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Case report

Primary lung invasive adenocarcinoma misdiagnosed as infectious pneumonia in ^{18}F -FDG PET/CT: A case report [☆]

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ABSTRACT

A 64-year-old woman presented to our hospital with cough and a large amount of white foam sputum. F-fluorodeoxyglucose positron emission tomography/computed tomography (F-FDG PET/CT) showed diffuse ground-glass opacities in both lungs, which was considered as infectious pneumonia. However, after ineffective anti-infection, the primary invasive mucinous adenocarcinoma was finally diagnosed. Pulmonary invasive mucinous adenocarcinoma is rare and special subtype of lung adenocarcinoma, it has a variety of imaging manifestations. When intense tracer uptake, air bronchial sign, honeycomb sign present in diffuse ground-glass opacities in F-FDG PET/CT, lung invasive mucinous adenocarcinoma should be highly suspected.

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Introduction

With the COVID-19 epidemic, people have a deeper understanding of Ground-glass opacities (GGOs). GGOs is a common lung abnormal image that can be seen in a variety of diseases such as interstitial lung disease, infection, diffuse alveolar hemorrhage and alveolar proteinosis, and the most common is infectious pneumonia, especially viral pneumonia [1–4]. Primary pulmonary invasive mucinous adenocarcinoma (IMAs) is a rare and special subtype of pulmonary invasive adenocarcinoma. It has a variety of imaging manifestations, which can be nodules, consolidation or GGOs [5–7]. Here we report a case

of diffuse GGOs in both lungs that is misdiagnosed as infectious pneumonia in ^{18}F -fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F -FDG PET/CT), and finally IMAS is histologically confirmed.

Case report

A 64-year-old woman developed cough and sputum 3 months ago before admission. The amount of sputum was large, white and foamy, about 800ml/d, accompanied by chest tightness,

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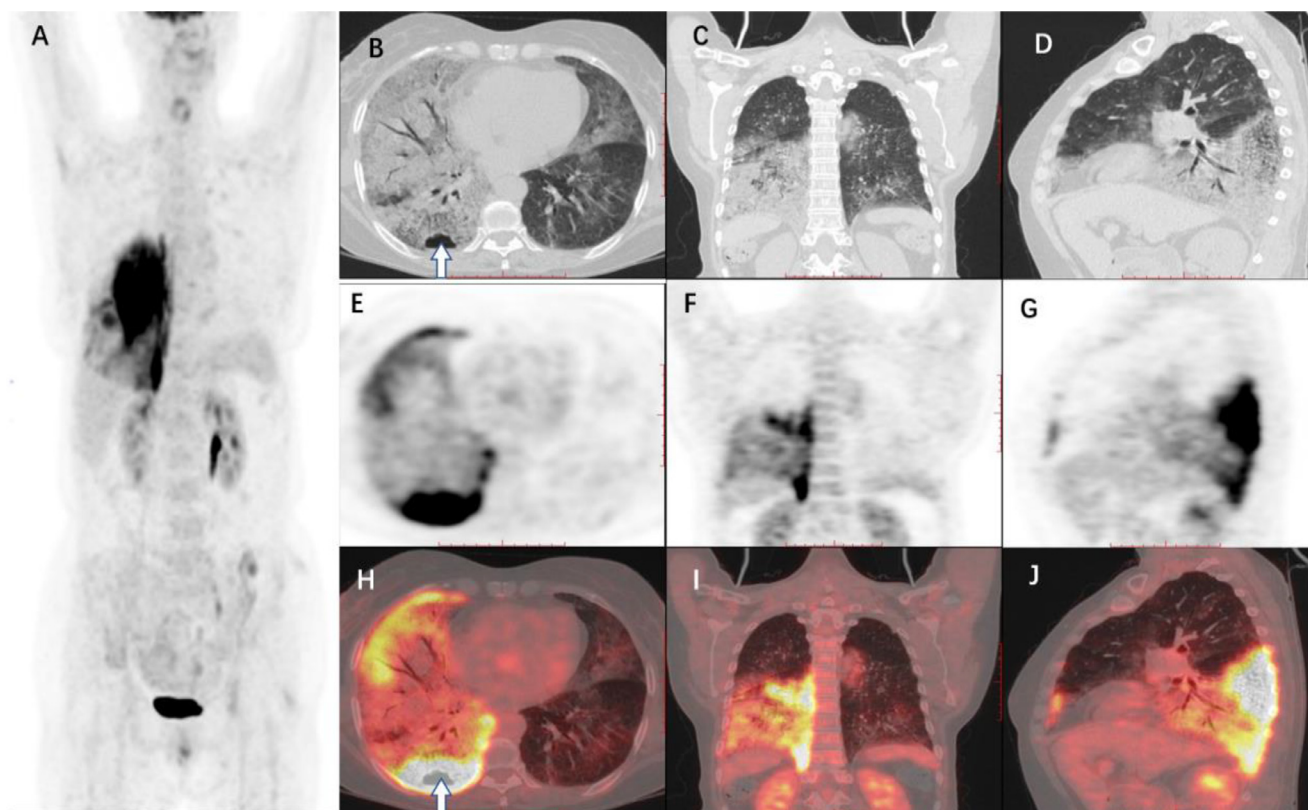


