Some Haematologic Aspects of Leiner's Erythroderma

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The metabolic lability peculiar to early childhood may give rise to certain pathologic changes which otherwise occur only under quite special conditions. Dehydration and atrophy are characteristic examples.

The syndrome to be discussed, another condition peculiar to infancy and not encountered in the adult, is erythrodermia desquamativa, also known as Leiner's disease or Leiner's erythroderma, after its first describer [20]. Numerous data to the still unclear pathogenesis have been contributed by Hungarian authors [2, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 21, 22, 23, 24, 25, 26, 27].

Leiner's erythroderma appears as a typical skin disease, as the external manifestation of various biochemical and metabolic changes. There is always some organic lesion (mainly of the liver and the pancreas), sometimes a primary constitutional defect (hormonal disorder), occasionally an antecedent infection (pemphigus, Staphylococcus albus); it appears to be proved that one of the causative factors is a dietary deficiency, especially a shortness in protein and vitamin supply [6, 7, 9, 16].

The condition which may show different degrees of severity from mild seborrhoeal changes in the newborn to grave morbid processes sometimes with lethal outcome can only be identified as a genuine case of Leiner's erythroderma if it fulfils all of the following 7 criteria.

(i) Age under 3 months.

(ii) Characteristic skin symptoms.

(iii) Hypoproteinaemia.

(iv) Anaemia.

(v) Steatorrhoea.

(vi) Susceptibility to dystrophy (associated with hepatic and pancreatic lesion).

(vii) Breast-milk feeding for the greater part.

Of these, hypoproteinaemia and anaemia, as the most general symptoms, have a decisive influence on the patient's functional balance, and deserve therefore to be discussed in some detail.

Eliasberg's report [4], which was the first to call attention to anaemia in Leiner's erythroderma, aroused little attention. Only Baar and Stransky [1], Kokil [19] and Balló [2] made mention of it before us [8].

The experimental results derived in 1952 from a comparatively small number of cases led us to the statement that (i) all infants affected are anaemic though in different degrees; (ii) anaemia grows progressively graver with the duration of the disease and the nature of the complications; (iii) the syndrome is frequently associated with a certain degree of megalocytosis.

The present paper which embodies an account covering 250 cases observed by us in a period of 10 years, is intended to furnish some data readily amenable to statistical estimation. The most comprehensive report up to now is that of ECKARDT and KUNAD [3], discussing 160 own cases and commenting on another 242 patients who had been under the care of their Department.

RESULTS AND COMMENTS

The haematological results of our own cases were as follows.

(i) *Red cell counts.* Blood counts were made once or several times in most cases. The average red cell count at admission was 3 550 000 (between 2 800 000 and 4 300 000). In patients who succumbed to the disease, it was 2 340 000 (between 1 500 000 and 3 600 000). The lowest values were recorded in patients with the so-called white form of the condition (see Table I).

These findings are in conformity with the data recorded by STEPANOVA in 1951 [32], as also with those in WOLFRAM's review dating from 1959 [33], and led us to the conclusion that in Leiner's erythroderma a red cell count of 3 million or thereabouts exposes the case as a severe one and claims from the prognostical point of view an even greater significance by calling attention at an early stage to the possible presence of a complication or focus eventually calling for surgery. The question is yet to be touched upon in connection with the smears.

(ii) *Haemoglobin.* The haemoglobin value was always determined together with the red cell count and gave an average of 11.3 g per 100 ml (from 7.8 to 15.6). In the lethal cases, all of them associated with marked macrocytosis, the average Hb content was 10 g per 100 ml (with 8.6 g and

TABLE I

Average counts in 250 cases of Leiner's disease

Cases	RBC	Hb g per 100 ml	WBC	RBC volume index	Serum protein g per 100 ml
Recovered	3.550.00 (2.8—4.3 m)	11.3 (7.8—15.6)	9.600 (6.000—18.400)	1.33—0.92	4.4 (3.5—5.5)
Dead	2.340.000 (1.5—3.6)	10.0 (8.6—13)	10.300 (6.200—20.200)		4.3

13 g as the lower and upper values). The data have fully confirmed our finding from 1952 that anaemia of varying severity always accompanies the disease.

