中文題目: 非結核分枝桿菌患者合併血清 CA199 及 CA125 顯著升高：個案報告

英文題目:Markedly elevated serum Ca-199 and CA-125 in a patient with Non-tuberculosis Mycobacterium infection: A Case Report

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Abstract: A 52-year-old male presented to our emergency department due to persistent hemoptysis. He was then admitted according to the chest film study with increased infiltration over right upper lung lobe and under the suspicious of pulmonary tuberculosis with reactivation. However, epigastric pain with heart-burning sensation was mentioned. After series examination, an abnormal raised serum cancer antigen-199 (CA-199) and cancer antigen-125 (CA-125) was noted. However, panendoscopy, coloscopy, abdominal sonography and abdominal CT did not reveal any gastrointestinal tract malignancy. After we initiated anti- Non tuberculosis Mycobacterium (anti-NTM) therapy, the serum CA-125 and CA-199 both decreased and CA-125 finally returned to normal range. From our case report, we observed these tumor markers (CA-125 and CA-199) could probably assess NTM treatment effectiveness in the future. To be brief, the measurement of serum CA-125 and CA-199 might offer an alternative follow-up tool to evaluate the therapeutic response of Non-tuberculosis Mycobacterium infection.

Introduction: Just as we known, cancer antigen-125 (CA-125) was a tumor marker which has been shown closely related to some malignancy (such as: breast, lung, pancreas, ovary) and some non-malignancy condition (such as: endometriosis, cirrhosis of liver). Otherwise, cancer antigen-199 (CA-199) was an another tumor marker which might imply several gastrointestinal cancers, such as: pancreatic cancer, colorectal cancer, hepatocellular cancer, and esophageal cancer. Some non-malignant condition, such as: pancreatitis, cirrhosis of liver, and obstruction of biliary tract, can also detect raised serum CA-199 concentration.

In the past, we observed some patients of pulmonary tuberculosis infection having high titer of cancer antigen 199 (CA-199) and cancer antigen (CA-125) while acute phase of disease. Some articles reported that a raised CA-125 might be associated with pulmonary tuberculosis. Some articles had focused on the validity of the cancer antigen-125 (CA-125) and cancer antigen-199 (CA-199) in the differential diagnosis of active pulmonary tuberculosis. Some studies observed that decreased serum CA-199 and CA-125 concentration after initiating pulmonary tuberculosis treatment, which might imply

pulmonary tuberculosis disease controlled. Other studies reported that higher serum CA-125 level in active pulmonary tuberculosis than inactive pulmonary tuberculosis.
Since Non-tuberculosis Mycobacterium (NTM) was an infectious disease with difficulty to evaluate treatment effectiveness at present. In our study, we reported a case of NTM infection with significant elevating CA-199 and CA-125 before the treatment initiating. Then we found an interesting phenomenon with gradually decreased CA-199 and CA-125 after starting NTM therapy. Hence, we supposed that cancer antigen-199 (CA-199) and cancer antigen-125 (CA-125) may use to evaluate the therapeutic response of Non-tuberculosis Mycobacterium (NTM) infection.

