Usefulness Of Touch Preparation Cytology In Postmortem Diagnosis: A Study From The University Hospital Of The West Indies

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Abstract

Touch preparation or imprint cytology has been shown to be of value in the diagnosis of surgical pathology specimens and a few studies have also suggested a role in postmortem examination. The use of the technique in postmortem diagnosis has not been previously reported from a developing country. We prospectively examined 40 autopsy cases (M:F ratio 1.2:1, mean age 50.7 +/- 22.3 years) at the University Hospital of the West Indies with touch preparation cytology in addition to routine histology. A total of 120 specimens were obtained from a wide range of organs with the cytologic diagnosis being malignant in most cases (75 %); the overall concordance between cytologic and histologic diagnoses was 92.2%. Touch preparation cytology proved to be an accurate, simple, fast and relatively inexpensive method of postmortem diagnosis, and is likely to be of particular value in areas where cost-containment is critical.

INTRODUCTION

In a landmark paper published in 1927, Dudgeon and Patrick first described the use of imprint smears of fresh tissues in the rapid microscopical diagnosis of tumours [1]. Subsequently, various publications have addressed the application of imprint or touch preparation cytology in the diagnosis of surgical specimens including intraoperative diagnosis [2,3,4,5,6,7]. The application of the technique in postmortem examinations has received far less attention, although the few publications on the subject have noted its potential value including much cheaper preparation costs relative to routine histologic sections [8,9,10].

The use of touch preparation cytology in postmortem diagnosis has not been previously reported from a developing country, and in an era in which cost-containment has become a critical factor in the operation of medical facilities in regions such as ours, we sought to investigate the diagnostic accuracy and usefulness of touch preparation smears in postmortem examinations at the University Hospital of the West Indies (UHWI).

MATERIAL AND METHODS

In a prospective study performed at the UHWI between May 1999 and November 2001, 40 autopsy cases (15 medicolegal/coroner's and 25 hospital/non-coroner's cases) were subjected to cytologic evaluation in addition to routine histology. The study investigators were notified by pathology residents when autopsies were being performed on patients with mass lesions or suspected tumours amenable to touch preparation cytology smears. Relevant clinical and gross autopsy findings were recorded using a pre-designed abstraction form. A total of 120 specimens were obtained from various sites as shown in Table 1.

The slides were prepared either by making direct imprints of the cut surface of the selected tissue, or by scraping the cut surface with an edge of a glass slide prior to imprinting, the latter technique being used for firm to hard tissues including bone marrow to facilitate cell removal [9]. The slides were then placed immediately in 95% ethyl alcohol and stained by the routine Papanicolaou method. In some cases immediate assessment of the smears was also performed using a rapid Papanicolaou method [11], with the rapid diagnosis facilitating the immediate sampling of additional organs.

Tissue sections were also taken for histologic evaluation in most cases; bone marrow sections were not taken. The tissue sections were fixed in 10% buffered formalin, routinely processed, embedded in paraffin, and stained with hematoxylin-eosin. Immunohistochemical studies were performed for cases diagnosed microscopically as malignant

lymphoma using a modified avidin-biotin peroxidase complex (ABC) method with a panel of standard lymphoma antibodies.

Cytologic diagnoses were classified as benign, indeterminate, suspicious for malignancy and malignant. Due to the nature of the sampling i.e. smears of the surfaces of whole masses/organs, there were no inadequate samples. The overall concordance between cytologic and histologic diagnoses was determined.

RESULTS

The 40 patients included in the study comprised 22 males and 18 females (M:F ratio = 1.2:1). One patient was less than 1 year of age (16 days old), and the age range for the others was 1 to 86 years (mean 50.7 +/- 22.3 years).

The sites sampled by touch preparation cytology smears included a wide range of organs as shown in Table 1, with lymph nodes, bone marrow, liver, lung and pleura representing the most commonly sampled tissues. Smears of the gastrointestinal tract included gastric and colonic lesions.

