EOSINOPHILIC LEUKEMIA

REPORT OF A CASE WITH AUTOPSY CONFIRMATION; REVIEW OF THE LITERATURE

By Theodore S. Evans, M.D., and Robert R. Nesbit, M.D.

IT IS FORTUNATE for the orderly and steady progress of medicine that there is, in the profession, a large group of observers slow to accept what is new and unproven; and so it has been true that as each form of leukemia has been described, there has always been a fairly large number of "doubting Thomases." This was true when the cleavage between myeloid and lymphoid leukemia was first asserted by Neumann in 1870 and proven by Naegeli and others in 1900. The description by Schilling of a third type of leukemia was greeted by a storm of protest; and the existence of monocytic leukemia is still denied by able and thoughtful observers some thirty-five years after Schilling's original contribution. The existence of basophilic leukemia was first predicated by Joachim in 1906, and more recently studies have appeared by Doan, Groat and others.

Individuals with leukemia showing a marked peripheral eosinophilia have been studied intensively by many workers. In 1912 Stillman described such a case, but many later observers have denied that this was a case of true leukemia. Our own studies indicate that this was probably the first reported case of chronic myeloid leukemia with marked eosinophilic predominance.

We have been impressed in the study of the subject by the following facts:

1. There are comparatively few reports of cases of eosinophilic leukemia, and its occurrence must be quite rare.
2. Many of the reported cases are lacking in essential data as to the maturity of the eosinophils in the peripheral blood, and their descriptions are often inadequate.
3. While many of the case reports include autopsy material, only a small number present evidence regarding the state of the bone marrow during life.
4. In only rare instances have the results of serial bone marrow studies been recorded.

If we accept as a fact that the normal definitive eosinophil is derived from the myeloblast via maturation stages in the bone marrow, then it would seem to be of value to report a case in which studies of both the blood and of the bone marrow showed at first a preponderance of mature eosinophils with later a gradual left shift until finally, myeloblasts replaced a large proportion of the granular cells in both marrow and blood. Hay and Evans, and Thomsen and Plum have reported such instances and have commented upon the value of such information. In our own case of acute eosinophilic leukemia, serial bone marrow examinations and blood films were studied over a period of three months, during which time the gradual change from mature eosinophils through eosinophilic myelocytes to
myeloblasts was evident. While it is impossible to prove that eosinophilic leukemia is a separate and distinct disease entity, paralleling in its life cycle the other well-established types, we believe, however, that the evidence presented adds strongly to previously accumulated data in support of this assumption.

Shapiro in 1919 reported a case of acute eosinophilic 'leukemia,' as did MacDonald and Shaw in 1922, whereas most of the earlier observers referred to their cases as coexistent eosinophilia and hyperleukocytosis, suggesting that the syndrome may be merely a variant of myeloid leukemia. On the other hand, McGowan and Parker, Stephens, Friedman et al., Thomsen and Plum and others hold that it is a disease entity. At this time there are many proponents of both points of view, and no general agreement has been reached.

REPORT OF A CASE

A. G., a 53-year old white female was admitted to the Hospital of St. Raphael* on June 26, 1946, and died on September 7, 1946.

For approximately five years prior to admission, the patient suffered periodically from itching 'lumps' on the legs. She had been treated with various ointments. These itching, subcutaneous lesions would disappear for long periods. In the summer of 1946 they had become fairly widespread and constant, and the patient was admitted to the hospital for study. In addition to these itching lumps, she complained of recurring attacks of bronchitis and upper respiratory infections which had been noted for many years. The rest of the systemic history was essentially negative. She had lost no strength or weight and slept well except for the pruritis.

Examination revealed an obese, poorly developed woman with rather flabby musculature. The skin was widely and deeply excoriated from scratching so that most of the lesions were almost unrecognizable, but a few relatively recent ones were found. The patient stated that they first appeared as lumps beneath the skin which later reached the surface and became red and itchy. Deep-seated masses were found in areas where there was no superficial redness and which did not itch, and other lesions which had reached the surface and had become red and itchy. The masses were rather firm. There was no lymphadenopathy.

The moderate fever was assumed to be due to the sepsis from scratching of the skin and consequent infection.

Four days after admission, clinical and roentgen ray evidence of broncho-pneumonia was found at both bases. She was treated with penicillin and a favorable response occurred, but during the ten weeks in the hospital, four similar episodes of fever and lung signs appeared, each of which she survived.