Case report: This is a 52-year-old male with previous systemic history of myasthenia gravis and thymoma status post operation since more than 10 years ago. However, he presented to our hospital due to symptom of hemoptysis. The laboratory data showed no leukocytosis and no elevation of CRP level (WBC=7020/uL, CRP=0.28 mg/dL). The chest film revealed infiltration over right upper lobe lung. He was then hospitalized in our isolation ward on 20140913 under the suspicious of pulmonary tuberculosis with reactivation according to the clinical symptom and chest film study.
We arranged chest high resolution CT scan (chest HRCT) after admission. The chest HRCT showed progression of bilateral bronchiectasis and bronchiolitis. Acid-Fast stain did not demonstrate bacilli. The TB PCR was negative. The patient was transferred to ordinary ward on 20140920 after exclude of pulmonary tuberculosis with reactivation. Bronchoscopy was arranged with bronchial brushing performing at the RB1, 3. However, we found interesting finding with significantly elevated tumor marker of CA-199 (CA-199 was 1050 U/ml). In the beginning, the cause of elevated CA-199 is unknown. Heart burning sensation was told by the patient. Panendoscopy was performed and demonstrated gastroesophageal reflux disease, LA grade A; and erosive gastritis over gastric antrum. The abdominal sonography revealed mild to moderate fatty liver. Besides, no significant abnormality in this abdominal sonography. Coloscopy was arranged with negative finding. He was discharged on 20140923.
After discharge and regularly followed at our out-patient department, the final TB culture disclosed Mycobacterium abscessus/chelonae infection. We initiated anti-NTM treatment since 20141007 (Rifampin 600mg QD, EMB 1600mg QD for two months, and Klaricid 500mg bid). However, we followed other tumor markers and CA-125 elevation was also detected (CA-125 was 49.57 U/ml on 20141118). Abdominal CT was checked and revealed no evidence of hyper-or hypo-vascular tumor in the pancreas. Pancreatic duct appears normal. Besides,

no intra-abdominal lesion was detected in the CT study. We initiated anti-non tuberculosis (anti-NTM) therapy in our out-patient department. Under anti-NTM treatment, we followed serum CA-199 and CA-125 level which showed a trend with gradually decreased titer as following:

