CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 12-1976

PRESENTATION OF CASE

First admission. A 35-year-old man was admitted to the hospital because of acute myeloblastic leukemia.

He was well until four weeks previously, when an upper-respiratory-tract infection developed and persisted. On the day of entry he came to the clinic, where an abnormal blood count was found, and was admitted to the hospital.

The temperature was 37.2°C, the pulse 90, and the respirations 18. The blood pressure was 100/70 mm Hg.

On examination the patient appeared robust. Enlarged lymph nodes were found in the cervical, supraclavicular and inguinal regions bilaterally. The lungs were clear, and the heart normal. The liver was not felt, and its vertical span was 8 cm; the splenic tip was barely palpable on inspiration.

The urine was normal. The hematocrit was 38 per cent; the white-cell count was 23,200, with 5 per cent neutrophils, 2 per cent band forms, 18 per cent lymphocytes, 2 per cent metamyelocytes and 73 per cent blasts; occasional Auer rods were noted. The platelet count was 49,000.

The patient was given cytosine arabinoside daily for one week and a three-day course of daunorubicin. The platelet count fell to 2000, the white-cell count to 300, and the hematocrit to 21.7 per cent; numerous ecchymoses appeared. Transfusions of platelets and of red cells were administered. Oral and esophageal moniliasis developed and did not respond to mycostatin; amphotericin B was instituted. On the 21st hospital day the hematocrit was 32 per cent, the white-cell count 3000, and the platelet count 170,000. A bone-marrow aspiration disclosed evidence of complete remission. He was discharged on the 22d hospital day to be followed in the clinic.

Second admission (three and a half months later). The patient returned periodically to the clinic, where maintenance doses of cytosine arabinoside and 6-thioguanine were administered. Bone-marrow relapse developed, and 10 days before admission he began to have a headache and fever. He returned to the hospital.

The temperature was 38.4°C, the pulse 100, and the respirations 16. The blood pressure was 100/70 mm Hg.

On examination he appeared pale. Conjunctival hemorrhages were observed in the right eye. Small cervical and inguinal lymph nodes were palpable. The lungs and heart remained normal. The edge of the liver descended 6 cm, with a vertical span of 16 cm; the spleen was 6 cm below the left costal margin.

The urine was normal. The hematocrit was 31 per cent; the white-cell count was 154,750, with 2 per cent neutrophils, 1 per cent basophils and 97 per cent blasts. The platelet count was 35,000. The glutamic oxalacetic transaminase (SGOT) was 127 U, the lactic dehydrogenase (LDH) 580 U, the amylase 7 U, and the alkaline phosphatase 13.6 Bodansky U. An x-ray film of the chest was normal. A lumbar puncture showed no abnormality, and multiple cultures yielded no bacterial growth.

The patient was given further doses of cytosine arabinoside, with vincristine, daunorubicin, cephalothin, gentamicin and orally administered mycostatin; platelets and frozen, washed red cells were transfused. On the sixth hospital day the hematocrit was 23.2 per cent, the white-cell count 13,600, and the platelet count 15,000. Three days later a bone-marrow aspiration revealed a large number of blast cells. On the 12th hospital day bilateral retinal hemorrhages were found. Monilial infection recurred and was treated with further doses of mycostatin and flucytosine (5-fluorocytosine).

On the 30th hospital day, after preparation with four sublethal doses of cyclophosphamide, the patient received approximately 700 ml of bone marrow from a sister who was identical by HL-A and mixed lymphocyte culture (MLC) methods. Prophylactic treatment with methotrexate was begun. Esophagitis recurred, and additional doses of amphotericin B were given. On the 36th hospital day a purpuric eruption appeared. A skin biopsy revealed a nonspecific reaction that included slight vacuolization in the region of the basement membrane and a sparse, superficial perivascular lymphohistiocytic infiltrate. Antibiotic therapy was discontinued. On the 44th hospital day a bone-marrow-aspiration smear was normal except for a shift to the left; a cytogenetic study revealed a female karyotype.

On the 45th hospital day grand-mal seizures developed; a lumbar puncture yielded grossly bloody cerebrospinal fluid under a normal pressure; stained smears disclosed no micro-organisms, and cultures gave no bacterial growth. A computed axial tomographic study (CAT-scan) of the brain and an electroencephalogram showed no abnormality. Phenytoin (diphenylhydantoin) sodium and phenobarbital were instituted, and seizures did not recur. On the 48th hospital day the hematocrit was 28.6 per cent, the white-cell count 2900, the platelet count 90,000, and the reticulocyte count 6.1 per cent. Methotrexate was continued. On the 52d hospital day the patient was discharged on a regimen of prednisone, mycostatin, phenytoin sodium and phenobarbital.

Final admission (10 days later). He felt well until two days

V C
Genetics

Air Products and Chemicals, Inc.
ALLENTOWN, PA.

28 May 1976

Office of:

W. Mayo Smith

cc: A. Ross Adams
W. L. Ball
J. T. Barr
T. L. Carey/H.L.Watson/J.C.Novak
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E. B. Tepper, M.D.

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Manufacturing Chemists Association

Minutes of Meeting

VINYL CHLORIDE RESEARCH COORDINATORS

Crystal City Marriott Hotel Arlington, Va.

