Changing Trends and Practices in Cytopathology

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Keywords

Cytopathology · Trends · Practice · Cytotechnology

Abstract

Objective: To explore the current and anticipated changes in the practice of cytopathology. **Study Design:** The present review is based on a review of recent literature and an evaluation of the authors' personal experiences. **Results and Conclusion:** In recent years the practice of cytopathology, nationwide and in our institute, has witnessed a major change affecting gynecologic and nongynecologic cytology. There has been a decline in the number of Papanicolaou tests which has affected the utilization of cytotechnologists and provoked a reorganization of their work flow. The "need to do more with less" in the era of targeted therapy/personalized medicine has resulted in an increasing preference for needle core biopsy when performing a rapid on-site evaluation. We feel that this change is unavoidable. It is pertinent that cytopathologists as a group recognize this change and prepare themselves and the trainees not only to become adapt but also to use this as an opportunity to discover the yet unexplored world of cytology.

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Introduction

In recent years the practice of cytology has changed in an attempt to adapt to revised American Congress of Obstetrician and Gynecologists (ACOG) guidelines and the onset of the era of personalized medicine. The ACOG guidelines [1] implemented in 2009 brought about a decreased number of Papanicolaou (Pap) tests, resulting in decreased cervical cytology screening and thereby reducing the number of cytotechnologist positions and prompting the closure of many cytotechnology programs nationwide. On the other hand, the dawn of the era of personalized medicine for targeted therapy has increased the pressure on cytopathologists to do more with less. The latter has caused a significant shift from rapid on-site evaluations (ROSE) performed on fine-needle aspiration (FNA) to touch imprint (TI) cytology of needle core biopsies (NCB). The trend towards a subspecialty histopathology sign out has also led to diversion of cytological specimens into the corresponding or appropriate subspecialty histopathology teams in favor of a better cyto-histocorrelation, an accurate diagnosis, and better patient care [2].

In the current review, we explore the changing trends and the anticipated challenges in the practice of cytology.

Fig. 1. Numbers of Papanicolaou (Pap) and human papilloma virus (HPV) tests per year, over the last 6 years, at the University of Mississippi Medical Center.

Discussion

Gynecologic Cytology

Routine screening of cervical cytology with a Pap smear, originating in the 1940s, is recognized as the standard of gynecologic care. Over the last 30 years, routine cervical cytology screening has contributed to a 50% reduction in the incidence of cervical cancer in the USA [1]. The mortality from cervical cancer has also decreased from 5.55 per 100,000 women in 1975 to 2.38 per 100,000 women in 2008 [1]. The development of cervical cancer is strongly associated with previous infection with the human papilloma virus (HPV), and cervical cancer represents 53.4% of the total number of HPV-associated cancers in women [3]. HPV testing for high-risk HPV genotypes, so far used to triage equivocal Pap test diagnoses, became an integral part of the cervical cancer screening program recently. The current guidelines for cervical carcinoma screening were created as joint recommendations of the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology in 2012 and they were accepted and promoted by the ACOG later that year [1, 4, 5]. Major highlights of the guidelines include: initiation of cervical carcinoma screening at 21 years of age, with cervical cytology testing exclusively until age 30 years; co-testing with cytology and HPV testing every 5 years for women aged 30–65 years; and discontinuation of screening in women over the age of 65 years without a history of cervical intraepithelial neoplasia grade 2 or higher and adequate negative prior screening results. In 2014, the FDA approved the cobas® HPV test as the first of its kind for use in place of cytology for primary screening for cer-