A dermatologist concluded that dermatitis herpetiforme was present. Treatment was ineffective.

A biopsy of the skin lesions gave no evidence of periarteritis nodosa, but mature eosinophilic granulocytes were seen in large numbers, particularly surrounding the blood vessels.

Because of the finding of anemia without any obvious bleeding, a hematologic survey was performed early in July. By this time, there was some enlargement of the lymph-nodular system, and the tip of the spleen could be felt. The peripheral blood showed marked achromia, aniso- and poikilocytosis and increased polychromatophilia. Platelets appeared to be present in normal numbers. There was very marked leukocytosis, and about 15 per cent of all white cells were adult eosinophils. These were very large, multilobulated, and well-filled with large granules staining deep red with Wright's stain. Lymphocytes and monocytes appeared to be present in normal numbers, proportion and morphology. Sternal puncture showed numbers of active megakaryocytes. There was a marked reduction in the number of nucleated red cells. All stages of myeloid cells were identified, from myeloblasts to adult polymorphonuclear cells. The most unusual feature of this marrow was the very large proportion of eosinophils which made up a large part of the total number of white cells.

There was only a slight tendency toward left shift. The eosinophils were very large with polymorphous nuclei. The granules seemed somewhat larger than are usually seen and appeared to be grouped less

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*Service of Dr. William Dennehy.
evenly in the cells. The granules also had a tendency to irregular staining with a few cells containing both red and blue staining elements. The average number of granules in each cell was somewhat less than usual. These changes have been described in whole or in part in the cases of Stillman, Shapiro, MacDonald and Shaw, Hay and Evans, and Thomsen and Plum.

Erythropoiesis seemed to have been depressed by the very large concentration of adult eosinophils. The erythro-granulocytic ratio was 2-9.

Tests of the urine, stools, blood nonprotein nitrogen, blood sugar, blood calcium, serology, bleeding, clotting and clot retraction time were normal. The basal metabolic rate was +15 per cent. The erythrocyte sedimentation time was normal. All other causes of eosinophilia appeared to have been eliminated so that the hematologic impression was granulocytic leukemia with marked eosinophilia. There was a constant eosinophilia during the last eight weeks of life. This varied from time to time but was always beyond normal limits. Serial bone marrow studies showed a steadily increasing tendency toward left shift in the myeloid series. At first many myelocytes 'C' were identified in the eosinophilic series. With each succeeding examination of the bone marrow, more 'B' and 'A' eosinophilic myelocytes were seen and finally the bone marrow became strongly blastic in character. The final examination of the bone marrow performed on the day before death revealed a large percentage of myeloblasts with many early (immature) eosinophils.

The patient's condition slowly but definitely worsened with increasing fever, tachycardia, weakness and anorexia. The spleen and liver increased slowly in size, and death ensued on September 7, 1946. The clinical diagnosis of leukemia of the myeloblastic type with marked persistent eosinophilia, i.e., "eosinophilic leukemia" was made.

Postmortem examination was performed ten and three-fourths hours after death. The body was that of a well-developed, moderately obese, middle-aged female. The external body markings of import were marked pallor of the skin and mucous surfaces, superficial ulcerations of the lips, edges of the tongue and buccal mucosa, and a recently incised focus on the left side of the back, which appeared to be healing. No evidence of the skin lesions mentioned in the clinical note was seen.

The peritoneal cavity contained no fluid, but showed a mass of dense adhesions around the gallbladder. Pleural and pericardial cavities were free of adhesions. Pericardial fluid was normal.

Heart: 420 Gm. The viscus was markedly pallid. The arteries were slightly thickened, but their lumina were patent. Section of the myocardium showed slight gray streaking. The endocardium and valves showed nothing of gross note.

Sections showed a mild degree of infiltration of the epicardial fat by leukemic cells, including blast forms, myelocytes and young lobulated forms. Many of these were of the eosinophilic class. The myocardium showed no infiltration, and the cells and fibers were normal. There was no fractionating of fibers, and striations were normal. The endocardium appeared normal.

Lungs: Rt. 710 Gm.; Left 605 Gm. The two lungs were grossly similar, presenting dark purple-red

<table>
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<td>%</td>
<td>%</td>
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markedly subcrepitant bases, with meaty texture, and very pallid, slightly subcrepitant upper lobes. Section revealed markedly increased blood content in the bases, and frothy blood-tinged fluid in the remainder, including the smaller bronchi. No foci of consolidation were demonstrable.