Fig. 1 – The MIP (A), transverse CT (B–D), corresponding PET (E–G), and fused (H–J) images revealed GGOs was diffusely distributed in whole lungs, especially in the middle and lower lobes of the right lung. The aerated bronchus shadow could be seen inside the GGOs, and FDG uptake increased in different degrees (SUVmax range 6.4–24.3). The trachea and bronchus were unobstructed and normal shape. In addition, an air-filled cavity (arrow) could be seen in the lower lobe of the right lung, and the surrounding lung tissue showed honeycomb changes.

shortness of breath and chest pain. Physical examination: body temperature 38.2°C, heart rate 92 beats/min, breathing 18 times/min, blood pressure 107/76 mm Hg, barrel chest, wet rales can be heard under both lungs. Laboratory examination: total number of white blood cells was $12.7 \times 10^9/L$ (the normal reference range of our hospital was $4.0\text{--}10.0 \times 10^9/L$, the same below), the ratio of neutrophils was 0.79 (0.50–0.70), and the number of red blood cells was $6.28 \times 10^{12}/L$ ($3.50\text{--}5.00 \times 10^{12}/L$), hemoglobin was 196g/L (110–150 g/L); procalcitonin was 0.074 ng/ml (0.000–0.046 ng/ml); C-reactive protein and erythrocyte sedimentation rate were normal; tumor and tuberculosis indicators were negative. No obvious abnormal cells were seen in the sputum smear. SARS-Cov-2 nucleic acid test was negative. Chest computed tomography (CT) showed diffuse ground glass shadows in both lungs. Based on the patient's symptoms and related examinations, infectious pneumonia should be considered, then regular anti-infection, expectorant and improving circulation were given.

After a period of treatments, the blood test showed that the total number of white blood cells and the ratio of neutrophils had dropped to normal, but the patient's symptoms did not significantly alleviate, and chest CT showed no significant changes in diffuse lung lesions. Then ^{18}F -FDG PET/CT was performed to identify the nature of lung lesions (Fig. 1).

From the image, we can observe that the GGOs were diffusely distributed in both lungs, especially in the middle and lower lobes of the right lung, and the FDG uptake value increased to varying degrees (standard uptake value, SUVmax range 6.4~24.3). The air bronchogram was seen in the ground-glass density shadows, and the lumen was unobstructed, with walked slightly stiff. In addition, an air-filled cavity (indicated by the arrow) was seen in the lower lobe of the right lung, the surrounding lung tissue showed honeycomb changes. and the FDG uptake value was the highest, with the SUVmax was 24.3. There were no obvious enlarged lymph nodes in the hilum and mediastinum. Combining the patient's medical history and PET/CT findings, we recommended a needle biopsy avoiding the cavity in the right lower lobe to rule out the presence of malignant tumors. Subsequently, the patient underwent a bronchoscopy. A large number of serous secretions in the bilateral lumens were seen, centered on the right lower lobe. After repeated washings, no obstruction or new tissue were seen in the lumen of each bronchus. Bronchoscopy lung biopsies was performed at the outer basal segment, posterior basal segment, dorsal segment of the right lower lobe and the dorsal segment of the left lower lobe. Combined with pathology, the primary invasive mucinous adenocarcinoma of the lung was further diagnosed (Fig. 2).