April 27, 1976

Chairman Torkelson convened the meeting at 9:00 p.m. The record of attendance is:

MEMBERS PRESENT:

T. R. Torkelson, Chairman	The Dow Chemical Company
Z. G. Bell, Jr.	PPG Industries, Inc.
W. D. Harris	UNIROYAL, Inc.
M. N. Johnson	B. F. Goodrich Chemical Company
H. L. Kusnetz	Shell Oil Company
W. M. Smith	Air Products & Chemicals, Inc.
R. N. Wheeler	Union Carbide Corporation
M. Freifeld	MCA Staff

GUESTS PRESENT:

W. R. Gaffey	Equitable Environmental Health, Inc.
R. V. Johnston	The Dow Chemical Company
M. W. Palshaw	Stauffer Chemical Company
B. A. Schwetz	The Dow Chemical Company
P. G. Watanabe	The Dow Chemical Company

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1. Birth Defects

The article on "Genetic Risks of Vinyl Chloride", by P. F. Infante et al., which appeared in Lancet recently, (reportedly identical to the article distributed to the Panel on March 17, 1976), attempts to implicate VC but its data base is very weak.

Currently, The Center for Disease Control (CDC) is conducting a study on this subject in Kanawha County, West Virginia. In the discussion of whether this group should recommend undertaking a study in this area, the conclusion was

reached that no feasible way of conducting it could be found. Hence, it was suggested that the matter be held in abeyance until the results of the CDC project are known.

Dr. Schwetz felt there was no need for additional animal testing with relation to birth defects. However, he thought other test should be considered. He pointed out that the Ames test is marginally positive with VC but dominant lethal and cytogenetic tests are negative. Therefore an approach such as heritable genetic translocation studies of the type conducted by Russel at Oak Ridge might be suitable.

The birth defects surveillance program of CDC was scheduled to be a major topic at a meeting April 21, chaired by Dr. E. Landau of The American Public Health Association and attended by Dr. Ken Johnson of the MCA staff. In the absence of Dr. John Herbert of CDC, who was to speak on this program, the discussion centered on a presentation by Dr. Theriault whose work is described in a paper, "Distribution of Primary Cancers of the Liver in the Province of Quebec", in CNA Journal, February 8, 1975, pages 305 to 307. Dr. Theriault sought additional funds to pursue his investigations and indicated a written proposal would be forthcoming. The Research Coordinators felt they would probably not be interested in supporting Dr. Theriault's work at this time, particularly since he did not plan to investigate birth defects.

The group decided to defer any recommendations on mutagenesis/birth defects until the results of the CDC study are known.

2. Continuation of Dow Metabolism Studies

The results of a letter ballot on this effort reported on by the Project Manager indicated the Panel was overwhelmingly in favor of continuing these studies. Only two of the ballots received indicated any reluctance on this score.

Dr. Watanabe outlined the next step of proposed studies as following the binding of VC to macromolecules including those containing sulfhydryl. Concurrently, in vitro investigations are planned to determine what happens to tissues of exposed animals.

No specific recommendations were felt necessary from this group in the light of the ballot results.

3. University of Louisville Proposal

In a letter of April 20, to Dr. Torkelson, Dr. Tamburro outlined studies on immunological systems and electron microscopic evaluation of liver tissues. This was a further description of areas the Panel previously found to be of interest.

An important aim of this proposed work is to develop new diagnostic tools, (mainly based on enzyme testing), for anticipating diseases due to VC exposure. This will complement Dr. Tamburro's major effort, supported by The National Cancer Institute, for applying known, accepted methods for diagnosis and treatment.

The support level requested was at about $235,000 per year but an alternate funding suggestion was at the rate of about $200,000 per year. Dr. Torkelson transmitted a sense of urgency, if indeed the group wanted to support this effort, so that Dr. Tamburro could keep his staff intact.

On motion made and duly seconded to support this program at the rate of $200,000 per year for three years, the vote was five in favor and two opposed.

4. Selection of Vice Chairman

Dr. W. Mayo Smith was unanimously elected as this group's recommendation to the Panel for Vice Chairman. The vacancy was created when Dr. Rinehart left Ethyl Corporation.

The meeting was adjourned at 11:30 p.m.

Milton Freifeld

Milton Freifeld

MF:ec

Minutes Subject to Approval

May 25, 1976

L. B. Lepper
Empl. Relations

CHEMICAL MARKETING REPORTER - MARCH 8, 1976

Disease Control Center Seeks Link With VCM In W. Va. Birth Defects

The National Center for Disease Control is doing an epidemiological study in the area of Charleston, W. Va., near where Union Carbide Corporation has one of its vinyl chloride polymerization plants.

The purpose of the study is to determine whether the higher than average rate of birth defects in the Charleston - S. Charleston area may be related to exposure to vinyl chloride monomer.

Between 1970 and 1953, fifty-three children with central nervous defects were born in this region. Based on the national average, thirty-one such births might have been expected.

National Center epidemiologists hope to interview the parents of all children in the region with central nervous system defects in order to find out where the parents work and how far away from the PVC plant they lived, especially during the early stages of pregnancy. Their experiences will be compared with those of a control group of parents with normal children.

This study is a follow-up of an earlier study done by the center in an area in Ohio near a PVC plant. That study, which was inconclusive, was prompted by earlier findings by a National Institute for Occupational Safety & Health epidemiologist who discovered an unusually high rate of birth defects, especially nervous system defects among children born in three cities in Ohio where VCM polymerization plants are located.

The epidemiologist, Dr. Peter F. Infante, has also reported a two- to threefold increase in the rate of stillbirths and miscarriages among the wives of vinyl chloride polymerization workers compared with wives of PVC fabrication and rubber workers. (CMR 2/9/76, pg. 34).

It was also reported last week that Environmental Protection Agency, in conjunction with American Public Health Association, is planning to study the rates of cancer, stillbirths, miscarriages, birth defects and other diseases that might be related to VCM.

Dr. Teppl

Dr. M. Johnson believes This will be a proper study. Whether it can be specific for VCM is a Big question mark in my mind because of the other industry in Charleston.

MBA
3/15

← Dictate
→ Protocol
Time
etc