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# CASE REPORT

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## THE CO-EXISTENCE OF CHRONIC LEUKEMIA AND PREGNANCY

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THERE is no unanimity of opinion among clinicians with regard to the influence of pregnancy on the prognosis of leukemia. Vignes<sup>1</sup> maintains that signs and symptoms of leukemia are temporarily enhanced by pregnancy, but usually improve with parturition. Angelucci<sup>2</sup> and Kasmak<sup>3</sup> are of the opinion that the symptomatology of leukemia becomes more marked with the progression of pregnancy. The latter author advocates the termination of pregnancy or induction of labor when the diagnosis of leukemia is established during the course of cyesis. Grier and Richter<sup>4</sup> also concur that pregnancy may induce a relapse of the leukemic process. On the other hand, Kaplan and Connery,<sup>5</sup> Forkner,<sup>6</sup> McGoldrick and Lapp,<sup>7</sup> Moloney and Heffernan,<sup>8</sup> claim that pregnancy has no influence whatsoever on the prognosis of chronic myelogenous leukemia. The data accumulated by these authors does not bear out the contention that pregnancy rapidly precipitates a fatal outcome for the patient. As a matter of fact, surgical intervention of pregnancy may be detrimental to the life of the mother because of possible precipitation of an acute phase of leukemia, or uncontrollable hemorrhage. Hochman<sup>9</sup> states that a leukemic patient has a good chance of carrying her pregnancy to term without undue harm to herself.

It is the purpose of this paper to report 4 primiparae with chronic myelogenous leukemia who carried their pregnancies uneventfully to term with the delivery of normal nonleukemic children.

### REPORT OF CASES

*Case 1.* Mrs. P. M. H., a 27 year old white housewife, 3 years prior to marriage, had received roentgen irradiation at varying intervals for chronic myelogenous leukemia. After 2 years of married life, the patient became pregnant. When first seen at the age of 23, the symptoms presented were insidious onset of tiredness and general malaise of approximately 2 months duration. There had been slight bleeding of the gums, and her skin bruised easily with slight trauma. There was no definite history of blood dyscrasia in the family, but a sister was thought to be anemic.

*Physical examination on first entry.* The patient appeared pale and asthenic, and showed evidence of recent loss of weight. The skin and mucous membranes were pale, but neither purpura nor petechiae were apparent. Moderately enlarged lymph nodes were felt in the neck, axillae, and groins. The liver edge was felt 2 cm. below the right costal margin. It was sharp and nontender. The spleen was enlarged down to the pelvic brim. There was no edema of the ankles.

*Laboratory data.* The blood examination revealed: hemoglobin, 57 per cent (Sahli); erythrocytes, 2,460,000 cells per cm.; leukocytes, 277,000 cells per cm. of blood. The differential count was: segmented polymorphonuclear leukocytes, 11.0 per cent; nonsegmented leukocytes, 50.0 per cent; small lymphocytes, 3.0 per cent; metamyelocytes, 7.0 per cent; myelocytes, 28.0 per cent; myeloblasts, 1.0 per cent.

*Diagnosis.* Chronic myelogenous leukemia.

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*Course of illness.* Total body roentgen irradiation was started soon after the diagnosis of chronic myelogenous leukemia was established. Within 1 month following repeated exposures to x-ray irradiation, the white blood count dropped to 11,650 cells per cm.; erythrocytes increased to 3,110,000 cells per cm. of blood, and the hemoglobin increased to 71 per cent (Sahli). During the subsequent 1½ years, the white blood count seldom exceeded 20,000 cells per cm. of blood, and the hemoglobin remained within a range of 90 per cent (Sahli). The spleen and liver were seldom palpable during this time.

During pregnancy, the patient was examined and the status of her blood evaluated at biweekly intervals. At no time during the entire period of gestation did the white blood count rise above 20,000 cells per cm. of blood, nor did the hemoglobin drop below 90 per cent (Sahli). Only the usually prescribed hygienic measures were observed during the prenatal period. Neither arsenic nor x-ray irradiation was given the patient. At term, a normal female child was born, exhibiting no evidence of leukemia. No complication was encountered during the postpartum period. Six months have passed since the birth of the child. When last examined, the patient appeared in good health and there had been no exacerbation of symptoms. The spleen was nonpalpable, and the blood count was: hemoglobin, 94 per cent (Sahli); erythrocytes 3,870,000 cells per cm.; leukocytes, 19,000 cells per cm. of blood.

