The Importance of Bone Marrow Examination in Haematology

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Marrow biopsy was performed in 1903 by Pianese who punctured the epiphysis of the femur by a trocar. In 1908 Ghedini trephined the tibia in its upper third. Ghedini's method was employed for several years but it became evident that the tibia is one of the later bones to react to haemopoietic stresses. In 1923 Seyfarth trephined the sternum. The material obtained by this method can be used for preparing smears, wet preparations for supravital staining and blocks for sectioning. Sternal puncture which is simpler to perform than trephining was first proposed in 1927 by Arinkin. This method can be repeated at frequent intervals and is the method most widely used. In children the iliac crest is used.

Bone marrow biopsy is of great help in haematological work. It is of particular value in those disorders of the haemopoietic system in which no demonstrable changes are found in the peripheral blood and in those cases in which the peripheral blood changes are so slight that only very tentative conclusions can be drawn. In many disturbances of haemopoiesis marrow biopsy aids in prognosis and in the evaluation of therapeutic methods and it has contributed to elucidiation of pathogenesis and classification of certain diseases.

The value of bone marrow examination in different haematological disorders will be considered.

DEFICIENCY ANAEMIAS.

The diagnosis of the different types of deficiency anaemias can usually be made from the peripheral blood changes i.e. blood count and picture, red cell diameter Mean corpusclar volume, Mean Corpuscular Haemoglobin, Packed cell volume etc. Marrow biopsy helps to confirm the impressions gained from the peripheral blood investigations and acts as an index to effective therapy.

a) Macrocytic Anaemia. Pernicious Anaemia and other allied macrocytic anaemias are characterised by megaloblastic hyperplasia. Cells of the red cell series make up 30 to 50% of all nucleated cells instead of 20% or less. Most of the cells consist of promegaloblasts and different megaloblasts (basophilic polychromatophilic and orthochromic). These cells are of large size with delicate nuclear chromatin and deeply basophilic cytoplasm. Normoblasts are few in comparison to the megaloblasts. There is also abnormal leukopoiesis. Bizarre forms of metamyelocytes are frequent and these are associated with multisegmented polymorphs (macropolycytes).

Following effective liver or Vit B12 therapy the marrow picture alters with extraordinary rapidity. Within a few hours the typical megaloblasts are greatly reduced in number and their place is taken by normoblasts.

b) Microcytic Anaemias. In this type of anaemia the Bone Marrow differs fundamentally from that of Pernicious Anaemia. The Bone Marrow shows hyperplasia which is normoblastic in type. All stages of erythropoiesis are more numerous particularly polychromatophilic normoblasts with scanty irregular grey rim of cytoplasm. As the blood is restored to normal by iron therapy the cellularity of the marrow likewise becomes normal.

LEUKAEMIAS.

In leukaemias associated with a high leucocyte count marrow puncture is not of diagnostic importance as the peripheral blood changes are quite typical. It is in the diagnosis of aleukaemic and subleukaemic cases that sternal puncture is

of great importance. These terms are generally used to refer to those cases in which the white count is normal or subnormal. The white count may be as low as 400 per c.mm. Persistent leucopoenia together with anaemia and thrombocytopoenia should always arouse suspicion of leukaemia. Immature white cells may be abundant or they may form only a small proportion of the circulating peripheral blood cells. Yet in the bone marrow these immature white cells are predominant and hence marrow puncture clinches the diagnosis. The increasing number of reports of aleukaemic leukaemias is probably due to more frequent resort to marrow puncture. This is fully confirmed by the increased number of aleukaemic leukaemias seen at St. Luke's Hospital Clinical Laboratory during the last 3 years.

LEUKAEMOID BLOOD PICTURES.

Certain diseases are sometimes accompanied by blood changes which if taken apart from the clinical picture may be suggestive of leukaemia. In difficult cases bone marrow examination at once settles the problem.

a) Glandular Fever may be confused with acute leukaemia especially if throat infection is also marked. In glandular fever there is no anaemia and no thrombocytopoenia. Although many of the leucocytes are abnormal very few of them contain nucleoli. Marrow puncture is chiefly of value to exclude leukaemia.

b) Tuberculosis. The marked leukocytosis which may occur consists chiefly of adult cells. The regenerative hyperplasis of the marrow is distinguishable from the disorderly proliferation of the leukaemoid marrow.

c) Sepsis. In sepsis most of the cells are adult granulocytes and the % of myelocytes is small.

d) Acute Infectious Lymphocytosis may simulate lymphatic leukaemia. The bone marrow does not show the great increase of lymphocytes seen in lymphatic leukaemia. The same applies to whooping cough.

e) Lymphadenoma may rarely show a very high white count. The marrow shows activity but no immaturity.

f) Intoxications. Myeloid blood pictures may sometimes occur in mercury poisoning mustard gas poisoning, in eclampsia and following serves burns.

g) Lymphosarcoma may be accompanied by leukaemic blood picture. This condition is termed leukosarcoma. There is no doubt that lymphosarcoma and lymphatic leukaemia are closely allied and Willis draws no sharp distinction between these two conditions.

