Nonfatal aplastic anemia associated with clopidogrel

Klopidogrel ile ilişkili ölümcül olmayan aplastik anemi

Thienopyridines inhibit the adenosine 5'-diphosphate P2Y12 receptor on platelets. These drugs reduce the overall rate of thromboembolic events in patients with atherosclerotic vascular disease after stent implantation. Ticlopidine is a first-generation thienopyridine. The use of ticlopidine has two major limitations, which are its safety profile and its inability to induce platelet inhibition rapidly. Thus, clopidogrel, a second-generation thienopyridine, has largely replaced ticlopidine. Clopidogrel therapy may also be accompanied by rare life-threatening side effects (1). Clopidogrel may be found to be associated with severe bone marrow suppression manifested as bone marrow failure (2), aplastic anemia, thrombocytopenia, neutropenia. We present a case of aplastic anemia caused by clopidogrel.

A 55-year-old man with acute coronary syndrome underwent bare metal stent implantation to target lesion in the circumflex coronary artery on May, 2008. He was started on clopidogrel (300 mg loading followed by 75 mg daily) for at least 12 months. His baseline hematologic findings were normal at that time. Eleven months after the introduction of clopidogrel, he was evaluated in our out-patient cardiology clinic because of mainly fatigue. He denied angina. At last, on his clinical and laboratory assessment, hematologic findings revealed severe pancytopenia. His hemoglobin level was 8.4 g/dL, erythrocyte count - $2.4x10^{12}$/L, white-cell count - $2.8x10^{9}$/L (neutrophils 62%, lymphocytes 31%, monocytes 6%, and eosinophils 1%), and platelets count - $31x10^{9}$/L. Bone marrow examination findings demonstrated severe hypoplasia of all three lineages without fibrosis. Results of cytogenetic analysis were normal (46, XY with no structural anomaly) and a Ham test was negative. There was no evidence of autoimmune disorders, hepatitis, parvovirus infection or other viral infections and other drugs use such as angiotensin-converting enzyme inhibitors. The serum levels of vitamin B12 and folic acid were normal. Ultrasound examination did not disclose splenomegaly or lymphadenopathy. Aplastic anemia was diagnosed, and resolved fourteen days after stopping clopidogrel. His symptoms were rapidly relieved.

The incidence of thrombocytopenia and neutropenia induced by clopidogrel was reported to be 0.26 and 0.10%, respectively in CAPRIE study (3). The mechanism of aplastic anemia induced by clopidogrel is not well understood (possibilities include cumulative toxicity or idiosyncratic reaction) (4). In a previous report, it was suggested that aplastic anemia occurred within 5 months of starting clopidogrel (5). In our case, aplastic anemia occurred within 11 months of starting clopidogrel.

As a result, clopidogrel may be a potential cause of aplastic anemia irrespective of the duration of treatment, though rarely seen. Therefore, careful clinical and hematological monitoring should be carried out in the course of treatment with clopidogrel.

Ömer Uz, Ejder Kardeşoğlu, Mustafa Aparcı, Ömer Yiğiner, Zafer Işılak, Namık Özmen
From Department of Cardiology, Haydarpaşa Gülhane Military Medical School, İstanbul, Turkey

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Address for Correspondence / Yazışma adresi: Dr. Ömer Uz
Department of Cardiology, Haydarpaşa Gülhane Military Medical School, İstanbul, Turkey.
Phone: +90 216 542 34 65 Fax: +90 216 348 78 80
E-mail: homeruz@yahoo.com

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A case of infective endocarditis, during pregnancy: should we keep the fetus?

Bir gebelik dönemi enfektif endokardit vakası: Fetusu korumalı mıyız?

Incidence of infective endocarditis during pregnancy is reported to be 0.006% (1). Among those patients, 22% have a history of valve disease, and etiology is variable among others (2).

A 27-year old female patient in the 14^{th} week of pregnancy began to have palpitations, pain in left shoulder, and became orthopneic. Echocardiogram demonstrated severe mitral stenosis (MS), moderate aortic regurgitation (AR) and mild aortic stenosis. Two days after her admission, she developed dyspnea, tachycardia and refractory hypotension. The repeat echocardiogram revealed echodense structures over the mitral valve, consistent with vegetations. Blood tests were insignificant except elevated leukocyte count ($18.6\ 10^{9}$/L), high erythrocyte sedimentation rate (72 mm/h). Therefore, infective endocarditis was considered to be complicating her valve disease. The patient was intubated and medical treatment including diuretics, digitals and broad-spectrum antibiotics was initiated. After two days, the patient was hemodynamically stable, and she underwent surgery for aortic and mitral valve replacement with St Jude® mechanical heart valve prosthesis. During the operation, a high flow (2.5 lt/min.m^2), high pressure (mean 60mmHg), and non-pulsatile perfusion with moderate hypothermia was achieved. Anesthesia protocol included a hypnotic (propofol, Diprivan®), a narcotic (fentanyl, Fentanyl Citrate®), a muscle relaxant (vecuronium bromide, Norcuron®) and an inhalation anesthetic (isoflurane, Forane®). Intravenous tocolytic (ritodrin, Prepar®) and antiepileptic (phenytoin, Epdantoin®) drugs were also administered