*Case 2.* Mrs. D. E. F., a 36 year old white housewife, was admitted November 11, 1943 to the University of California Hospital, complaining of a progressive enlargement of her abdomen and the appearance of hemorrhagic spots over her lower extremities. Ten months prior to this entry, the patient had consulted her physician because of amenorrhoea, and was told that she was 3 months pregnant. Incidental findings at this time were an enlarged spleen and a leukocytosis of 205,000 cells per cm. of blood. No anemia was recorded. The patient was advised to have x-ray irradiation, but she refused to co-operate in carrying out this therapeutic procedure. X-ray irradiation, therefore, was not used in the patient during the period of gestation. The pregnancy progressed without untoward symptoms, and a normal male child, showing no stigmata of leukemia, was delivered at term. The postpartum period was complicated by a slight thrombophlebitis of the right leg which subsided in about a month's time. The white blood cells had remained within a range of 300,000 cells per cm. of blood during the pregnancy. The patient was asymptomatic until three months after parturition when the spleen, which had been previously moderately enlarged, began to increase in size and became markedly tender. There was also a recurrence of the tendency to bruise easily.

*Physical examination at the time of entry.* The patient was thin, pale, and appeared younger than the stated age of 36 years. She seemed to suffer acute pain in the left upper quadrant of the abdomen on sudden motion of the body. Small, discrete, firm lymph nodes were found in the anterior cervical regions, axillae, epitrochlear and inguinal regions. Ecchymoses, about 6 cm. in diameter, appeared over the right knee and over the left thigh. The liver edge was firm, and could be felt about 3 cm. below the right costal margin. The spleen, tremendously enlarged, filled the entire left side of the abdomen and extended into the pelvis, and was markedly tender. No dependent edema of the tissues was apparent.

*Laboratory data.* The blood examination showed: hemoglobin, 49 per cent (Sahli); erythrocytes, 2,740,000 cells per cm.; leukocytes, 478,000 cells per cm. of blood. The differential count was: segmented polymorphonuclear leukocytes, 9.0 per cent; nonsegmented leukocytes, 62.0 per cent; eosinophiles, 1.0 per cent; basophiles, 0.5 per cent; metamyelocytes, 14.0 per cent; myelocytes, 10.5 per cent; promyelocytes, 2.0 per cent; myeloblasts, 1.0 per cent. The platelets were 360,000 per cubic mm. of blood.

*Diagnosis.* Chronic myelogenous leukemia.

*Course of illness.* The patient was treated with radio-active phosphorus, starting with an initial dose of 165 mc. Subsequently she was given varying doses of radio-active phosphorus, 136 to 315 mc. intravenously, at 2 to 8 day intervals. After 8 weeks had elapsed, the hemoglobin was recorded at 77 per cent (Sahli); erythrocytes, 2,630,000 cells per cm.; leukocytes, 282,000 cells per cm. of blood. Then, because of the scarcity of the radio-active salt, total body x-ray irradiation was substituted. In another 4 weeks, the hemoglobin was 90 per cent (Sahli), the erythrocytes count was 4,710,000 cells per cm.; and the white blood count was 18,000 cells per cm. of blood. During this time, there was a gradual reduction in the size of the spleen so that it was felt only with great difficulty. Since then, exposures of the patient to x-ray irradiation have been so spaced as to maintain the level of the circulating white blood cells below 20,000 cells per cm. of blood. The hemoglobin has remained within the range of 90 per cent saturation. The liver and spleen have become vaguely palpable only on occasions.

Three years have passed since the termination of pregnancy. The patient is living and well, and her child appears physically normal.

*Case 3.* Mrs. M. B., a 20 year old white housewife, was first seen July 14, 1938, at the University of California Hospital, with the presenting complaint of insidious weakness, and general malaise over a period of 1½ years. Previous to this hospital entry, the patient had been married for 8 months and had become pregnant shortly thereafter. The period of gestation was uneventful until the seventh month of pregnancy at which time, she had a severe attack of vaginal bleeding which lasted 7 days and necessitated vaginal packing to check the hemorrhage. The patient was well for the next 2 weeks when she went into labor. The pregnancy was only of 7½ months' duration, but the child appeared to be a normal male on examination. No unusual bleeding was encountered at the time of delivery. A routine blood count disclosed: hemoglobin, 63 per cent (Sahli), erythrocytes, 3,170,000 cells per cm.; leukocytes, 115,000 cells per cm. of blood. The differential count was: segmented polymorphonuclear leukocytes, 38.5 per cent; nonsegmented leukocytes, 22.5 per cent; small lymphocytes, 5.5 per cent; monocytes, 4.5 per cent; metamyelocytes, 13.5 per cent; myelocytes, 16.5 per cent.

