A Single Liver Metastasis from Pleural Biphasic Mesothelioma

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Abstract: Virtually any malignancy can metastasize to the liver. Large solitary metastases are rare and can be difficult to distinguish from primary tumors. Malignant mesothelioma is often considered as a locally invasive cancer but tumor dissemination to extra-thoracic sites is possible, and the liver can be involved. Herein, we present a rare case of pleural mesothelioma with a solitary large liver metastasis diagnosed postmortem in a ninety-two-year-old man with 35 years of exposure to asbestos. Results of immunohistochemical staining of the pleural and liver tumor were similar, both positive for low-molecular weight keratins, calretinin, vimentin, and podoplanin, and negative for Claudin-4, TTF1, CEA, BerEP4, CK7, CK19, CK20, BAP1, Hep Par1, p40, and WT1. Fluorescent in-situ hybridization (FISH) for p16/CDKN2A was also performed and a homozygous deletion was detected in both tumors, supporting the diagnosis of mesothelioma. Reporting this case, we would like to point out that extra-thoracic dissemination from pleural mesothelioma, even if exceptional, can occur. In cases where differential diagnoses are challenging, the value of ancillary techniques and a practical approach to diagnostic work-up is of primary importance.

Keywords: autopsy; malignant pleural mesothelioma; liver; metastasis; asbestos exposure
Figure 1. Autopsy was performed in a ninety-two-year-old male at the request of his son, on the suspicion of an occupational disease of legal concern. The patient died at home; in the last month he had presented weight loss, coughing, chest pain, fever, and general malaise. Chest CT-scan revealed an intrathoracic mass in the right upper lobe measuring 6.7 × 6.5 cm, of probable pleural origin; numerous bilateral pleural plaques were also detected. The patient, bedridden due to the serious general conditions, was not subjected to further investigations and died in few weeks. Gross examination revealed multiple nodular bilateral scleral hyaline plaques of the costal, parietal, and diaphragmatic pleura (A, arrow). At the upper lobe of the right lung, a nodular mass, 9 cm in diameter, adhered to the thoracic surface (A, inset). The right pleural surface was thickened (1 cm). At histology, the thoracic mass was characterized by a proliferation of epithelioid malignant cells showing a solid pattern, vesicular round nuclei with small nucleoli, and an admixture of pleomorphic epithelioid and spindle cells (B, hematoxylin and eosin, scale bar: 300 µm; inset: pleomorphic features). The right lobe of the liver was entirely occupied by a partially necrotic mass, 10 cm in diameter (C), and the liver cancer showed prevalent large necrosis foci and neoplastic aggregates with similar microscopic features (D, hematoxylin and eosin, scale bar: 300 µm).
According to the recent guidelines [1,2] a panel of immunohistochemistry antibodies was used in both tumors, eliciting positive reactions to: calretinin (A, scale bar: 200 µm; B, scale bar: 300 µm), podoplanin (D2-40) (C, D, scale bar: 300 µm), CK5/6 (E, F, scale bar: 300 µm), and vimentin (G, H, scale bar: 300 µm), and negative reactions to CEA, TTF-1, p40, CD34, HMB45, Melan-A, CK7, CK19, CK20, PAX8, FLI-1, and BAP1 (using lymphocytes as positive control). Immunostaining for WT-1 was also performed, resulting negative in both lung and liver.
the mesothelial cell layer over the Glisson’s capsule are also reported, rarely associated to asbestos hyperchromasia, large nucleoli, and rare multinucleation [12]. However, the examination of the pattern [11] and pleomorphic type [12], more likely affected by an aggressive behavior and sharing malignancy. The epithelioid type is often easy to identify and is associated with the best prognosis. Immunohistochemistry antibodies and molecular analyses can help pathologists to diagnose this rare exposure [9]. Diagnosis of these rare tumors can be very challenging. Using a large panel of antibodies may be variable. Specifically, in our case, the WT1 negativity was not an unexpected finding, could also be helpful in these challenging cases. Nevertheless, the sensitivity and specificity of some antibodies may be variable. Indeed, some epithelioid cells showed pleomorphic features, with nuclear enlargement, hyperchromasia, large nucleoli, and rare multinucleation [12]. However, the examination of the whole tumors revealed the coexistence of two different and distinguishable components, epithelioid and sarcomatoid, thus orienting toward a biphasic form. Immunohistochemical and molecular analyses could also be helpful in these challenging cases. Nevertheless, the sensitivity and specificity of some antibodies may be variable. Specifically, in our case, the WT1 negativity was not an unexpected finding, as this is reported to be expressed in less than half of high-grade mesotheliomas [14,15]. Similarly, other marker expressions can be lost in the sarcomatoid component, such as calretinin and CK5/6, whose sensitivity ranged from 10 to 60% and 13 to 29%, respectively [14]. Conversely, podoplanin is frequently detected in high-grade tumors (with a sensitivity of up to 90%), but its specificity is low [14].
In our patient, the combination of different immunohistochemical markers, together with the detection of p16/CDKN2A deletions, most frequently reported in mesotheliomas [1,16], permitted a confident identification of the mesothelial lineage of the neoplastic cells.

In conclusion, our case confirms the value of ancillary techniques and of a practical approach to the diagnostic work-up for diagnosing mesothelioma, particularly in challenging cases. Malignant pleural mesothelioma should be considered a neoplasm with an extra-thoracic metastatic capacity like most cancers, and this aspect should be taken into account in clinical practice.

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