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Miscellanea.

The Neutropenic (Pancytopenic?) Type of Bacillary Dysentery

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Leucopenia is a wellknown consequence of bacterial infections as typhoid, paratyphoid and tuleraemia. Probably it also has been described in other infectious ailments, which due to their rare—or ill documented—occurrence, did not deserve a place in the usual textbooks. One of these—first described by FELSEN (1935)—is bacillary dysentery and it is to draw more attention to this probably not so uncommon entity that the following case histories are presented.

Case I. Th. E., a 76-year-old negroid male, was admitted to the hospital on May 13, 1964. He complained about fever and anorexia since 3 days, accompanied by mucous containing stools twice daily. He had been treated with guanimycin during two days without any result. Patient did not take any alcohol for years.

Examination did not show abnormalities.

Laboratorium: BSR 14 mm after 1 h, Hb 13.8 g%, WBC 3,350/mm³. Differential: Eo 1%, stabs 16%, segments 48%, lymphoc. 28%, monoc. 10%. SGOT 30 U. SGPT 40 U. Creatinine 9.2 mg/l. Sodium 136 maeq/l. Potassium 4.2 maeq/l. Chlor 90 maeq/l. Urine: no abnormalities. Stools: no parasites; culture: *shigella flexner* 2a. Bonemarrow examination showed a maturation arrest at the promyelocyte level. X ray chest: normal.

Course: The *sh. flexner* 2a infection was successfully cured with sulfaguanidine. A slight leucopenia was present as may be seen in Table 1.

TABLE 1. Th. E.

	14/5	15/5	16/5	17/5	19/5	21/5	20/7
RBC × 10^3	4,100	3,950	3,830	3,840	—	3,990	4,450
Ret. %	—	—	—	—	—	2.8	—
WBC	3,350	2,150	2,950	4,400	2,900	3,800	8,600
Gran. %	62	68	—	—	55	—	68
Platelets	—	229,100	203,000	245,800	—	375,100	324,000

RBC: red bloodcells/mm³. Ret.: reticulocytes. WBC: white bloodcells/mm³. Gran. %: granulocytes per 100 white bloodcells. Platelets/mm³.

Conclusion: A 76-year-old negroid male was admitted with a three days lasting diarrhoea due to a *sh. flexner* 2a infection. In spite of a disappointing response to guanimycin, a good result was obtained with sulfaguanidine. Furthermore a transient leucopenia was observed.

Case II. J. H., a negroid male of 71 years, was admitted August 5th, 1964, as he had collapsed in the office of his general practitioner. Since six days he

suffered from a blood and mucous containing diarrhoea, which had been stopped by the use of guanimycin. The day before admission his stools had become normal, but he still ran a fever.

Examination of this old, demented and dehydrated man presented a palatoschisis and a spleen which was enlarged to one finger below the left costal margin. Temperature 40.2°C.

Laboratorium: BSR 42 mm after 1 hour. Hb 11.2 g%, RBC 3,630,000/mm^3, WBC 1,100/mm^3. Differential: stabs 13%, segments 16%, lymphoc. 46%, monoc. 24%. Thymol T.T. 1.5 U. Alk. phosph. 1.4 U. (Bessy). Total protein 6.5 g%. Sodium 137 maeq/l. Potassium 4.4 maeq/l. Chlor 103 maeq/l. Creatinine 10 mg/l. Urea 190 mg/l. SGPT 19 U. Fasting bloodsugar 103 mg%. G 6 P.D. 160 U%. Agglutination typhoid O: 1/40 pos., typhoid H: 1/40 pos., paratyphoid B. O: 1/40 pos., H: neg. Urine: no abnormalities. Stools: no parasites; culture negative. X ray chest: In the right middle field were slight changes suggestive of an infiltrative process. The bonemarrow was essentially normal.

Course: Patient had been suffering from diarrhoea which had not been cultured and seemed successfully treated with guanimycin. Agglutination tests showed titers against: *sh. flexner* 1^b 1/160 pos., *sh. flexner* 2^a 1/40 pos., *sh. flexner* 4^a 1/1280 pos., *sh. flexner* 6 1/160 pos. Repetition 4 weeks later gave the same titers, making an infection with *sh. flexner* 4^a most likely. His son was admitted 2 weeks later suffering from a *sh. flexner* 2^a diarrhoea. He furthermore presented a fever and a bronchopneumonia which subsided after the administration of chloramphenicol during 5 days.

