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Megaloblastic, Dyserythropoietic Anemia Following Arsenic Ingestion

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ABSTRACT

Following acute arsenic ingestion, a 35 year old woman experienced multiple organ failure, including renal and respiratory insufficiency, toxic hepatitis, peripheral neuropathy, and encephalopathy. In addition, she developed an anemia; the bone marrow showed a striking dyserythropoiesis with megaloblastic features. Her recovery was heralded by normalization of the bone marrow morphology, followed by improvement in all other organ dysfunction except for the peripheral neuropathy.

Arsenic poisoning is a cause of megaloblastic anemia; early hematologic recovery suggests favorable prognosis.

Acute arsenic poisoning is uncommon. It is usually the result of accidental or suicidal ingestion of insecticides or pesticides. Toxicity is manifested by nausea, vomiting, abdominal pain, circulatory collapse, and often results in death. Hematological abnormalities include anemia, leukopenia and/or thrombocytopenia. The anemia is generally normocytic and normochromic. Basophilic stippling is often present.[1,2,3,4,5] In the case to be described, the bone marrow initially exhibited a striking dyserythropoiesis. Marrow recovery preceded normalization of other clinical abnormalities.

Case Report

A 35 year old woman was admitted to Northwestern Memorial Hospital 20 hours following the unintentional ingestion of an arsenic-containing insecticide. She presented with nausea, vomiting, abdominal cramping, and diarrhea. Physical examination revealed an alert and cooperative female whose vital signs were normal. The only physical abnormality was a III/VI systolic ejection murmur at the apex. An electrocardiogram showed a sinus tachycardia (100 beats/min), prolongation of the QT interval (0.48 sec) and T wave inversion in the precordial leads. An abdominal radiograph showed radiopaque material in the right upper quadrant. Her hemoglobin was 13.5 g per dl; hematocrit, 40 percent; red blood count, 4.18 M per μl; white blood count, 23,400 per

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μl with a normal differential. The platelet count was 600,000 per μl and the reticulocytes, 0 percent. Prothrombin time and partial thromboplastin time were normal. Lactic dehydrogenase was 286 mU per ml (Nl, 0 to 250); alkaline phosphatase, 89 mU per ml (Nl, 0 to 85); serum glutamic oxalacetic transaminase, 110 mU per ml (Nl, 0 to 30); creatine phosphokinase, 3680 mU per ml (Nl, 0 to 125) with 92 percent MM and 8 percent MB isoenzyme fractions. A technetium T_c99m pyrophosphate myocardial scan showed no evidence of infarction. A serum arsenic level was 113 μg per 1 (Nl, < 1 μg per 1) and urine arsenic was 27.5 mg per 1 (Nl, < 0.15 mg per 1).*

The patient was transferred to the intensive care unit for cardiac monitoring and was treated with 2,3 dimercapto-1-propranol (BAL) and cathartics. During the first few days following admission, there was a progressive fall in the hemoglobin to 9.1 g per dl and the hematocrit to 26 percent. The reticulocyte count remained at 0 percent. An examination of the bone marrow showed normal cellularity with a myeloid to erythroid ratio of 5:1 (figure 1). Granulopoiesis and thromboiesis were adequately represented and showed normal maturation. Erythropoiesis revealed megaloblastic changes with nuclear irregularity, maturation delay, and frequent karyorrhexis. Iron stores were slightly decreased.

* Kindly performed by Dr. E. Berman, Hektoen Institute, Cook County Hospital.

The first week in the hospital was complicated by respiratory failure, renal insufficiency, pulmonary edema, toxic hepatitis, malabsorption, encephalopathy, and peripheral neuropathy. The patient was treated with folate, intravenous fluids, and antibiotics. On the 14th day, the reticulocyte count increased to 3.2 percent. The following day, a repeat marrow examination showed slight granulocytic hypoplasia and normoblastic erythropoiesis with disappearance of the previously observed megaloblastic changes and karyorrhexis. Iron stores were abundant (figure 1). Subsequently, the function of other organs improved, although the peripheral neuropathy persisted. Her hemoglobin eight weeks following admission had increased to 12.3 g per dl and hematocrit to 37.6 percent.

