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Case Report

Cryptococcemia in an Elderly Woman with Retroperitoneal Diffuse Large B-cell Lymphoma after Rituximab-containing Chemotherapy☆

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SUMMARY

Cryptococcemia is a bloodstream fungal infection caused by encapsulated yeasts of *Cryptococcus neoformans*. We reported an 88-year-old woman in whom *C. neoformans* colonies of smooth and mucoid phenotypes were sequentially cultured from the blood during treatment of retroperitoneal diffuse large B-cell lymphoma using rituximab-containing chemotherapy. The most likely cause was disease progression of pulmonary cryptococcoma. She was successfully treated with optimal antifungal therapy.

1. Introduction

Cryptococcus neoformans is the most common encapsulated yeast that causes opportunistic cryptococcosis in immunocompromised patients. The molecular type of *C. neoformans* can be subdivided into VNI, VNII, VNB (*C. neoformans* var. *grubii*), VNIV (*C. neoformans* var. *neoformans*), and VNIII (a hybrid form of 2 varieties). The subtype VNI is the leading cause of cryptococcosis worldwide, including Taiwan[1]. The morphology of *Cryptococcus* colonies can be depicted as smooth (SM) or mucoid (MC)[2]. Fries et al[2] described the morphology change between SM and MC as phenotypic switching. It is a reversible process, in which colony morphology changes to another variant at a higher frequency than would be expected from random somatic mutation.

Rituximab-containing cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisolone (CHOP) chemotherapy is one of the regimens indicated for diffuse large B-cell lymphoma. Rituximab is a monoclonal antibody for CD20-positive B lymphocyte. However, opportunistic infections have been reported due to the immunosuppressive effect of rituximab[3,4].

2. Case Report

An 88-year-old woman had a history of right breast cancer, Stage IIA postmastectomy, and lymph node dissection in April 2010. Since then she has received oral tamoxifen adjuvant therapy until December 2012. In December 2012, she presented with right flank and abdominal pain with weight loss of <10% of body weight (5 kg) within 3 months. A large soft tissue lesion (9.3 cm × 5.4 cm × 9.3 cm) in the retroperitoneal aortocaval and para-aortic region was found by abdominal computed tomography scan. Biopsy of the retroperitoneal mass revealed CD20-positive diffuse large B-cell lymphoma. In addition, one 2-mm peripheral nodule at the right upper lung and another 3-mm nodule at the left upper lung without definite characteristics on chest computed tomography scan (Figure 1A) were found during staging workup. Bone marrow needle biopsy showed no bone marrow involvement. Thus, her diffuse large B-cell lymphoma was classified as Stage IIA disease. Her Eastern Cooperative Oncology Group performance score was 2. The level of lactate dehydrogenase was 261 IU/L. The International Prognostic

☆ Conflicts of interest: All contributing authors declare that they have no conflicts of interest.

