CASE REPORT

A Case of Erythremic Myelosis
(Di Guglielmo's Anemia)

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In erythremic myelosis neoplastic changes are found in the primitive red cells of the bone marrow and in nucleated red cells in the peripheral blood; it is sufficiently uncommon to warrant reporting.

The abnormal erythroid cells show changes similar to those which affect the myeloid series in myeloid leukemia, and although one should expect the condition to occur more often it has seldom been reported in British literature. Four hitherto unpublished cases have been brought to the knowledge of one of us (I. M.) and we therefore feel that the incidence is greater than the number which has been published. It is hoped that the publication of this case will help to bring the condition before clinicians and pathologists, and thus bring more cases to light.

So far as we can ascertain there are two acceptable cases in British medical literature (Neumark and Emery). Moeschlin considered that 12 cases in the literature could be substantiated up to 1947. Neumark thought that the case published by Israels should be classified as an erythroleukemia. He further lists 40 instances of erythremic myelosis, which have been published by continental authors. A certain confusion may arise from the similarity between the marrows in erythremic myelosis and erythroleukemia, but Blackburn and Lajtha have clearly pointed out the analogy or the gradations between erythremic myelosis, erythroleukemia and myeloid leukemia.

The case to be described had abnormal nucleated red cells in the peripheral blood and in the bone marrow, and showed a persistent granulopenia and thrombocytopenia throughout. There was, in addition, a well defined reticulo-endotheliosis.

Case Report

A married woman of 28 years was admitted to hospital on October 10, 1950, with severe anemia and pyrexia.

She had been perfectly well until three weeks before, when she had a severe attack of vomiting associated with shivering and a headache. This was followed by a transient jaundice, and she steadily became weaker and tired, and complained of a sore tongue and loss of appetite. Her doctor had given her iron...
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by mouth, and Anahaemin by injections for her obvious anemia, but with no clinical response.

Previous History

She had had no serious illnesses in her life, and was the mother of two healthy children. One sister had died at the age of 25 years, probably from subacute bacterial endocarditis. No other relatives had suffered from jaundice or anemia.

Examination and Investigations

On admission, she was extremely pale, and there were bruises on the body and petechiae on the soft palate. The tongue was smooth and pale, and she had several carious teeth. There was no koilonychia but the nails were brittle. A soft apical systolic murmur was present but the heart was not enlarged. There were coarse basal crepitations and some ankle and sacral edema. The liver was two fingerbreadths enlarged and the spleen could be tipped on deep inspiration.

She was Group A, rh negative, and the Coombs test was negative. Hemoglobin 3.0 Gm.; RBC 570,000 per cu. mm.; WBC 8,200 per cu. mm.; reticulocytes 1 per cent; platelets 13,000 per cu. mm.; nucleated red cells in peripheral blood 1,300 per cu. mm. (normoblasts 32 per cent, late erythroblasts 20 per cent, intermediate erythroblasts 22 per cent, megaloblasts 19 per cent and hemoglobinizing megaloblasts 8 per cent).

P.C.V. 10; M.C.Hb. 36.8; M.C.H.C. 32 per cent; M.C.V. 115 cu.; M.C.D. 6 μ. The serum bilirubin was 0.84 mg. per cent; and the Van den Bergh gave a slight positive direct reaction. Red cell fragility was normal.

The blood urea was 36 mg. per cent. There was a trace of albumin in the urine, but no excess of cells.

A histamine fractional test meal revealed no free acid, and an x-ray of the chest was clear.

Sternal Marrow. The marrow was comparatively cellular; most of the primitive cells were erythroblasts but many were proerythroblasts. Other more mature forms were present, and many had the megaloblast-like nuclear pattern (fig. 1). Reticulum cells were increased, and occasionally it was found that there were clumps of cells with a central reticulum cell having intermediate erythroblasts grouped around it (fig. 2). Some of the erythroblasts had double nuclei, and rarely one could be seen with three nuclei (fig. 3).

Table 1 shows the general sternal marrow pattern, which did not vary much during her illness. It was not uncommon, as the disease ran its course, to find more mature abnormal erythroblasts, some of which were hemoglobinized, and an appreciable number showed bizarre, atypical and aberrant mitoses. An essential feature was the persistence of the megaloblast-like nucleus in cells of megaloid and more mature type both in the bone marrow and in the peripheral blood.

Progress

She was treated with penicillin and streptomycin and vitamin B₁₂, together with repeated transfusions of stored blood for four weeks, during which time she ran a remittent temperature of up to 103 F., and the spleen increased in size. It was found that during the first 14 days she failed to retain the transfused blood and transfusions were necessary every second or third day. The levels of
hemoglobin and red cells fluctuated from 5 to 8 Gm., and 1.5 to 2.5 million per cu.mm., respectively. After four weeks she was able to maintain a level of 8 Gm. of hemoglobin and 3 million red cells for a further three weeks before she required
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further transfusion. Then at the end of seven weeks from the commencement of treatment, she was given a transfusion of fresh blood, and allowed to go home at her own urgent request. It is interesting to observe that following the transfusion of fresh blood she was able to live for nine weeks without transfusion, but at the end of this time she was re-admitted for further transfusions following an attack of influenza to which her husband was also a victim.

Her spleen was now palpable 5 inches below the costal margin, and her serum contained auto-agglutinins. The Coombs test gave a very weak positive reaction.