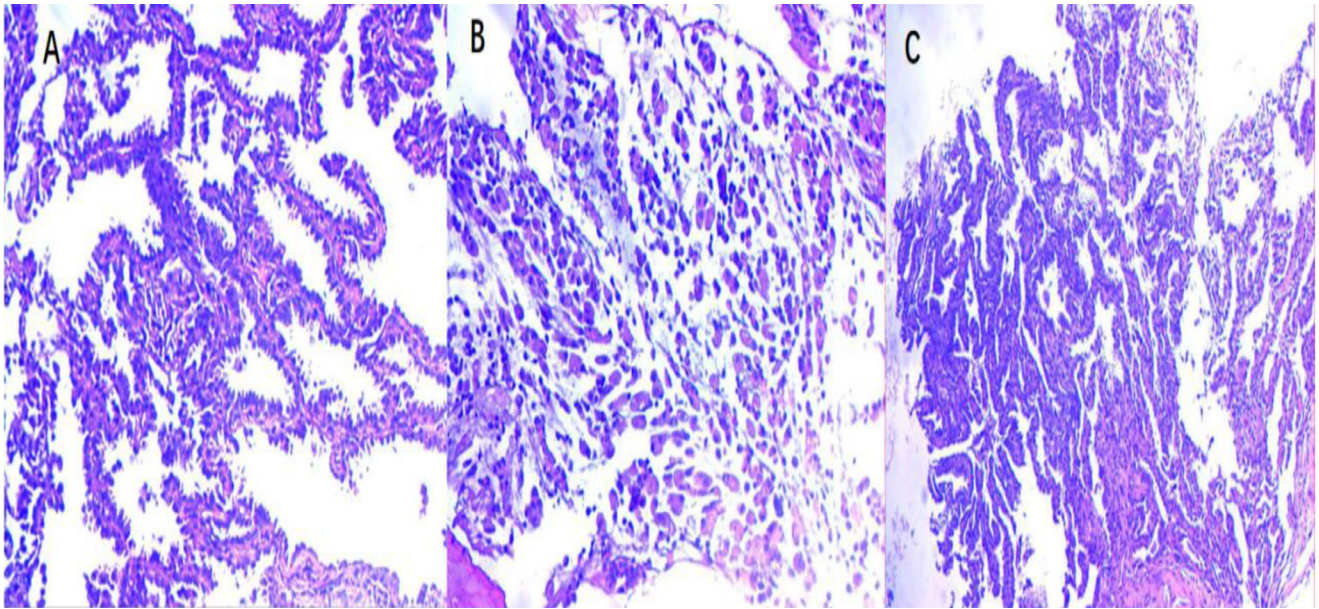


Fig. 2 – Microscopic examination (A–C, hematoxylin-eosin stain; original magnification, $\times 200$) showed the cancer cells were papillary and not typical adenoid arrangement, with nuclei slightly enlarged, hyperchromatic and abnormality. Immunohistochemistry showed CK7 (+), TTF-1 (+), NapsinA (+), CK5/6 (+), P63 (-), P40 (-), Syn (-), ALK (D5F3) (-), Ki-67 positive cell number <10%.

Discussion

The 2015 version of the new WHO lung tumor histological classification divides lung adenocarcinoma into pre-invasive lesions, micro-invasive adenocarcinoma and invasive adenocarcinoma [8], among which IMAs are a rare and special subtype of invasive adenocarcinoma, accounting for approximately 2%-10% of lung adenocarcinoma [5]. It usually occurs around the lungs and grows along the alveolar walls. The pulmonary interstitium, pleura and blood vessels of the lung are generally unaffected. Tumor cells in IMAs are highly discrete, poor adhesion, easily spread widely through alveolar pores and small airways, which is an important reason for its diffuse distribution [9,10]. Middle-aged and elderly people are susceptible to this disease, and the incidence rate is higher in women than in men. The general clinical symptoms lack specificity. Coughing a large amount of white foamy sputum is considered to be one of its characteristics, but it is generally rare [11]. In addition to cough and sputum, this patient also had mild fever and the white blood cells elevated. It may be caused by the secretion of a large amount of mucus that was not easy to cough up and caused obstructive pneumonia. This is also an important reason why this case was misdiagnosed as infectious pneumonia.

