中文題目：退行性大細胞淋巴癌罕見以開洞性肺部腫瘤合併高血鈣表現

英文題目：A Rare Presentation of Anaplastic Large Cell Lymphoma as a Cavitary Pulmonary Mass with Hypercalcemia

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Introduction

Cavitary pulmonary mass with hypercalcemia is a common manifestation of squamous cell carcinoma. However, it occurred in an anaplastic large cell lymphoma (ACLC), which is not so common and has a similar pathologic morphology to carcinoma. Although the prognosis of ALK negative ACLC is inferior to those with ALK positive, the 5-year survival rate could be near 50%.[1] It is worthy for our attention. Here we presented a case with cavitary pulmonary mass and hypercalcemia and was diagnosed as ACLC then.

Case presentation

This 48-year-old male smoker with a history of hypertension and alcohol consumption presented with intermittent fever up to 39℃ for two weeks, accompanied with severe back pain, weight loss 20 kilogram in six months, and coughing with purulent blood-tinged sputum. He admitted to a local hospital, where chest radiography showed a well-defined mass with cavity over right lower lung field, multiple scattered pulmonary nodules, and osteolytic lesions in right clavicle. Computed tomography (CT) revealed a well-defined thick wall cavitary mass with irregular inner border, several pulmonary nodules, and multiple osteolytic lesions. Because of persistent fever after 5-day duration of ampicillin-sulbactam and fluconazole, and 4-day duration of ceftazidime and sulfamethoxazole-trimethoprim then, declined consciousness, no clear diagnosis after CT-guided biopsy, and 2-week hospitalization, he was transferred to our hospital.

The physical examination showed disoriented consciousness, body temperature of 39.4℃, blood pressure of 136/97 mm Hg, pulse rate of 133 beats per minute, respiratory rate of 18 breaths per minute, and oxygen saturation level of 100% while breathing under nasal cannula 3 liter per minute. Chest auscultation disclosed bilateral rales. Laboratory data demonstrated an elevated leukocyte counts of 28,100 per mL with a differential of 92% neutrophils, 2.7% lymphocytes, and 4.1% monocytes; a raised C reactive protein up to 17.6 mg/dL; a declined hemoglobin of 8.5 g/dL; platelets of 274,000 per mL. We also noted elevations of serum blood urea nitrogen (32 mg/dl), creatinine (1.62 mg/dL), corrected serum calcium level (13.5 mg/dL); and lactate dehydrogenase (346 IU/L). Infectious disease or metastatic malignancy was

suspected. Ceftaroline and voriconazole were prescribed to cover possible pathogens. Hydration and zoledronic acid were administered for the hypercalcemia. The assays of gram stain and acid-fast stain of sputum, serum *Mycoplasma pneumoniae* IgM, serum and sputum *Aspergillus* galactomannan test yielded negative results. The inflammatory scan for the fever source evaluation showed abnormally intense gallium uptake in the right lung region and multiple sites of skeleton. Endobronchial ultrasound guided biopsy was done for the pulmonary mass and rapid on-site evaluation showed carcinoma-like tumor cell. But final pathologic report demonstrated a picture of anaplastic large cell lymphoma, which consisted of isolated large, atypical lymphocytes with abundant cytoplasm. The immunohistochemical staining revealed positive for common leucocyte antigen and CD30, and negative for CD3, CD20, CD79a TTF-1, p40, p53, CK (AE1/AE3), EBER, Alk, and CD15.

However, pulseless ventricular tachycardia occurred suddenly at ward, and he had return of spontaneous circulation after cardiopulmonary resuscitation and defibrillation for 8 minutes. Although targeted temperature management and anti-convulsion medications were done, he was still in deep coma due to hypoxic encephalopathy related status epilepticus. No further lymphoma related therapy was done for the comatose patient with mechanical ventilation dependence.

Discussion

Anaplastic large cell lymphoma (ALCL) presented as a pulmonary mass is uncommon, and it is even rare as a cavity with hypercalcemia, like this case. Although the prognosis is poor for the ALCL, 5-year overall survival could reach 49% if timely and proper treatment is given. It is important for clinician to consider ALCL as a differential diagnosis in a cavitary mass concomitant with hypercalcemia.

Many pathologic processes cause pulmonary cavitary diseases, and the differential diagnosis could be narrowed down by careful history review and other clinical evidence. Maximum wall thickness more than 15 mm, an irregular internal wall, absence of centrilobular nodules, and upper lobe predominance are more likely to be malignancy.[2,3,4,5]As the presentation of our case with smoking history, pulmonary cavitary mass, and hypercapnia, SqCC is more likely to be the cause. [6] However, it was not at all. Other possible differential diagnosis for pulmonary mass with hypercalcemia are tuberculosis, sarcoidosis, chronic fungal infections, and lymphomas. [7] The usual mechanisms of hypercalcemia include osteoclastic bone resorption, or humoral hypercalcemia (tumor cell secretion of parathyroid hormone-related protein), 1,25(OH)2D3 secreting lymphoma, and ectopic hyperparathyroidism.[8] Hypercalcemia was less seen with ALCL, and one case report mentioned 1,25(OH)2D3-mediated hypercalcemia in ALCL. [9] In our patient, multiple

osteolytic lesions might be the cause of hypercalcemia.

ALCL is a newly described type of non-Hodgkin's lymphoma (NHL) with usual presentation of T-cell phenotype and frequently follows an aggressive clinical course. It is characterized by pleomorphic large cells expressing the CD30 antigen. [10,11] Primary systemic ALCL accounts for 8% of non-Hodgkin lymphomas. [12] Although lung involvement may occur as a result of dissemination, primary pulmonary ALCL has only been reported in rare cases. [13] While patients with anaplastic lymphoma kinase positive (ALK+) had a superior outcome than those with ALK negative (5-year overall survival, 70% vs 49%; P=0.016), [1] our patient with ALK negative still have near 50% 5-year survival rate if the ACLC diagnosis earlier.

Conclusion

Because of the common manifestations of SqCC in a rare diagnosis of ACLC, it is easy to misdiagnosis and delay the treatment for ACLC. Though this case, we want to remind physician to consider anaplastic large cell lymphoma as a possible diagnosis for the patient with a cavitary pulmonary mass associated with hypercalcemia.

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