At the end of a further seven weeks she was discharged again, and given urethane. There was no response to urethane, and she was unable to tolerate it for long. Within a month she was re-admitted in a very acute phase, with signs of consolidation at the bases of both lungs. She was also very anemic. At this time the hemoglobin was 6.6 Gm., and the red cells 1,600,000 per cu.mm.; nucleated

**Table 1.—Sternal Marrow on Admission**

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myeloblasts</td>
<td>4.5</td>
</tr>
<tr>
<td>Myelocytes</td>
<td>8.5</td>
</tr>
<tr>
<td>Metamyelocytes</td>
<td>0</td>
</tr>
<tr>
<td>N. Polymorphs</td>
<td>3.5</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>5.5</td>
</tr>
<tr>
<td>Turck Cells</td>
<td>0.5</td>
</tr>
<tr>
<td>E. Myelocytes</td>
<td>0.5</td>
</tr>
<tr>
<td>Megakaryocytes less than 0.5%</td>
<td>1</td>
</tr>
<tr>
<td>Hemoeytoblasts</td>
<td>1</td>
</tr>
<tr>
<td>Proerythroblasts</td>
<td>3</td>
</tr>
<tr>
<td>Megaloblasts</td>
<td>14</td>
</tr>
<tr>
<td>Early erythroblasts</td>
<td>8</td>
</tr>
<tr>
<td>Intermediate erythroblasts</td>
<td>19</td>
</tr>
<tr>
<td>Normoblasts</td>
<td>28</td>
</tr>
<tr>
<td>Mitotic red cells</td>
<td>4</td>
</tr>
</tbody>
</table>

Myeloid/Erythroid ratio is 1 to 3

Differential count of 200 cells (per cent)
red cells in the peripheral blood 40,000 per cu.mm.; white cells 4,200 per cu.mm. The platelets which had always remained low were now 11,000 per cu.mm. She died on the day after admission, having survived for eight months from the time of her original admission and nine months from the onset of the disease.

Postmortem Examination

The body was that of a very emaciated young adult woman, and there were a few petechiae on the trunk. The gums were hemorrhagic and spongy. The scalp, skull, meninges and brain were macroscopically normal. There was bilateral pulmonary consolidation and many small infaracts which had become septic. An

Fig. 4.—Section of liver showing increase in reticulin and deposition of blood pigment, mainly in peripheral zones of the liver lobule. Silver impregnation. (X 90)

acute fibrinous pneumonia was present. The heart was small and pale, and had slatey blue valves which were apparently functionally competent. The liver weighed 2350 Gm. and was pale brown in color with small blue areas around large bile ducts. It was of soft consistency. The spleen weighed 2,800 Gm., and showed multiple recent infaracts. Two small splenomegaly were present. The kidneys showed no morbid lesion other than pallor, and the pancreas, adrenals, thyroid and pituitary were macroscopically normal. The liver, spleen, pancreas and kidneys gave an immediate prussian blue color on testing with acidic ferrocyanide of potassium. The sternal and femoral bone marrow was rather gray in color and appeared to be hyperplastic.

Histologic Examination

There was general increase in reticulum and deposition of iron pigment in the liver and spleen (fig. 4). The liver structure showed wide variations, and certain
areas closely resembled the liver of an erythroblastotic infant by reason of the
gross infiltrations of erythropoietic tissue (fig. 5). The same increase in reticulin
accompanied by loss of normal architecture could be seen in many lymph glands.
An interesting difficulty was encountered in distinguishing splenic tissue from
bone marrow, because of the widely dilated sinuses, many foci of erythropoiesis
and increase in reticulin; but the bone marrow lacked evidence of hemosiderosis.
Abnormal nucleated erythroblasts could be seen in both, and there was very
little fat in the bone marrow.

Fig. 5.—Section of liver showing marked infiltration of hepatic sinus by erythroblasts,
and distortion of liver structure. Hematoxylin and eosin. (× 90.)

The presence of an acute fibrinous pneumonia was confirmed. The infarcts
showed peripheral infiltrations of erythroblasts around the necrotic centers, and
we feel that the infarcts arose from necrosis of pulmonary deposits of erythropoietic
tissue. The kidneys showed small erythroblastic infiltrations, and scanty,
but nevertheless appreciable, deposits of iron pigment.

Death was due to an acute fibrinous pneumonia in association with erythremic
myelosis.

SUMMARY

A case of erythremic myelosis is described which was characterized by a severe
anemia from the beginning. There was irregular remitting fever, splenomegaly
and hepatomegaly. The peripheral blood showed immature erythroblasts, granulo-
penia and thrombocytopenia. The bone marrow showed hyperplasia of erythrophy-
poiesis with maturation arrest, and a persistent megaloblastic type of nucleus in
abnormal red cells. There was also a well defined proliferation of the reticulo-
endothelial system. The course was that of the subacute variety of erythremic
myelosis, but it began with an acute phase and ended acutely.
A remission of nearly three months without transfusion followed a transfusion of fresh blood. While this may be coincidental with a spontaneous remission we feel that it is probable that a maturation factor in the fresh blood was responsible. For this reason we feel it is reasonable to suppose that other cases of erythremic myelosis will benefit more from fresh blood than from stored blood; and, as in our case, the inevitable fatal outcome after two months or less can be postponed for an appreciable number of months.

REFERENCES

Case Report: A Case of Erythremic Myelosis (Di Guglielmo's Anemia)

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