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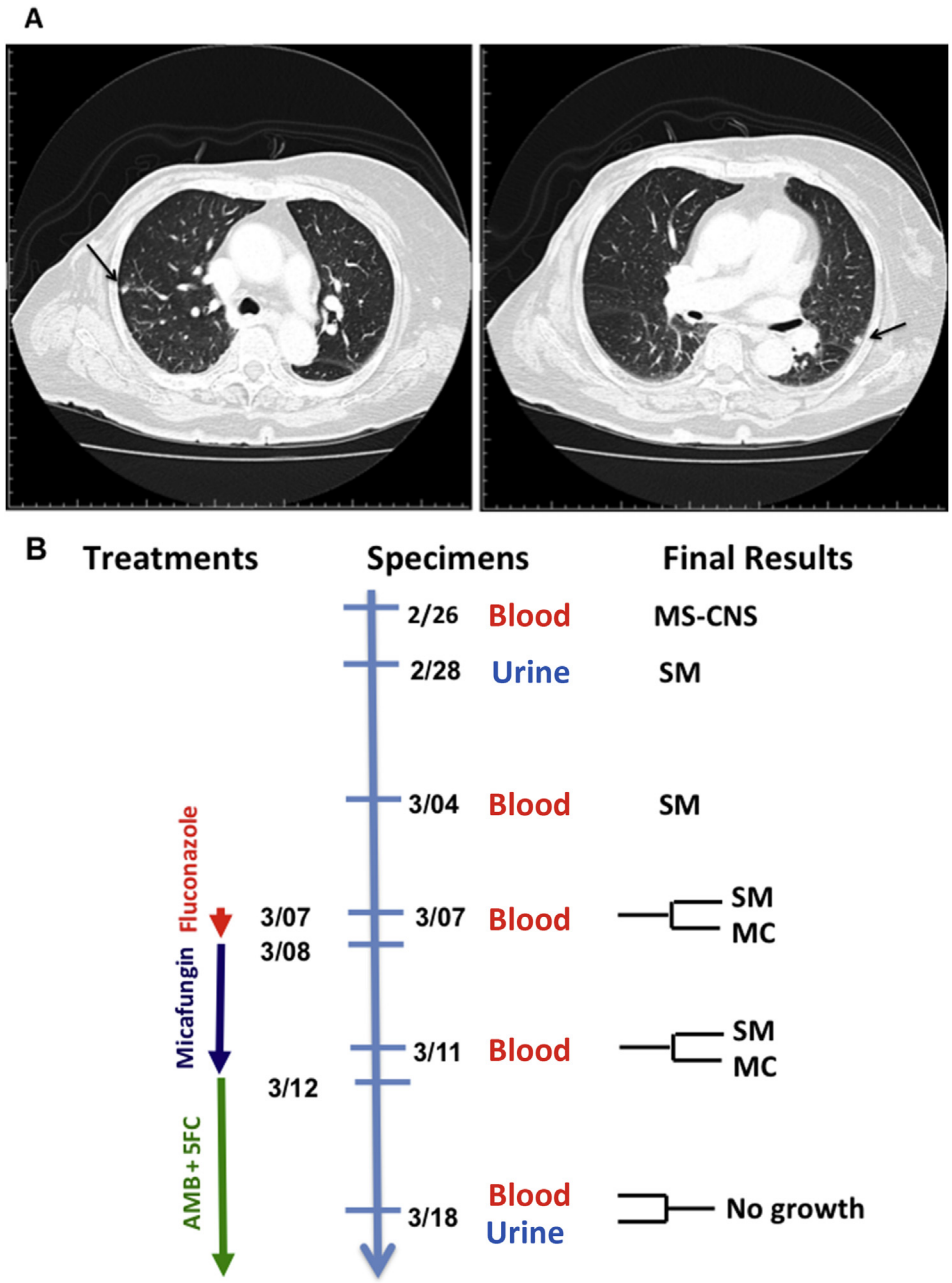

Figure 1. (A) Chest computer tomography revealed two peripheral nodules (black arrows). (B) Summary of morphology change and antifungal treatment. AMB + 5FC = amphotericin B plus flucytosine; MC = mucoid; MS-CNS = methicillin-susceptible coagulase-negative *Staphylococcus*; SM = smooth.

Index score was 3, which placed her in the high–intermediate risk group. She was first treated with a prephase therapy containing dexamethasone plus vincristine in January 2013. One week later, she was treated with rituximab, cyclophosphamide, vincristine, and prednisolone combination chemotherapy. The dose of rituximab was 375 mg/m^2 during treatment. Three weeks later, she received a second course of treatment with rituximab and prednisolone to minimize side effects.

On the third admission for chemotherapy, rituximab, vincristine, and prednisolone combination therapy was given on February 19, 2013 (Day 0). Fever developed 8 days later, and she received empirical antibiotics after obtaining urinalysis and blood culture (BACTEC FX culture system; Becton Dickinson, Inc., Sparks, MD, USA). Laboratory data (Day 8) showed that white blood cells count was 1600/μL with 4% band, 64% neutrophil, and 26% lymphocyte. She had a C-reactive protein level of 5.18 mg/dL, procalcitonin level of 0.063 ng/mL, and creatinine level of 0.8 mg/dL. Granulocyte colony-stimulating factor was administered due to neutropenia. Blood culture yielded methicillin-susceptible coagulase-negative *Staphylococcus*; fever subsided gradually after adequate antibiotic use. However, her urine culture yielded yeast (Figure 1B). On March 4, 2013 (Day 13), we repeated blood cultures due to neutropenic fever. Three days later (Day 16), the preliminary report from blood culture revealed yeast. Initially, a 400-mg dose of intravenous fluconazole was administered empirically; the antifungal regimen was then pre-emptively switched to micafungin 100 mg once daily on the next day (Day 17) to cover clinically suspected azole-resistant *Candida*.