His leucopenia of unknown origin, which needed continuous penicillin to counteract secondary infection, was the reason of his prolonged admission. In spite of all kinds of treatment (Table 2) it was impossible to reach normal values. Also a slight depression of the number of platelets was observed.

TABLE 2. J. H.

	Pen-strep			Chloro		Vit. B 12 and folic acid.		Testeron	
	5/8	8/8	10/8	11/8	14/8	22/8	26/8	7/9	12/9
RBC × 10^3	3,630	3,640	3,620	3,700	3,790	3,560	3,530	3,560	3,960
Ret. %	—	0.9	1.0	0.5	0.6	2.2	2.0	2.3	2.8
WBC	1,100	600	325	350	650	120	800	1,300	1,050
Gran. %	29	26	30	—	32	—	56	56	58
Platelets	—	80,100	108,600	159,100	231,600	130,600	197,700	181,560	213,800

	Testeron and prednisolon			Vit. B 12 and folic acid.		ACTH and tetracycline		
	17/9	26/9	30/9	8/10	14/10	21/10	23/10	13/11
RBC × 10^3	3,640	3,980	4,120	4,710	—	5,350	4,600	4,400
Ret. %	2.1	2.4	2.5	3.5	1.8	0.8	0.9	0.6
WBC	800	1,900	3,800	2,000	700	1,900	900	1,400
Gran. %	44	76	87	81	62	69	12	33
Platelets	145,600	155,200	247,200	245,300	—	110,100	110,400	140,800

For explanation abreviations see Table 1.

October 29th the prophylactic penicillin was stopped for a few days resulting in a raised temperature. Patient died Nov. 15th of a coma due to pulmonary incompetence. At post mortem examination a generalised septicaemia was found with a severe bronchopneumonia. The spleen was enlarged and showed the characteristic changes of a septicaemia.

Conclusion: A 71-year-old negroid male was admitted with a history of diarrhoea, which had been successfully treated with guanimycin. He presented a leucopenia, fever and an enlarged spleen. It appeared impossible to correct the leucopenia and patient died of a generalised sepsis with a bronchopneumonia.

Case III. P. M., a 48-old-negroid in-patient of the mental hospital, suffered since 2 weeks from diarrhoea due to a *sh. flexner* 2c infection, which was treated with sulfaguanidine. He appeared to have 2,700 white bloodcells/mm^3 after which it was decided to give him chloramphenicol. The next day he was transferred to the general hospital as he still ran a fever. Here the chloramphenicol was not continued. For his epileptic insults during already considerable time patient received 200 mg phenobarbital and 200 mg dilantin daily.

Examination of this not so very cooperative patient demonstrated no gross abnormalities. Temp. 40°C.

Laboratorium: BSR 20 mm after 1 hour. Hb 15 g%. WBC 1,950/mm^3. Stabs 2%, segments 35%, lymphoc. 46%, monoc. 17%. Natrium 135 maeq/l. Kalium 4.8 maeq/l. Fasting bloodsugar 90 mg%. Vit. C 0.1 mg%. Urine: no abnormalities. Figlutest neg. Bonemarrow normal. Stools: no parasites; culture negative.

Course: Patient presented during this admission only once a loose stool which had a negative culture. Two bloodcultures failed to reveal bacterial growth. Treatment was started with 4 million units Pen. G. daily to counteract secondary infection in a granulocytopenic patient. This resulted in a normal temperature on the fifth day. The leuco- and thrombocyto-penia (Table III) corrected themselves spontaneously.

TABLE 3. P. M.

	2/9	3/9	5/9	7/9	10/9	12/9	15/9	18/9	21/9
RBC × 10^3	3,870	4,160	4,430	4,290	3,860	3,520	3,410	3,390	3,710
Ret. %	0.9	0.6	0.2	0.5	0.8	0.9	1.3	1.8	2.2
WBC	1,950	1,700	1,600	2,400	2,850	2,350	3,050	2,850	3,150
Gran. %	38	37	19	18	20	26	23	27	36
Platelets	100,600	112,300	53,200	55,770	77,200	306,200	259,200	237,300	316,200

Conclusion: A 48-year-old mental patient since 2 weeks suffering from a *shigella* 2c infection presented a leucopenia and thrombocytopenia which disappeared without any specific treatment.

