中文題目：一名腎移植患者於肺部影像發現單一肺結節

英文題目：Solitary pulmonary nodule in a Renal Transplant Recipient

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Introduction: The definition of solitary pulmonary nodule (SPN) is an isolated radiographic opacity with size less than 3 cm and surrounded by lung parenchyma. The differential diagnosis of a SPN is broad and can be divided into benign etiology and malignancy. Common benign etiologies include nonspecific granuloma, infectious granulomas, hamartomas and miscellaneous benign lesions. Infectious granulomas may be caused by tuberculosis, coccidioidomycosis, histoplasmosis, cryptococcosis and aspergillosis (1). Common malignant causes include primary lung cancer, carcinoid tumors, and lung metastases. Diagnostic tools include sputum analysis, biochemistry, bronchoalveolar lavage fluid analysis, chest computed tomography (CT), positron emission tomography, and image-guide biopsy or diagnostic wedge resection (2). Herein, we report a kidney transplant recipient presented with fever with solitary pulmonary nodule. A diagnosis of pulmonary mucormycosis was established.

Case Presentation: A 42-year-old man from Taiwan presented with fever and chillness for three days. He had undergone kidney transplantation 2 years previously, with a history of acute pyelonephritis of the transplanted kidney and acute T cell mediated rejection, grade IIA, for which he had been receiving treatment with mycophenolate mofetil, tacrolimus and prednisolone. He also complained urinary burning sensation, but denied cough, dyspnea, chest tightness or abdominal pain.

On examination, the temperature was 38.3 °C, the blood pressure 175/79 mmHg, and the pulse 78 beats per minute. The body-mass index (the weight in kilograms divided by the square of the height in meters) was 33.7. His breath sounds were clear to auscultation bilaterally, and no cardiac murmurs were heard. Swelling scrotum of left side was noted. Laboratory studies showed white blood cell counts of 3500 /uL, hemoglobin of 5.5 g/dL, platelet count of 165000/uL, serum blood urea nitrogen of 70 mg/dL, serum creatinine of 4.71 mg/dL, serum sodium of 128 mEq/L and C-reactive protein of 61.5 mg/L. Chest radiography revealed an ill-defined nodular density over right lower lung (RLL) (Figure 1A). With the tentative diagnosis of left epididymo-orchitis, empirical antibiotic of levofloxacin 750mg qd was administrated. Blood culture yielded no microorganism after 7 days of incubation. Subsequent CT of chest revealed one 1.6cm solid nodule over RLL abutting the right major fissure [Figure 1B]. Pulmonologist and thoracic surgeon were consulted regarding diagnosed therapeutic options of SPN. Bronchoscopy examination was performed and disclosed not much secretion and no endobronchial lesion via endobronchial ultrasonography. No specific pathogen was

identified by microscopic examination and culture of bronchoalveolar lavage fluid. Therefore, thoracoscopic wedge resection of right lower lung for tissue proof was carried out. Histopathologic diagnosis was necrosis with acute and chronic inflammation. Broad and wide branching fungal hyphae was identified by periodic-acid Schiff stain, suspicious for mucormycosis [Figure 1C]. Mold isolates recovered from lung tissue were sent for identification by morphological characteristics and sequence analysis of the internal transcribed spacer (ITS) region. Mucorales (*Cunninghamella bertholletiae*) was confirmed (Figure 1D). Liposomal amphotericin B was then administrated for five weeks and shifted to oral posaconazole for three months. Antifungal susceptibility testing was performed later according to Clinical and Laboratory Standards Institute M38-A3 broth dilution. The minimum inhibitory concentration (MIC) of amphotericin B against the *C. bertholletiae* strain was 2 μg/mL, posaconazole 1 μg/mL and isavuconazole >16 μg/mL. Finally, the patient was discharged home and then got recovery.

Discussion: Invasive mold infections are comparatively frequent complications of immunosuppression in haemato-oncological patients, and, albeit to a lesser extent, in solid organ transplant (SOT) recipients. *Aspergillus* spp. are the main aetiological agents, followed by Mucorales. Infection rates by Mucorales have been reported to be as high as 3% in SOT patients (3). Patients with early graft rejection or graft dysfunction, or active or latent infection in the donor or recipient at the time of transplantation, are at particularly high risk to develop opportunistic infections. Corticosteroids and other immunosuppressive agents used in SOT not only reduce the risk of organ rejection, but also increase the susceptibility of transplanted patients to infections by several opportunistic and obligate pathogens. Mortality rates are high for all invasive mold infections that develop in SOT recipients(3).

Pulmonary mucormycosis occurs after inhalation of sporangiospores into the bronchioles and alveoli (4). The most common symptoms are persistent fever, cough, chest pain, dyspnea and hemoptysis (5). Radiological manifestations of pulmonary mucormycosis include multiple nodules (≥10), pleural effusion, consolidation, cavitation and reverse halo sign, a ground-glass pulmonary opacity surrounded by a ring of denser consolidation, on CT(6, 7). A single pulmonary nodule was a rare presentation. A global guideline recommends an early complete surgical treatment for mucormycosis in addition to systemic antifungal treatment. If lung resection is performed, patients may benefit from emergency surgery to prevent bleeding as well as from elective surgery, which has been shown to increase survival (4). In this report, the clinician early arranged aggressive diagnosis procedure for SPN for the immunocompromised patient, obtained the diagnosis opportunely, and early initiated appropriate antifungal agents, all of that facilitate better outcome of the patient.

