Biphasic malignant mesothelioma with epithelioid and sarcomatoid components (dedifferentiated mesothelioma) and intrapulmonary growth: a rare entity mimicking desquamative interstitial pneumonia

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CLINICAL QUESTION

The patient was a 54-year-old man with symptoms of chronic obstructive pulmonary disease (COPD) who had smoked for many years. A thoracic CT showed bilateral bullae and a tumour measuring 35×25 mm in the right upper lobe (figure 1). Radiological features were consistent with an intraparenchymatous lung tumour. A right upper lobectomy was performed. Gross examination of the surgically excised specimen revealed a nodular lesion measuring 5×5 cm in diameter.

Review the high quality interactive digital Aperio slide at http://virtualacp.com/JCPCases/jclinpath-2019-206379.R1/ and consider your diagnosis.

WHAT IS YOUR DIAGNOSIS?

A. Biphasic malignant mesothelioma with intrapulmonary growth.
B. Desquamative interstitial pneumonia.
C. Inflammatory sarcomatoid carcinoma.
D. Lymphohistiocytoid mesothelioma of the pleura.
E. Pulmonary adenocarcinoma, intra-alveolar variant.

The correct answer is after the discussion.

DISCUSSION

Biphasic malignant mesothelioma (BMM) is characterised by an admixture of epithelioid and sarcomatoid (spindle cell) components that may be abruptly juxtaposed to each other or blend imperceptibly.[1]

Microscopically, the tumour mass was strikingly biphasic. There was a morphologically uniform proliferation of epithelioid cells with eosinophilic cytoplasm and atypical vesicular nuclei filling pre-existing air spaces (lined by TTF-1-positive epithelium). This epithelioid component transitioned to a very poorly differentiated pleomorphic malignant spindle cell component with areas of necrosis and a chronic inflammatory infiltrate.

The uniform epithelioid component was multifocally positive for pan-keratin, WT-1 and calretinin. Stains for CAM5.2, TTF1, MDM2, SMA, desmin, CD34, CDK4, GATA3, Napsin-A, D2-40 and DOG-1 were negative in both the epithelioid and pleomorphic spindle cell components (figure 1). This second component failed to stain with any of these antigens. The abrupt transition between the components and the complete lack of expression of any mesothelial antigens in the sarcomatoid area lead us to use the term 'dedifferentiated mesothelioma'. In some areas, these epithelioid cells grow into the alveolar spaces with heavy inflammatory infiltration resembling desquamative interstitial pneumonia. A similar presentation was described by Larsen *et al*[2] in five unusual cases of malignant diffuse mesothelioma masquerading interstitial lung disease (ILD). The hallmark of this variant of mesothelioma was diffuse intrapulmonary growth, and absent or rare pleural involvement that clinically simulated ILD. Other differential diagnosis included inflammatory sarcomatoid carcinoma,[3] adenocarcinoma intra-alveolar variant[4] and lymphohistiocytoid mesothelioma.[5]

Diagnosis was even more challenging as the radiological features were consistent with an

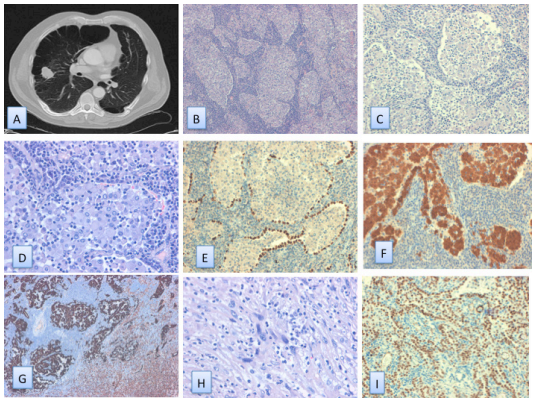

Figure 1 (A) CT scan showing bilateral bullae and a tumour in the right upper lobe. (B) Microscopic appearance showing epithelioid cells filling alveolar spaces and heavy interstitial lymphocytic infiltrate (H&E ×100). (C) Alveolar spaces containing epithelioid cells mixed with lymphocytes (H&E ×200). (D) Atypical epithelioid atypical cells showing round nuclei and large eosinophilic cytoplasms mimicking desquamative pneumonitis (H&E ×400). (E) Epithelioid cells filling pre-existing air spaces lined by TTF-1 positive epithelium (TTF-1 stain ×200). (F) Epithelioid component showing strong, diffuse calretinin staining (calretinin ×200). (G) Cytokeratin showing abrupt transition between the epithelioid component (upper part, positive) and the spindle cell component (lower part, negative) (AE1:AE3×40). (H) spindle cell component showing nuclear pleomorphism (haematoxylin-eosin, ×100). (I) Nuclei of epithelioid component stained with WT-1 (WT-1, ×200).

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intraparenchymatous lung tumour (histologically BMM, with extension of tumour into the underlying pulmonary parenchyma) due to the infolding of the mesothelium.

ANSWER

A. Biphasic malignant mesothelioma with intrapulmonary growth.

Take home messages

- Malignant mesothelioma may appear as an intraparenchymatous lung tumour due to the infolding of the mesothelium.
- The epithelioid component in biphasic malignant mesothelioma (BMM) may exhibit intra-alveolar growth, mimicking desquamative pneumonitis.
- The sarcomatoid component of BMM may be devoid of mesothelial markers but cytokeratins, which eventually may be a source of misinterpretation with sarcomatoid carcinoma, especially in small biopsies.
- Familiarity with the features described above can help to prevent BMM from being misinterpreted as an inflammatory interstitial disease, such as desquamative interstitial pneumonitis, especially on core biopsies, as the presence of interstitial lymphocytic infiltration and an intra-alveolar epithelioid proliferation can be a source of confusion.

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