

NOTICE

This material may be
protected by copyright
law (Title 17 U.S.C. 101-105)

PLAINTIFF'S
EXHIBIT

907

Myeloid Metaplasia as a Result of Chronic Benzene Intoxication

MURRAY PORT, M.D.
New York City

JULIAN B. HYMAN, M.D.
New York City

From the Department of Internal Medicine,
New York Polyclinic Medical School and Hospital

CHRONIC EXPOSURE to the inhalation of benzene (benzol) frequently results in depression of one or more elements of the bone marrow.^{1,2} The period of exposure necessary to produce this effect varies from individual to individual. The time interval between exposure and the production and clinical recognition of bone marrow elements may differ considerably. There may be occasional stimulation of the bone marrow with the presence of a leukocytosis prior to the appearance of the depression. In several instances acute leukemia has occurred many years after benzene poisoning.^{3,4} One patient exposed to benzene for thirteen years developed an aplastic anemia from which he recovered. Fifteen years after recovery he developed acute leukemia.⁵ The development of myeloid metaplasia as a consequence of exposure to chronic benzene intoxication is known,⁶⁻⁸ but the cases reported in the literature are few in number. Other manifestations such as aplastic anemia, leukopenia, and leukemia are more frequently observed.

Since benzene intoxication may still represent a problem in certain industries, we are presenting this unusual additional case

of myeloid metaplasia resulting from chronic benzene intoxication. The patient was asymptomatic, and the disease was recognized only at the time of an acute condition necessitating operation.

Case report

A fifty-year-old Negro woman entered the New York Polyclinic Hospital on September 11, 1963, with a diagnosis of right inguinal hernia that had suddenly become painful on the day of admission. She had always enjoyed good health except for a hysterectomy in 1945. She had worked continuously as a hand presser in several cleaning factories in Georgia for a period of thirty years and had been subjected to chronic inhalation of cleaning fluids containing benzene (benzol) in poorly ventilated establishments.⁹ She had continued to work in cleaning factories up to three weeks before admission.

When examined in the emergency room of New York Polyclinic Hospital she complained of severe pain in the right groin. She was admitted to the surgical service, and an emergency right inguinal herniorrhaphy was performed.

On admission the patient's blood pressure was 160/86 mm. of mercury, her pulse was 84 beats per minute and regular. Examination of the eyes, ears, nose, and throat was unremarkable. No lymph nodes were felt in the cervical, axillary, or inguinal regions. The lungs were clear.

The heart revealed the presence of a Grade III systolic murmur at the apical region propagated slightly to the left. The abdomen was soft and nontender. The liver was smooth, nontender, and palpable 4 cm. below the right costal margin. The spleen was felt 6 to 8 cm. below the left costal margin. There was a firm, non-fluctuant mass, easily reducible, and tender to touch in the right inguinal region. The rectal and vaginal examinations showed negative results. The admitting hemoglobin was 10.2 Gm. per 100 ml., hematocrit 33, with 11,250 white blood cells, 77 segmented neutrophils, 22 lymphocytes, and 1 eosinophil per cubic millimeter of blood. The erythrocyte sedimentation rate 24 mm. per hour (Westergren), the fasting blood sugar was 124 mg. per 100 ml., and blood urea nitrogen was 9 mg. per 100 ml.

FIGURE 1. Section magnification. (E)

After the right the patient was service because and hepatosple was questioned tory without a being obtained. hematologic dis- own past histor or drug intake the fact that she same type of at ing in the same of chemicals an

Additional F the following re. volume was 10: globin 31 mic count 2 per ce 376,000 per cub eral smear rev moderate aniso macrocytes, an sickle cell and erations showe function studi the prothrombi control twelve was 0.6 mg. pe alkaline phospho dansky units, th in twenty-four 9.7 units, total 100 ml. with 4. Gm. of globuli 100 ml., trans. and selfobrom. tention in forty electrolytes we On Septemb

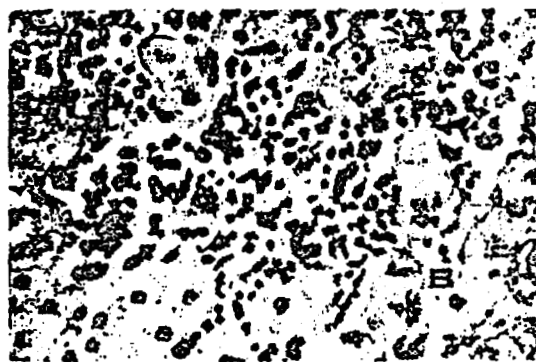


FIGURE 1. Section of liver tissue showing focal areas of extramedullary hematopoiesis. (A) Low-power magnification. (B) Higher magnification. (Hematoxylin and Eosin Stain)

After the right inguinal herniorrhaphy, the patient was transferred to the medical service because of the findings of anemia and hepatosplenomegaly. The patient was questioned again about her past history without any additional information being obtained. She denied any known hematologic disease in her family or in her own past history. She denied any alcohol or drug intake. She again emphasized the fact that she had always worked in the same type of atmosphere, "always breathing in the same steam that had the smell of chemicals and benzene."

Additional hematologic study yielded the following results: the mean corpuscular volume was 100 cubic microns, the hemoglobin 31 micromicrograms, reticulocyte count 2 per cent, and the platelet count 376,000 per cubic millimeter. The peripheral smear revealed slight hypochromia, moderate anisocytosis, poikilocytosis, many macrocytes, and a few target cells. The sickle cell and lupus erythematosus preparations showed negative results. Liver function studies showed the following: the prothrombin time was sixteen seconds (control twelve seconds) serum bilirubin was 0.6 mg. per 100 ml. The serum alkaline phosphatase was less than 4 Bodansky units, the cephalin flocculation 1 plus in twenty-four hours, thymol turbidity 9.7 units, total serum proteins 7 Gm. per 100 ml. with 4.5 Gm. of albumin and 2.6 Gm. of globulin, cholesterol 214 mg. per 100 ml., transaminase (SGOT) 16 units, and sulfobromophthalein 6 per cent retention in forty-five minutes. The serum electrolytes were within normal limits.

On September 25, 1963, a liver biopsy

was performed. The report of this study showed a well-preserved architecture in the section of liver tissue. There were focal areas with sinusoidal dilatation and accumulation of immature hematopoietic cells including megakaryocytes within the sinusoidal space. The interpretation of the section was liver tissue consistent with myeloproliferative disorder (Fig. 1). A bone marrow aspiration was performed on October 3, 1963. There was diminished cellularity throughout the marrow with increased fat present. The erythroid series was revealed to be undergoing normoblastic maturation. The myeloid series revealed a distinct shift to the left with an increase in promyelocytes suggesting a maturation arrest. No foreign cells were seen. The megakaryocytes were diminished in number. The bone marrow was interpreted as being hypoplastic and compatible with a diagnosis of myeloid metaplasia.

Comment

The presentation of this case is of interest for several reasons. As stated in the introduction it re-emphasizes the potential danger of the inhalation of a toxin which may produce marrow hypoplasia or aplasia. Benzene, sometimes called benzol, has been used extensively in industry because of its solvent property for rubber, gums, resins, and fats. It is not to be confused with benzine, a mixture of short-changed aliphatic hydrocarbons.

Also of importance is the relationship between the development of myeloid metaplasia and chronic benzol intoxication.

Myeloid metaplasia occurs frequently