Sections revealed an increasingly prominent leukemic infiltration from above downward. Sections of the upper portions showed moderate crowding of the vessels of the alveoli with cells of the leukemic infiltrate, but more marked was filling of the alveolar spaces with precipitated, pink-staining albuminous material, in which was a scattering of “heart failure” cells, some containing phagocytosed erythrocyte debris; and a few erythrocytes. Sections of the lower lobes revealed intense plugging of the capillaries, so much so that the walls of alveoli appeared to be composed of hyperchromatic cells, mostly round cell types, which are identifiable as blast and myelocytic forms. These were seen to be just outside of the alveolar epithelium, in markedly distended capillaries. The erythrocyte content of these capillaries was practically nil, so great was the plugging with the leukemic cells. In many instances there had been rupture of capillaries and adjacent walls of the alveoli, so that the alveolar spaces were completely filled with infiltrating leukemic cells and a moderate number of erythrocytes. Large foci were seen that represented confluent ruptured alveoli, with air-bubbles in the mass of blastic and myelocytic cells. Other fields showed compression of alveolar spaces by the leukemic cells in distended neighboring alveoli.

### Table I.—Bone Marrow. Differential Counts

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E. M. ratio approximately 1:9. 45% of the nucleated white cells were eosinophils, and most of these were adult cells. A few B and A eosinophilic myelocytes were seen.

45% of the total number of white cells were eosinophils, but there was a left shift throughout the myeloid series, including the eosinophilic strain.

On this examination there was seen to be a very marked left shift with the presence of 29% myeloblasts. In addition 38% of the eosinophils were myelocytes, and there were some cells in which both blue and red staining granules are identified. Many cells were seen in mitosis.

Spleen: 1235 Gm. This organ was greatly enlarged, and its capsule tense, and “ironed” out, but the consistency was of a tensely fluctuant nature rather than hard. When sectioned, the cut surface everted and rolled the stretched capsule back. The cut surface was predominantly gray in color, and the pulp, greatly increased, was essentially of gray color. To touch, this surface was greasy.

Sections revealed sinusoids packed with leukemic cells of the type already described, and large foci of acute necrosis, some of which could be seen to be splenic follicles. These foci contained neutrophilic polymorphonuclears and macrophages, in a mass of necrotic cells. Some other foci showed replacement fibrosis of these necrotic islands, this of varied age, some partly hyalinized, others with young fibroblasts proliferating in foci still showing some of the acute process. Besides the leukemic cells, there were, in the sinusoids, scatterings of macrophages containing engulfed cell fragments, and pigment. The endothelial lining cells were not remarkable except that they were generally flattened by the widely distended sinusoids.

Pancreas: 85 Gm. Grossly, the pancreas showed normal surface and section markings, and its duct appeared normal.

Sections showed infiltration, essentially perilobular, and in only rare instances was there any infiltration from the perilobular connective tissues into the gland itself. The capillaries contained the leukemic cells in large numbers, but they were noticeably absent from the parenchyma of the gland. The islet and alveolar cells appeared normal and retained normal staining reactions.
<table>
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<th>Author</th>
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<th>Range of eosins</th>
<th>Type of eosins</th>
<th>Organs affected</th>
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<td>Hay and Evans 1929, Case 1</td>
<td>41</td>
<td>weeks</td>
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<td>83*</td>
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<td>33</td>
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**Chronic Cases**

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<td>27</td>
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<td>6</td>
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<td>1</td>
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<td>90</td>
<td>62% Mature, Later 81% Myeloblasts</td>
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* Terminal
Fig. 1.—Liver section, showing the intense and essentially portal infiltration by the leukemic cells the resulting fatty degeneration; also pyknotic nuclei more centrally, and the fading into parenchymatous degeneration near the central vein which is seen to contain large numbers of hypochromatic cells with large nuclei, the leukemic cells. Phloxine hematoxylin. X 450, enlarged from 35 mm. film.

Fig. 2.—Kidney section, showing intense infiltration of the interstitial tissues, and at right the concentration of the infiltrating cells in the capillary about Bowman's capsule. The appearance of a round cell stroma is typical of all sections. Phloxine hematoxylin stain, enlarged from 35 mm. using X 450.
FIG. 3.—Smear of first bone marrow aspiration showing mature polynuclear neutrophiles, eosinophiles and late myelocytes.