In a global review of reported cases of mucormycosis, *Rhizopus* spp. (47%) were the most frequently reported causes of culture-confirmed mucormycosis, followed by *Mucor* spp. (18%), *C.*

bertholletiae (7%), *Apophysomyces elegans* (5%), *Lichtheimia (Absidia)* spp. (5%), *Saksenaea* spp. (5%), and *Rhizomucor pusillus* (4%), with a variety of other uncommon species representing the remaining 8% of culture-confirmed cases (8). The species of the order Mucorales causing pulmonary mucormycosis in the present case was *C. bertholletiae* which was identified by initial morphological characteristics and confirmed by further ITS sequencing from the sterile specimen. Jeong W. et al reported *Cunninghamella* spp. were isolated primarily in patients with pulmonary or disseminated disease and associated with significantly higher mortality than other Mucorales (9). Amphotericin B is considered the most active drug against Mucorales and is active in vitro against most species within this order except *Cunninghamella* spp (4). Posaconazole may be considered to treat mucormycosis caused by *C. bertholletiae.*

Conclusions: Immunocompromised host have an increased susceptibility to miscellaneous infections and clinical manifestations may be non-specific. Once SPN is found in immunocompromise host, it is necessary to obtain diagnosis aggressively to avoid delayed treatment.

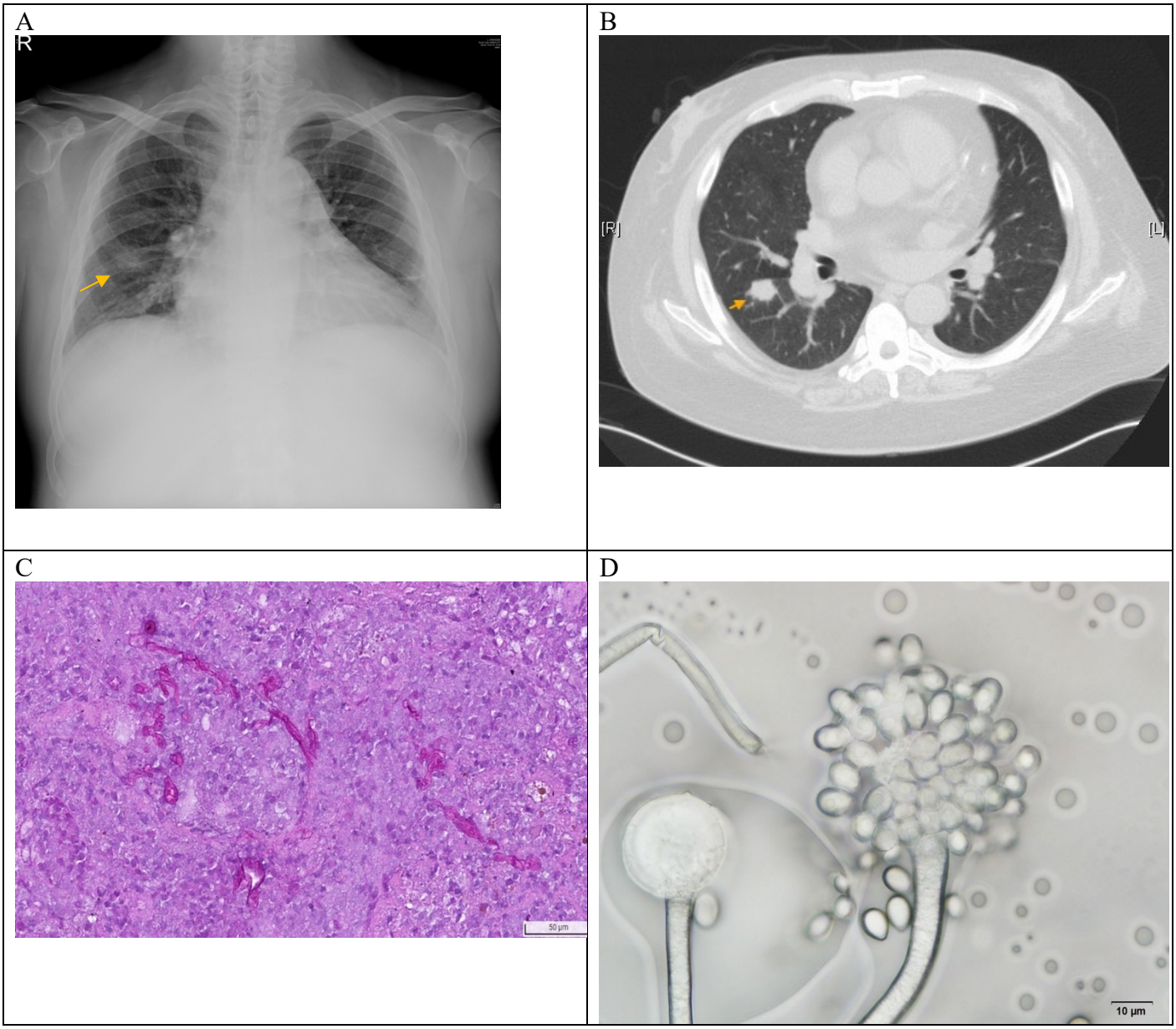

Figure 1. (A) Chest radiography: an ill-defined nodular density over right lower lung (RLL) (B) Chest computer tomography: one 1.6cm solid nodule over RLL abutting the right major fissure. (C) Histopathological examination showing broad and wide branching fungal hyphae by periodic-acid Schiff stain, 400X. (D) Microscopic morphology of *Cunninghamella bertholletiae* showing simple sporangiophores forming a swollen, terminal vesicle around which single-celled, globose to ovoid sporangiola develop on swollen denticles

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