Comment

Arsenic poisoning is usually associated with leukopenia, anemia, and thrombocytopenia, secondary to depression of the bone marrow.[3] Megaloblastic erythropoiesis is unusual and has been reported only once previously.[7] In that patient, serum B_{12} and folate levels were normal, and the megaloblastosis was

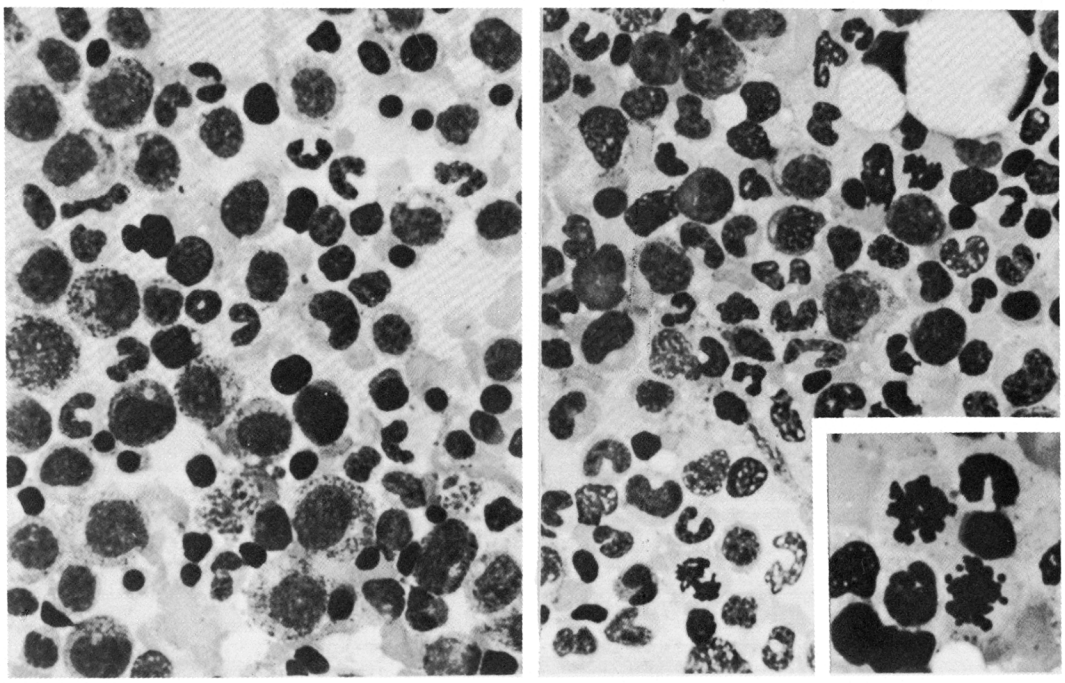

FIGURE 1. Right: First marrow showing frequent karyorrhexis (inset) and megaloblastic changes in the red cell precursors. May-Grunwald Giemsa (×300). Left: Second marrow displaying normoplastic erythropoiesis and disappearance of karyorrhexis (×300).

thought to be a direct toxic effect of the arsenic. Similarly in our patient, folate deficiency would not account for the morphologic abnormalities, since the megaloblastic anemia developed while the patient was in the hospital receiving adequate dietary folate.

The mechanism of arsenic induced megaloblastosis is speculative. Investigators measuring the incorporation of ^{14}C-labeled sodium formate into nucleic acid purines of control and arsenic-fed mice showed that potassium arsenite reduced incorporation of formate into nucleic acid precursors, thereby inhibiting nucleic acid synthesis.[6]

Recovery from the toxic effects of arsenic in our patient was heralded by the development of reticulocytosis and a normalization of the marrow abnormalities. Subsequently, there was improvement in other organ systems. It is suggested that the findings of reticulocytopenia, megaloblastosis, and karyorrhexis should raise the suspicion of arsenic intoxication, and that repeated hematologic evaluations are valuable in assessing the prognosis for recovery.

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