

CA125 and CA15-3 Tumor Markers are Closely Associated with Disease Activity in a Patient with Diffuse Large B-cell Lymphoma

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ABSTRACT. A 67-year-old woman suffered from right supraclavicular and axillary lymph node swelling, fever and a cough. She was diagnosed with a diffuse large B-cell lymphoma from the results of a lymph node biopsy done at a local hospital. Her CA125 and CA15-3 tumor markers were high. When she was admitted to our hospital, we determined that the lymphoma had invaded her lung, spleen and bone marrow; thus we diagnosed her as clinical stage IV BN+M+ with International Prognostic Index as high risk. We instituted CHOP chemotherapy combined with rituximab. After 6 courses of CHOP and 8 of rituximab, the patient gained complete remission. The markers returned to normal one after another in order of LDH, CA125, sIL-2R, and CA15-3.

Several recent reports have shown that CA125 values are well associated with the clinical stage and prognosis of patients with non-Hodgkin's lymphoma (NHL). However, there are few reports about CA15-3 related to lymphoma. Here we report a case in which the CA125 and CA15-3 markers were well associated with the disease activity of NHL; therefore, indicating that these markers are useful for an initial diagnosis of the disease.

Key words ① CA125 ② CA15-3 ③ non-Hodgkin's lymphoma

The CA125 is used as a tumor marker for epithelial ovarian cancer, and is also suggested to be a good marker for the disease activity and prognosis of non-Hodgkin's lymphoma (NHL). On the other hand, CA15-3 is mainly used as a tumor marker for advanced breast cancer, while its relation with lymphoma is unclear. Here we report a case of NHL, in which the CA125 and CA15-3 tumor markers were closely related with disease activity and prognosis in a patient with NHL.

CASE REPORT

Patient: A 67-year-old woman.

Chief complaints: Right supraclavicular and axillary lymph node swelling, dyspnea, and fever.

Past History: Lumbar spine compression fracture in 1995.

Family History: An elder sister had gastric cancer.

History of the present illness: The right supraclavicular and axillary lymph nodes were swollen, and fever, cough and dyspnea were noted on February 2005. CA125 and CA15-3 serum markers were 315U/ml and 49.3U/ml, respectively. She was diagnosed with a diffuse large B-cell lymphoma from the results of right supraclavicular and axillary lymph node biopsies done at a local hospital.

Physical findings: Height, weight, temperature, and pulse rate were 160 cm, 59.6kg, 36.7°C, and 72/min, respectively. She had a slight conjunctival anemia. The right supraclavicular lymph node of 7cm was palpable, as was the right axillary lymph node of 3cm. There was no cardiac murmur. There was attenuation of her breath sound in the right lung field. The liver was one side finger-palpable but the spleen was not.

Laboratory findings: The number of white blood cells was slightly increased and slight anemia was found on examination of peripheral blood. Serum lactate dehydrogenase (LDH) and soluble interleukin-2 receptor (sIL-2R) were increased to 263IU/l and 7,930U/ml, respectively, but β 2-microglobulin (β 2-MG) level was normal. Serum CA125 and CA15-3 were 315 and 49.5 U/ml, respectively.

Computed tomographic scan and magnetic resonance imaging showed swelling of multiple lymph nodes in the right supraclavicular and subclavicular. A bulky mass of about 10 cm in diameter invaded from the right subclavicular to the 1~3 rib bones. As well, remarkable pleural effusion and a right upper lung field infiltrative shadow were seen. ^{67}Ga scintigraphy showed an accumulation of enhancement from the right supraclavicular to the axilla. Bone scintigraphy showed an accumulation of enhancement in the second rib bone, which suggested invasion into the bone. Multiple mass lesions were found in the spleen by abdominal ultrasonography.

Lymphoma cells were not found in the pleural effusion. The CA125 value in the pleural effusion was 1,223 U/ml, which was four times higher than in serum. CA125 antigen was detected in mesothelial cells by immunostaining (Fig. 1). The CA15-3 value in the pleural effusion was 15.4 U/ml.

No aberrations were noted on gynecological and breast region examinations. We diagnosed the patient with NHL with a clinical stage of IV BN+M+, and the International Prognostic Index (IPI) was high risk.

