BONE MARROW STUDIES IN HODGKIN'S DISEASE

WOODROW M. CAMPION, M.D.,* and LEMUEL W. DIGGS, M.D.**

Osseous involvement in Hodgkin's disease has been reported in numerous papers, with a varying percentage of cases showing typical bone lesions either by roentgenologic study or by microscopic examination of the pathologic tissue. In 172 cases studied, Craver and Copeland[1] found bone involvement in 15.7 per cent. Goldman[2] reported roentgenologic evidence of disturbances of the osseous system in 6.6 per cent of 212 cases. Lymphogranulomatous foci of the bone marrow were found in 11 of 14 cases of Hodgkin's disease examined by Steiner,[3] and in 7 of the 11 cases examined the sternal marrow was involved. It has been shown repeatedly that the bones containing active hematopoietic tissue, such as the vertebrae, sternum, pelvis, skull, and ribs, are most often affected.

Morrison and Samwick[4] reported bone marrow aspirations to be a diagnostic aid in 8 cases of Hodgkin's disease in which clinical signs and symptoms and routine blood examinations failed to be of assistance. They noted that the red cell mechanism showed slightly increased activity but that, on the other hand, there was an increase in reticulum cells and a moderate eosinophilia and increase in megakaryocytes. Varadi[5] was able to make the diagnosis of Hodgkin's disease by sternal puncture in 1 case. The aspirated material contained a mixture of blood, fat droplets, lymphocytes, and large cells with enormous nuclei, containing nucleoli, which were considered to be Sternberg cells. In the same case Sternberg cells were found on puncture of a lymph gland and also on histologic examination. X-ray examination of the sternum revealed no pathologic finding except for slight rarefaction.

Paraf *et al.*[6] reported a case of Hodgkin's disease with clinical and roentgenologic evidence of involvement of the sternum which could not be diagnosed by sternal puncture, as the repeated aspirations revealed hypoplasia of the bone marrow. In this case, Sternberg cells were abundant in biopsy studies of an involved lymph gland and also of cutaneous nodules.

Materials and Methods

In this paper are recorded the observations made at Cleveland Clinic on the bone marrow smears of 8 patients with Hodgkin's disease. The diagnosis was confirmed in all cases by biopsy of lymph nodes or by autopsy. All of these patients either had enlarged lymph nodes at the time of examination or gave a history of glandular enlargement during the course of their illness. Three patients had hepatomegaly and 4 had splenomegaly; 1 patient had both.

* *Medical Arts Clinic, Liberal, Kansas. Former Fellow in the Department of Medicine.*
** *University of Tennessee Medical School, Memphis, Tennessee. Formerly of the Department of Clinical Pathology.*

The temperatures of these patients varied from 99 to 104 F. at the time of their initial examinations. All gave a history of weight loss. One patient had regained and maintained his weight after having received x-ray therapy one year previously. Roentgenograms of the chest were made on all patients, and evidence of mediastinal disease or hilar gland enlargement was noted in four instances. Four patients had received x-ray therapy prior to the sternal punctures. The Wassermann and Kahn tests were negative in all patients. The peripheral blood picture varied in different patients but in all cases was consistent with the diagnosis of Hodgkin's disease.

The marrow preparations were made on coverslips from material aspirated from the sternal marrow. A minimal amount of marrow was aspirated in order to avoid dilution with peripheral blood. The smears were stained with Wright's stain. In making the differential count 200 or more cells were examined.

