References

Testing for Neuroendocrine Immunohistochemical Markers Should Not Be Performed in Poorly Differentiated NSCCs in the Absence of Neuroendocrine Morphologic Features according to the 2015 WHO Classification

In Response:
In contrast to the recommendations of the 2015 World Health Organization (WHO) classification of tumors, Derks et al. suggest that testing for neuroendocrine (NE) immunohistochemical markers should be performed on all poorly differentiated non–small cell carcinomas (NSCCs) lacking NE morphologic features and reported. We considered this suggestion in our preparation of the WHO classification, and the topic was discussed in detail. For the 2011 International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society lung adenocarcinoma classification, we conducted an evidence-based review that addressed this topic specifically. Because there are no consistent evidence-based data in the literature to support any clinical relevance (diagnostic, prognostic, or therapeutic) of a positive NE marker in the absence of NE morphologic features, the 2015 WHO Classification recommends that testing for NE markers not be performed on all poorly differentiated NSCCs in the absence of NE morphologic features. This recommendation is specifically presented on page 20 of the WHO blue book, and this detail could not be included in the short review provided for the Journal of Thoracic Oncology. Only if there is a suggestion of NE morphologic features is testing for NE immunohistochemical markers appropriate. In addition, the problem of NSCC with NE differentiation...
Genetic Basis of Mesothelioma—More Than Asbestos Exposure

To the Editor:
A combination of pathogenic organisms, environmental carcinogen, and genetic predisposition can contribute to carcinogenesis. No causative viruses for mesothelioma have been identified to date, and even though mesothelioma has been attributed largely to asbestos exposure, the genetic basis underlying the disease has lately received attention. Such interest is warranted because asbestos alone cannot explain the varying incidence of mesothelioma among patients with comparable exposure, and most diseases have a multifactorial etiology.

Thus, researchers were excited to find that mutations in a tumor suppressor gene, breast cancer 1–associated protein 1 (BAP1), were found in families with a high incidence of mesothelioma, as well as in sporadic cases.1 Interestingly, both germline and somatic mutations were found, which indicated a possible inheritance of the disease, as well as establishment of BAPI as a target of mutations. All family members had nonoccupational, residential asbestos exposure; thus, the relationship between BAPI mutations and asbestos might be additive, synergistic, or both.

Recently, Nasu et al.2 found somatic mutations of BAPI in more than 60% of 22 frozen mesothelioma biopsies, and they duplicated their finding in another 70 biopsy samples. There was no significant correlation between frequency of BAPI mutations and asbestos exposure among patients, which implied that the pathogenesis of mesothelioma may be multifactorial and possibly polygenic.

For instance, germline and somatic mutations in transcriptional regulators such as mammalian switch/sucrose nonfermentable (mSWI/SNF) chromatin remodeling complex were noted in mesothelioma.3 Such mutations may cause low acetylation of histone and affect transcription, thereby contributing to the development of mesothelioma. Even though these results were obtained from eight mesothelioma cell lines from patients who all had a history of asbestos exposure, they supported interplay between genetic predisposition and asbestos as a contributor to development of disease.

Furthermore, somatic mutations were reported in tumor suppressor genes, including neurofibromatosis type 2 (NF2), large tumor suppressor 2 (LATS2),

References