Therapy and clinical course of the disease (Fig. 2):

Initially, we administered prednisolone at 50mg and then started CHOP chemotherapy (cyclophosphamide 1100mg, adriamycin 70mg, vincristine 1.5mg, and prednisolone 50mg). The pleural effusion

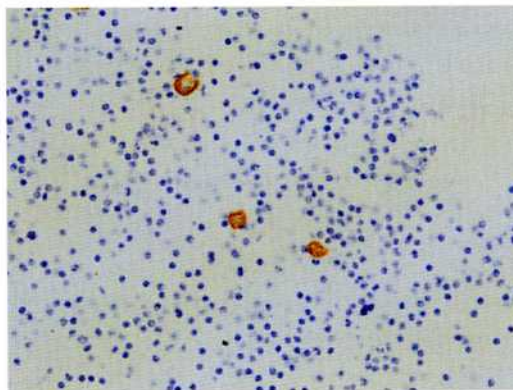


Fig. 1. The CA125 antigen was detected in mesothelial cells by immunostaining (pleural effusion). $\times 40$

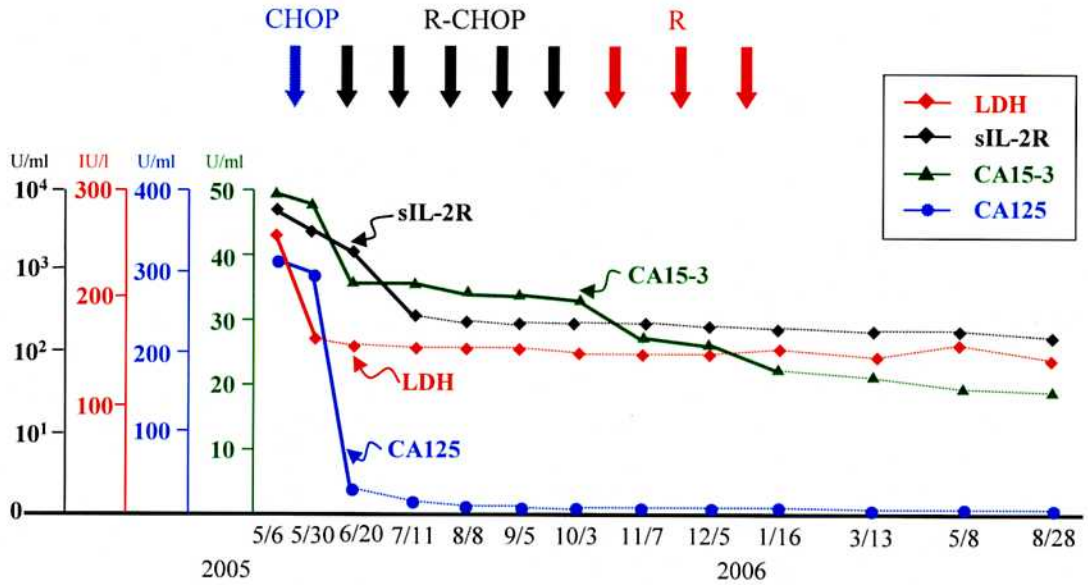


Fig. 2. Clinical course

The patient underwent Rituximab(R) and chemotherapy(CHOP).

— abnormal range normal range

decreased after the first course of chemotherapy, and fever and respiratory symptoms disappeared. We also used Rituximab 560mg together with CHOP chemotherapy after the second course. We performed 6 courses of CHOP chemotherapy and 8 of Rituximab. The patient eventually gained complete remission. Markers returned to normal one after another in the order of LDH, CA125, sIL-2R, and CA15-3, and have remained normal to this day, 18 months after treatment.

DISCUSSION

From 1997 to 2006 there have been many reports showing that the CA125 marker closely correlates with LDH and β 2-MG, and is that it is useful for monitoring the progress of NHL and the effect of treatment⁽¹⁾⁻¹²⁾. A high level CA125 value at the initial diagnosis is progressive and tends to invade lungs, pleura, gastrointestinal tract, and indicates a poor prognosis^(7)-9),12). On the other hand, there are few reports about CA15-3 as a marker for NHL⁽¹⁰⁾. In the present case, high CA125 and CA15-3 levels closely correlated with high LDH and sIL-2R levels, but not with β 2-MG, which remained normal. However, the cause of the increased level of CA125 in NHL patients remains unclear. It is thought that in the present case, CA125 may have been produced from mesothelial cells in response to cytokines such as interleukin-1 β (IL-1 β) and tumor necrosis factor- α (TNF- α) released from NHL cells⁽¹³⁾. There may also be another way; that is, CA125 is secreted directly from NHL cells⁽¹⁾. In the present case, no lymphoma cells were detected in the pleural effusion while CA125 antigen was detected in mesothelial cells; indicating that the mesothelial cells produced CA125. The cause for the high level of CA15-3 in NHL observed in the present case is unknown. To clarify this point, more cases need to be analyzed in respect to the transition of CA15-3 values in NHL.

It has been reported that at an initial diagnosis of NHL, cases with high CA125 level make up

40-70%^{10, 12)}, and those with high CA15-3 level, 17.5%¹⁰⁾. When these tumor markers are high at the initial diagnosis, clinicians need to follow the transition of these values during their treatment of NHL, and then confirm the normalization of the value after treatment.

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