vical cancer by detection of high-risk HPV genotypes in women aged 25 years or older [6]. The interim guidelines state that, because of its equivalent or superior effectiveness, primary high-risk HPV screening can be utilized as an alternative to cytology [7, 8]. As an effect of the guidelines, in the last 4 years our institution has witnessed a decline in cervical Pap tests and an increase in HPV testing (Fig. 1). In order to manage the annual load of up to 60,000 Paps, cytotechnologists were spending most of their time screening Paps. The approximately 30% decline in Pap smears in the last 5 years prompted the department to reorganize the service contribution by the cytotechnologists. A program was initiated to train cytotechnologists to perform ROSE and screen FNA/NCB specimens. With the evolution of molecular testing in surgical pathology and cytopathology, cytotechnologists were utilized to assist pathologists in screening and evaluating ROSE and triaging specimens for molecular testing. Cost cutting and hospital budget containment also required cytotechnologists to contribute to administrative duties. It is possible to further expand the role of cytotechnologists to enhance the pathologist's efficiency in other ways as well, including screening for and locating microorganisms on special stains, grossing small biopsies, evaluating the adequacy of renal biopsies, enumerating tumor purity for Sanger sequencing, capturing and annotating digital images, and selecting slides for molecular tests [9]. Cytotechnologists as "pathologist extenders" add value in prescreening cytology and other specimens for the identification of abnormalities. The College of American Pathology (CAP) Pap proficiency program and nongynecologic interlaboratory comparison programs have consistently demonstrated that pathologists are less skilled than

Fig. 2. Numbers of fine-needle aspirations (FNA) and needle core biopsies (NCB) per year, over the last 6 years, at the University of Mississippi Medical Center.

cytotechnologists at detecting abnormalities on Pap tests and that cytotechnologists perform as well as pathologists in identifying most lesions [9]. Besides, cytotechnologists performing ROSE help to offset the reduced reimbursement for pathologists performing adequacy assessments.

Nongynecologic Cytology

During the last decade, pathologists have witnessed an accelerated growth in the field of molecular pathology. With new technologies and better resolution of computer tomography, ultrasound, and magnetic resonance imaging, the number of diagnostic procedures has increased and the demand for ancillary testing on smaller specimens is greater than before. Cytology specimens have proven to be an excellent source for molecular testing, yielding the maximum information with use of a minimally invasive technique [10]. Cytopathologists are an important link of personalized medicine with minimally invasive techniques and they are well versed in the art of ROSE on FNA smears for adequacy of diagnosis and triaging of the tissue for ancillary studies. More recently NCB has become the preferred method for obtaining tissue, especially for molecular testing, resulting in the need for cytologists to become familiar with the nuances of performing ROSE on TI.

According to the 2015 CAP nongynecologic survey, more than half of the laboratories that participated in the survey performed ROSE of TI of NCB. On-site assessment of the TI was performed by a pathologist in 82% of the laboratories surveyed [11]. In our own institute, over the last few years the number of ROSE for FNA has doubled and the number of ROSE for TI has increased by 50% (Fig. 2). Most NCB are obtained under image guidance,

including CT (CT-NCB), endoscopic ultrasound (EUS-NCB), and endobronchial ultrasound (EBUS-NCB). At our institution, the most common body sites for NCB are the lungs, abdomino-pelvic masses, soft tissue, and bone, including the spine. NCB is the favored method for providing tissue to pathologists for diagnosis as it ensures adequacy of the tissue for molecular testing if indicated. In order to accommodate their requests, we let the radiologist choose the tissue type (FNA/NCB) based on the procedure that is best for the patient and their diagnostic/therapeutic needs. If the TI on the first core shows lesional cells, other cores are directly submitted in formalin or used for flow cytometry or microbiology as the need may be. Multiple paraffin blocks are made if multiple cores are available, with each block containing one core to ensure adequacy of the tissue. As per the 2015 CAP NGC education survey, the majority (50.5%) of laboratories accession the entire specimen as a surgical specimen, followed by 28.4% which accession it as a cytology specimen and some (15.5%) which accession TI as a cytology specimen and NCB as a surgical specimen. At our institute the entire specimen (TI and NCB) is accessioned as a cytology specimen as the cytologist has the advantage of being present during the procedure, reviewing the images, and discussing the case with the radiologist. Besides, a single report incorporates the ROSE findings and the final diagnosis and documents ancillary studies if performed in a more complete manner.

