

DEVELOPMENT OF THE NEUTROPENIA ASSOCIATED WITH SOMATOSTATIN: A RARE CASE REPORT

SOMATOSTATİNE BAĞLI GELİŞEN NÖTROPENİ: OLGU SUNUMU

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ABSTRACT

Somatostatin is a form of polypeptide hormone, which is usually used in the treatment of gastroesophageal variceal bleeding, endocrine tumours and fistulas, and may lead side effects such as nausea, vomiting and abdominal pain. Drug-induced neutropenia is a rare case; however, it is a serious side effect which threatens life. In this report, we are presenting a 32-year-old male patient with cryptogenic liver cirrhosis who developed neutropenia and started somatostatin infusion twice due to the esophageal variceal bleeding. This case was evaluated as a definitive drug side effect according to Naranjo scale and in the literature; it is the first case of neutropenia associated with somatostatin.

Key words: Somatostatin, Neutropenia, Naranjo scale

ÖZET

Somatostatin gastroözofageal varis kanamaları, barsakların endokrin tümörleri, intestinal ve pankreas fistülleri tedavisinde kullanılmakta olup en sık karşılaşılan yan etkileri bulantı, kusma ve karın ağrısıdır. İlaça bağlı nütropeni nadir görülmekle birlikte ortaya çıktığında hayatı tehdit eden ciddi bir yan etkidir. Vakamız gastroözofageal varis kanamasıyla acil servise iki kez başvurmuş kriptojenik karaciğer siroz tanılı 32 yaşında erkek hastadır. Somatostatin infüzyonu verilen hastada nütropeni gelişti ve kontrollerde nütropenin düzeldiği görüldü. Naranjö skorlamasına göre nütropenin somatostatin ile ilişkili olduğu kesinleşti. Nütropeni somatostatinin sık görülen yan etkileri arasında olmamakla birlikte, somatostatine bağlı gelişen ilk nütropeni vakası olarak sunulmuştur.

Anahtar kelimeler: Somatostatin, Nütropeni, Naranjö skorlaması

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Introduction

Somatostatin is an endogenous peptide hormone secreted by the central nervous system, gastrointestinal tract, retina, peripheral neurons and pancreatic D cells of the islets of Langerhans (1). Somatostatin is used for the treatment of cirrhosis-related gastroesophageal variceal bleeding, endocrine tumours of the gut, and intestinal and pancreatic fistulae (2). The most common side effects of somatostatin include gastrointestinal side effects such as abdominal pain, nausea, vomiting and diarrhoea. Neutropenia is not currently listed as an adverse effect and not included even among the rare adverse effects of somatostatin (3).

Drug-induced neutropenia is a potentially serious and life-threatening adverse event that may occur secondary to therapy with a number of agents. The annual incidence of this relatively rare condition is 2 to 15 cases per million. Cytotoxic chemotherapy may cause a predictable and dose-dependent decline in neutrophil count. Neutropenia secondary to other medications tends to be idiosyncratic reaction either as an immune-mediated reaction or due to direct myeloid cell line damage. This effect has been associated with a variety of medications including but not limited to clozapine, dapsone, methimazole, penicillin, rituximab and procainamide (4, 5).

No cases of neutropenia induced by somatostatin have ever been reported until this date. This is the first report of a case of neutropenia associated with somatostatin.

Case Presentation

A 32-year-old male patient diagnosed with cryptogenic liver cirrhosis who was being followed since September 2006 presented to the emergency room in June 2009 due to bleeding esophageal varices. At presentation his WBC/Neutrophil count was 5/3.5 $10^3/\text{mm}^3$. Band ligation was performed and somatostatin treatment was started with a bolus injection of 250 mcg, followed by 250 mcg/hour administered by continuous infusion over 3 days. On the third day of somatostatin infusion, his WBC/Neutrophil count decreased to 1.6/0.9 $10^3/\text{mm}^3$. His follow-up blood count at 1 month after treatment showed recovery of WBC/Neutrophil count to normal range (WBC/Neutrophil count: 7.3/5.4 $10^3/\text{mm}^3$). In April 2016, the patient readmitted to the emergency room with bleeding esophageal varices and following a 250 mcg bolus injection of somatostatin, 250 mcg per hour of somatostatin was given by infusion over 3 days and band ligation performed. His WBC/Neutrophil count was 4.4/3.6 $10^3/\text{mm}^3$ at presentation which declined to 1.3/0.8 $10^3/\text{mm}^3$ on the third day of somatostatin infusion. Consistent with his first episode, his WBC/Neutrophil count returned to normal as observed on follow-up at one month (WBC/Neutrophil count: 5.6/3.3 $10^3/\text{mm}^3$) (Figure 1).