Figure 1

Table 1: Cytologic diagnoses by site

Site	Benign	Indeter-minate	Primary Cancer	Metastatic Cancer	NHL	MM	MH	Total	%
Lymph node	1	2		5	9	1	1	19	15.8
Bone marrow	4	1		6	5	1	1	18	15.0
Liver	3	2		8	4	1		18	15.0
Lung/pleura	1		5	2	3	1		12	10.0
Spleen	1	1			7	1	1	11	9.2
Adrenal	1	1		3	1			6	5.0
GIT			3			2		5	4.2
Prostate	2		3					5	4.2
Heart		1			3	1		5	4.2
Kidney		1	1	1	1			4	3.3
Mediastinum	1	2						3	2.5
Thyroid	2	1						3	2.5
Pancreas			1			1		2	1.7
Peritoneum				2				2	1.7
Ovary				1	1			2	1.7
Breast			1					1	0.8
Gall bladder						1		1	0.8
Orbit					1			1	0.8
Brain				1				1	0.8
Skin	1							1	0.8
Total (%)	17 (14.2)	12 (10.0)	14 (11.7)	29 (24.2)	35 (29.2)	10 (8.3)	3 (2.5)	120 (100.0)	100

NHL = Non-hodgkins lymphoma; MH = malignant histiocytosis; MM = malignant melanoma; GIT = gastrointestinal tract

Most specimens, including bone marrow, yielded very cellular samples. The overall quality of the cytologic material including slides assessed by the rapid staining technique was generally good, although in some cases effects of autolysis were noted including cellular dissociation with loss of the usual architectural patterns such as gland formations or papillae, spindling effect of the cells, as well as loss of some cytoplasmic and nuclear details. It is noteworthy however that in these cases the quality of the touch preparation smears was still usually superior to the corresponding histologic slides.

The cytologic diagnosis was malignant in most cases (75 %) with Non-Hodgkin's lymphoma (NHL) being the most common category followed by metastatic and primary cancers. The 35 samples positive for NHL were obtained from 10 patients. Slides from 8 patients exhibited cytologic features typical of adult T-cell lymphoma (ATL), typified by polymorphous, pleomorphic populations of malignant lymphocytes inclusive of "flower cells" with cleaved nuclei, and bizarre giant cells. All 8 cases were confirmed to be of T-cell phenotype by immunohistochemical analysis, while the other 2 NHL cases showed positive staining with B-cell markers. The contribution of malignant melanoma to the overall number of malignant diagnoses was due to samples from one patient with disseminated disease that was extensively sampled.

Clinical and gross anatomical findings were useful adjuncts in the interpretation of the slides providing important clues in the differential diagnosis. For example, cytologic impressions of medullary carcinoma of the kidney, Graves' disease of the thyroid and neurofibroma of the skin were consistent with the clinical diagnoses of sickle cell disease, hyperthyroidism and neurofibromatosis, respectively. Gross parameters such as size and circumscription or encapsulation of masses, presence and extent of metastases provided important information in the overall assessment. Indeterminate diagnoses largely represented cases in which malignancy needed to be excluded after consideration of clinical, gross and cytologic findings, such as the thymomas where histology was necessary for the determination of invasiveness.

A total of 102 (85%) specimens had corresponding histology; the overall concordance between cytologic and histologic diagnoses was 92.2% (Table 2). All 8 non-concordant cases (8% cases with histology) had indeterminate cytology, and 7 of these showed benign lesions on histology (2 reactive lymph nodes and 1 case each of benign thymoma, rhabdomyoma of the heart, nodular goiter, splenic hyperplasia and normal liver). The remaining case was shown to be a malignant thymoma.

Figure 2

Table 2: Concordance between cytologic and histologic diagnoses

	Cytologic diagnosis		
Histologic outcome	Benign	Indeterminate	Malignant
Benign	13	7	
Indeterminate		2	
Malignant		1	79
Total	13	10	79

DISCUSSION

This series from the UHWI represents the first report of the application of touch preparation cytology in postmortem diagnosis from a developing country. One limiting factor encountered in the study was the presence of moderate tissue autolysis in some cases. Our department does not routinely perform postmortem examinations on warm bodies, and allows for the examination within four days of death. Autolysis is encountered in some cases despite this time limitation, and can affect cellular morphology as seen in both cytologic and histologic samples. We have documented the cytologic effects of autolysis in this series including cellular dissociation and loss of normal architectural patterns which, along with the general increased cellular yield obtained, should be taken into consideration in the interpretation of postmortem touch preparation cytology. It is noteworthy that even in these cases with varying degrees of autolysis, the quality of cytology slides is still usually superior to the histologic counterparts.

