CASE REPORT

Chronic Granulocytic (Myelogenous) Leukemia and Pregnancy

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WE HAVE RECENTLY had the opportunity of observing a case of chronic granulocytic (myelogenous) leukemia which underwent a rapid and dramatic transition from a stage of remission to an acute fulminating myeloblastic exacerbation coincident with pregnancy. This striking change prompted us to re-evaluate the effect of pregnancy on the patient with chronic granulocytic leukemia. A critical review and analysis of the literature indicates that pregnancy shortens the average life expectancy of a definite proportion of such patients.

CASE REPORT

This was the third and final admission on October 22, 1951 of M. F., a 20 year old Puerto Rican female. Her present illness apparently began in the summer of 1949, twenty seven months prior to this, when she first noticed a large solid swelling in the left side of her abdomen. One year later, in June 1950, the patient was hospitalized at another institution because of weakness, weight loss, periods of amenorrhea and gingival bleeding. A diagnosis of chronic granulocytic leukemia was established at that time, and she was given x-ray therapy.

The patient was first admitted to the Flower and Fifth Avenue Hospitals on July 19, 1950. The diagnosis of chronic granulocytic leukemia was confirmed (table 1), and she was started on 1 Gm. of urethane by mouth three times a day. She was discharged subjectively improved on this medication on August 30, and followed in the out-patient department.

She was readmitted on December 11 for the purpose of considering the advisability of radiation therapy. The patient had remained essentially the same since her previous discharge, save for increasing splenomegaly. The urethane was discontinued and the patient discharged on December 15. Radiation therapy was started one week later on an ambulatory basis.

The patient was then seen infrequently until the final admission, when she came to the hospital complaining of progressive anorexia, fatigue, insomnia, "feverishness" and increasing swelling of her abdomen of five weeks' duration. At this time she also stated that she was pregnant, having had her last menstrual period on May 20, 1951.

Past History

She had an illness consisting of recurrent chills and fever for about one month in the summer of 1948, and a purulent infection of the small toe of the left foot in 1949. Past history was otherwise noncontributory.

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Physical Examination

The patient was an emaciated, pale olive-skinned, small boned, female who appeared chronically ill. Her blood pressure was 105/60, pulse 120 with occasional premature beats, respirations 36 and temperature 100.4 F.

Her mucous membranes and conjunctivae were pale, and several teeth were missing. There were several firm pea-sized lymph nodes palpable in the left posterior cervical triangle, and a few larger nodes in each axilla.

The lungs were clear to percussion and auscultation, but there was a harsh systolic murmur over the entire precordium, heard best at the apex. The breasts were tense and enlarged, and showed increased areolar pigmentation.

The edge of the liver was palpated four finger-breadths below the right costal margin. The spleen was firm and enlarged to the midline and below the left iliac crest. The fundus of the uterus was palpated at the level of the umbilicus, and the findings of an active fetus with a fetal heart rate of 150 per minute, confirmed a gestation of approximately five and one-half months.

TABLE 1.—*Hemograms of Patient*

			Treatment: Urethane and x-ray							Pregnancy					
	7/24/50	7/31	8/29	10/6	12/16	12/29	1/12/51	2/8	4/17	7/17	10/23	10/29	11/2	11/5	11/10
Hemoglobin, %	52	55	53	57	52	63	52	64	61	60	25	36	54	43	31
R. B. C. (in millions)	2.74	2.85	2.54	2.92	2.8	3.2	2.85	3.4	3.46	3.6	1.62	1.58	—	—	—
W. B. C. (in thousands)	720	650	208	189	120	42.4	19.2	8.6	9.5	5.3	36	4.9	4.8	4.2	2.8
Neutrophils (segmented)	19	40	48	53	52	47	68	68	70	86	4	4	4	—	
Neutrophils (nonsegmented)	15	10	17	8	5	13	14	—	—	—	3	1	5	—	
Eosinophils	5	—	1	2	2	2	2	3	8	—	—	1	—	—	
Basophils	—	4	2	—	2	4	1	—	—	1	—	1	—	—	
Myelocytes	35	38	31	18	19	28	10	4	—	—	3	7	3	—	
Myeloblasts	20	4	—	2	—	2	—	1	—	—	81	64	81	—	
Lymphocytes	6	4	1	9	17	2	5	22	22	12	9	22	7	—	
Monocytes	—	—	—	8	3	2	—	2	—	1	—	—	—	—	
Platelets (in thousands)	190	—	—	—	350	—	385	130	260	140	55	100	80	50	

Hospital Course

Hematologic examination disclosed a leukocyte count of 36,000 with marked predominance of myeloblasts. Bone marrow aspiration revealed a markedly hypercellular marrow consisting almost entirely of myeloblasts and "stem cells." On October 26, daily intravenous infusions of urethane were begun along with small, carefully administered blood transfusions.

