ACQUIRED FACTOR VIII DEFICIENCY IN A PATIENT WITH GASTRIC CANCER
(CASE REPORT)

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Özet


Anahtar kelimeler: Mide Kanseri, Faktör VIII inhibitörü, Immunosıpressif tedavi

Summary

Acquired haemophilia A associated with gastric cancer is a very rare condition. Here in this case we report a patient who experienced a successful immunosuppressive treatment of haemorrhagic episodes due to FVIII inhibitors associated with gastric cancer. The combination of immunosuppressants (cyclophosphamide and prednisone) were administered, and significant improvement occurred. Both the APTT and the level of factor VIII inhibitor decreased. Haemorrhagic episodes were ceased.

Key words: Gastric cancer, Factor VIII inhibitor, Immunosuppressive therapy
Introduction

The most common spontaneous development of inhibitors to any clotting factor constitute against factor VIII (FVIII) in persons without a history of bleeding diathesis, and leads to an acquired haemophilic state. The inhibitors in this state usually are autoantibodies that inhibit the function of specific coagulation factor. Whereas, FVIII inhibitors in haemophilia A are alloantibodies and may develop in 20-30% of multitransfused patients with haemophilia. None the less, acquired haemophilia A is very uncommon cause of fatal haemorrhagic diathesis.

The most commonly reported conditions associated with the development of antibodies against FVIII are autoimmune disorders such as rheumatoid arthritis and systemic lupus erythematosus, the postpartum period, drug reaction, dermatological disorders. Antibodies against coagulation factors occur rarely in nonhaemophiliac persons (0.2-1/1,000,000/year). Approximately 10% of patients with acquired haemophilia have an underlying malignancy. The cases of gastric cancer associated with acquired FVIII inhibitors have been rarely reported (1-4).

Case

A 65-year-old man with no history of haemorrhagic diathesis was diagnosed to have gastric cancer, and total gastrectomy with cholecistectomy was performed a year ago. Histology of tumour showed adenocarcinoma. The pathological stage of tumour was T2N2M0 in surgical specimen. The coagulation tests were within normal limits at the time of surgery. The patient was given three chemotherapy course (5-FU, Folinic acid) after surgery, but it did not continue. About a year after surgical intervention, the patient was admitted to our department complaining of epigastric pain, ecchymoses on the right hip, lumbar and inguinal region. Computed Tomography (CT) revealed haematoma in retroperitoneal region (4x5 cm) and between muscles of gluteus maximus and medius (6x6 cm). Also, metastatic lesion in the liver was revealed by CT. Laboratory results were as follows: haemoglobin (Hb): 5.5 g/dL, WBC count: 7.7 X10⁹/L, platelet count: 300X10⁹/L, total bilirubin: 3.5 mg/dL, direct bilirubin: 1.0 mg/dL, reticulocyte: 3.5%, lactic dehydrogenase (LDH): 1120 U/ml, aPTT: 87.50 sec. Bleeding time and PT were in normal range.

Assay for specific coagulation factors revealed a moderately decreased FVIII (3.3%). Other coagulation factors were within normal limits. The assay for FVIII inhibitors were performed according to the Bethesda method. FVIII inhibitor titre at the time of diagnosis was 9 Bethesda unit (BU). According to these findings, acquired haemophilia A was diagnosed. Since Hb level is low, 5 U of packed red blood cell was administered first to the patient. Then, bleeding was controlled with fresh frozen plasma (FFP) at a dose of 15 ml/kg every 12 hours. At the same time, cyclophosphamide at dose of 900 mg/d (for 1 day) in combination 100 mg prednisolone (5 day) was administered to the patient. Two weeks after starting therapy, the bleeding did not occurred, and Hb level had been stable, and APTT decreased to 58.9 sec., and FVIII inhibitor was 0.22 Bethesda units. CT revealed reduced diameters of hematoma from 4x5 cm, 6x6 cm to 2x2, 3x4 cm in retroperitoneal region and in between muscles, respectively.

Discussion

FVIII inhibitors in patients with malignancy pose a clinical dilemma and a potentially life threatening haemorrhage for 25% of the patients (5).

The patient had no prior history of haemophilia. When total gastrectomy with cholecistectomy was performed a year ago, routine coagulation tests were within normal limits. A year after surgery, extensive ecchymoses was noted in gluteal region. At the same time, gastric cancer recurrence and liver metastasis also observed.

The most common solid organ tumour associated with FVIII inhibitors is prostate carcinoma. Also, the most common histologic type of solid tumours associated with FVIII inhibitors has been reported as adenocarcinoma. However, It has been reported a few cases of gastric cancer associated with FVIII inhibitors. At the time of diagnosis of the inhibitor, the tumour has been reported as advanced in 27% of patients. In our patient also was established liver metastasis at the time of diagnosis of the inhibitor. It has been reported that the most common haemorrhagic episodes (25%) involved soft tissues. Whereas, in our patient bleeding involved muscles and retroperitoneal region (3,5).

The underlying mechanism is not completely understood, but occurrence of antibodies are possibly due to immune dysfunction caused by abnormal T cell response to unknown antigen or to abnormal interaction between the B and T lymphocytes (4).

In the majority of cases, the clinical course is characterised by severe bleeding episodes. For treatment of bleeding episodes of patients with acquired FVIII inhibitors, there are several therapeutic method such as prothrombin complex concentrates,
FFP, porcine FVIII, human FVIII concentrates, plasmapheresis, immunosuppressive therapy. A recent report suggested that treatment of coagulation inhibitors with extracorporeal immunoadsorption was safe and well-tolerated. It has been reported that the most popular and most effective treatment of coagulation inhibitors was combination of immunosuppressants (cyclophosphamide and prednisone) (3-6). Bleeding episodes of the patient were treated successfully with cyclophosphamide in combination with prednisolone. Both the APTT and the level of factor VIII inhibitor moderately decreased. Haemorrhagic episodes were ceased.

It is necessary to consider an acquired inhibitor against FVIII as a cause of spontaneous bleeding among patients with malignancy.

References


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