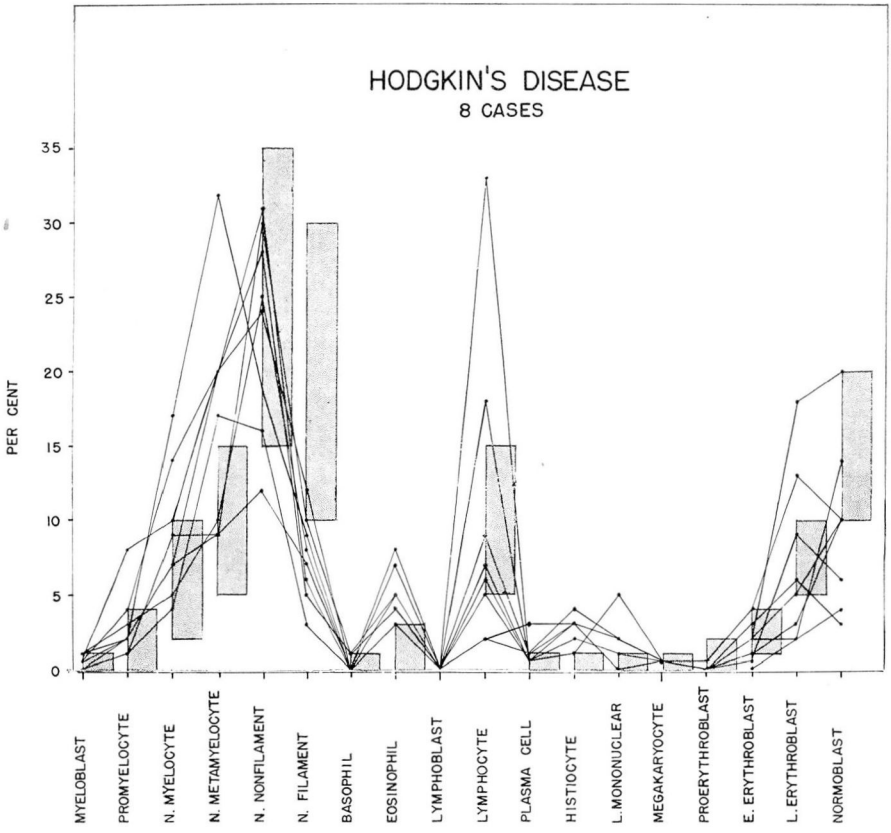

FIG. 1. Cell distribution in bone marrow smears. Normal range of variation represented by shaded areas.

The megakaryocyte counts were made, noting the number per 10,000 consecutive nucleated cells. The megakaryocytes were classified as megakaryoblasts, immature, intermediate, and mature megakaryocytes, or a naked nuclei. Twenty-five or more megakaryocytes were examined in each case.

Observation

The distribution of the various cell types in the 8 cases of Hodgkin's disease is graphically represented in fig. 1.

The sternal marrow was found to be cellular in 7 cases and hypoplastic in 1. This patient had received a large amount of x-ray therapy. There was a tendency toward a shift to the left in the myeloid series. There was an increase in eosinophils in 5 cases, and the level of these cells was at the upper limit of

