中文題目:以微血管病變所引發溶血性貧血為臨床表現的轉移性大腸癌

英文題目: Metastatic colon cancer presenting with microangiopathic hemolytic anemia

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Background: Cancer-related microangiopathic hemolytic anemia (CR-MAHA) is a RARE paraneoplastic syndrome characterized by Coombs-negative hemolytic anemia with schistocytes and thrombocytopenia. **Case Presentation:** A 74-year-old man presented at our emergency department (ED) complaining of multiple bone pain for three weeks. Two weeks ago, the patient developed spiking fever with common cold symptoms. Other symptoms included anorexia, constipation, and passage of bloody stool. Meanwhile, the patient's body weight dropped from 72 to 65 kilograms. Upon physical examination at the ED, the patient was oriented and vital signs were stable with no acute distress initially. His extremities were warm and well perfused, with normal range of motion and muscle power. No edema was noted. At the ED, the patient's white blood cell (WBC) count was mildly elevated (10.02 k/uL) with the presence of myelocytes and metamyelocytes. His hemoglobin (7.6 g/dL) and platelet counts (48 k/uL) were decreased. Mean corpulscular volume was 89.4 fL. Creatinine was 2.1 mg/d. A chest X-ray film was taken and had no significant findings. Because of the presence of bloody stool, anemia, and abnormal liver tests, the patient received a blood transfusion and was initially admitted to gastroenterology division. During his admission, an upper gastrointestinal panendoscopy revealed superficial gastritis and several small ulcers (A2) in the gastric antrum. The ulcers were considered incompatible with the severe anemia and bloody stool. A bone marrow aspiration and biopsy was performed and the touch imprint cytology of bone marrow biopsy revealed clusters of malignant cells and the trephine biopsy pathology later confirmed that there were adenocarcinoma and suggested it could be from gastrointestinal tract. The following studies showed worsening leukocytosis (12.68 k/uL), anemia with polychromatophilia, and thrombocytopenia (32 k/uL). Total bilirubin/direct bilirubin was 1.65/0.60. Lactate dehydrogenase (1795 IU/L) was elevated. Haptoglobin (<7.44 mg/dL) was decreased. Direct antiglobulin test, anti-nuclear antibody, and cold agglutinin were all negative. D-dimer was beyond 10000 ng/mL A colonoscopy revealed that there was a mucosal lesion with swollen mucosa causing the narrowing of the lumen at the sigmoid colon and the scope was

unable to advance further. Specimens were collected during the procedure and a pathology report later confirmed a diagnosis of adenocarcinoma. An abdominal computed tomography scan showed 3 non-enhancing tumors in the patient's liver. A Technetium-99m bone scan and whole body positron emission tomography revealed enhanced signals in the liver, multiple lymph nodes, bone marrow, and multiple bones. Finally, he was diagnosed to have adenocarcinoma of sigmoid colon with liver and multiple bone and bone marrow metastases associated with CR-MAHA.

The patient's condition deteriorated quickly. He began to experience fever and dyspnea, especially at night. Chest X-ray films showed reticular ground-glass infiltrations and small amounts of pleural effusions in the bilateral lungs. Procalcitonin level (1.93 ng/mL) was mildly elevated. Cardiac enzymes were within normal limits, and the highest level of N-terminal of the prohormone brain natriuretic peptide (NT-proBNP) recorded was 887 ng/mL. The patient's oxygen demands were gradually upgraded to oxygen mask with flow of 10 L/hr. The patient's ECOG performance status score went downhill to a score of 4. On the fourteenth day of admission, a chemotherapy with FOLFIRI regimen was started. **Result:**The CR-MAHA, thrombocytopenia, hypoxemia, transfusion requirement and critical condition were all resolved one month after starting chemotherapy. He was still alive and receiving chemotherapy with improved performance status three months after initial diagnosis of CR-MAHA at the time of writing up the abstract**. Discussion:** The pathogenesis of microangiopathic hemolytic anemia in patients with CR-MAHA is unknown. Most cases of CR-MAHA have been reported in patients with mucin producing adenocarcinomas, predominantly gastric and breast cancer, in addition to being reported in patients with widely disseminated malignancies. To the best of our knowledge, the present study is one of the few report describing metastatic colon adenocarcinoma presenting with microangiopathic hemolytic anemia. Though severe deficiency of von Willebrand factor-cleaving protease was initially proposed as a key pathogenetic factor for thrombotic thrombocytopenic purpura, subsequent studies involving patients with CR-MAHA did not find as severe a deficiency of von Willebrand factor-cleaving protease as is seen in idiopathic cases of thrombotic thrombocytopenic purpura. The plasma exchange is ineffective in CR-MAHA. There is evidence that some cases of CR-MAHA responding to antitumor therapy had a superior survival compared to patients without chemotherapy. **Conclusion:**The prognosis of cancer-associated TMA is quite poor, with a majority of patients dying within weeks of diagnosis. Thus the early recognition of hemolytic anemia and identification of malignancy followed by prompt treatment of an underlying malignant process is the key in the successful management of CR-MAHA in these patients.