During the first week of hospitalization, the patient's condition remained unchanged, except for several episodes of mild epistaxis, gingival bleeding, and the appearance of purpuric spots on her arms. However, after ten days, she began to complain of shortness of breath, coughing, pain in the abdomen, and pain in her arms and legs. The patient became increasingly restless, and died on November 11, 1951.

DISCUSSION

Although chronic granulocytic leukemia is quite common, case reports of its coexistence with pregnancy are infrequent. This unexplained paradox has limited analysis of the effect of pregnancy on the disease and has led to conflicting conclusions. Thus, Grier and Richter[1] state, "The course of the disease in the chronic

TABLE 2

Case	Author	Year	Age	Relation of Onset to Gestation	Duration of Gestation	Death of Mother Postpartum	Total Duration of Disease
1	Jaggard[2]	1890	?	6th month	Term	11 months	14 months
2	Jürgens[3]	1938	27	6th month	8 months	2 hours	12 weeks
3	Erf[4]	1938	33	10 months prior	7-7½ months	7 months	24 months
4	Erf[5]	1941	21	Near term	Term	16 months	17 months
5	Erf[5]	1941	38	Near term	Term	12 months	13 months
6	Bates[6]	1941	38	8 months prior	Term	5 months	22 months
7	Moloney[7]	1942	32	2nd month	Term	Living 2 weeks +	—
8	McGoldrick[8]	1943	31	9 months prior	Term	Living 6 months +	—
9	Angelluci[9]	1944	22	4th month	Term	—	—
	(Erf)[10]			12 months prior	Term	8 months	29 months
10	Hochman[11]	1944	25	22 months prior	2 months	4 months	28 months
11	Hochman[11]	1944	23	18 months prior	Term	10 months	37 months
12	Holmgren[11]	1944	40	18 months prior	Term	Living 14 months +	—
13	Miles[11]	1945	30	6 months prior	Term	Living 4 months +	—
14	Miles[11]	1945	30	Prior	8 months	Living 13 months +	—
15	Wolff[12]	1946	21	6 months prior	Term	Living 6 months +	—
16	Erf[10]	1947	25	4 months prior	Term	4 months	17 months
17	Li[13]	1947	27	5 years prior	Term	Living 6 months +	—
18	Li[13]	1947	36	6th month	Term	Living 3 years +	—
19	Li[13]	1947	20	8th month	8 months	24 months	24 months
20	Li[13]	1947	22	Term	Term	Living 1 month +	—
21	Williams[11]	1948	27	7th month	Term	Living 1 year +	—
22	Slentz[3]	1948	25	7 months prior	3 months	—	—
				23 months prior	3 months	6 months	30 months
23	Slentz[3]	1948	25	Near term	Term	23 months	23 months
24	Slentz[3]	1948	23	18 months prior	Term	7 weeks	30 months
25	Shub	1952	20	22 months prior	5 months	5th month pregnancy	27 months

cases (myelogenous leukemia) was about the same as that commonly stated when pregnancy was not involved." In the same paper, however, one also finds

the following statement, "In the chronic forms (of leukemia) pregnancy should be avoided, because of the acute exacerbations which occur at the time."

With our review of the literature, plus the case herein presented we found a total of 53 cases of coexistent pregnancy and chronic myelogenous leukemia. In only 25 of the 53 cases are sufficient data available regarding the apparent onset of the leukemia in relation to conception and survival after pregnancy.

TABLE 3

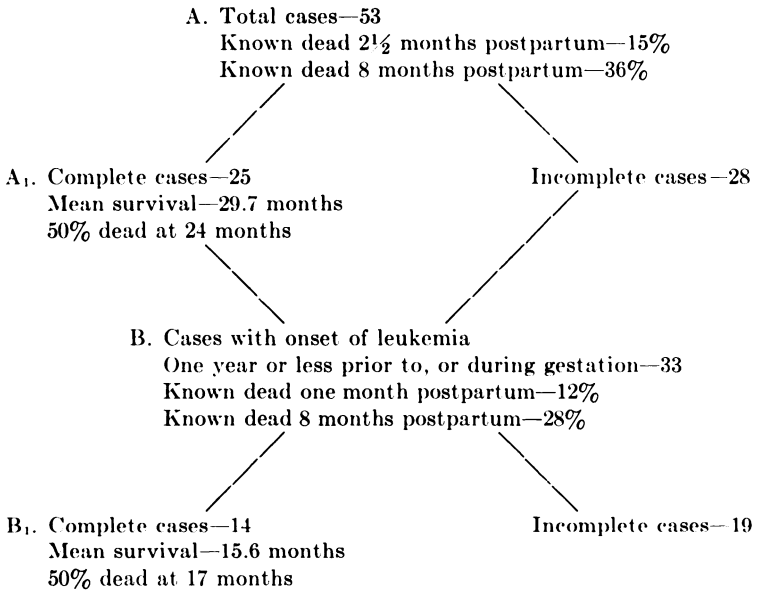

TABLE 4

Series	Months	
	50% Dead	Mean Survival
Shimkin et al.	36	39.6
* S.-B.-S.—A_1	24	29.7
S.-B.-S.—B_1	17	15.6

