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Agranulocytosis Associated With Gentamicin

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GENTAMICIN is an aminoglycoside antibiotic derived from *Microspora purpurea*. It has broad-spectrum antibacterial action against most strains of *Staphylococcus*, *Escherichia*, *Enterobacter*, and *Pseudomonas*,¹ and has been widely used in clinical practice with satisfactory results. However, like many other antibiotics, it is not without side-effects. The more frequently reported adverse reactions are nephrotoxicity, neurotoxicity, and allergic skin reactions.²

No serious hematologic complications have been recorded although transient granulocytopenia has been observed.^{3,4} We recently encountered a patient who had agranulocytosis associated with gentamicin and who recovered without any serious incident.

Report of a Case

A 68-year-old man was admitted to the Veterans Administration Hospital, Dayton, on May 6, 1974, with chief complaints

of shortness of breath and chronic cough from an acute exacerbation of chronic obstructive lung disease. On admission, the patient was emaciated, appeared chronically ill, and was in moderate respiratory distress. Vital signs included a temperature of 37.3 C (99.2 F), pulse rate, 104 beats per minute, and blood pressure, 100/62 mm Hg. He had moderate cyanosis of the tongue and lips. The jugular venous pressure was markedly increased with the patient tilted at 45°. Breath sounds were diminished, but no rales or wheezes were heard. The heart had strong parasternal and epigastric heaves with soft S₁ gallops. The liver extended 4 cm below the right costal margin at the right midclavicular line, but the spleen was not palpable.

Admission laboratory studies showed a white blood cell (WBC) count of 10,700/cu mm, with 80% neutrophils, 15% lymphocytes, and 5% monocytes; red blood cells (RBCs) 4.68 million/cu mm; hemoglobin value, 14.9 gm/100 ml; and hematocrit reading, 46.9%. Urinalysis showed bacteriuria and pyuria. Urine culture showed *Klebsiella* organisms, more than 100,000/ml of urine. Electrolyte values were essentially normal, but blood urea nitrogen (BUN) level was 32 mg/100 ml and creatinine value, 1.0 mg/100 ml. Arterial blood gas studies showed a pH of 7.40, Pco₂, 54.0 mm Hg, and oxygen pressure, 35.5 mm Hg, bicarbonate, 32.2 mEq/liter, and oxygen saturation, 69%. Chest x-ray film showed evidence of pulmonary emphy-

sema. The sputum culture yielded normal flora.

The patient was treated with intravenous fluids, oxygen, and bronchodilators. Treatment with ampicillin sodium, 500 mg every six hours, was begun. He showed marked clinical improvement on supportive treatment. Ampicillin therapy was discontinued on the eighth hospital day. On the 17th hospital day, gentamicin sulfate treatment, 60 mg intramuscularly every eight hours, was begun for the urinary tract infection with the *Klebsiella* organism. Eight days after institution of gentamicin treatment, the hemogram showed moderate leukopenia (WBC count, 4,100/cu mm, with 9% neutrophils, 86% lymphocytes, and 5% monocytes). It was suspected that gentamicin was causing the granulocytopenia, and treatment with the drug was immediately discontinued. The hemogram on the following day showed a WBC count of 4,400/cu mm, with 1% neutrophils, 65% lymphocytes, 3% eosinophils, 1% basophils, and 30% monocytes; RBC count, 4.54 million/cu mm; hemoglobin value, 12.9 gm/100 ml; hematocrit reading, 42%; reticulocytes, 0.8%; and platelet count, 372,000/cu mm.

The patient had no evidence of further infection and follow-up granulocyte counts slowly returned to normal (Fig 1). Bone-marrow aspiration was obtained on June 14, 1974, five days after withdrawal of gentamicin. Marked granulocytic hyperplasia was noted with a high percentage of mye-