FIG. 4.—Smear of third bone marrow aspiration showing many young cells and no mature polynuclears.
Gastro-intestinal tract: No gross abnormalities were noted. There were no foci of hemorrhage and no ulcerations. The lymphoid patches showed some swelling, but no ulceration.

Liver: 162 Gm. There was marked enlargement of the liver, which had a rounded edge, and a pale mixed yellowish-brown and white color, both on its capsular and cut surfaces. The cut surface bulged prominently and felt greasy. Markings were almost obliterated. No gross abnormalities of the biliary system were demonstrable.

Microscopically, there were two notable processes, both most marked in the portal zones of the lobules, and fading as the central zones were reached. These were an intense leukemic infiltration of the entire portal region, and a likewise intensely marked fatty degeneration of the hepatic cells. This was combined with moderate crowding of the sinusoids with the leukemic cells, though the latter was much less prominent than the portal infiltration. The cells of the liver cords were in varied stages of necrosis as well as fatty degeneration, and pyknotic nuclei and disintegrating cytoplasm were common. In the midst of the leukemic process, the bile capillaries stood out and appeared remarkably unaltered. No cirrhotic process was seen, and there was no bile duct proliferation. The vessels of the portal region all contained an excess of the leukemic cells as did the central veins. The cells nearest the central veins showed some parenchymatous degeneration but were comparatively well-preserved.

Gallbladder: In the ampullary region of the cavity was a partially impacted calculus, 1 cm. in diameter, composed of concentric layers of cholesterol and pigment about a pigment nucleus.

Adrenals: Rt. 7 Gm.; L. 6 Gm. Aside from marked autolysis of the medullae, the glands were not grossly remarkable. Sections showed very mild spotty infiltration in cortical and medullary zones. Aside from this and marked autolysis of the medullary cells, the glands were essentially normal.

Kidneys: Rt. 40 Gm.; L. 42.5 Gm. These two organs were similar in gross. They were large and pale. The capsules were free and stripped with ease. The external and cut surfaces were pallid and mottled, and the cut surfaces greasy. Markings were largely obliterated, but the cortico-medullary ratio was retained, though both were greatly increased in width.

Sections showed an intense infiltration of the interstitial tissues by leukemic cells. Of especial note was an intensely marked infiltration of the pericapilar region, apparently in the capillaries, with no similar distention of the capillaries of the glomerular tufts. The glomeruli stood out normally in the round cell background, with normal appearing subcapsular spaces surrounding them, and normal Bowman's capsules around the whole. The tubules, all classes, showed prominent parenchymatous degeneration. The interstitial tissues were so completely infiltrated that in many instances, normal tissues were invisible, or appeared fragmentarily in small foci. The infiltration extended to the places and calices, where it was seen just beneath the epithelium, the latter appearing normal.

Lymph nodes: All nodes were greatly enlarged, gray-white in color and tense but not hard. Their cut surfaces bulged prominently and were gray and greasy to sight and touch.

Sections revealed a process similar to that in the spleen with the exception of necrosis. Sinusoids were crowded with the leukemic cells, and the architecture of the nodes was destroyed by its intensity. The follicles were practically absent, and the nodes largely replaced by the leukemic infiltrate.

The bone marrow was abundant and almost white, but sections were not satisfactory, probably because of the long postmortem period before removal.

A clot in the pulmonary artery was used for Wright's staining and demonstrated the leukemic cells amply. The cells were essentially of the eosinophilic classes of myelocytes, with numerous blasts present, and a moderate number of mature forms in all classes. Of the mature forms, most were eosinophils and the remainder were neutrophils in their staining reaction. A few lymphocytes were seen.

The essential findings were leukemic in origin, being most marked in the liver, spleen, kidneys, lymph nodes and lungs. Other changes such as those of fatty degeneration of the liver were secondary to the process. Especially notable were the massive infiltrations of the lungs, the essentially portal infiltration of the liver, and the interstitial infiltration of the kidneys. The collection of the infiltrating cells in the pericapilar capillaries of the glomeruli was outstandingly prominent.

