPV 59 % only).

DISCUSSION

Imprint cytology (IC) and frozen section (FS) are renowned techniques of per-operative cytology and the diagnostic accuracy of both is comparable. Liu et al have investigated the utility of intraoperative touch preparation with comparison of frozen section in 122 cases. The rate of correct diagnosis for touch preparation was 88.5% as compared to 86.1% for frozen section. The rate of incorrect diagnosis for touch preparation was 4.1% as compared to 2.5% for frozen.[1]

Scucchi et al compared 2,250 intraoperative cytology with frozen section with the final diagnosis achieved on paraffin sections. The diagnostic accuracy of each technique alone was 94.9%. For frozen section the sensitivity was 89.9% and specificity 97.9% as compared to the touch cytology, which had a sensitivity of 94.9%, and specificity of 96.8%.[2]

Guarda et al carried out a comparative study of the two techniques and found the accuracy of cytology and frozen section 98.4% and 99.2% respectively.[3]

The greatest advantage of IC examination is of not having artifacts, resulting in superb nuclear and cytological details.[1] IC provides better and crisp cellular morphological details and even some tissue architecture.[4] Very small fragments of tissue provide sufficient cells for IC, but difficult to process and report on FS. The diagnosis of very small lesions is therefore facilitated and tissue is saved for permanent section.[5] Certain tissues that cannot be studied by frozen section i.e. bone, necrotic tissue and fat etc. give accurate results on touch preparations.[1] IC was found to be more valuable in the field of neuro-pathology, lymph node and most of the epithelial tumours.[3] Parathyroid glands are correctly identified by IC, slightly more sensitive than FS.[5]

Used intraoperatively, the imprint method can provide valuable information when frozen-section interpretation is equivocal. IC is particularly valuable in the diagnosis of certain neoplastic lesions which can simulate inflammatory lesions on FS eg. Well differentiated Pancreatic cancer, metastatic signet ring cell carcinoma in LN (can be mistaken for reactive sinus histiocytosis on FS). Certain benign inflammatory lesions can simulate malignancy on FS e.g. Organizing pneumonia (anaplastic carcinoma), intense sinus histiocytosis (can simulate metastatic carcinoma) that can be diagnosed with IC.[5]

Well-differentiated tumours and tumours with a dense fibrous stroma cannot be diagnosed by imprint cytology method.[5]

On the other hand Frozen Sections provided more tissue architectural details. It is well recognized, however, that the freezing and sectioning techniques of frozen section results in unavoidable distortions and artifacts, rendering diagnosis difficult in many instances.[1]

The diagnostic accuracy in distinguishing benign from malignant lesions by combined procedures was 100%. There were no false positive or false negative cases.[4] To increase diagnostic accuracy many people recommend the combined use of imprints and frozen sections.[5]

For diagnosing specific subtypes of malignancy, the diagnostic accuracy of each method alone was 96.6% with a sensitivity of 86% and specificity of 100% and the combined sensitivity 90%. The benefit of frozen section is that the tissue architecture closely approximates permanent histology sections.[4]

By virtue of our experience from this study, we would like to emphasize upon these few points:-

1. Imprint cytology is a reliable method to rule out malignancy in a short time. It may help surgeons to make changes in the previously made treatment plan. The confirmation of malignancy can help an oncologist to start therapy earlier without waiting for the results of final biopsy.
2. This method can be used to find out adequacy of biopsy specimen. Many times we are not sure while taking core biopsies (may be sonography or CT guided) that correct specimen is retrieved or not. Immediate imprint cytology from biopsy specimen will tell us that the tissue contains viable tumour, necrosed tissue or normal tissue. If the biopsy is not representative of disease we can take more samples immediately, hence to save time, patients' comfort and cost.
3. The imprint cytology can differentiate between a normal parathyroid gland and a lymph node with or without metastasis. This may help head and neck surgeons in per-operative confirmation of normal parathyroid glands before using them for auto-implantation. Now days, it is highly emphasised not to implant parathyroid glands without histological confirmation.
4. The imprint cytology is not a reliable investigation for sub-typing of cancer. It cannot differentiate between the grades of differentiation from well to poorly differentiated cancers. Its reliability on differentiating lung cancer into various subtypes like small cell, squamous cell or adenocarcinoma is not acceptable. Also it can't differentiate among various grades of dysplasia and early invasive cancer. This limitation should always be kept in mind.
5. Frozen section needs a good cryostat and other specialized materials along with experienced pathologist and technician. The cost of the setup ranges from Rupees 4 lac to 20 lac. There are problems regarding maintaining low temperature in the range of minus 15 to 20 ^{0} centigrade (sometimes even lower) with the cheaper cryostats along with issues regarding wastage of precious sample and poor quality of slides with cheaper devices. To make frozen section cost effective a centre should have at least 5 specimens for frozen section per day. This is the basic reason why frozen section is not available in majority of the hospitals even in big cities.

CONCLUSION

Imprint cytology is a cheap and reliable method for per-operative diagnosis of malignancy, and can be used in place of frozen section, where such facility is not available. It can be used for per-operative confirmation of parathyroid glands before auto-implantation.

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Table 1: The results are shown with categorization of various specimens.

S. No.	Tissue of origin of specimen	Total No.	Positive for malignancy by Imprint Cytology (IC)	Positive for malignancy by Paraffin Section (PS)
1	Metastatic nodules	13	12	12
2	Breast lump	6	6	6
3	Ovary	2	2	2
4	Cervix/uterus	2	2	1
5	Lymph nodes (LN)	15	14	15
6	Parathyroid gland for confirmation	4	3	3
7	CT/ USG guided biopsies	25	22	22
8	Stomach cancer	2	1	2
	Total	69	62	63