Micropapillary pattern in lung adenocarcinoma: aspect on $^{18}$F-fluorodeoxyglucose positron emission tomography/computed tomography imaging

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Abstract

We diagnosed a non-small cell lung carcinoma in a 49-year-old female patient with the histopathological diagnosis of stage IIIB mixed bronchioloalveolar and papillary adenocarcinoma with extensive micropapillary feature, which was not visualized on the preoperative multimodality imaging with positron emission tomography (PET) and computed tomography (CT). The micropapillary component characterized by a unique growth pattern with particular morphological features can be observed in all subtypes of lung adenocarcinoma. Micropapillary component is increasingly recognized as a distinct entity associated with higher aggressiveness. Even the most modern multimodality PET/CT imaging technology may fail to adequately visualize this important component with highly relevant prognostic implications. Thus, the pathologist needs to consciously look for a micropapillary component in the surgical specimen or in preoperative biopsies or cytology. This may have potential future treatment implications, as adjuvant or neoadjuvant chemotherapy may be of relevance, even in the early stages of the disease.

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1. Introduction

Adenocarcinomas with a micropapillary component have been receiving increasing attention in the past 10 years in the breast and bladder, and more recently in the ovary, lung and salivary glands [1, 2]. They are characterized by a unique growth pattern and particular morphological features characterized by small papillary tufts lying freely in alveolar spaces or encased within small walls of thin connective tissue [2]. There is rising evidence of higher aggressiveness associated with a micropapillary component, even when only focally present in a primary tumor [1]. The micropapillary variant of lung adenocarcinoma has recently been recognized as a distinct entity [2], which may be observed in association with all subtypes of lung adenocarcinoma: acinar, papillary, solid and bronchioloalveolar. The extent of the micropapillary component can vary greatly from 5 to 10% up to 74%, and is often found in the periphery of the tumor. It is associated with more frequent lymph node and intrapulmonary metastases as well as with pleural invasion [3, 4]. Thus, the presence of a micropapillary component is of prognostic significance and it has been proposed to include this feature in the TNM staging system [3].

2. Case report

This report concerns a 49-year-old never-smoking woman who presented with a refractory cough and recurrent episodes of acute bronchitis. Subsequent workup including computed tomography (CT) scan, positron emission tomography (PET) and bronchoscopy with lavage was consistent with well-differentiated adenocarcinoma of stage IIIA (cT3 cN1 cM0) as well as moderate emphysema. She underwent a right middle and inferior lobectomy. The definitive postoperative diagnosis was pT4[positive pleural fluid] pN0M0, stage IIIB mixed bronchioloalveolar and papillary adenocarcinoma with extensive micropapillary features. To improve accuracy of preoperative staging, she underwent imaging with $^{18}$F-fluorodeoxyglucose (FDG) PET/CT, which has been proved to be superior to CT or PET alone [5].

Fig. 1 shows the correlation between the PET/CT and the macroscopic and microscopic surgical specimen. While the classical papillary adenocarcinoma (Fig. 1g) was visible on CT and clearly showed increased FDG activity on PET
transition between the aerogenous spread of the micropapillary component into the adjacent lung parenchyma did not show any significant FDG uptake on PET or any abnormality on CT. Note the abrupt transition between the aerogenous spread of the micropapillary component and the other part of the tumor.\(^{(f)}\)

(standardized uptake value = 12.3 g/ml), extensive aerogenous spread of the micropapillary component into the adjacent lung parenchyma did not show any significant FDG uptake on PET (Fig. 1e). The presence of an increased FDG uptake in a right hilar lymph node on PET imaging (cH1) corresponded on the microscopic examination to a lymph node with important anthracosis with histiocytosis and no metastasis (pN0), which is a known pitfall of nodal staging [6, 7]. Adjuvant chemotherapy was recommended, but refused by the patient. Fifteen months after the initial diagnosis the patient appears to be free of disease and well. However, she did not want to undergo any repeat imaging and is receiving alternative herbal therapy.

3. Discussion

Recognizing the micropapillary features has a number of highly relevant clinical implications. Firstly, the pathologist needs to be consciously looking for a micropapillary pattern in the surgical specimen, in particular in the periphery of the tumor, or in preoperative biopsies or cytology [3, 8], and its presence or absence should be clearly mentioned on the surgical pathology report. Secondly, the outcome of patients with early stage non-small cell lung cancer appears inferior for adenocarcinomas with a micropapillary component, thus adjuvant or neoadjuvant chemotherapy may be worth considering even in very early stage disease. Recently, Nagano et al. showed that among a series of 156 patients with stage I adenocarcinoma, the 5-year survival was significantly lower when the micropapillary pattern was present (76% vs. 96% for micropapillary pattern – negative cases) [9]. Lastly, modern clinical staging with anatomic-functional FDG PET/CT imaging [5] may fail to adequately visualize such micropapillary involvement and extension [10]. This may lead to an underestimation of potentially important prognostic factor.

4. Conclusion

Even the most modern multimodality PET/CT imaging technology may fail to adequately visualize this important component with highly relevant prognostic implications – as illustrated in our case report. Thus, the pathologist needs to consciously look for a micropapillary component in the surgical specimen or in preoperative biopsies or cytology and note its presence or absence in his report. This may potentially have future treatment implications, as adjuvant or neoadjuvant chemotherapy may be of relevance, even in the early stages of the disease.

References