COMMENT

A complete search of some of the more recent literature has been impossible, since many of the foreign journals are not yet available. Only a few cases of eosino-
philic leukemia have been studied by means of both serial bone marrow spreads and postmortem material. The marrow studies in this case showed a progressive development of the leukemic process. In the earlier study, most of the eosinophils were adult cells. Gradually there was replacement of these mature granulocytes by younger forms (early eosinophilic myelocytes) and eventually a shift to blast cells. The early myelocytes contained both red and blue staining granules within the same cell. These have been noted before by MacDonald and Shaw, Hay and Evans in eosinophilic leukemia and by Doan and Reinhart in basophilic leukemia and have been considered to be evidence of "left shift." Additional evidence of left shift is seen in the presence of mitotic figures. The increasing number of young marrow cells appeared largely in the eosinophilic strain—from 15 per cent in the first study to 22 per cent and finally to 38 per cent. The same sequence of events was seen to a lesser extent in the peripheral blood where blasts to the number of 20 per cent appeared at one time. The finding of 45 per cent eosinophils in the peripheral blood of which 30 per cent were young eosinophil granule cells was made on one occasion.

The separation of eosinophilic leukemia from many other conditions which result in secondary eosinophilia in the peripheral blood is always difficult. Stewart has reviewed the literature on familial eosinophilia and Paviot and others, that on eosinophilia associated with malignant disease. Henschen has written a comprehensive review of the whole subject. Reports of eosinophilia with recurrent attacks of lung infiltration (Loeffler's syndrome) are becoming increasingly frequent in the literature. Although our patient had several attacks of "pneumonia" during the period of observation, there were too many clinical facts at variance with this condition, and the autopsy findings were too definitely conclusive of leukemia to place our case in that category. Periarteritis nodosa was also considered in the differential diagnosis of this case, but skin biopsy was negative for this condition, and postmortem examination did not support this diagnosis.

The diagnosis of eosinophilic leukemia may be initially and tentatively advanced on the persistent presence of a large percentage of eosinophils in the circulating blood. If a considerable and increasing number of these cells are eosinophilic myelocytes, reflecting predominance in the bone marrow, the evidence is still further supportive; and if the disease is fatal and there is invasion of all the organs by these abnormal cells as shown at postmortem examination, the diagnosis may be said to have been established. All of these criteria were present in our case, including the observation of the progressive left shift in the eosinophil granule myelocyte to the myeloblast which predominated terminally.

Doan and Reinhart have reported the presence of an acute dysfunction of the bone marrow, resulting in fulminating basophilic leukemia. They have called attention to the fact that immature "elements of the different cell strains may be present at the same time in the blood of a given patient." They have also noted the fact that both basophilic and eosinophilic granules were found in the same cell in basophilic granular cell leukemia but that the basophilic granules were present in larger proportion. Our case is similar in that both types of granules were present in individual cells but differs from theirs in that eosinophilic granules were preponderant. A further parallel to their cases is seen in the fact that our case also
showed "a left shift" to the primitive cells; however, our case progressed to the blastic phase through eosinophilic granule myelocytes, whereas theirs reached the ultimate state of myeloblastosis through basophilic granule myelocytes. Doan and Reinhart conclude that there is "an initial benign, perhaps metabolic disturbance in the granulopoietic equilibrium,—in the normal reciprocal relationships which seem to characterize the body cells in health,—to be followed sooner or later, especially in the later decades of life, by a very differently acting, invasive, metastasizing process much more closely related in clinical course and cellular pathology to the malignant hyperplasia and anaplasia which characterize tumor growths arising in other organs."

The total and proportional number of eosinophil granule cells in our case did not reach the extremely large numbers reported by some other observers, but it should be pointed out in this connection that this patient died in the acute stage of the disease. Death in other types of leukemia often occurs with low peripheral blood counts but with all other evidences of leukemia, and it has been assumed that this is so because the disease is fatal before a massive cellular response is seen in the blood.

**Summary**

1. The data in a case of fatal leukemia with predominant eosinophilia in the peripheral blood and bone marrow are presented; we believe that this case was one of eosinophilic leukemia.

2. During the period of observation, these eosinophils showed progressive immaturity as the symptoms became more severe. Eventually this "left shift" became so marked that a large proportion of the cells were terminally myeloblasts in both the blood and the bone marrow.

3. Autopsy revealed invasion of many of the tissues and organs with these mature and immature eosinophil granulocytes and with myeloblasts.

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**References**


DOAN, C.: Personal communication.


ET AL.: La eosinofilia massiva a tipo leucemoide de origen infeccioso y evolucion regressiva, comouna nueva. Bol soc. cubana de pediat. 15: 913, 1944.

WISMAN, B.: Personal communication.
EOSINOPHILIC LEUKEMIA: REPORT OF A CASE WITH AUTOPSY CONFIRMATION; REVIEW OF THE LITERATURE

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