Two weeks after parturition, the patient had another occurrence of severe vaginal hemorrhage which confined her to the hospital for 16 days. When discharged from the hospital, she was gaining in strength, but was conscious of an enlarged mass at the upper left quadrant of her abdomen which was tender upon pressure.

*Laboratory data.* The blood examination disclosed: hemoglobin, 68 per cent (Sahli); erythrocytes, 2,580,000 cells per cm.; leukocytes, 183,000 cells per cm. of blood. The differential count was: segmented polymorphonuclear leukocytes, 14.0 per cent; nonsegmented leukocytes, 21.0 per cent; metamyelocytes, 45.0 per cent; myelocytes, 16.0 per cent; myeloblasts, 4.0 per cent. The platelet count was 346,000 per cm. of blood.

*Diagnosis.* Chronic myelogenous leukemia.

*Course of illness.* The patient was given small doses of radio-active phosphorous (200 to 400 mc.) intravenously at weekly intervals. In 8 weeks' time, the hemoglobin was recorded to be 80 per cent (Sahli), erythrocytes, 4,090,000 cells per cm.; leukocytes, 16,000 cells per cm. of blood. The spleen became gradually and progressively smaller until it was no longer palpable. Her leukocytes were maintained at a level below 20,000 cells per cm. of blood by periodic injections of small doses of radio-active phosphorous. The patient was well for the next 18 months and able to carry on with her housework without difficulties. At the end of this period, the patient had an acute exacerbation of symptoms. Her spleen became progressively enlarged and tender in spite of repeated radio-active irradiation therapy. Roentgen irradiation to the spleen had no effect in reducing its size. A progressive anemia developed but the leukocytes remained at the range of 6,000 to 10,000 cells per cm. of blood at all times. This phase of the disease lasted 2 months and terminated with the death of the patient. Her child remained normal in all respects with no evidence of leukemia.

*Case 4.* Mrs. E. E., a 22 year old white housewife, had consulted her physician a year previously because of amenorrhoea, and was told that she was pregnant. She had been married for 3 years but had had difficulty in conceiving during all this time. A routine physical examination and complete blood examination were found to be within normal limits at that time. The entire period of gestation progressed uneventfully, except for a moderate hypochromic anemia of 60 per cent (Sahli), discovered during the second trimester of the pregnancy. A difficult labor was encountered at term because of foot presentation of the child with persistent arrest of the occiput in the posterior position. The delivery was long and difficult, requiring the use of forceps, and the infant was delivered dead. The postmortem examination disclosed that the child was normal without evidence of leukemia but atelectasis of the lungs was found to be the cause of death. On the second day postpartum, the patient had a rise in temperature to 38° C. A routine blood count disclosed a leukocytosis of 180,000 cells per cm. of blood, and a hemoglobin of 40 per cent (Sahli). A sternal marrow aspiration was done and the marrow was found to be moderately hyperplastic with a preponderance of promyelocytes and myelocytes. It is compatible with the diagnosis of chronic myelogenous leukemia.

*Physical examination.* The patient appeared to be well developed and well nourished. The skin and mucous membranes were pale, but no petechiae or ecchymoses were present. Discrete, small lymph nodes

were found in her cervical region, axillae and groins. The liver edge was felt 6 cm. below her right costal margin. A firm, tender spleen was found to be enlarged down to the level of the umbilicus. There was no dependent edema.

*Laboratory data.* A hematologic examination revealed: hemoglobin, 37 per cent (Sahli); erythrocytes, 1,310,000 cells per cm.; leukocytes, 160,000 cells per cm. of blood. The differential count was: segmented polymorphonuclear leukocytes, 10.0 per cent; nonsegmented leukocytes, 34.0 per cent; monocytes, 3.0 per cent; lymphocytes, 4.0 per cent; eosinophiles, 1.0 per cent; basophiles, 2.0 per cent; metamyelocytes, 21.0 per cent; myelocytes, 23.0 per cent, and myeloblasts, 2.0 per cent.

*Diagnosis.* Chronic myelogenous leukemia.

*Course of illness.* After repeated transfusions, the hemoglobin was noted as 73 per cent (Sahli); and erythrocytes, 3,810,000 cells per cm. of blood. Three weeks after the initial transfusion, the patient became markedly jaundiced with moderate tenderness over the liver. The icterus index was 140 units. Herpes simplex were found on her perioral regions. There was progressive enlargement of her spleen. A course of roentgen irradiation directed over the spleen was started. At the time this paper was being prepared, the patient was still in the hospital but was gaining strength.

