EDITÖRE MEKTUP / LETTER TO THE EDITOR

A chronic myeloid leukemia case with two ischemic cerebrovascular attacks during nilotinib therapy

Nilotinib tedavisi sırasında iki kez iskemik serebrovasküler atak geçiren bir kronik miyeloid lösemi olgusu

Gül İlhan
Mustafa Kemal Üniversitesi Tıp Fakültesi, Hematoloji Bilim Dalı, Hatay, Turkey

Sayın Editör,

Nilotinib (NIL) is one of the BCR/ABL tyrosine kinase inhibitor drug. It has been approved both first and second line chronic myeloid leukemia (CML) treatment. Generally it is well tolerated but has some side effects such as pancreatitis, hyperbilirubinemia, and hyperglycemia. However atherosclerosis and peripheral arterial occlusive disease (PAOD) were reported. We presented a patient who had two ischemic cerebrovascular accident (CVA) during NIL therapy\(^1\).

A 68-year-old male patient with coronary artery disease, hypertension and diabetes mellitus was diagnosed with CML 5.5 years ago. He was initially treated with imatinib (IM) 400 mg daily. At the first month of IM treatment, because of no hematologic response dose was escalated to 600 mg daily. Major molecular response (MMR) was achieved at the first year. But at the second year hematologic response was lost. Dasatinib (DAS) 100 mg daily was started. After two weeks he was hospitalized due to pulmonary edema. DAS was stopped. A few weeks later, NIL was started (200 mg twice daily). But the second year of NIL, MMR was lost and we escalated NIL dose to 400 mg twice daily. After 6 months he patient presented with partial aphasia, left hemiparesis due to an ischemic CVA. Clopidogrel was added and acetylsalicylic acid dose was changed to 300 mg daily At the first year of NIL, MMR was gained again 12 months. Unfortunately, he had a second ischemic CVA 7 months later from the first attack. We sendred T315I mutation and stopped NIL therapy and changed it to DAS 50 mg daily.We planned to give him diuretic therapy routinely and follow him closely for fluid retention.

NIL is generally well tolerated but incidence vascular events was found increased. The 6 year cumulative cardiovascular events were 9.9%, 15.9% and 2.5% among patients treated with NIL 300 mg twice daily, NIL 400 mg twice daily and IM 400 mg daily respectively\(^2\). Other side effects are headache, skin rashes, indirect hyperbilirubinemia (10%), hyperglycemia (10-20%) and rarely pancreatitis (1-2%)\(^3\). NIL-associated vascular events reported in small cohorts of patients. In one of these studies one patient's sudden death and one patient's PAOD and coronary artery disease were reported\(^4\).

Aicherberger and collegeas reported 8 of 24 patients had vascular diseases PAOD, sudden death, myocardial infarction, spinal infarction, subdural hematoma during NIL therapy\(^5\). However severe cases of NIL-associated PAOD have recently been reported, occurring in as many as 17% of patients treated. In a retrospective study of 233 patients 5 patients had vascular events during NIL therapy. One of them was CVA, the others were PAOD. In all cases NIL was stopped\(^6\).

Jager et al. reported a case with coronary ischemic attack and three CVA after NIL therapy. The mechanisms by which NIL could cause these serious side effects are poorly understood. Potential

---

Yazışma Adresi/Address for Correspondence: Dr. Gül İlhan, Mustafa Kemal Üniversitesi Tıp Fakültesi Hastanesi, Hematoloji Bilim Dalı, Antakya, Hatay, Turkey E-mail: gulihan2002@yahoo.com

Geliş tarihi/Received: 24.09.2016  Kabul tarihi/Accepted: 02.10.2016
roles of discoidin domain receptor 1 (DDR1), KIT and the platelet derived growth factor receptor (PDGFR) are suggested. In our case there were some risk factors of vascular disease such as diabetes mellitus and hyperlipidemia. Beginning of CVAs were after NIL, there were no cardiologic cause for embolism and we he was taking two antiagregant therapy before the second attack. These factors made me us think of the etiology may be NIL.

In conclusion clinicians should be aware of the potential role of NIL in the development of vascular events and take this knowledge into account during clinical decision-making, for example in patients with pre-existing cardiovascular risk factors.

REFERENCES