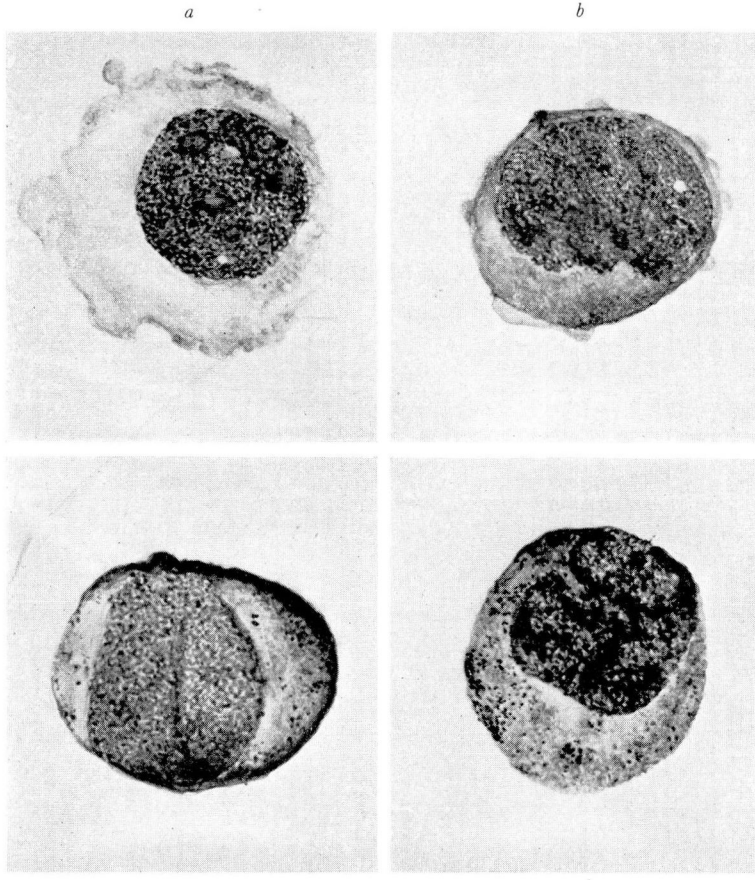

FIG. 2. Cell types found in the bone marrow, Hodgkin's disease. (a) Undifferentiated reticulum cell. (b) Early cell with indented nucleus and pseudopods. (c, d) Large atypical granular mononuclears.

normal in the other 3 cases. Basophils were rarely found. Lymphocytes were increased in 2 cases. Plasma cells constituted 3 per cent of the nucleated cells in 1 case but in the other 7 cases were 1 per cent or less. The mononuclear count varied from 1 to 5 per cent. Reticulum cells were slightly increased in all cases, the percentage varying from 1 to 4.

Atypical cells which were morphologically on the border line between reticulum cells, large mononuclears, and promyelocytes were demonstrable in all smears but usually constituted less than 1 per cent of the nucleated cells. These atypical cells were large, having a diameter greater than the usual myeloblast or promyelocyte. The shape of the nucleus varied from round to lobulated. The majority of cells were indented and had brain-like convolutions or folds. In most of the cells there was a well-defined, delicate chromatin

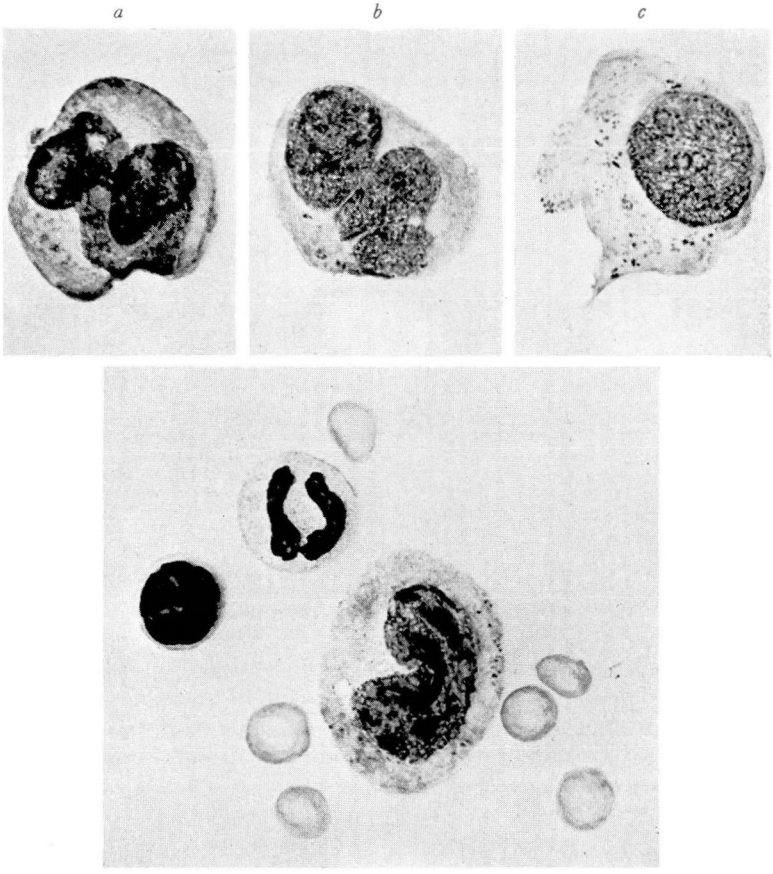

FIG. 3. Cell type found in bone marrow, Hodgkin's disease. (a, b) Atypical large mononuclears. (c) Histiocyte. (d) Atypical large mononuclear, showing size in relation to red cells, lymphocyte, and filamented neutrophil.

