

Peripheral Blood and Bone Marrow Changes in Chronic Renal Failure (Investigation of 50 Cases)

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Anemia almost always develops in chronic renal failure with nitrogen retention, and it is not uncommon for a patient with chronic uremia to seek medical advice in the first instance because of anemia (4,6,7). Anemia is not related to the type of disease causing the renal failure, although it may be more severe in renal failure associated with infection, e.g. chronic pyelonephritis. It develops with primary disease of the kidney or urinary tract, i.e. chronic nephritis, chronic pyelonephritis, cystic disease of the kidney, urinary tract obstruction and tuberculosis of the kidney and with the systemic diseases which cause renal impairment, i.e. systemic lupus erythematosus. The severity of the anemia is quantitatively related to the severity of renal failure (4).

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The anemia is usually normocytic and normochromic; it may be hypochromic and rarely macrocytic (4,8). Moderate anisocytosis is common, poikilocytes with spiny projections, called burr cells, are seen in advanced cases. In 1949 Schwartz and Motto described burr cells for the first time (10). Crenated forms, triangular and helmet-shaped red cells are also present, rarely spherocytes are seen (4). Reticulocyte count is normal but in advanced uremia is slightly increased. Leucocyte count is normal or slightly increased but definite leucocytosis occurs when infection or other complications occur. Neutrophilia sometimes occurs (4). Eosinopenia is usual and lymphopenia may be present (10). Platelets are normal in number but occasionally mild to moderate thrombocytopenia occurs (4,6).

The bone marrow cellularity is normal or slightly increased. Erythropoiesis is normoblastic with normal or increased activity but when the renal failure is advanced mild erythoid hypoplasia may occur. Myeloid and megakaryocytic series are normal or slightly increased in activity. The marrow iron content is normal or increased (2,4).

Because of different hematological aspects of anemia in chronic renal failure and predominant hypochromic anemia in our patients, this communication aims at investigating the causes of these variations and finding the reasons for these morphological differences, compared to what is generally accepted as normochromic normocytic anemia.

Materials and Methods

The patients were between 14 and 62 years old, (the majority were between 20 and 40 years) comprising 32 females and 18 males.

Duration of the illness in 15 cases was less than one year, in 12 about one year, in 9 unknown and in the rest was between one and 4 years.

11 patients had chronic or subacute glomerulonephritis, 6 chronic pyelonephritis, there was one case of advanced hydronephrosis, one of amyloidosis two with generalized tuberculosis and the causes of the rest were undetermined. 9 of the patients had mild epistaxis which did not seem to contribute to their anemias. 8 patients had occult blood in their stool, 16 negative and in the rest stool was not examined for occult blood.

Blood urea corresponding BUN was between 60 and 601 mg % (BUN 28-280 mg %), with 8 cases between 60 and 100 (BUN 28-47), 13 from 101 to 200 (BUN 47-93), 16 from 201 to 300 (BUN 94-140) and the rest between 301 and 601 mg %, (BUN 140-280).

Full blood examination was carried out in all patients; this consisted of hemoglobin, hematocrit, reticulocyte count, leucocyte count, platelet count and differential leucocyte count with special attention to the red cell morphology, (in all cases red cell morphology accorded with MCHC). Finally the marrow examination including Prussian blue staining for iron was also carried out.

Results

All patients were anemic, hemoglobin varied from 3.2 to 11.5 g % and hematocrit from 10 % to 36 %. Anemia was moderate when blood urea was less than 200 mg % (BUN 93) and it was more marked when the blood urea was more than 200 mg % (BUN 93). With blood urea from 250 to 400 mg % (BUN 117-187) anemia did not progress any more and there was only a slight fall in hemoglobin concentration when the blood urea exceeded 401 mg % (BUN 187) (Table-1).

Type of anemia: 32 patients (64 %) had normocytic or microcytic hypochromic anemia, 4 (8 %) macrocytic hypochromic and 14 (28 %) normocytic normochromic anemia. Altogether 72 % had hypochromic anemia, 14 (28 %) of them had concomitant iron deficiency anemia.

Out of 29 patients with blood urea above 200 mg % (BUN 93) 16 (55 %) had burr cells, while in those with blood urea below 200 mg %, 21 cases, only 8 (38 %) had burr cells. Crenated red cells in 22 % and anisocytosis in 58 % were prominent.

