Agranulocytosis during Nifedipine Treatment in a Hemodialysis Patient

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Dear Sir,

Nifedipine is widely used in hypertensive patients with chronic renal failure [1]. This drug may cause headache, flushing, dizziness, gastrointestinal symptoms and fluid retention with edema. Other potential, although rare, side effects include an impaired glucose metabolism, interactions with other drugs, allergic hepatitis and abnormal liver function tests, rash, muscle cramps, immunocomplex glomerulonephritis [2]. Only 1 case of agranulocytosis as a suspected consequence of nifedipine treatment is reported in the literature [3]. We wish to report a case of reversible agranulocytosis possibly related to nifedipine.

A 53-year-old man underwent regular dialysis treatment, in March 1986, for chronic renal failure, due to left kidney agenesis and chronic pyelonephritis. Since 1979, the patient had been treated with a low-protein diet and α-methyldopa, which was replaced by nifedipine in July 1985. In July 1986, the patient underwent surgical repair of an abdominal aortic aneurysm with application of a Dacron prosthesis; the postoperative course was without complication. On July 19, the patient had a myocardial infarction. The nifedipine therapy was stopped and patient was given nitroderivates. After a few days, the patient developed a hemorrhagic herpes zoster lesion on the left upper lip. He was treated with acyclovir (500 mg/day) for 6 days with complete recovery of the herpetic lesion. On September 6 the patient was discharged and continued hemodialysis as an outpatient. The previous therapeutic regimen, i.e. nifedipine, vitamin D, aluminium hydroxide, digoxin and nitroderivates, was reassumed. On October 1, 1986, the patient developed fever, severely sore throat and marked asthenia. He presented with high fever (39 °C), tachycardia (96 beats/min) and extensive ulcerations of the soft palate and pharynx. Admission laboratory data included a hemoglobin value of 8.8 g/dL, a leukocyte count of 1,070/mm3 and a platelet count of 225,000/mm3. The differential leukocyte count showed 75% lymphocytes, 9% neutrophils, 13% eosinophils and 3% basophils. Bone marrow biopsy revealed severe myeloid hypoplasia and marked megakaryocyto-sis; no morphologic atypias were observed in the white cell series; the few neutrophils still present showed toxic cytoplasmic granulations. Prednisolone (75 mg/day) was then given and nifedipine was stopped. Ten days later, white cell count rose to 6,200 (41% neutrophils, 49% lymphocytes, 5% monocytes, 4% eosinophils, 1% basophils).
the patient had an unexpected gastric hemorrhage and died. Autopsy showed acute ulcerative gastric lesions; no findings other than those correlated with chronic uremia were present.
The involvement of nifedipine in this case of agranulocytosis is indicated by the pattern of myeloid damage (suggesting a toxic origin) and by the prompt recovery of the bone marrow after stopping nifedipine administration. We have also considered the fact that the patient had received nifedipine during the previous 2 years without any side effects. This delayed reaction could be explained by the fact that the patient did not receive nifedipine during treatment for the myocardial infarction, and that the nifedipine therapy was reassumed after treatment with a DNA synthesis inhibitor, acyclovir. Since there is considerable evidence of the significant role played by calcium in regulating the mytotic process [4–6], the possibility that the previous treatment with acyclovir facilitated the development of agranulocytosis during nifedipine administration cannot be ruled out. On the other hand, no case of agranulocytosis due to acyclovir has been reported and this drug was administrated for only a few days 2 months before the appearance of the myeloid involvement.

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References