#### DISCUSSION

It is unusual for leukemic women to become pregnant. The reason for the infertility of patients has not been established. Perhaps their poor physical health and the amenorrhoea generally associated with the disease are some of the influential factors. In studying postmortem materials, it is not unusual for the reproductive organs to be heavily infiltrated with leukemic cells. The entire ovary and the mucosal surface of the uterus may be destroyed; therefore, ovulation and gestation are almost impossible. This is especially apparent in lymphogenous leukemia.

Although the occurrence of leukemia has been reported in newborn infants,<sup>10</sup> there is no evidence that leukemia is an hereditary disease. Cameron<sup>11</sup> calls attention to the efficacy of the placenta as a barrier in keeping the leukemic cells from entering the fetal circulation. Burchenal<sup>12</sup> has been unable to transmit leukemia from the diseased mouse to its offspring. The fear of the leukemic mother having a leukemic child is no indication for termination of the pregnancy.

The deleterious effects of irradiation on the fetus have been pointed out by Rolleston,<sup>13</sup> Murphy, Shirlock and Doll.<sup>14</sup> Angelucci<sup>2</sup> advocates the use of a solution of potassium arsenite (Fowler's solution) in pregnant leukemic women, resorting to roentgen irradiation over the long bones, spleen and mediastinum only when the former medication is no longer effective. The fetus is not exposed to the irradiation by this means.

#### SUMMARY

The co-existence of pregnancy in 4 patients with chronic myelogenous leukemia has been reported. One patient was known to have had chronic myelogenous leukemia 3 years prior to her pregnancy. The diagnosis of leukemia was made during the course of pregnancy in the remaining 3 patients; 1 in the first trimester, the other 2 in the third trimester. No specific therapy was required in any of the patients during pregnancy. Their children at birth showed no stigmata of leukemia.

Current literature on the subject has been reviewed. The consensus is that pregnancy does not influence the prognosis of chronic myelogenous leukemia. During the period of gestation, the symptoms can be controlled by administration of a

solution of potassium arsenite (Fowler's solution) and irradiation therapy over long bones, spleen and mediastinum without exposing the fetus.

## REFERENCES

- <sup>1</sup> VIGNES, H.: Leucemie et grossesse. *Presse méd.* 47: 1460, 1939.
- <sup>2</sup> ANGELUCCI, H. M.: Myelogenous leucemia complicating pregnancy. *Am. J. Obst. & Gynec.* 48: 125, 1944.
- <sup>3</sup> KOSMAK, G. W.: Splenic leucemia associated with pregnancy. *Am. J. Obst. & Gynec.* 1: 485, 1921.
- <sup>4</sup> GRIER, R. M., AND RICHTER, H. A.: Pregnancy with leucemia; case report and review of literature. *Am. J. Obst. & Gynec.* 37: 412, 1939.
- <sup>5</sup> KAPLAN, I. I., AND CONNERY, J. E.: Pregnancy in the course of leukemia. *Am. J. Med. Sc.* 183: 209, 1932.
- <sup>6</sup> FORKNER, C. E.: Leucemia and allied disorders. New York, Macmillan Co., 1938.
- <sup>7</sup> MCGOLDRICK, J. L., AND LAPP, W. A.: Leucemia and pregnancy. A case report and review of literature. *Am. J. Obst. & Gynec.* 46: 711, 1943.
- <sup>8</sup> MOLONEY, W. C., HEFFERNAN, R. J., AND KASDON, S. C.: Leucemia in pregnancy. *J. A. M. A.* 122: 1170, 1943.
- <sup>9</sup> HOCHMAN, A.: Leukaemia and pregnancy. *J. Obst. & Gynec. Brit. Emp.* 51: 231, 1944.
- <sup>10</sup> MORRISON, M., SAMWICK, A. A., AND RUBINSTEIN, R. I.: Congenital leukemia with "chloroma." *Am. J. Dis. Child.* 58: 332, 1939.
- <sup>11</sup> CAMERON, J. C.: Influence of leukaemia upon pregnancy and labor. *Am. J. Med. Sc.* 95: 28, 1888; 100: 479, 1890.
- <sup>12</sup> BURCHENAL, J. H.: Experimental studies on relation of pregnancy to leukemia. *Am. J. Cancer* 39: 309, 1940.
- <sup>13</sup> ROLLESTON, H.: Critical review: The harmful effects of irradiation (x-rays and radium). *Quart. J. Med.* 23: 101, 1930.
- <sup>14</sup> MURPHY, D. P., SHIRLOCK, M. E., AND DOLL, E. A.: Microcephaly following maternal pelvic irradiation for the interruption of pregnancy. *Am. J. Roentgenol.* 48: 356, 1942.