* Present series (Shub, Black, and Speer)

Of these 25 cases, 10 were obtained from Grier and Richter's total of 28[1] and 15 from the 25 in table 2. The 25 cases with adequate available data, are referred to here as the complete cases (A_1 table 3). In order to evaluate the data in table 3 more properly, we have compared them to data derived from the paper by Shimkin et al.,[14] who analyzed the incidence, distribution and fatality of chronic granulocytic leukemia from 1910 to 1948. The comparison of these two groups of data is shown in table 4. Since Shimkin et al. limited their analysis to those cases followed from onset of the disease to death, comparison with our complete

cases is consistent. Their analysis includes untreated cases as well as those treated by various methods available at the time, and the calculated mean survival excludes the small minority of cases which lived ten years or more.

As previously stated, the coexistence of pregnancy and leukemia is rare. Among the possible causes of this infrequency is the tendency of leukemia to induce alteration in ovarian function as evidenced by amenorrhea. This occurred in our own case while the disease was only moderately active. In view of the probability that the patient who is seriously ill with leukemia would not be expected to become pregnant, those cases in which pregnancy and leukemia were found to coexist more probably represent a group of women who were in remission or whose disease was quiescent. Patients with chronic leukemia undergo slow progressive debilitation before death, a process which may take six months or more and tends to be gradual. We have found that an acute transition from a stage of remission to acute exacerbation and death is unusual. In our case, apparently coincident with pregnancy, just such an acute process occurred with a well defined myeloblastic picture in the peripheral blood and bone marrow.

That this case was not unique in showing a rapid demise after becoming pregnant is evident by an examination of data from the literature. Eight of the 25 complete cases or a minimum of 15 per cent of the total cases (53) were known to be dead within two and one-half months postpartum. This is an unusually rapid death rate for cases who must have been in a relatively quiescent state at the time of conception.

Since the previous duration of the leukemia might influence subsequent survival with or without coexisting pregnancy, it was pertinent to evaluate the survival in a group of cases of only limited duration before the advent of pregnancy. To this end we have separately analyzed those cases wherein the diagnosis of leukemia was made one year or less prior to, or during pregnancy (B, table 3). This group consisted of 33 cases, of which the total duration of the disease was known in 14. (B_1, table 3). Despite the fact that these cases were of relatively short duration before the advent of pregnancy and should have been in generally good health as indicated by their ability to become pregnant, their total survivals are decidedly sub-average. Thus, the mean survival of group B_1 was only 15.6 months as compared to the mean survival of 29.7 months in group A_1. This contrast is even greater when compared to the mean survival of 39.6 months found by Shimkin et al. in their analysis where pregnancy was not a factor. In addition it should be noted that whereas 50 per cent of our cases in group B_1 were dead in 17 months, Shimkin's data reveals that 36 months were required to attain a 50 per cent death value. Thus, it appears that the group B_1 cases are mainly responsible for the contrast in data between the 25 complete cases (A_1) and those of Shimkin et al. as seen in table 4.

The effect of pregnancy on the course of the leukemia is also apparent in the postpartum survivals of this group of cases (B). Thus, 4 of the 14 complete cases or approximately 12 per cent of the total 33 cases are known to be dead in less than one month postpartum. Within eight months postpartum, 9 of the 14 complete cases (B_1) or a minimum of 28 per cent of the total group B are known to

be dead. Since this postpartum mortality is similar to that found for the entire series eight months postpartum (36 per cent of 53 cases, Group A), it is evident that the reduced postpartum survivals are not merely the result of the chance occurrence of pregnancy in leukemic cases having a previously long duration wherein one would expect only a limited subsequent survival. In contrast, the data indicate that the occurrence of pregnancy is of far greater importance in limiting subsequent survival than the previous duration of the leukemia. If anything, the data listed in table 4 would suggest a greater deleterious effect of pregnancy on those cases of shorter duration.

Our findings indicate that approximately one-third of the cases of chronic myelogenous leukemia complicated by pregnancy will be dead within 8 months postpartum. Since these deaths are unrelated to the previous duration of the disease, they must therefore be attributed to the adverse affect of pregnancy on the leukemia.

Summary

1. An additional case of coexistent pregnancy and chronic granulocytic (myelogenous) leukemia is reported.

2. Coincident with pregnancy the leukemia in this patient underwent a transition from the chronic phase in remission to acute myeloblastic disease with rapid exitus.

3. The pertinent literature concerning pregnancy and chronic granulocytic leukemia has been reviewed and evaluated.

4. Our findings indicate that pregnancy may have a deleterious effect on the course of the patient with chronic granulocytic leukemia, and may initiate an acute exacerbation of the disease.

5. In approximately one-third of the cases of chronic granulocytic leukemia complicated by pregnancy, an exacerbation and death occurred within eight months postpartum.

6. In chronic granulocytic leukemia, pregnancy should be avoided.

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