The Pelger-Huet Anomaly and Megaloblastic Anemia

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The Pelger-Huet anomaly of leukocytes is characterized by the presence of an oval, indented or bilobed ("pince-nez") nucleus in the neutrophil polymorphonuclear leukocytes which replaces the normal nuclear segmentation of these cells (Pelger1). It is inherited as an autosomal dominant characteristic (Huét2), the incidence being 1 in 6000 of the population (Davidson3). By contrast, megaloblastic anemia is characterized by an increase in the number of lobes in the neutrophil nucleus. The combination of addisonian pernicious anemia in a family with the Pelger-Huet anomaly enabled us to observe the effect of the megaloblastic process on the morphology of the cells exhibiting the Pelger-Huet trait. This paper reports our observations.

CASE REPORT

W. P., female aged 39, was seen in 1959 with attacks of asthma which had been present for 2 years. However, during the past 3 months she had noticed increasing fatigue.

Hematology: The hemoglobin concentration was 8.9 Gm. per 100 ml., packed cell volume 31 per cent, red cell count 2.6 million per cu. mm. and reticulocytes 1.0 per cent. The total white cell count was 10,000 per cu. mm. The stained peripheral blood film showed well-marked macrocytosis with some anisocytosis. The differential count was normal and the neutrophils appeared normal (fig. 1). Sternal marrow aspiration showed megaloblastic erythropoiesis with prominent giant metamyelocytes (fig. 2).

Other investigations: There was no hydrochloric acid in the gastric juice following 0.5 mg. of histamine, and a gastric biopsy showed total atrophy. The serum vitamin B12 concentration was abnormally low (35 μg. per ml.) and she failed to absorb an oral dose of Cr51-B12, the urinary excretion in the Schilling test being 3.1 and 0.4 per cent in two tests. Fecal fat excretion on a normal ward diet was 3.0 Gm. per day.

Progress

The patient was treated with monthly injections of 200 μg. of vitamin B12. The reticulocytes reached 15 per cent on day 6 following the initial dose. The hemoglobin concentration reached 14.8 Gm. per 100 ml. 8 weeks later and has been maintained in this region.

The total white count remained between 7000 to 9000 per cu. mm. The stained blood now showed the disappearance of the three- and four-lobed neutrophils which had been present before treatment with vitamin B12 and their replacement by neutrophils with their one or two lobes as seen in the Pelger-Huet anomaly (fig. 3).

Family Studies

The father died in 1942, 48 hours after admission to Hammersmith Hospital, with a severe megaloblastic anemia (red cell count 0.7 million per cu. mm.).

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The neutrophil shows the sex chromatin appendage. The red cells show variation in size with a tendency to macrocytosis.

Fig. 1.—Peripheral blood film (Case W. P.) before treatment with vitamin B\textsubscript{12}. Total gastric atrophy and marrow hyperplasia were found at autopsy. The mother is well and shows the Pelger-Huët anomaly. There are eight siblings, five of whom were available for study. Two of these carried the Pelger-Huët anomaly. One also had a low serum vitamin B\textsubscript{12} level (100 \(\mu g\) per ml.), but apart from the anomaly the blood film appeared normal.

Fig. 2.—Sternal marrow film (Case W. P.) showing a giant metamyelocyte at the top, a megaloblast on the left, and a five-lobed neutrophil leukocyte.

Observations of the Neutrophil Leukocytes

Segmentation of the neutrophils was assessed in two ways: firstly by noting the percentage of cells with one, two, three, four and five or more lobes among...
100 neutrophils, and secondly by adding the total number of nuclear lobes in 100 cells and dividing the value by 100. This latter value has been called the average lobe index (A.L.I.) and the normal range is 2.5 to 3.1 (mean 2.8). The observations are summarized in figure 4. In normal subjects, less than 3 per cent of the neutrophils contain five or more nuclear segments. By contrast, in untreated megaloblastic anemia there is an increase in the hypersegmented forms and an increase in the A.L.I. In our patient the A.L.I. before treatment with vitamin B₁₂ was 2.5, which is within the normal range, and the general distribution of nuclear segments approximated normal. However, a further nuclear count carried out on a blood film made 4 weeks after therapy showed an A.L.I. of 1.7 and a preponderance of single and bilobed forms.

While in relapse, the characteristic drumsticks of the sex chromatin were present in 6 per cent of the neutrophils containing three or more lobes. These bodies were no longer evident with the return of the Pelger-Huët form following treatment with B₁₂.

**DISCUSSION**

Although the neutrophils in the Pelger-Huët anomaly are morphologically different from the normal, they have been shown to behave normally in other respects. Thus they show normal phagocytic activity and have a normal survival in the circulation. Whether the neutrophils showing the Pelger-Huët morphology show an increase in nuclear segmentation in response to a megaloblastic form of hemopoiesis has not hitherto been described. The A.L.I. in our patient was 1.7 in her normal state and this shifted to 2.5 in the presence of megaloblastic hemopoiesis. By contrast, pernicious anaemia of corresponding severity in a patient without the Pelger-Huët anomaly produced a change in the A.L.I. from 2.8 to 3.3. Thus the Pelger Huët neutrophils respond in the usual manner during the megaloblastic process.
THE PELGER-HUET ANOMALY

Fig. 4.—The distribution of nuclear segments in the neutrophils in an untreated patient with addisonian pernicious anemia, in a normal subject, and in Case W. P. before and after treatment, with vitamin B₁₂. The average lobe index is also given.

Skendzel and Hoffman⁹ were unable to identify the sex chromatin body (drumstick) in the neutrophils in females with the Pelger-Huët anomaly although the sex chromatin was evident in buccal smears. In our patient the sex chromatin appendage could not be identified following treatment with vitamin B₁₂. With the appearance of three- and four-lobed forms in the megaloblastic state, the characteristic X chromatin pattern was evident and was present in normal numbers (fig. 1).

SUMMARY

A patient is described with addisonian pernicious anemia and with the Pelger-Huët anomaly of leukocytes. Before the patient was treated with vitamin B₁₂, her peripheral blood contained three- and four-lobed neutrophils, but with therapy almost all the neutrophils showed the characteristic bilobed
form of the Pelger-Huët anomaly. Before treatment the sex chromatin appendage was present in the neutrophils in normal numbers, but these could not be identified after treatment.

SUMMARIO IN INTERLINGUA

Es describite un patiente con anemia pernicioso de Addison e le anomalia leucocytic de Pelger-Huët. Ante que le patiente esseva tractate con vitamina B₁₂, su sanguine peripheric contineva tri- e quadrilobate neutrophilos, sed con le therapia quasi omne le neutrophilos monstrava le characteristic forma bilobate del anomalia de Pelger-Huët. Ante le tractamento le appendices de chromatina de sexo esseva presente in le neutrophilos in normal numeros. Post le tractamento illos non esseva identificabile.

REFERENCES


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