LEUCO ERYTHROBLASTIC ANAEMIAS.

In this group there is anaemia with large numbers of nucleated red cells and few or many myelocytes in the peripheral blood. This condition may be found:

a) Secondary tumour marrow deposits. Sternal puncture may make the diagnosis of malignant disease but this is not an early diagnosis as such cases must have skeletal metastases. The tumour cells are foreign to the marrow and mostly recognisable but groups of cells are necessary to make the diagnosis. Histological examination of the marrow increases the reliabilit of the diagnosis.

b) Myeloma. In a number of instances marrow puncture decides the diagnosis and clarifies an otherwise obscure clinical picture if typical myeloma cells are found. These cells may or may not be found in the peripheral blood.

c) Myelosclerosis. Sternal puncture is valuable as a diagnostic measure. If the puncture is successful the picture is different from that of leukaemia. In the hyperplastic cases the florid picture of leukaemia is lacking. As the disease progresses the hyperplasia will lead to hypoplasia, aplasia and fibrosis. During the latter stages marrow puncture is characteristically unsuccessful and usually very little blood is all that is withdrawn.

APLASTIC ANAEMIA.

Sternal puncture is of great value in the

diagnosis and assessment of prognosis in this condition. In fact it is in the differentiation between aleukaemic leukaemia, aplastic anaemia and thrombocytopoenic purpura that marrow examination during life achieves its greatest usefulness.

The marrow may show the following pictures.—

a) Aplasia. The material obtained consists chiefly of red cells. 60 to 100% of the nucleated cells are lymmphocytes. Such a finding makes it desirable to obtain a larger specimen of marrow (by trephening) in order to be sure that one has obtained actual marrow and also to see how fatty the marrow is.

b) Maturation arrest with primitive marrow. The cells seem to be arrested at the myeloblast and myelocyte stages.

c) Hyperplastic Marrow the cells seem to be destroyed as soon as they enter in the peripheral blood.

PURPURA HAEMORRHAGICA.

A number of studies have shown that in this condition the megakaryocytes are plentiful but show various morphological changes. Platelet production appears to be greatly reduced. Dameshek and Miller (1946) found platelet production in only 8 to 19% of the megakaryocytes instead of 68.6%. Following splenectomy platelet production was found in 69 to 85% of the megakaryocytes. In acute Leukaemias and other diseases invading or destroying the bone marrow the megakaryocytes were greatly reduced although those remaining were of normal morphology.

HAEMOLYTIC ANAEMIAS.

Mylogram shows extreme hyperplasia of erythropoietic tissue with marked increase in proerythroblasts and basophilic normoblasts. 75% of the marrow cells may be nucleated red cells. Reticulocytes are very abundant. Relative granulocytopoenia is usual. Following splenectomy in Familial Haemolytic anaemia the marrow usually returns to normal.

In the infective and toxic groups of Haemolytic Anaemia the marrow changes are usually milder.

Di Gugliemo's disease is a disorder of the red cell series analogous to leukaemia. It is characterised by enormous erythroblastic hyperplasia.

GAUCHER'S DISEASE.

This rare disease of lipoid storage is characterised by splenomegaly, anaemia, leucopoenia, and thrombocytopoenia. This disease may frequently be diagnosed at an early stage by marrow puncture, where the typical Gaucher cells are seen.

Likewise the diagosis of *Niemann-Pick's disease* can be made by the finding of 'foam cells' in the marrow smears.

Hand-Schuller-Christian's disease. Fat storing reticulum cells may be found in the marrow and peripheral blood. Differential diagnosis on the basis of marrow findings only is not possible owing to the similarity of the cells. Diabetes insipidus exophthalmos and irregular bony defects form the three cardinal points.

KALA-AZAR.

Marrow puncture is of great help in establishing the diagnosis of Kala-Azar by finding the typical Leishmann-Donovan bodies in marrow smears.

Likewise marrow puncture may help in the diagnosis of malaria and in some cases of filariasis.

LUPUS ERYTHEMATOSUS.

In acute lupus enthumatesus the finding of L.E. cells in the blood or marrow establishes the diagnosis. The typical L.E. cell is a mature neutrophil leucrcyte which contains within its all membrane one or more masses of nuclear material called L.E. bodies.

Investigations into the metabolism of blood and marrow cells and into their defensive mechanisms and also tissue culture of marrow cells have produced results important in both clinical and academic fields. Though many problems still await investigation and solution, marrow biopsy has proved its value in diagnosis, prognosis and even in therapeutics and has given invaluable help in the elucidiation of many haematological problems.