Reticulocytosis and Hypoxemia as Prognostic Signs in Congestive Heart Failure

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THE APPEARANCE of immature red blood cells in the peripheral blood of patients with congestive heart failure has been well documented in the literature.[1-4] Frumin and colleagues[1] reported that nucleated red cells found in the blood of patients in congestive heart failure indicated a poor prognosis and attributed this to anoxemia resulting from the cardiac decompensation. Groen and Godfried[2] suggested that normoblasts found in patients with cardiac disease signified massive pulmonary infarction. These reports emphasized the presence of nucleated red blood cells, or normoblasts, in the peripheral blood as an unfavorable prognostic sign in patients with cardiac insufficiency. The purpose of this study is to observe this phenomenon further, and to determine if reticulocyte counts may be used to reflect the degree of arterial oxygen unsaturation and thus serve as a prognostic sign in congestive heart failure.

Method

The study is composed of observations on 15 patients with severe congestive heart failure* who were admitted to the medical service of George W. Hubbard Hospital of Meharry Medical College. The etiology of the heart disease was distributed as follows: hypertensive and arteriosclerotic, 10; arteriosclerotic without hypertension, three; syphilitic and rheumatic, one each. Venous pressure, circulation time, and nonprotein nitrogen were recorded on each subject. Arterial blood was collected from the femoral or brachial artery in oiled heparinized syringes and capped immediately. Oxygen determinations were performed in the Van Slyke manometer. None of the patients had received oxygen less than 12 hours before the sample was obtained. Venous blood was drawn at the same time for the hematologic studies. Serial red blood cell and reticulocyte counts, hemoglobin, and hematocrit determinations were performed on all subjects.

Results

Within 1 month after admission, five of the 15 subjects died. There was no demonstrable clinical difference between the deceased and the now living subjects, and some of the deceased patients had a better clinical prognosis than did those in the latter group. All of the patients who died had a reticulocyte count greater than 3.0 per cent, the range being 3.0 to 4.9 per cent, with an average of 4.0 per cent. On the other hand, the 10 patients that improved, and are now living, had a reticulocyte count less than 2.2 per cent, with an average of 1.5 per cent. These findings are significant at the .001 level according to the t-test for difference between means.

In all patients except one, the arterial oxygen saturation was reduced; the average of these findings indicates a reciprocal relationship between the degree of hypoxemia and the reticulocytosis (table 1). The average arterial oxygen saturation of the five deceased patients was 83 per cent as compared to an average of 88 per cent in the patients that survived. This, however, was not a statistically significant difference. Two of the five patients that died had nucleated red cells in the peripheral blood. In all cases except one, the nonprotein nitrogen was slightly elevated but none of the patients was uremic. The white blood cell and differential counts were normal in all subjects.

Case five is particularly interesting in that serial oxygen and reticulocyte determinations were obtained (fig. 1). The patient was

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*Functional capacity Class IV and therapeutic Class E, Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Blood Vessels by the Criteria Committee of the New York Heart Association, Inc., 1953.

Table 1

Peripheral Blood Analysis of 15 Patients in Congestive Failure

Case no.		Venous pressure ml. water	Circulation time, sec.	WBC cells/mm.^{3}	RBC cells/mm.^{3} X 10^6	Hemoglobin Gm. %	Hematocrit vol. %	Reticulocytes %	Nucleated red cells/100 WBC	O_2 sat. %	Nonprotein nitrogen mg. %
1	Dead	300	65	7,600	5.54	17.0	49	3.0	1	86	59
2	Dead	280	40	8,500	4.84	15.0	46	3.1	0	81	62
3	Dead	295	30	7,350	4.31	12.5	38	4.5	1	88	30
4	Dead	285	55	4,600	4.33	14.5	39	4.9	0		78
5	8/26/60	250	60	7,100	3.94	12.0	36	1.1	0	90	49
	Dead 9/12/60	190	75	5,800	3.65	11.5	36	2.1	0	86	55
	9/13/60			5,750	3.20	12.0	38	4.4	0	76	41
6	Alive	210	50	7,150	5.55	16.5	48	1.9	0	88	38
7	Alive	290	35	9,950	5.68	18.5	61	2.2	0	89	49
8	Alive	265	35	10,550	3.96	13.0	37	1.4	0	81	68
9	Alive	270	47	5,100		17.0	48	1.2	0	91	43
10	Alive	200	40	8,700	5.44	19.0	52	1.2	0	86	36
11	Alive	280	35	7,050	4.44	13.5	38	2.1	0	82	84
12	Alive	245	40	6,000		16.5	49	1.2	0	90	54
13	Alive			12,500	3.84	11.5	36	1.3	0	78	36
14	Alive	115	42	4,750	4.10	11.5	35	1.3	0	96	55
15	Alive	280	40	8,000	4.44	15.0	43	0.9	0	98	40

