CORRESPONDENCE

The Morphological and Molecular Diagnosis of Lung Cancer

by Prof. Dr. med. Iver Petersen in volume 31–32/2011

Laboratory Tests to Ascertain Tumor Resistance to Drugs Are Available

Individualized treatment, which is promoted as the optimum treatment modality nowadays, makes it desirable for the diagnosis of a neoplasm to be able to confirm not only the malignancy of the tumor tissue but also its growth characteristics and responsiveness to therapy.

New morphological and molecular diagnostic procedures for lung cancer enable differentiation between main types and subtypes. However clinically relevant characteristics of these groups can be defined only to a limited extent, which means that the number of patients benefiting from this approach is currently still small.

Drug treatment of lung cancers is difficult owing to the high rate of intrinsic tumor resistance. This is induced by the body's own resistance to toxic substances—for example, toxins contained in cigarette smoke (1). The detoxification mechanisms thus induced consequently also inactivate toxic chemotherapeutic drugs. A laboratory finding of tumor resistance to drugs is possible by using morphological and molecular diagnostic methods. Tumor resistance to drugs can be diagnosed by means of immunohisto-chemical tests of tumor resistance factors—for example, overexpressed substances of the group of ABC transport proteins (2). Methods that can test the non-response to anticancer drugs in living biopsy specimens have also been available for some time (3). For the patient, the diagnosis means that he or she is spared ineffective pharmacotherapies. However, more research is needed to optimize the methods for routine tests.

In recent years, drug resistance testing has met with increased interest and has been used in many cases. The National Comprehensive Cancer Network (NCCN) reported a while ago that in treating ovarian cancer, resistance tests were used in selecting the drugs for treatment (3). In the diagnostic evaluation of tumors, testing drug resistance provides pathologists with an opportunity to also act as pilots in identifying a suitable therapeutic regimen.

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In Reply:

Professor Lippert rightly points out the clinical relevance of tumor classification. He requests specifically that the diagnostic evaluation should provide information regarding the behavior of a tumor in response to systemic treatment. The studies he cites give an interesting insight into currently available methods. They allow conclusions about the possible resistance of a tumor to certain chemotherapeutic regimens. By comparison, predicting a positive therapeutic response—that is, the sensitivity to a particular cytotoxic agent—is subject to far greater uncertainty.

Pathologists have recognized this problem. The relevant subspecialty is known as "predictive pathology," and in molecular tumor diagnosis, differentiation is made between diagnostic, prognostic, and predictive biomarkers (1, 2). However, the boundaries between these markers are fluid. A confirmed activating epidermal growth factor receptor (EGFR) mutation, for example, is associated not only with sensitivity to treatment with an EGFR tyrokinase inhibitor, but also with a better prognosis for the patient. The mere morphological distinction of small cell and non-small cell lung cancers is already predictive for initial sensitivity or resistance to conventional chemotherapy. Equally, the new, morphology-based classification of adenocarcinoma of the lung yields prognostic as well as predictive information (3, 4). It confirms in an exemplary way that a tumor's histomorphology and cytomorphology contains characteristics whose clinical relevance has hitherto remained unidentified. It may therefore be assumed that differentiated morphological diagnostic evaluation will continue to have a key position in tumor classification. It will be complemented by selective, targeted use of biomarkers to identify clinically relevant subgroups. The challenge for pathologists is therefore in possessing in-depth knowledge of molecular mechanisms in tumor biology and tumor therapy, in addition to having a good eye for morphology.

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