This series has documented the largest number of lymphoma diagnoses by postmortem cytology to date. Non-Hodgkin's lymphomas are among the leading malignancies in Jamaica in both males and females with age standardized incidence rates of 7.0 per 100,000 and 5.6 per 100,000 respectively [12]. The majority of these lymphomas in our population are of T-cell phenotype, and are associated with infection with the Human T-cell lymphotropic virus type 1 (HTLV-1) [13]. These HTLV-1 associated NHL are known as ATL, and exhibit characteristic morphologic findings [14], as exemplified by most of the NHL in this series. These features allow for a relatively specific and accurate cytologic diagnosis especially with supporting clinical data.

Other findings in this series are similar to those that have been reported from developed countries [8,9,10]. Firstly, the potential application of touch preparation cytology to a wide variety of tissue types has been confirmed, including sampling of hard tissues such as bone marrow that can be technically difficult to section and sample by other means. The scraping of the cut surface with the edge of the slide prior to imprinting facilitates the harvesting of cells. Multiple sites can also be sampled depending on the clinical and/or gross impressions, for example in the determination of the degree of tumour spread.

Secondly, cytologic sampling has the advantage of being readily amenable to rapid assessment. Walker and Going described the use of Diff-Quik or hematoxylin and eosin rapid staining in their autopsy series[10], but our staff are more comfortable with the interpretation and diagnosis of cytologic slides stained with the standard Papanicolaou stain, and we have recently reported our modification of the rapid Papanicolaou staining method for use in fine needle aspirations [15]. We adopted the same technique in some of the postmortem cases with the rapid assessment facilitating immediate additional tissue sampling if necessary. The ability to render definitive diagnoses promptly can be used to revive clinicians' interest in utilizing autopsy services, as it has been shown that despite the autopsy remaining the gold standard of diagnosis, autopsy rates worldwide have been declining [16,17,18].

Touch preparation cytology in post-mortem diagnosis has consistently demonstrated excellent diagnostic accuracy. Our cytologic/histologic concordance of 92.2% compares well with the previously reported accuracy rates of 96.3% and 95% by Suen et al and Walker and Going respectively [9,10]. The interpretation of the cytologic slides is assisted by the available clinical data and gross pathologic findings which can allow for relatively specific diagnoses that might otherwise be difficult to make based on cytology alone. As highlighted in the results, recognized clinical syndromes such as sickle cell disease and neurofibromatosis are associated with specific pathologic lesions such as renal medullary carcinoma and multiple nerve sheath tumours; information that can be taken into account when interpreting the slides. Gross features of organs or mass lesions can also clearly influence the final diagnosis; for example with touch preparation smears of thyroid gland yielding sheets of bland follicular epithelium, the classic degenerative changes of nodular goitre disease help to distinguish a hyperplastic nodule from a follicular neoplasm. In tumour diagnosis, cytologic slides can be used for example to confirm the gross impression of metastatic spread to various sites.

Cases which remained indeterminate after consideration of the clinical, gross and cytologic findings in this series (8% of cases with follow-up) were all resolved with histologic

examination and most were in fact shown to be benign. This finding points to a continued role for histologic sampling in postmortem diagnosis, but also indicates that it can be restricted to selected cases if cytologic sampling is used, with the latter facilitating definitive diagnosis in the majority of cases.

Finally, the use of cytologic preparations in post-mortem diagnosis has the potential for major cost savings. A previous study showed that touch preparation cytology slides were approximately 40 times cheaper to prepare than histologic slides of formalin-fixed tissue [8]. Glass slides and relevant stains are the basic tools needed for touch preparation slides, while various processing equipment are additional requirements for histologic samples. The significantly lower costs for cytologic assessment can be a very useful advantage in the provision of health care, particularly in centres such as ours in the developing world.

CONCLUSION

In conclusion, we have shown that touch preparation cytology is a useful procedure for post-mortem diagnosis in our setting. The technique can be applied to a variety of tissue types, and is simple, accurate and fast while costing much less than traditional histologic preparations. Relatively unusual or uncommon diagnostic entities can be diagnosed cytologically, particularly when relevant clinical and gross pathologic findings are considered.

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