

Miliary Adenocarcinoma of the Lung with Lepidic Pattern: A Morphological Conundrum

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Clinical Summary

Miliary multi-focal bilateral pulmonary adenocarcinoma with lepidic predominant pattern is an unusual morphological presentation and is seen in females who are non-smokers. This gross morphology can be confused with infectious diseases, like tuberculosis, histoplasmosis or with pulmonary metastasis.

Investigations

A 70-year-old female, non-smoker presented with breathlessness, dry cough and low-grade fever since six months. She had a past history of tuberculosis for which she had been receiving anti-tuberculosis treatment since two months. On examination, she had bilateral crepitations and decreased air entry in the infra-scapular and infra-axillary regions. Chest radiograph revealed bilateral diffuse reticulonodular shadows and bilateral pleural effusion. She died within 24 hours of hospital admission. At autopsy 400cc of haemorrhagic pleural effusion was evident. On gross pathological examination, the lungs showed multiple greyish white tiny nodules of 1-2 mm diameter size scattered diffusely over the entire pleural and parenchymal surfaces resembling miliary tuberculosis (Figure 1). On histopathological examination, the nodules were composed of tumour arranged predominantly along the alveolar lining characteristic of the lepidic pattern (Figure 2). The individual tumour cells were relatively uniform, columnar-shaped with moderate eosinophilic cytoplasm and vesicular nuclei. On further sectioning there were focal areas showing micro-papillary pattern (5%). The tumour cells were seen infiltrating the pleura and there were occasional lympho-vascular emboli. The tumour cells tested positive for thyroid transcription factor (TTF) on immunohistochemistry. The final histopathological diagnosis was infiltrating bilateral pulmonary miliary adenocarcinoma with predominantly lepidic pattern.



Figure 1. Gross specimen photograph showing multiple grayish white tiny nodules scattered diffusely over the entire lung.

Diagnosis

Infiltrating bilateral pulmonary miliary adenocarcinoma with predominantly lepidic pattern.

Discussion

Pulmonary adenocarcinoma on gross morphology has a wide range of presentations. Most commonly these

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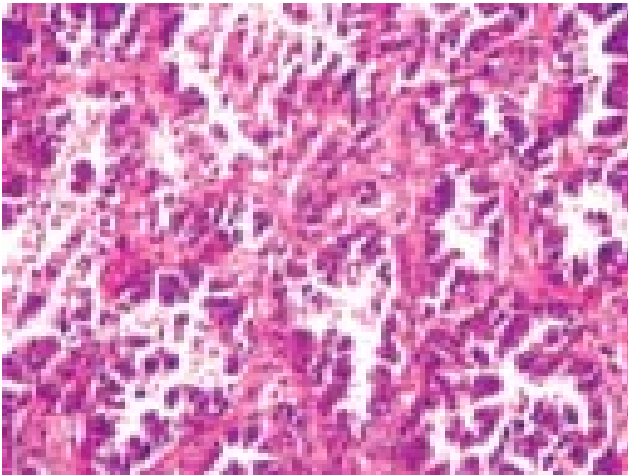


Figure 2. Photomicrograph showing tumour cells lining the alveolar septa suggestive of lepidic pattern (Haematoxylin and Eosin, $\times 400$).

present as peripheral nodules with scarring and puckering. The other patterns include centrally located tumours, diffuse pneumonia like consolidated pattern, diffuse bilateral nodularity of varying sizes, pseudomesotheliomatous pattern and adenocarcinoma with dense scarring and fibrosis.^{1,2} Centrally located tumours are seen more commonly in the Asian population. Primary lung adenocarcinoma may be synchronously or metachronously multifocal.³ Our case showed miliary pattern with most of the nodules measuring 1-2 mm. There are very few case reports where infiltrating bilateral miliary type of gross morphology of adenocarcinoma has been described.⁴ In a recent study,⁵ five non-smoker patients with miliary adenocarcinoma of the lung and their strong association with epidermal growth factor receptor (EGFR) exon 19 deletions was reported. Miliary adenocarcinoma was more common in women and responded well to EGFR tyrosine kinase inhibitors.⁵ In-frame deletion in EGFR exon 19 is more commonly associated with lung adenocarcinoma in never-smoker females.⁶

Radiologically and on gross pathological examination, our case could be confused with many other lung conditions. The differential diagnosis of miliary pattern on chest radiography includes miliary

tuberculosis, other conditions like histoplasmosis, sarcoidosis and metastases.⁶ Microscopically because of the predominantly lepidic pattern metastasis needs to be ruled out.

In our case no primary tumour could be identified in any of the organs. Microscopically, it showed predominantly lepidic pattern (95%) and occasional micropapillary pattern (5%). The glandular pattern usually seen with these patterns in cases of adenocarcinoma lung was absent and there were vascular and pleural metastases. Final diagnosis in our patient was infiltrating bilateral pulmonary miliary adenocarcinoma with predominantly lepidic pattern. Thus, in our case both radiographic and gross appearances were deceptive with the extensive lepidic pattern also leading to difficulties in diagnosis.

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