Leucocyte count: 2 patients (4 %) had leucopenia (less than 4,000 per cumm), 34 (68 %) had normal leucocyte count (20 % from 4,000 to 6,000 and 48 % from 6,100 to 10,000), 7 (14 %) had mild leucocytosis (10,000 to 15,000), 7 (14 %) had definite leucocytosis (15,000-24,000); neutrophilia occurred (28 % of cases) when leucocytosis was present; 5 (10 %) had mild eosinophilia 15 (30 %) eosinopenia and the rest (60 %) had normal eosinophil count; 3 (6 %) had mild basophilia and the others (94 %) had a normal number of basophils; one (2 %) had lymphocytosis, 18 (36 %) lymphopenia and 62 % had a lymphocyte count within normal limits; 7 (14 %) had monocytosis and the rest 86 % had normal monocyte count (Table-2).

Platelets: We had 5 patients (10 %) with thrombocytopenia (platelets from 75,000 to 120,000) and all the others had normal platelet counts.

Bone marrow: 2 (4 %) had hypercellular marrow, 3 (6 %) had hypocellular, 88 % had bone marrow with normal or slightly decreased cellularity; we had one blood tap (2 %). Erythroid series were hyperplastic in 4 cases (8 %), hypoplastic in 3 patients (6 %) and 42 (84 %) had normal activity. Myeloid series had increased activity in 2 cases (4 %), 5 (10 %) had myeloid hypoplasia and 84 % had normal activity. Megakaryocytes were normal in all. Stainable iron was absent in 7 cases (14 %), in 7 (14 %) reduced, in 22 (44 %) normal and 12 (24 %) had increased amount of iron. We had one blood tap and in another case the bone marrow was not stained for iron.

Table - 1: Relation between blood urea and hemoglobin

Blood urea /mg% (BUN mg%)	Number of patients	Hemoglobin mg/100ml. (Mean \pm S D).
60-150 (20-70)	14	8.3 \pm 2.35
151-200 (70-93)	7	8 \pm 1.7
201-250 (94-117)	10	7.2 \pm 2.3
251-300 (117-140)	6	7.4 \pm 2.7
301-400 (140-187)	7	7.1 \pm 2.5
401-601 (187-280)	6	6.4 \pm 1.7

Table - 2: Differential leucocyte counts demonstrating percentages of normal cases and of various deviations.

White blood cells	Normal %	Increased %	Decreased %
Leucocytes	68	28	4
Neutrophils	72	28	—
Eosinophils	60	10	30
Basophils	94	6	—
Lymphocytes	62	2	36
Monocytes	86	14	—

Discussion

Anemia occurs almost invariably in chronic renal failure with uremia; it has two main causes namely depression of erythropoiesis and increased red cell destruction (4,6). Erythropoiesis suppression is due to the toxic effects of waste products which do not seem to be urea (4), and to diminished erythropoietin production.

Roscoe observed that, on average, the blood hemoglobin decreases 2 gm per 100 ml for each increase of 50 mg % (BUN 23) in blood urea (4) but increase in blood urea beyond 250 mg % (BUN 117) is not accompanied by any further progress of anemia; however there is considerable individual variation in the rate of hemoglobin fall. Callen and Limarzi (8) found that in patients suffering from chronic glomerulonephritis, hemoglobin is significantly lower when BUN exceeds 100 mg % (blood urea 214 mg %) and they state that some investigators have found a closer relationship between blood urea and hemoglobin concentration but the data are not convincing. Our findings are similar to those of Callen and Limarzi, because anemia was moderate when blood urea was less than 200 mg % (BUN 93), more marked with blood urea more than 200 mg %; with blood urea from 250 to 400 mg % (BUN 117-187) anemia did not progress and there was only a slight fall in hemoglobin concentration when the blood urea exceeded 401 mg %. Like Callen and Limarzi we did not find closer relation between blood urea and hemoglobin concentration.

The type of anemia in chronic renal failure is normocytic normochromic in most of the cases studied (4,8). In our country, where most low class inhabitants suffer from factor deficiency anemia, mostly due to iron deficiency, anemia presents a quite different hematological picture when they suffer from chronic renal failure. This has been the subject of our extensive study in recent years. The majority (72 %) of our patients had normocytic, rarely macrocytic, or microcytic, and hypochromic anemia; 28 % of them (14 cases), 8 females and 6 males, had reduction or absence of stainable iron in their bone marrow. This was interpreted as iron deficiency anemia, where

the morphology of red cells was hypochromic and microcytic; the remaining 44 % (22 cases), 17 females and 5 males, had normal or increased amount of iron in the marrow and hypochromia of their red cells was not related to iron deficiency. The reason for this has not yet become clear. Since it is generally accepted that the most critical index of iron deficiency anemia is the absence or reduction of iron in the marrow (3,4,9), we accepted this criterion as a guide to distinguish our iron deficient from our non iron deficient cases. 3 out of 14 patients with concomitant iron deficiency anemia had occult blood in their stool, 5 were negative and in the rest stool was not examined for occult blood.