The techniques used to perform TI are not standardized and vary from just touching the NCB on the slide to rolling the NCB on the slide and rarely to a crush/squash preparation. The percentage of cells transferred onto the slides depends on the inherent nature of the tissue (friable

Table 1. Advantages of touch imprint of needle core biopsy over fine-needle aspiration

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- There is good cellular detail with preservation of the architecture of the lesion
 - It is useful in lesions with desmoplastic or sclerotic stroma (less exfoliation of cells)
 - Touch imprints of needle core biopsies are a relatively simple technique
 - It preserves the original sample for permanent fixation
 - More tumor cells are available for different ancillary and molecular studies
 - It is cost-effective
 - There is a wider use and acceptance of touch imprints of NCB
 - It is less time-consuming for the cytopathologist, the radiologist, and health care personnel
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Table 2. Disadvantages of touch imprint over fine-needle aspiration

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- It has a limited utility for the assessment of cystic lesions
 - The presence of cohesive fragments and fewer single cells impedes evaluation of cytological features
 - There are artifacts that pathologists may not be familiar with
 - It involves a learning curve
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Table 3. Differences in CPT codes for touch imprint vs. fine-needle aspiration

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- The billing codes for rapid on-site evaluations performed on fine-needle aspiration (88172, 88173, and 88177) are different from the billing codes for touch imprint performed on needle core biopsy (88333 and 88334)
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tumors vs. benign fibrous lesions) and on the increasing length of the drag. Excessively vigorous TI can deplete the core of cells. The DNA content lost is directly related to each centimeter of imprint, thereby impacting the material available for molecular testing and other ancillary studies [11]. Rekhtman et al. [12] described an imprint of a NCB as touching the CNB to the slide with minimal sliding along the slide surface and recommended the horizontal drag method. Other factors that can affect the quality and quantity of the NCB material include the type and location of the target lesion and the number and type of needle passes [12, 13].

The shift to and preference for NCB over FNA is related to the ability of radiologists to provide multiple cores at the same time through the use of a coaxial NCB system and the flexibility for pathologists to triage the tissue adequately for ancillary studies including immunohistochemistry, histochemistry, microbiologic cultures, molecular studies, and flow cytometry [14, 15]. Historically, cytology texts and literature and training of cytologists have been based on descriptions of morphologic findings of cellular material retrieved through FNA, even though it has been shown that TI of NCB are comparable to FNA for the purposes of ROSE [16, 17]. TI involves artifacts different from FNA [16, 18]. Intuitively, the process of acquiring material is different in the two procedures; aspiration is an active process that generally yields a cell-rich preparation without much stroma, compared to NCB which is a relatively passive process and includes

cells and stromal elements in the same specimen. The smears made from aspirated tissue are therefore generally composed of widely scattered, smaller cell clusters with more single cells. The TI in contrast contains much larger and more cohesive cell groups, highlighting architectural details [16]. The advantages of FNA and TI over each other are summarized in Tables 1 and 2. It is important to keep in mind that the CPT billing code for both procedures is also different (Table 3).

Clearly, there is a learning curve involved in getting familiar with the differences in morphologic features in smears and TI in order to confidently perform a ROSE.

Charles Darwin said, “It is not the strongest of the species that survive, nor the most intelligent, but the one most responsive to change.” Cytopathologists have acknowledged and embraced the change. Cytopathology is a study based on examination of cells and so a trained cytopathologist is the best to do “most” with “less.” In the future, we anticipate that cytopathologists will be even more intimately involved in triaging and choosing tissue for molecular testing besides making the “final diagnosis” on miniscule tissue from different parts of the body.

Disclosure Statement

None of the authors has any conflict of interests, financial or otherwise.

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