structure and nucleoli. In later and partially degenerate forms pyknosis was demonstrable. Although the nucleus was large the cytoplasm was also ample. The granules varied in size and distribution (figs. 2 and 3). Vacuoles and small multiple or large pseudopods were sometimes observed. Transition forms between the abnormal cells and undifferentiated reticulum cells, histiocytes, and mononuclears can readily be demonstrated.

Erythroid elements were within normal limits with the exception of 1 case in which they were present in decreased numbers. Megakaryocytes were considered to be moderately increased in the 7 cases counted (table). The megakaryocytes tended to be mature except in the case with purpura. Platelets appeared to be present in normal numbers, but in the case of purpura they were markedly decreased.

TABLE

MEGAKARYOCYTES IN BONE MARROW STUDIES

Case	Megakaryocytes per 10,000 nucleated cells	Differential Count			
		Immature	Intermediate	Mature	Naked Nuclei
1	29	4	28	52	16
2	23	0	8	8	84
3	18	0	16	76	8
4	14	0	5	65	30
5	35	4	12	84	0
6	28	0	5	75	20
7*	32	20	68	12	0
Normal	4–20	0–10	9–36	50–80	0–26

* *This patient also had purpura.*

Discussion

The greatest value of the bone marrow examination in diseases characterized by enlargement of the lymph glands is the differentiation of leukemia from other conditions. In monocytic or lymphoid leukemia there is a replacement of the marrow cells by monocytes or lymphocytes, some of which are immature. In myeloid leukemia there is predominance of early myeloid cells. In the leukemias the nucleated red cells and megakaryocytes are significantly decreased in the later stages of the disease.

Occasionally in sarcoma or other malignant diseases one may find diagnostic tumor cells in the bone marrow, but this is the exception rather than the rule. The bone marrow examination is of little value in differentiating Hodgkin's disease from tuberculosis and other chronic inflammatory diseases, for in these conditions there is also a hyperplastic marrow with a pleomorphic cellular reaction and atypical reticulum cells.

Summary

The bone marrow smears from 8 patients with Hodgkin's disease examined at Cleveland Clinic revealed fairly consistent abnormalities which, while not diagnostic, are considered to be of value in differential diagnosis and of confirmatory value in suspicious cases. The marrow is usually cellular and the myeloiderythroid ratio essentially normal. There is slight myeloid immaturity. The eosinophils, mononuclears, histiocytes, and sometimes the lymphocytes are slightly increased. Large, atypical cells characterized by folded, indented, or lobulated nuclei, early nuclear structure, and variable granularity are demonstrable. Megakaryocytes are present in increased numbers and are of mature variety.

References

1. Craver, L. F., and Copeland, M. M.: Changes in bone in Hodgkin's granuloma. Arch. Surg. **28**:1062-1086 (June) 1934.
2. Goldman, L. B.: Hodgkin's disease; analysis of 212 cases. J.A.M.A. **114**:1611-1616 (April 27) 1940.
3. Steiner, P. E.: Hodgkin's disease; incidence, distribution, nature and possible significance of the lymphogranulomatous lesions in bone marrow; review of original data. Arch. Path. **36**:627-637 (Dec.) 1943.
4. Morrison, M., and Samwick, A. A.: Clinico-hematologic evaluation of bone marrow biopsies. Am. J. M. Sc. **198**:758-773 (Dec.) 1939.
5. Varadi, S.: L'infiltration lympho-granulomateuse du sternum. Sur un cas de maladie de Hodgkin diagnostiqué par ponction sternale. Sang. **12**:106-110, 1938.
6. Paraf, J., Fischgold, H., Abaza, A., and Lewi, S.: Maladie de Hodgkin a localisation osseuse et cutanee (donnees de la ponction sternale). Sang. **13**:797-803, 1939.