Britton stated that burr cells were found in 70 % of uremic subjects but they are not specific to the disease since they are also found in a high proportion of cases of gastric carcinoma, bleeding peptic ulcer and some neurological conditions (10); 48 % of our patients had burr cells but the majority of them were among those with blood urea above 200 mg % (BUN 93). 58 % of our patients had mild anisocytosis and 22 % crenated red cells; reticulocyte count was normal in the majority of our patients and slightly increased in others; these nearly accord with other findings.

Leucocyte count was normal, or slightly increased in 82 % of our patients; definite leucocytosis, with neutrophilia, occurred in 7 (14 %) patients. Only one of them had chronic pyelonephritis but there was no apparent reason for the others. According to Britton eosinopenia is usual in uremia (10) but only 30 % of our patients had eosinopenia. Jenson stated that lymphopenia may be found in uremia (10), we had 36 % lymphopenia.

Platelets are normal in number in most patients and thrombocytopenia occurs in 20 % of cases (4,6). 5 (10 %) of our patients had mild to moderate thrombocytopenia, 4 of them had blood urea above 160 mg % (BUN 75), two of them had concomitant leucopenia. In certain patients with chronic uremia the spleen is enlarged, due to increased immunological activity (1), and hypersplenism will cause leucopenia, thrombocytopenia and aggravation of the anemia; none of our patients had apparent splenomegaly.

Bone marrow was hypercellular in 2 patients (4 %), with normal or slightly decreased cellularity in 44 (88 %), and was hypoplastic in 3 (6 %). These 3 had depression of both myeloid and erythroid series and two of them had blood urea above 500 mg % (BUN 234) (one with pancytopenia). Erythroid series were hyperplastic in 4 (8 %), their blood urea being more than 216 mg % (BUN 100), with normal activity in 42 (84 %) and hypoplastic in 3 cases (6 %) which were accompanied by bone marrow hypoplasia. Myeloid series had increased activity in 2 patients (4 %), their leucocyte count was more than 12,000/ cumm, 5 (10 %) had hypoplasia, 3 of them with bone marrow hypoplasia and 84 % had normal activity; we had one blood tap. Megakaryocytic series were normal in all. According to Cartwright and de Gruchy stainable iron is normal or increased in chronic uremia (2,4); we had 68 % with normal or increased stainable iron, it was reduced in 7 (14 %) and absent in 7 (14 %) patients.

Finally we conclude that our results in Iran in many ways, are in accordance with other findings but with some differences as follows:

1. There was a slight fall in hemoglobin concentration when blood urea exceeded 401 mg % (BUN 187); this finding contrasts with what Roscoe previously reported.
2. The majority of our patients (72 %) had hypochromic rather than normochromic anemias; 28 % of them had reduction or absence of stainable iron in their marrow.

Summary

Anemia and morphological features of the hemopoietic system in 50 Iranian patients suffering from chronic uremia was investigated. The results were compared with the results observed by others; our findings in most instances are nearly in accordance but with the following differences: When

blood urea was above 401 mg % (BUN 187) there was a slight fall in hemoglobin concentration; anemia was normocytic, rarely macrocytic, or microcytic, and hypochromic in 72 % of our patients, 28 % of them had concomitant iron deficiency anemia demonstrable by absence or reduction of stainable iron in their marrow.

Resumé

Etude de 50 cas de l'anémie et les modifications morphologiques de système hématopoiétique chez les malades atteintes de l'urémie chronique en Iran révèle:

— Il y a une concordance relative entre nos résultats et celles de la littérature, mais en plus nous avons les constatations suivantes: Quand l'urée sanguin est supérieur de 401 mg % (BUN 187) le taux de l'hémoglobine est diminuée par comparaison avec des chiffres antérieurs. Chez 72 % de nos malades l'anémie est hypochrome et normocytaire ou microcytaire très rarement macrocytaire. Dans 28 % de ces cas il existe une déficite ferrique que nous avons interprétée comme une diminution ou déficite du fer du moelle osseuse.

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