IMAs has a variety of imaging manifestations, which can be nodules, consolidation or GGOs. IMAs with consolidation or GGOs is sometimes difficult to distinguish from infectious pneumonia. Therefore, in recent years, this type of lung cancer is often named pneumonic-type lung carcinoma. High resolution chest CT is still the main examination method for diagnosing pneumonia-type IMAs, but the first diagnosis is

easy to be misdiagnosed as infectious pneumonia, interstitial lung disease, diffuse alveolar hemorrhage and other benign lung lesions. The possibility of pneumonia-type IMAs should be highly suspected when the following signs appear on chest CT [6,7]: (1) honeycomb transparent area in the lesion (vacuole sign); (2) air bronchogram sign; (3) interlobar fissure bulging fissure sign; (4) angiogram sign. Magnetic resonance imaging (MRI) is rarely used in the diagnosis of lung diseases, but Gaeta M et al. found that MRI water-sensitive sequences is of great significance in distinguishing pneumonia-type mucinous adenocarcinoma from infectious pneumonia [12]. The appearance of white lung sign in MRI water-sensitive sequences highly suggests the possibility of pneumonia-type mucinous adenocarcinoma. As an important and accurate non-invasive imaging method, FDG PET/CT can reflect the anatomical and metabolic information of the lesion at the same time, and has important value for tumor diagnosis, staging, prognosis and curative effect evaluation. Zheng N et al. found that FDG PET/CT early imaging is of limited value in the diagnosis of IMAs, and dual-phase or delayed imaging can significantly improve the accuracy of diagnosis [13]. In addition, studies have found that the pathological infiltration area of IMAs is closely related to SUVmax, and the SUVmax of tumors with an infiltration area of ≤ 5 mm is significantly lower than those with an infiltration area of > 5 mm [14,15]. The case we reported is a diffuse invasive mucinous adenocarcinoma, involving both lungs, and the highest SUVmax value reached 24.3, which is consistent with the results of previous studies. Another important role of FDG PET/CT is to guide biopsy. In this case, the SUVmax of diffuse ground glass density shadow in both lungs was significantly higher than the SUVmax of infectious pneumonia we have encountered in the past. In or-

der to rule out the existence of malignant tumors, we recommended a needle biopsy at the highest FDG uptake in the right lower lobe because the most active area of FDG uptake is often marked as the most meaningful biopsy. In the end, the clinician adopted our suggestion and performed bronchoscopy lung biopsy in multiple lower lobes of both lungs. The pathological diagnosis was IMAs.

The existing literature is controversial about the prognosis of IMAs. Some studies believe that the prognosis of IMAs is relatively poor compared with other types of lung adenocarcinoma [16]. Boland JM et al. proved that there is no difference in the rate of recurrence-free survival between IMAs and non-mucinous adenocarcinoma [17]. For mass adenocarcinoma, surgical treatment is the best choice. But for diffuse invasive mucinous adenocarcinoma, which cannot be surgically removed, timely diagnosis, early chemotherapy is a better treatment option. The patient in this case gave up treatment after diagnosis, so the treatment and prognosis cannot be followed up.

Conclusion

The clinical symptoms of IMAs lack specificity, and one of the characteristics is coughing a lot of white foamy sputum. Imaging findings are often difficult to distinguish IMAs from infectious pneumonia. When we find the honeycomb sign, the air bronchogram sign etc. in imaging, IMAs is highly suspected. Anti-inflammatory treatments are generally ineffective. Pathological biopsy or cytologic examination is the gold standard for diagnosing the disease.

Patient consent

The patient has provided consent to the submission of the case report to the journal, and has passed the human ethics review.

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