(iii) *RBC volume index.* In the cases examined in 1952 [8], the average volume index was usually above 1, at admission 0.92 and 1.33, at discharge. This suggested that in some cases there had been macrocytosis during the preclinical phase, a fact by no means disproving that the anaemia was mostly due to sideropenia. KHO and TUMBELEKA's recent study [18] in cases with kwashiorkor, a condition the clinical course of which is known to resemble that of Leiner's erythroderma, has furnished evidence that although the characteristic anaemia in nutritional deficiency is hypochromic, megaloblastosis may also occur. STRANSKY [30], studying infantile protein deficiency anaemia, observed changes of a pernicious character in peripheral blood but none in the bone marrow. The good results recorded by WOODRUFF [34] in megaloblastic anaemia with vitamin B_{12}, are obviously in some connection with the fact that SALMI [28] was able, just like ourselves, to induce remission with the same drug in Leiner's erythroderma.

The bone marrow showed but a slight degree of megalocytosis [12, 21].

(iv) *White cell count.* There was practically no difference in the average WBC between the recovered (9600) and lost (10 300) cases. ECKARDT and KUNAD [3], however, regard moderate leucocytosis (14 000) with a marked shift to the left a characteristic symptom.

(vii) *Smears.* There was little difference between the results for the patients with Leiner's erythroderma and those for normal infants about 2 months of age. The results are shown in Table II.

TABLE II

Comparison of smears, values per 100 WBC

	normal 2 mo	Leiner's erythroderma	
		re-covered	died
Neutrophiles			
young	—	0.4	0.5
unsegmented	2	3.2	5.0
segmented	36	30.9	35.5
Eosinophils.....	2.5	3.5	2.5
Lymphocytes	58	58.7	54.3
Monocytes	1.5	3.3	2.2

Little diagnostic value was attributed to minor shifts to the left, especially observed in severe cases.

Much more indicative of complications were some changes in the smears and so were the abnormally great shifts of certain cell types. For instance, in a case there was an increase in the lymphocyte count from 50 per cent at admission to 71 per cent short before death with a corresponding reduction to 0 of the original eosinophil count of 4. In another case the lymphocyte count fell from the initial 82 per cent to 28 per cent on the last day of life, while the eosinophil count rose from 2 to 8. The cause of these changes

is unknown, but presumably a functional deterioration of the bone marrow is responsible for them.

Most complications were affecting the ears and involved changes in the smears similar to those observed in the lethal cases. Hence any deviation from the normal or any marked shifts in the counts recorded at periods when the occurrence of some complication is suspected, is suggestive of a lesion in the haemopoietic system, moreover, of one involving a focus. The qualitative count may therefore present a prognostical aid and assist in the indication for surgery.

Otogenic complications occurred in 65 cases, i. e. in a quarter of the material; 44 of them were subjected to operation. In our experience failure of the usual treatment in bringing about improvement of the characteristic symptoms (skin, weight, faeces, etc.) combined with aggragavation of the anaemia points to a suppurative process. If neither the tympanic cavity nor the adenoid region, the skin, the uropoietic system, etc. present any sign of a secondary pyogenic lesion, antral empyema suggests itself as the plausible diagnosis, especially if the smear exhibits the above-described shifts. In young infants not even a focus is likely to produce any considerable rise in the white cell count and changes in the leucocyte count are diagnostically less conclusive than qualitative changes.

(vi) *Hypoproteinaemia*, described by SCHIFF and BAYER [29] as a characteristic and necessarily accompanying symptom of Leiner's disease, was present in every case. The serum protein value varied from 3.5 to 5.5 g per 100 ml, with 4.4 as the average in 250 cases. The average albumin-globulin ratio was 0.85.

Fig. 1 shows our findings concerning the average erythrocyte count, haemoglobin value, white blood cell

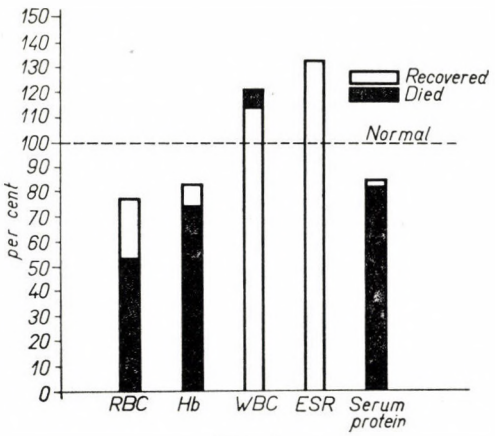

FIG. 1

count, erythrocyte volume index and serum protein value in the recovered (white sections) and died (shaded sections) patients as related to the corresponding normal values.

