INTRODUCTION

Ticlopidine is a platelet aggregation inhibitor that is used to decrease the occurrence of atherothrombotic arterial events such as cerebral infarction, cerebral transient ischemic attack, myocardial infarction and peripheral arterial disease\textsuperscript{[1]}. Hematologic effects, including pancytopenia, thrombotic thrombocytopenic purpura, leukopenia, and agranulocytosis, are the most serious adverse reactions. Sporadic cases were reported in which anemia and leukopenia developed simultaneously, or leukopenia and thrombocytopenia\textsuperscript{[2-5]}. We report an additional case of agranulocytosis and anemia due to ticlopidine with a favorable outcome, after the cessation of the drug and treatment with G-CSF and broad-spectrum antibiotics.

CASE REPORT

A 63-year-old man was admitted with a 6-day history of generalized weakness, sore throat, and fever. Ticlopidine had been used at a daily dose of 500 mg for 2 months prior to admission due to transient ischemic cerebral stroke. The concurrent drug used was glipizide 5 mg/day for type 2 diabetes mellitus. At the time of the initiation of the ticlopidine therapy, the leukocyte count was 7.5 x 10\textsuperscript{9}/L, the hemoglobin level was 16 gr/dL and the
Ticlopidine was an effective antiplatelet agent that inhibits the binding of adenosine 5'-diphosphate to its platelet receptor[6]. The platelet inhibition persists for 7 to 10 days after therapy is stopped. Ticlopidine is used for the secondary prevention of strokes, transient ischemic attacks, peripheral vascular disease and unstable angina. The Ticlopidine Aspirin Stroke Study (TASS) demonstrated that ticlopidine was somewhat more effective than aspirin in reducing the risk of death from any cause or the risk of a nonfatal stroke in patients with recent transient ischemic attack or mild stroke[7,8].

Ticlopidine is known to cause diverse severe hematological side effects including agranulocytosis, and, more rarely, thrombocytopenia or severe aplastic anemia[9-12]. Sporadic cases were reported, in which anemia and leukopenia or severe aplastic anemia[2-4]. Agranulocytosis occurs 1-3 months after treatment began and resolves within three weeks of ticlopidine discontinuation[7]. In our patient, agranulocytosis occurred 2 months after the start of ticlopidine therapy. Ticlopidine was administered with glipizide, which is unlikely to have been involved in the development of hematologic toxicity. He had been treated with glipizide for 2 years and this drug was continued during agranulocytosis and neutrophil recovery, suggesting that this drug was not the cause of hematologic toxicity. He continued to take glipizide and has had no further episodes of neutropenia. Certain viral infections, for example, infectious mononucleosis, infectious hepatitis and human immunodeficiency virus infection may cause neutropenia and pancytopenia due to infection of hemopoietic precursor cells. But in this case, screening was negative for viral agents.

Agranulocytosis is a potentially lethal toxic effect of ticlopidine, especially in older patients who are the usual population treated with ticlopidine[3,4]. The episode of neutropenia is associated with the arrest of the maturation of the granulocytic cell line. When agranulocytosis is detected, ticlopidine should be discontinued permanently. Great efforts should be directed at preventing and managing infection accompanying agranulocytosis, since it is the major cause of death. Admission to the hospital is advised for febrile patients and those exhibiting systemic infection. G-CSF regulates hematopoietic neutrophil progenitor colony growth and stimulates the release of bone marrow neutrophil storage pools resulting in an apparent rise in circulating neutrophils. G-CSF is now widely used to overcome neutropenias of various origins[12,13]. There are some reported cases of successful use of G-CSF in ticlopidine-induced neutropenia and pancytopenia[14,17]. Altho-
Address for Correspondence:
Ali KESKİN, MD
6006 Sokak, No: 21 Daire: 5
Çamlık, Denizli, TURKEY