PERSISTENT NEUTROPHILIC LEUKOCYTOSIS ASSOCIATED WITH IDIOPATHIC FUNCTIONAL ASPLENIA

Richard P. Spencer, Peter McPhedran, Stuart C. Finch, and Walter S. Morgan

Yale University School of Medicine, New Haven, Connecticut

Persistent neutrophilic leukocytosis of unknown cause can be a troublesome diagnostic problem. Such a leukocytosis suggests occult inflammatory or neoplastic disease, or an incipient myeloproliferative syndrome. In some patients, however, none of these conditions emerge, even after prolonged observation. Ward and Reinhard recently described a group of 32 such patients followed over a 20-year period and referred to the hematologic finding as "chronic idiopathic leukocytosis" (*1*). These authors expressed the view that the high white counts were "normal" for their patients although they were outside 95% confidence limits for the general population. Recently we have had under observation a patient with neutrophilic leukocytosis of at least 11-year duration. Our patient's leukocytosis appears not to be a normal variant but rather the consequence of a specific organ dysfunction, functional asplenia. This mechanism may have to be considered in other patients with persistent neutrophilic leukocytosis of unknown cause.

CASE REPORT

The patient is a 41-year-old white, married nurse who has been followed since September 1970 for persistent leukocytosis, chorioretinitis, and hypertension. Unexplained leukocytosis was first noted in 1960 when her white count was 30,000 (see Table 1) during an episode of dermatitis treated briefly with prednisone. Mild hypertension also was noted at that time. In 1962 she had a transient episode of blurred vision lasting several weeks which resolved without treatment. In 1964 her white count was recorded as 24,900 on hospital admission for surgery for bilateral ovarion cystadenomas (left salpingo-oophorectomy and partial right oophorectomy). In 1969 her white count was 30,000 at the time of consultation with an ophthalmologist for recurrence of blurred vision. Chorioretinitis was diagnosed and treatment consisted of a 3-week course of dexamethasone. In July 1970 blurred vision again recurred and a 1-month course of dexamethasone was given again. On August 5, 1970, she consulted an internist who found a white count of 31,600 as well as hypertension. The visual blurring had cleared, and the dexamethasone was stopped. Her white count remained elevated, however, and she was admitted to the Yale-New Haven Hospital on September 28, 1970.

On physical examination, she was a mildly obese woman in no physical distress but suffering from moderate anxiety. She was normotensive and afebrile. The only abnormalities were ocular fundus changes of Grade II hypertensive retinopathy and a healed, midline sub-umbilical scar. Her hematocrit was 45, platelet count 660,000, and white count 16,200 with 62 segmented neutrophils, 8 bands, 2 eosinophils, 19 lymphocytes, and 9 monocytes. Occasional target cells and giant platelets were noted. About one Howell-Jolly body per five oil immersion fields was seen. Repeat white counts on this admission were 26,200 and 22,600, and the platelet count was 500,000. Reticulocyte count was 2.4%. Leukocyte alka-

Received Nov. 4, 1971; original accepted Nov. 14, 1971.

For reprints contact: Richard P. Spencer, Yale University School of Medicine, 333 Cedar St., New Haven, Conn. 06510.

TABLE 1. SERIAL LEUKOCYTE DETERMINATIONS

Year	Leukocytes/mm³ × 10³ Total	Neutrophils*	Lymphocytes	Monocytes	Eosinophils
1960†	30.0+	—	—	—	—
1964	24.9	16.9	5.5	1.5	1.0
1969†	30.0	—	—	—	—
1970†	31.6	26.9	3.5	1.3	—
	20.5	—	—	—	—
	16.2	11.3	3.4	1.5	0.3
1971	18.5	14.1	3.9	0.6	—

* Normal range: 1.8–7.7.
† Associated with corticosteroids.

line phosphatase score was 84 Kaplow units (normal 13–130). Bone marrow was moderately hypercellular with a normal myeloid-erythroid ratio and slight increase in megakaryocytes. Serum uric acid was 6.4 mg%. Indirect fluorescent antibody titer for toxoplasmosis was 1:256 ("possible" toxoplasmosis) (*2*). Urinalysis, stool benzidine, electrolytes, liver function tests, haptoglobin, G6PD, and a search for Heinz bodies after heating of red cells were all normal or negative. An IVP showed irregularities in the outline of the right kidney suggestive of old pyelonephritis.

The rather unusual finding of occasional Howell-Jolly bodies in the red cells of the peripheral blood led to the request for a splenic scan, for the purpose of evaluating spleen size and function. The technique consisted of the intravenous administration of 1 mCi of ^{99m}Tc-sulfur colloid followed by an abdominal scan in 30 min. The spleen was not visualized either by posterior or anterior scan (Fig. 1).

Repeat indirect fluorescent antibody tests for toxoplasmosis in January 1971 remained at 1:256. In the year since hospital discharge the leukocytosis and thrombocytosis have persisted.