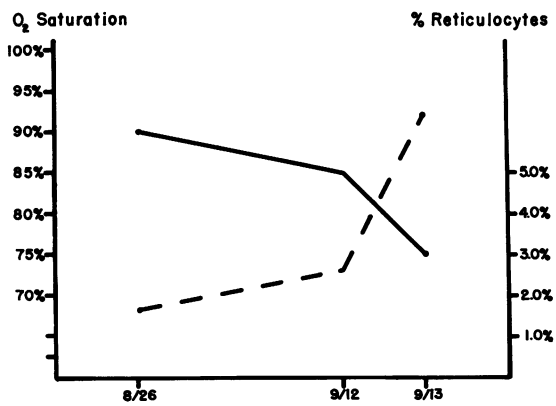

Figure 1

Relationship of reticulocytosis and hypoxemia in case 5. Solid line, oxygen saturation; broken line, reticulocytes.

a 50-year-old man with aortic insufficiency due to syphilis and, in addition, portal cirrhosis. The outstanding findings on physical examination were distended neck veins, jaundice, moist rales in both lung fields, aortic diastolic murmur, hepatomegaly, and marked ascites. At the time of admission dyspnea was not a prominent symptom. The reticulocyte count was 0.9 per cent and arterial oxygen saturation was 90 per cent on admission. After 2 weeks of hospitalization he became increasingly more dyspneic and the jaundice increased. The reticulocyte count was elevated to 2.4 per cent and the arterial oxygen saturation decreased to 86 per cent. After 2 days the reticulocyte count increased to 4.9 per cent and the arterial oxygen saturation decreased to 76 per cent. He died the following day.

Discussion

These studies emphasize the importance of reticulocytes and other immature forms of red blood cells in the peripheral blood of patients with congestive heart failure. Groen and Godfried[2] attributed the appearance of normoblasts to anoxia related to massive pulmonary infarcts or mural thrombi. Such a relationship was not established in this study. The observations here correlate with the findings of Waller, Blumgart, and Volk,[3] who noted increased red cell fragility and reticulocytosis in patients with pronounced congestive heart failure. These findings were attributed to stasis and anoxemia.

Nucleated red cells were found in the blood of only two of the five patients who died, whereas reticulocyte counts above 3.0 per cent were found in all patients who died. Although four of the patients had mild anemia, there was a good correlation between the reticulocyte count and the arterial oxygen saturation. The direct bilirubin of case 5 was increased, as a result of long-standing portal cirrhosis with superimposed congestive heart failure. The correlation of arterial oxygen saturation with the appearance of immature red blood cells in the peripheral blood of patients in congestive heart failure has not, to the knowledge of the writers, been previously reported.

Conclusions

Reticulocytosis and nucleated red cells in the peripheral blood of patients with congestive heart failure suggest an unfavorable prognosis.

The arterial oxygen saturation was decreased in all patients studied except one.

The findings suggest that a rise in the reticulocyte count in patients with congestive heart failure suggests a grave prognosis, and is a more useful tool than the nucleated red cell count.

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Religio Medici

For my Religion, though there be several Circumstances that might perswade the World I have none at all, (as the general scandal of my Profession, the natural course of my Studies, the indifferency of my Behaviour and Discourse in matters of Religion, neither violently Defending one, nor with that common ardour and contention Opposing another;) yet, in despight hereof, I dare without usurpation assume the honourable Stile of a Christian.—SIR THOMAS BROWNE. *Religio Medici,* 1642, edited by W. A. Greenhill, M.D., Oxon., London, MacMillan and Co., Limited, 1950, p. 7.

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