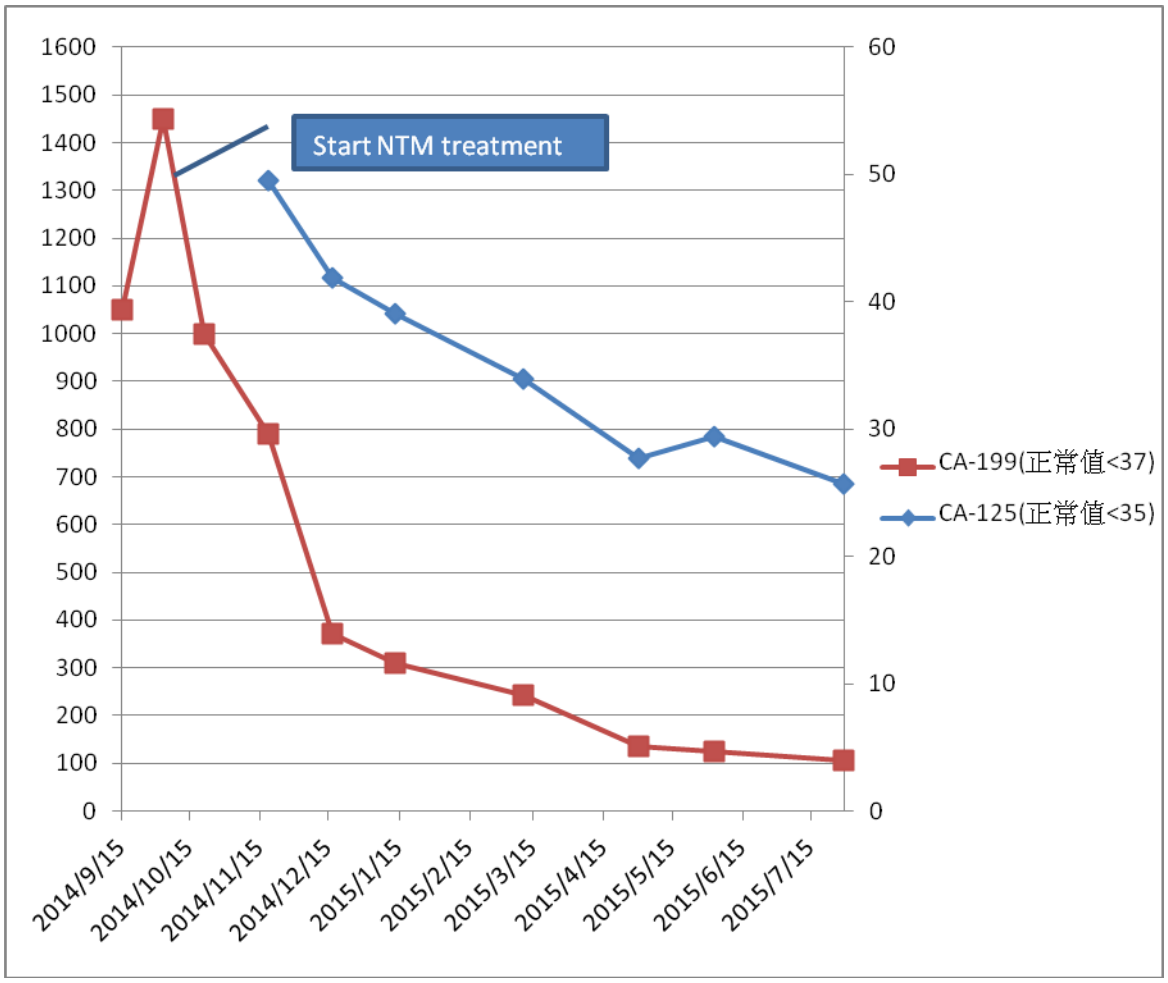

Figure1: This is a line graph which left vertical coordinate indicates serum CA199 titer, right vertical coordinate indicates serum CA125 titer, and horizontal coordinate indicates date of blood sampling. The figure demonstrates gradually decreased serum CA-199 and CA-125 titer after initiating anti-tuberculosis therapy.

From this case, we found an interesting phenomenon with elevating serum CA-199 and CA-125 while NTM infection flared up, but decreasing when NTM disease controlled. So we made a hypothesis that elevating CA-199 and CA-125 could not only imply probable gastrointestinal tract malignancy, it might also associate and probably imply worsening NTM infection or reactivation. In contrast, if CA-199 and CA-125 decreased, it might demonstrate disease controlled of NTM infection. So we conclude that CA-199 and CA-125 might use to evaluate the therapeutic response of Non-tuberculosis Mycobacterium (NTM)

infection in the future.

Discussion: From this case, the patient presented with hemoptysis and epigastric tenderness with heart-burning sensation. Chest film revealed increased infiltration over right upper lobe lung. Pulmonary tuberculosis was suspected initially. However, raised serum CA-199 and CA-125 level was noted after series examinations. Then sputum TB culture confirmed the diagnosis of non- Mycobacterium infection (Mycobacterium abscessus/chelonae). We conducted series study, including panendoscopy, coloscopy, abdominal sonography, abdominal CT scan, and chest high resolution CT scan which did not detect any malignancy. We started NTM therapy according to the TB culture result. Then the serum CA-125 and CA-199 titer decreased gradually during the period of NTM treatment.
From our study, we found an interesting phenomenon with positive relationship between CA-199, CA-125 titer and disease activity of NTM infection. Since Non-tuberculosis Mycobacterium (NTM) was an infectious disease with currently difficulty to evaluate treatment effectiveness, we conducted an observational result which might make the hypothesis that these tumor markers (CA-125 and CA-199) could probably assess NTM treatment effectiveness. Just as we known, these tumor markers are widely tested and might imply some malignant and non-malignant conditions. Cancer antigen-125 (CA-125) was a tumor marker which has been shown closely related to some malignancy (such as: breast, lung, pancreas, ovary) and some non-malignancy condition (such as: endometriosis, cirrhosis of liver). Otherwise, cancer antigen-199 (CA-199) was an another tumor marker which might imply several gastrointestinal cancers, such as: pancreatic cancer, colorectal cancer, hepatocellular cancer, and esophageal cancer. Some non-malignant condition, such as: pancreatitis, cirrhosis of liver, and obstruction of biliary tract, can also detect raised serum CA-199 concentration. However, we could use this simple test to evaluate the therapeutic response of Non-tuberculosis Mycobacterium infection. In addition, it also seems to suggest that NTM infection must be taken into consideration in the differential diagnosis of patients with elevated serum CA-125 and CA-199 concentration. However, further well-designed studies might be needed to support our hypothesis and define the precise role of CA-125 and CA-199 in the diagnosis and follow-up process of NTM.

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