Q&A column, 5/16

Editor: Frederick L. Kiechle, MD, PhD

Submit your pathology-related question for reply by appropriate medical consultants. CAP TODAY will make every effort to answer all relevant questions. However, those questions that are not of general interest may not receive a reply. For your question to be considered, you must include your name and address; this information will be omitted if your question is published in CAP TODAY.

Submit a Question

Q. What laboratory test should be used to monitor the effect of the heart failure medication Entresto (sacubitril/valsartan)?

A. There is no consensus at this time about which biomarkers should be measured once a patient is treated with Entresto. On the one hand, the simplistic argument would be to simply measure NT-proBNP, as this biomarker is not adversely affected by the drug and monitoring of the benefit of Entresto is possible. While the most straightforward approach, this may not be practical for institutions that do not run NT-proBNP, so clinicians are faced with either not measuring a natriuretic peptide in their patients or measuring BNP and trying to interpret it. Unfortunately, we do not know if the effect of Entresto extends to all BNP assays, and if it does, whether they are affected the same.

Also, in order to interpret BNP in a patient taking Entresto, it's important to emphasize we do not yet know how much of an increase in BNP to expect from Entresto treatment, or the durability of such a rise. It is clear that in the PARADIGM-HF trial, patients showed an approximate 25 percent increase in their BNP concentrations (measured using the Siemens BNP method) after initiation of the drug. This rise seems to be relatively durable, suggesting that the effects of Entresto on BNP do not "wear off."

Lastly, much as a fall in NT-proBNP may indicate benefit, it has been suggested by some that measuring BNP might be done to look for the rise in the marker to suggest effectiveness of the drug. I believe this latter approach is foolish and not advisable because a rising BNP might very well indicate a decompensating patient, and such decompensation would be missed if it was assumed the rise in BNP is due to Entresto.

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Q. After getting a consultation report, I usually issue an addendum without changing my own diagnosis. Some of my colleagues use an amended report with their own diagnosis changed. They say this will help clinicians with patient management. I do not feel confident about many of these difficult cases, so I do not want to change my diagnosis. We would like to establish a department policy to address this. Can you provide guidance?

A. Difficult diagnostic cases in surgical pathology may be sent out for extramural review for a variety of reasons: pathologist generated (the original pathologist is uncomfortable with the diagnosis of the case), patient generated (the patient doesn't trust the pathologist's diagnosis), clinician generated (the clinician doesn't trust the pathologist's diagnosis), or system generated (the patient is presenting for a second clinical opinion to an institution in which protocol mandates that the consulting institution's pathologists review the diagnostic material). The CAP's anatomic pathology checklist requirement ANP.10150 requires laboratories to have a policy for handling

extra-departmental consultations. The records of these consultations can be maintained within the official surgical pathology report or kept separately, as long as they can be readily linked and accessible.

A number of studies of interinstitutional review have shown modification of diagnoses in 1.4 to 11.3 percent of cases, with about half resulting in significant changes in the clinical management of the patient. A caveat is that in eight percent of second institution diagnoses, additional consultation has shown the original diagnosis was, in fact, the correct one; hence the second opinion should not, by reflex, be considered the gold standard.

Thus, the question about whether the original diagnosis should be changed depends on whether the original pathologist feels comfortable with the consultant's diagnosis. If not, then something must be done to address the discrepancy in the diagnoses. A report with two potential variant diagnoses, or a report that could possibly be misinterpreted, is not in the best interests of the patient, and one or two instances of such will quickly cause clinicians to lose confidence in the pathology department.

If the discrepancy may lead to a delay in clinical treatment, a responsible clinician should be notified as soon as possible about the disagreement and a plan for resolving the diagnostic dilemma should be devised, whether it involves additional immunohistochemical stains, additional sections, or a plan to send the case to a "tiebreaker" consultant. Ideally, the original pathologist, the consulting pathologist, a responsible clinician, and in some cases the patient should be included in the decision tree, especially if it is a complex case. If a definitive answer still cannot be reached, that should be reflected in a consensus report, which may culminate in a request for additional tissue via another surgical procedure.

It is important to document the change in diagnoses in the medical record, and it should be done consistently. "Amended reports," "supplementary reports," "addendum reports," and other synonymous terms abound. There should be a department policy that governs the standard use of these terms. Reports signaling a major change in diagnosis (usually called "amended reports" in most institutions) should be flagged in some way—by font (bold or bold italic, red color if feasible), a flashing warning on the LIS screen, or all capital letters, depending on the sophistication of the computer system. Ideally, given that not all systems work all the time, overlapping systems will be in place. The corrected report should show up first on the screen and be printed first when paper copies are obtained. Any major change in diagnosis should be communicated orally to a responsible attending clinician before a report is issued, and a record of the communication should be included in the amended report, including the means of communication (telephone, in person), date, and time. The report should state clearly the reason for the change (consult, additional information, additional stains), and the diagnostic field should highlight the changes.

Addendum reports ("supplementary reports") as a general rule signify a report reissuance to reflect ancillary studies such as cytogenetic results or special stain results that are received after the final diagnosis is issued, or they may be used to indicate an extramural consult in which the consulting pathologist agrees with the original diagnosis. All members of the department should use the same terms for the same sorts of report changes, making sure, most importantly, to avoid the use of the "amended" or "corrected" designation (if adopted) for less significant changes to reports.

Every pathology department should have a standard list of clinical situations in which a change in diagnosis, however discovered, requires urgent communication. While some would be obvious, such as benign-to-malignant or malignant-to-benign diagnoses, some nonmalignant errors may be critical, such as no evidence of a lumen in a fallopian tube or vas deferens segmental excision for fertility termination. Errors in this area have led to well-documented successful litigation against pathologists and laboratories. Every department should devise its own list, with clinician input. All pathologists should have a copy, and it should be reviewed and updated regularly.

The frequency of extramural consultations should be tracked by type (who requested the consult) and the results should be monitored, not only by original pathologist but also by organ system. Both can reveal individual as well as departmental weaknesses, which may be addressed through additional training or by hiring an expert in a burgeoning subspecialty area.

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