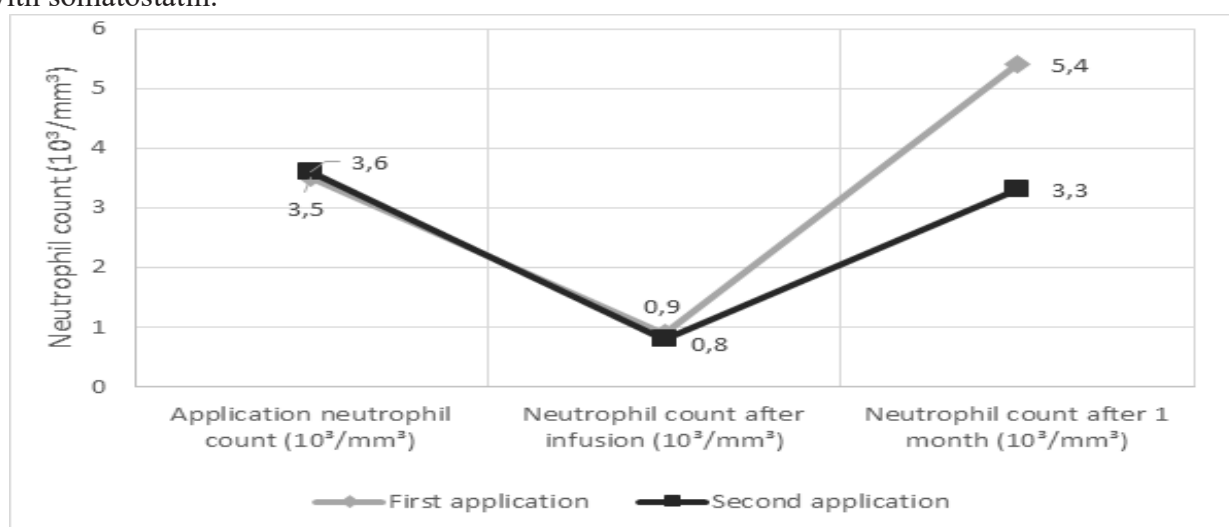


Figure 1. Neutrophil count in patient's applications

Discussion

Acute neutropenia evolves within a few days and occurs when neutrophil use is rapid and production is impaired. Chronic neutropenia may last for 3 months or longer and is a result of reduced production, increased destruction or excessive splenic sequestration of neutrophils (6). Acute neutropenia is most commonly associated with viral and bacterial infections (7). At the time of admission for variceal bleeding, our patient had normal CRP with no fever, which led to exclusion of infectious causes. Drug-induced neutropenia is often a multifactorial and complex condition and its mechanism has yet to be fully elucidated. Haptens and toxic metabolites of certain medications which are produced via oxidation were demonstrated to attack neutrophils. Additionally, genetic factors such as polymorphisms in the genes encoding human leukocyte antigens (HLA) have been linked to drug-induced neutropenia. Other mechanisms proposed for drug-induced neutropenia include autoimmune responses, formation of an immune complex or damage to myeloid stem cells and growth factors directly or via complement pathway (8-10). One or more of these mechanisms may have been effective in our case. Somatostatin was considered as the sole cause of neutropenia in our patient because of the absence of known history of previous medication use, temporal relationship of development of neutropenia with somatostatin infusion, full recovery of neutropenia observed on follow-up and neutropenia recurrence on readministration of somatostatin (positive rechallenge). Our patient had a score of 9 on the Naranjo scale, which confirmed the causal relationship with somatostatin (5).

Conclusion

Several drugs have been implicated in drug-induced neutropenia and it should be borne in mind that although rarely, neutropenia may occur in patients receiving somatostatin.

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Conflict of interest

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