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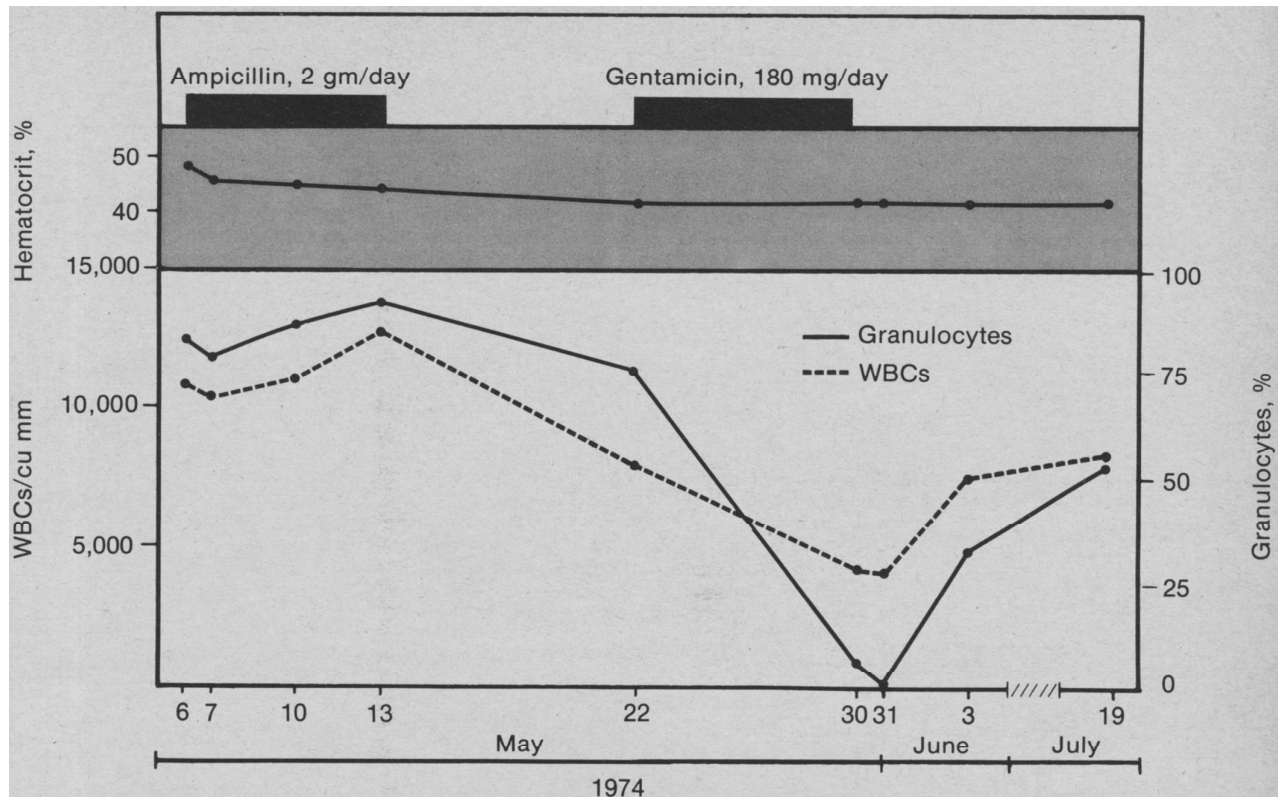


Fig 1.—Total white blood cell count, percentage of granulocytes, and hematocrit value of peripheral blood, and drugs received during patient's hospital stay.

lyocytes and metamyelocytes, suggesting synchronization of granulocytes during the recovery period after drug-induced bone-marrow depression (Fig 2).

The patient had an uneventful recovery from agranulocytosis and was discharged without any complications.

Comment

There is little doubt that this patient had gentamicin-induced agranulocytosis, since the development of granulocytopenia was characterized by severe peripheral blood neutropenia, monocytosis, and lymphocytosis that appeared within seven days after the institution of treatment with the drug. After discontinuation of gentamicin therapy, hematologic recovery was evident in three days, and the bone-marrow findings of granulocytic hyperplasia and synchronization of granulocytes were compatible with the idiosyncratic type of agranulocytosis caused by selective bone-marrow depression of granulopoiesis.

Although the patient had agranulocytosis, no severe infection occurred because the period of granulocy-

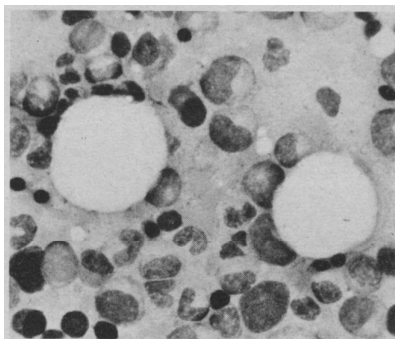


Fig 2.—Bone marrow aspirate on third day after discontinuation of gentamicin treatment showing marked granulocytic hyperplasia with synchronization of granulocytes at myelocyte and metamyelocyte stages.

topenia was rather short and the recovery of WBCs was prompt. It was thought that the patient had less chance of serious infection, because during the early phase of granulocytopenia he probably had an effective level of gentamicin, which, with its broad and highly effective bactericidal action, afforded protection against most pathogenic microbial organisms.

It is believed that gentamicin is not normally toxic to the bone marrow. The drug has been widely used in clinical practice in the past decade in the United States with, as far as we know, no published reports of fatal blood dyscrasia. Agranulocytosis seen in this patient was the result of a hypersensitivity reaction. However, it is wise to consider the possibility of such a complication in those receiving the drug.

Nonproprietary Names and Trademarks of Drugs

Gentamicin sulfate—*Garamycin*.
Ampicillin—*Amcill*, *Omnipen*, *Penbritin*, *Principen*, *Supen*.

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