(vii) *The erythrocyte sedimentation rate* was usually low, varying between 2 and 6 mm per hour and agreed with the values for normal infants about 2 months of age, as observed also by BALLÓ [2]. In two gravely anaemic "white" cases the rates were as high as 20 to 35 mm.

(viii) *Paper electrophoresis.* In 50 cases the albumin level was diminished, associated for the greater part

with a conspicuous rise in alpha$_2$ globulin, a characteristic feature of the hypoproteinaemic syndromes. The low gamma globulin level partially explained the susceptibility to infection of the patients with Leiner's erythroderma. The average results were albumin, 48.5 per cent; alpha$_1$ 7.5 per cent; alpha$_2$ 15.5 per cent; beta, 13 per cent; gamma, 15.5 per cent.

(ix) *Blood group and Rh factor.* 175 patients were examined for blood groups and 65 for Rh factor. The results are shown in Table III.

The average duration of treatment was 53 days in cases with complications and 22.2 days in uncomplicated ones.

The increase in body weight during hospital treatment was 116 g for the recovered patients and nearly as much, 113 g, was the loss of weight of those who died.

(x) A further point is the mother's haematological state. Its influence on the infant is perhaps more important in Leiner's erythroderma than in any other infantile disease.

In 1954 when we first made a study of Leiner's disease in breast-fed infants, we observed a fairly high degree of anaemia in the mothers. In the present material the maternal red cell count was 3 500 000 on the average and the Hb value 11.4 g per 100 ml, i. e. hardly more than the values for their children at the age of 2 months (see Table IV).

Marked anaemia occurred in 20 per cent of the mothers, sometimes with an erythrocyte count as low as

TABLE III

Incidence of blood groups and Rh factor, in per cents

	Blood group				Rh factor	
	O	A	B	AB	+	−
Normal controls	32	42	18	8	86	14
Leiner's erythroderma recovered	41 (70)	30 (50)	19 (30)	10 (17)	78 (51)	22 (14)
died	—	(1)	(4)	(2)	—	—

(Figures in brackets show the number of cases)

What claims attention in Table III is the frequency of group 0 and the unproportionally high death among group B patients; the figures are too low, however, to permit of any statistical evaluation.

The fact should be noted that the number of Rh negatives exceeded the average Hungarian incidence; a similar experience has been emphasized in connection with other infantile diseases [9].

TABLE IV

Average data of the mothers

RBC	Hb g per 100 ml	Serum protein g per 100 ml	Maternal milk protein mg per 100 ml
3 500 000 (2.8—4.2 m)	11.4 (8.1—14.7)	7.1	1140 (830—1800)

2 800 000. This was due partly to the delivery and earlier affections, partly to a diet poor in protein and other factors. Treatment with liver extract, iron and blood transfusion in the graver cases, together with a protein-rich diet soon brought about improvement of both the haematological state and the quality of the milk, raising in the latter within 10 days the original 900 to 1000 mg protein content to a level sometimes as high as 1200 mg per 100 ml [10]. All this confirms our opinion first expressed by SEMENOVA [31], that treatment of Leiner's erythroderma should always be extended to the nursing mother in order to improve her haematological state.

As to the infant itself, local skin therapy and antibiotic hormonal (steroid) treatment must go hand in hand with an increased intake of nutrients to make up for the shortage prevailing mainly in the vitamin and protein supply, all this by the only possible way of re-establishing the haematological state of equilibrium. Moderately anaemic subjects should be given plasma, in addition to iron and vitamin B_{12}; in graver cases, transfusions of blood are necessary.

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SUMMARY

Observations made in 250 infants with Leiner's erythroderma have been reported. Anaemia was present in all of them and in most of the mothers. A relationship between the pathological course and the severity of anaemia has been established. When there are pyogenic complications or some focal process, marked shifts occur in the qualitative counts. Group 0 and Rh negativity were prevalent among the afflicted infants. The importance of simultaneously treating the mother with her child and the significance of improving the haematological state have been emphasized.

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