Pulmonary cryptococcosis due to a capsule-deficient strain confused with metastatic lung cancer

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Abstract

A patient with hepatocellular cancer developed pulmonary cryptococcosis due to infection with a capsule-deficient Cryptococcus neoformans. Pulmonary lesions initially diagnosed as metastatic cancer by chest x-ray film and CT scan were subsequently found to be fungal granulomas by autopsy. Although morphologic studies of the fungi were insufficient to render a specific mycologic diagnosis because of the absence of encapsulated yeasts, fluorescent antibody studies confirmed the diagnosis of cryptococcosis. The use of various stains and electron microscopy for the pathological differential diagnosis of cryptococcosis caused by capsule-deficient yeasts is discussed.

Key words: capsule-deficient, Cryptococcus neoformans, immunofluorescence study, lung, metastatic cancer

Introduction

Cryptococcosis is a chronic, subacute, or acute pulmonary, systemic, or meningitic infection caused by the encapsulated yeast Cryptococcus neoformans (C. neoformans). Evidence that other species cause this infection is not convincing [1]. The radiographic findings of pulmonary cryptococcosis manifest infiltrates, nodules or mass like lesions. The most common roentgenographic picture resembles tumor: single or multiple circumscribed masses or nodules [2]. The present report describes a case of pulmonary infection caused by capsule-deficient C. neoformans that was radiographically confused with metastatic lung cancer. Since reports of cryptococcal infection due to poorly encapsulated or capsule-deficient C. neoformans have been increasing [3], the differential pathological diagnosis of such disease is discussed.

Case history

A 58-year-old Japanese woman with liver cirrhosis was followed for five years. Magnetic resonance imaging demonstrated multiple tumors of the liver, and liver cancer was diagnosed. She was admitted to Kinki University hospital to receive transcatheter arterial embolization therapy to the biggest cancer nodule. At admission, pancytopenia due to liver cirrhosis was evident. Leukocyte count was 2600 per microliter with 55% segmented neutrophils, 35% lymphocytes and 8% monocytes. An admission x-ray film of the chest disclosed multiple small nodular infiltrates of the left lung. CT scan exhibited these lesions in segmentum apicodorsale, superius, ventrobasale and dorsobasale. The nodules were round to oval shaped ranging in size from 5 to 10 mm in diameter. The patient sometimes presented low-grade fever lower than 38 °C which was believed to be related to liver cancer. It is regrettable that sputum was not cultured because of no suspicion of pulmonary infection. Neither chronic cough, chest pain nor bloody sputum was presented. She did not have any significant contact with pigeons. Based on the data
available, the nodules were diagnosed as pulmonary metastasis of the liver cancer. Since no effective treatment for the metastatic lung cancer is available, she was discharged on the 45th hospital day.

She was followed up twice a month at an outpatient clinic without chemotherapy. Leukocyte count was between 1400 and 3000 per microliter. She gradually started to suffer from ascites. Seven months after the discharge, she was admitted to the hospital again because of the liver dysfunction. At this time, an admission chest radiograph revealed similar nodular shadows which looked somewhat smaller than that on the previous film. Her general condition deteriorated and she died of hepatic coma on the 25th hospital day. Clinically, no evidence of pneumonia or other infection was evident.

Autopsy findings

Cancer was detected only in the liver without any metastasis to extrahepatic organs. In the subpleura of the left lung, five round to stellate-shaped granuloma-like nodules, 2 to 8 mm in diameter, grayish white to orange in color, were noted. Culture of these lesions was not available because lungs were cut several days after the autopsy. Sections stained with hematoxylin and eosin revealed that the nodules were granulomas composed of epithelioid histiocytes and multinucleated giant cells (Figure 1a). No caseous necrosis was evident. A few lymphocytes infiltrated in the granulomas but no polymorphonuclear leukocytes were disclosed. Numerous faintly stained or almost translucent yeast forms were present within and outside the histiocytes and giant cells. These organisms were readily demonstrated with Grocott’s silver stain (Figure 1b) and the Fontana-Masson stain. They were spherical or crescent, 2.5 to 5 μm in size, without distinct capsules. Buds were characteristically attached to parent cells by narrow necks. Granular black material with Grocott’s silver stain was found within the cytoplasm of