EDITORIAL

Errors in the pathology laboratory**M. Beatriz S. Lopes, MD, PhD**

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IN the article titled “Conflicting pathological reports: a diagnostic dilemma,” Dr. Shahar and colleagues¹¹ report a scenario that many of us may have unfortunately encountered in our professional careers—the possibility of human error that may harm our patients. Surgical specimen mix-up is occasionally seen in busy surgical pathology laboratories. This type of error, however, is much less common than that seen in other laboratory tests that can fortunately be more readily rechecked or retested, like blood and secretions testing.^{2,10} Similarly to the case presented by Shahar et al., an inaccurate diagnosis due to a laboratory error may lead to additional diagnostic procedures and/or unnecessary treatment.

While the molecular era expands into breakthroughs in the investigation of tumor-specific genetic alterations and guides clinicians and surgeons for treatment planning, histopathological diagnosis of diseases and tumor entities still relies on the pathologist’s assessment of morphological features in processed and stained tissue samples. Processing of surgical tissue samples for pathological diagnosis has undergone minimal changes in the last century, despite advances in equipment and technology. Furthermore, in spite of the introduction of automation in surgical pathology laboratories, several steps during the gross processing, embedding, and cutting of tissue samples are performed by histotechnologists, pathologist assistants, and pathologists themselves. Therefore, the potential for human error(s) is yet a possibility regarding which we all should be vigilant.

Several standards pertaining to laboratory testing and tissue analysis are in place as part of the accreditation and inspection practices of pathology laboratories. For example, in the US and several other countries, the great majority of pathology laboratories is accredited by the College

of American Pathologists and adheres to the College standards and guidelines for laboratory quality improvement (<http://www.cap.org/apps/cap.portal>). The process of accreditation and re-accreditation is a rigorous one, with annual self- and peer-reviewed inspections and adjustments to new guidelines and standards.

As briefly reviewed by the authors, surgical pathology errors have traditionally been categorized into three phases during the testing process: a preanalytical phase, consisting of specimen collection, labeling, and transport from the operating room to the pathology laboratory; an analytical phase, corresponding to the specimen accession, gross and histological processing, and microscopic interpretation; and a postanalytical phase involving the reporting of the pathology test results and clinical interpretation.⁶ Preanalytical phase errors, including specimen identification and accession, have been well examined and several safeguards have been introduced in the past decades for prevention of surgical specimen misidentification in a combined effort from outpatient clinics and operating room coordinators and surgical pathology laboratories.^{1,5,8} In particular, the introduction of automation or computerization of the surgical pathology laboratory labeling process from the specimen accession to labeling of tissue cassettes and ultimately glass slides has substantially decreased errors in surgical pathology laboratories.¹³ Ideally, a comprehensive computerized system would link the institutional database to the pathology laboratory system for confirmation of the patient’s identity, the physician test order submission with mandated entry of the clinical history, accountability of the specimen’s arrival in the pathology laboratory, patient’s identification at accession with subsequent labeling of blocks and slides, and finally identification of the final pathology report.⁷

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Regrettably, despite all efforts toward automation in surgical pathology laboratories, the problem described by the authors in the case report was a human error. Through a root cause analysis, it was concluded that the most likely phase of tissue mix-up occurred during the processing of the biopsy at the gross processing bench, resulting in “contaminant” tissue in the subsequent paraffin blocks and then in the glass slides analyzed by the pathologist.¹¹

Contaminants or extraneous tissue in microscopic sections may be caused by two main mechanisms: incorrect tissue embedded in a given patient’s paraffin block at the gross processing bench, or a superficial contaminant from the water bath at the time of block sectioning or staining area, also known as a “floater.” The origin of a floater is more readily detected because it is usually present only once, implying that it floated onto a single slide; tissue contaminant present within the paraffin block is more difficult to assess.¹² Regardless of its source, extraneous tissue creates serious problems for the pathologist and her/his final diagnosis.

In a large study of cross-contamination or extraneous tissue analysis comprising 275 pathology laboratories endorsing the College of American Pathologists Q-Probes quality improvement program, it was estimated that 0.6%–2.9% of slides reviewed had cross-contamination.³ More than 90% of extraneous tissue originated in the pathology laboratory, and the most frequently observed sites of potential cross-contamination were during frozen section or gross processing, at the time of cutting of histological sections, and during the staining process. Fortunately, the degree of diagnostic difficulty caused by cross-contamination was judged to be severe in only 0.4% of the slides analyzed prospectively and in 0.1% of the slides analyzed retrospectively.³

Over the years, most pathology laboratories have implemented a variety of quality control measures for reduction of the risk of tissue cross-contamination. Many laboratories avoid serial accession and gross processing of similar specimens; for example, breast biopsies would be interspersed with other types of biopsies to reduce the risk of misidentifying two consecutive specimens. Another example is the use of different cassette colors for specific types of tissues. Tidiness and cleanliness of gross processing benches, water bath, and cutting areas are also objects for quality control and improvements by specific guidelines and standards (<http://www.cap.org/apps/cap.portal>). Likewise, histotechnologists’ proficiency and continued competency are monitored by local institutional committees, accreditation organizations, and professional societies (<http://www.ascp.org/Board-of-Certification/Certification-Maintenance-Program-CMP>). First and foremost, a high degree of suspicion even of minor discrepancies, including size and number of tissue fragments as assessed by gross inspection; clinical history; and laboratory and imaging data must be constantly monitored by pathologists and health care workers in a pathology laboratory.⁹

Standard workup when cross-contamination is suspected may include clinical and laboratory correlation, specialized laboratory testing, and, potentially, molecular analysis. The latter is most useful when contaminant

tissue is present in the paraffin block, so residual tissues may be available for molecular probing. Molecular DNA fingerprinting for tissue and sample identity, as used in the case reported by Dr. Shahar and colleagues,¹¹ has been critical for this type of analysis.^{4,12}

A final step in preventing errors is safety measures at the postanalytical phase involving the interpretation of a pathology report in view of the clinical presentation and other laboratory data by the pathologist and the clinical team. In this sense, system redundancy should be established for error detection not only at the pathology department itself but also in the settings of clinicopathological conferences and tumor board reviews. Multidisciplinary team evaluation of a new diagnosis or recurrence seems to be the best practice for elucidation of errors in a systematic manner.

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Response

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We thank Dr. Lopes for her insightful editorial. There is an increasing awareness of potential mistakes during processing of surgical specimens, and efforts are being made to prevent such errors. Unfortunately, whenever humans are involved, errors will occur and may lead to inappropriate treatment of our patients. Modern pathology laboratories use multiple modalities to overcome the inherent potential for error in a complex process of surgical pathology analysis. These include stringent labora-

tory guidelines and standardized procedures, the use of automated systems where possible, built-in prevention and detection systems that include continuous quality assurance, quality-control monitoring, and adequate personnel training.

The final barrier before a patient is erroneously treated (based on an erroneous pathological report) is when the clinician applies a strict clinical perspective to the tentative pathology report, and preferably shares such a perspective ahead of time. For this part of the process the dialog among the clinical team members and the pathologist is crucial, and as stated in the editorial, critical evaluation of a newly diagnosed patient by a multidisciplinary team seems to be the best way to prevent clinicians from constructing the treatment plan based on an erroneous pathology report.