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EDITORIAL

Diagnosing malignant pleural mesothelioma

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The diagnosis of malignant pleural mesothelioma is a difficult clinical task. A suspicion of mesothelioma should always arise, when a patient with a case history of reasonable asbestos exposure is examined for pleural effusion or pleural masses of unknown aetiology [1]. In addition to asbestos exposure a hereditory predisposing factor has been suggested to be of importance for the development of malignant mesothelioma [2, 3]. Analyses of pleural fluid have been of limited value. The sensitivity of cytological examination of pleural fluid for detecting malignant mesothelioma has been low [4–6]. Elevated content of hyaluronic acid in pleural fluid is associated with malignant mesothelioma [6–8]. However, many mesotheliomas do not produce hyaluronic acid, and other causes of elevated hyaluronic acid content occur [7, 8].

The morphological variability of the tumour is the main cause of diagnostic problems. Malignant mesothelioma cells are difficult to distinguish from benign reactive mesothelial cells [4, 5, 9]. Furthermore, malignant mesothelioma may morphologically mimic other neoplasms metastatic to the pleura, especially adenocarcinomas [6, 9]. These difficulties have made access to tissue specimens of crucial importance for a correct diagnosis. Reports have shown that thoracoscopy is significantly superior to cytology ([6, 10] or Abrams needle biopsy [10], and is almost as good as thoracotomy [10] for diagnosing mesothelioma. Pathologists, if offered an option, would still prefer thoracotomy due to the larger amount of tissue available for examination [9].

Initially the microscopic patterns of expression were classified as epithelial, fibrous-sarcomatoid and biphasic [11]. Recently, this classification has been revised, and a great number of morphological patterns are now recognized. In a review of several reports, including a total of 819 cases of mesothelioma, 50% were of the epithelial tumour type, 16% were of the sarcomatoid type and 34% biphasic [12]. At least half of the epithelial mesotheliomas show morphological patterns which make a diagnosis of mesothelioma the most plausible. There are no diagnostic difficulties regarding the biphasic tumour type and seldom with the fibrous-sarcomatoid tumour type. An experienced lung pathologist using traditional stainings with the addition of stainings for mucosubstances (periodic acid-Schiff) and hyaluronic acid (Alcian blue/Toluidine blue) should thus be able to correctly reveal about 70% of all cases of mesothelioma provided he has had sufficient biopsies for microscopic evaluation. As for the remaining (about 30%) cases, development of new histopathological methods has greatly improved possibilities for a definite diagnosis. The new techniques include above all immunohistochemistry and electron microscopy.

Immunohistochemistry has developed rapidly in recent years. Antibodies to carcinoembryionic antigen (CEA), epithelial membrane antigen (EMA) and vimentin seem to be promising in distinguishing epithelial mesotheliomas from adenocarcinomas. CEA is reported to stain positive in about 10% of all mesotheliomas, as compared to 90% of all adenocarcinomas of the lung [13–15]. EMA stained positive in 33 out of 43 mesotheliomas in one study [16]. Vimentin positive staining is an expression of mesenchymal origin and is, as such, positive in many mesotheliomas but negative in adenocarcinomas [17, 18]. Reports in this journal by AL-SAFFAR and HASLETON [19] and by MANNES *et al.* [20] present further support for the diagnostic value of CEA and vimentin staining. AL-SAFFAR and HASLETON [19] also noted that the sensitivity of vimentin staining varied with greater sensitivity in surgically obtained tumour tissue as compared to postmortem tissue.

Malignant mesothelial cells can also be distinguished from adenocarcinomas with the use of electron microscopy [21]. By contrast electron microscopy is of less value for distinguishing malignant mesothelial cells from benign reactive mesothelial cells. Mesothelioma cells have long thin microvilli showing both secondary and tertiary branching. A length-to-diameter ratio greater than 10:1 is characteristic for microvilli of mesothelioma cells but is rare for microvilli of adenocarcinoma cells. The micovilli of all adenocarcinomas, with the exception of adenocarcinomas derived from müllerian epithelium, are shorter and thicker.

A combination of immunocytochemical technique and electron microscopy has been used on pleural fluid samples in one study [22]. Electron microscopy showed positive labelling of the villous surface of malignant mesothelioma cells with a monoclonal anti-EMA antibody E29. In contrast the villi of reactive mesothelial cells were not labelled at all.

As a result of the developments of modern immunohistochemical and electron microscopic techniques, diagnostic difficulties have declined, and there is a chance that pleural fluid examinations in the future could be sufficient for diagnosing malignant mesothelioma.

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