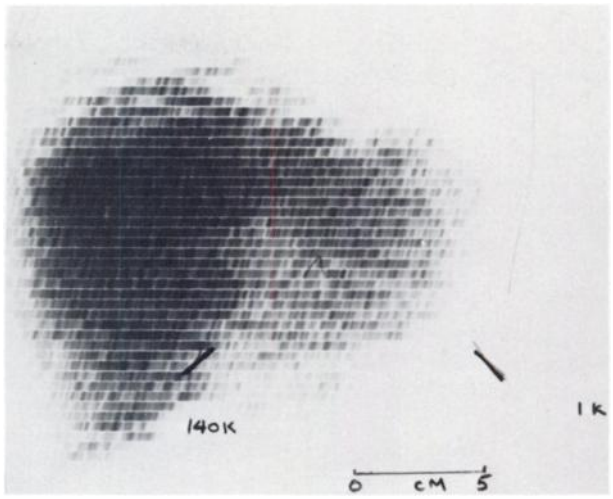

FIG. 1. Anterior abdominal scan, following intravenous administration of ^{99m}Tc-sulfur colloid. By 140 K is meant that liver showed 140,000 cpm. Splenic area revealed 1,000 cpm which was equal to general background. In addition, no splenic tissue was visualized on posterior view.

DISCUSSION

The mechanism responsible for persistent leukocytosis in our patient would appear to be splenic dysfunction, either as a consequence of an acquired disease or a congenital absence of the spleen. The concomitant finding of thrombocytosis, Howell-Jolly bodies in the red cells and nonvisualization of the spleen on technetium-sulfur colloid scan all support this conclusion. Alternatively, a myeloproliferative state such as chronic granulocytic leukemia could account for the patient's leukocytosis. However, the absence of splenomegaly, the long duration of the leukocytosis without significant change, the absence of immature granulocyte forms from the blood, and the normal leukocyte alkaline phosphatase are against this diagnosis. Chromosome studies would have been desirable but were not obtained at the time of the initial marrow examination, and the patient has refused further study. The possibility that our patient's leukocytosis has been due to drugs must also be raised. Corticosteroids may have contributed to elevation of the white counts of 1960, 1969, and July 1970, but do not alone cause this degree of leukocytosis and were not involved in the leukocytosis observed at other times. Neither hypertension nor chorioretinitis are likely to be associated with marked neutrophilic leukocytosis. Toxoplasmosis, a possible cause of the chorioretinitis in this patient, may cause lymphocytosis or eosinophilia but not neutrophilia (*3*).

Absence of the spleen after surgery can cause persistent neutrophilic leukocytosis. Lipson and coworkers observed the hematologic changes in 105 individuals splenectomized at the Mayo Clinic for followup periods of 4 months to 11½ years (*4*). Leukocytosis was present in 35% and thrombocytosis in 29% of followup determinations. Most of the white counts were in the range of 10,000–15,000, but counts as high as 22,500 were recorded. Neutrophilia was recorded in 14% of followup counts. Lymphocytosis, monocytosis, and eosinophilia were more common.

Functional asplenia, as defined by the inability of the reticuloendothelial system to accumulate a radioactive colloid, has been described in sickle cell anemia and a variety of other disorders (*5,6*). In our patient, however, the etiology of the functional asplenia remains obscure. Splenic infarction due to splenic artery thrombosis is one possible cause. If this is the cause of her leukocytosis, it has occurred outside of the usual settings. There is no history of trauma to the area, no underlying hypercoagulable state, and the patient has not had peripheral vascular thrombosis.

Although the cause of functional asplenia in our patient remains obscure, we believe this mechanism of leukocytosis deserves consideration in patients such as those reported by Ward and Reinhard. Platelet count and a careful search for Howell-Jolly bodies should be performed, and spleen scan strongly considered in all such patients.

SUMMARY

Persistent neutrophilic leukocytosis in association with idiopathic functional asplenia is described in a

40-year-old woman. It is suggested that a search for evidence of functional asplenia be undertaken in patients with persistent, unexplained leukocytosis.

ACKNOWLEDGMENT

This work was supported by USPHS CA06519, CA11106, HE05316-10; and by T-492A from the American Cancer Society.

REFERENCES

1. WARD HN, REINHARD EH: Chronic idiopathic leukocytosis. *Ann Intern Med* 75: 193–198, 1971

2. MILLER LH, BROWN HW: The serologic diagnosis of parasitic infection in medical practice. *Ann Intern Med* 71: 983–992, 1969

3. CONRAD ME: Hematologic manifestations of parasitic infections. *Sem Hematology* 8: 267–303, 1971

4. LIPSON RL, BAYRD ED, WATKINS CH: The post-splenectomy blood picture. *Amer J Clin Path* 32: 526–532, 1959

5. PEARSON HA, SPENCER RP, CORNELIUS EA: Functional asplenia in sickle cell anemia. *New Eng J Med* 281: 923–926, 1969

6. SPENCER RP, PEARSON HA, BINDER HJ: Identification of cases of "acquired" functional asplenia. *J Nucl Med* 11: 763–766, 1970