Case IV. F. K., a 43-year-old negroid male and known potator, was admitted on February 10th, 1964. The day before he had been watching a footballmatch in apparently good health. At 10 h p.m. he got shiverings followed by abdominal cramps and diarrhoea. The stools consisted of blood and mucous only. The doctor, called for the next day, advised admission in view of the dehydration. Patient was sure not to have used any drug during the last weeks.

TABLE 4. F. K.

	10/2	11/2	12/2	13/2	15/2	16/2	18/2
RBC × 10^3	4,410	3,940	3,810	3,540	3,640	2,950	4,010
Ret. %	0.5	0.5	—	0.3	0.2	0.1	0.1
WBC	250	300	1,950	3,900	3,050	3,500	2,300
Gran. %	25	17	75	85	93	94	92
Platelets	97,000	122,100	—	14,160	2,050	2,950	20,000

	21/2	24/2	26/2	28/2	4/3	7/3	23/3
RBC × 10^3	4,680	4,260	4,030	3,510	3,330	3,050	2,470
Ret. %	—	0.3	0.7	0.8	0.6	0.7	5.4
WBC	4,400	5,400	3,400	5,050	—	—	8,300
Gran. %	90	90	76	—	—	—	77
Platelets	9,300	55,400	60,500	42,100	103,200	128,100	385,100

Examination showed him to be delirious and severely dehydrated. He had a "facies abdominalis" and a quick and superficial respiration. Pulse 148; bloodpressure 70/40; temperature 40.6°C.

Above both lower lung-fields a few rhales were heard due to a bronchopneumonia, as was confirmed on the X ray. Abdomen distended, tympanitic, painful on palpation; weak peristaltic sounds.

Laboratorium: Hb 14.4 g%, WBC 250/mm^3, platelets 96,000/mm^3, reticulocytes 0.5%. Differentiation: eos 2%, juveniles 2%, stabs 13%, segments 8%, lymphoc. 52%, monoc. 23%. The segmented cells had vacuoles in the protoplasma. Sodium 118 maeq/l. Potassium 3.2 maeq/l. Creatinine 39.3 mg/l. Figlutest positive. Stool: no parasites; culture *sh. flexner* 2[a].

Course: Patient was immediately treated with saline-dextrose terramycin and cortef intravenously. The day after admission he showed slight improvement. The temperature fell, the pulse-rate became slower and the bloodpressure was 135/70. Patient was however still soporous, the abdomen was still more enlarged by meteorismus and no peristaltic sounds could be heard. It was decided to administer continuous suction by a duodenal tube and to feed patient parenterally.

From this moment we were faced with 3 problems: dysentery, leucopenia with thrombocytopenia and uraemia.

The dysentery resulted in a severe colitis and was followed by chronic constipation.

The data of the leucopenia and thrombocytopenia have been given in Table 4. This thrombocytopenia gave rise to intestinal haemorrhages which were treated with 500-1,500 ml EDTA blood daily. In respect of the grave situation it was decided not to withhold any drug that might be of value. This resulted in a polypragmasia which made it impossible to evaluate any of used medicines.

The uraemia was partly due to the dehydration causing a lower nephronnephrosis, and partly due to the intestinal haemorrhages.

Conclusion: A 43-year-old patient presented a *sh. flexner* 2a dysentery with leucopenia and thrombocytopenia. It was possible, thanks to heroic treatment, to save patient's life, after which he seemed to have made a complete cure.

Discussion.

These four case histories have in common a *sh. flexner* infection —be it of different subtype—and a leucopenia as a sign of a possibly more complicated haematological disturbance. As these patients have been all encountered during 1964, it seems likely that the combination dysentery and leucopenia is much more frequent than generally thought.

A relative leucopenia—according to our experience—seems more frequently met with in the tropics than in the moderate climates and we therefore want to define the existence of a leucopenia if the number of white bloodcells falls below 3,000/mm^3.

Two reports have been available to us reporting this combination of dysentery and leucopenia. FELSEN (1935) presented two cases of rsp. *sh. flexner* and *sh. sonnei.* The third case described by him would at present be classified as a paratyphoid infection. VAN DER SAR (1955) reported on one proven and one possible case of flexner dysentery.

A thrombocytopenia was observed in our patients J. H., P. M., F. K., between the 5th and 17th day of the onset of the disease. In one of these patients the thrombocytopenia persisted a considerable time longer than the leucopenia.

A depression in the activity of the red bonemarrow, which is followed by a hyperactivity during convalescence, also seems to be present during the period of the thrombocytopenia if we may consider the number of reticulocytes an indicator of the red cell production.

It is hard to understand why some patients with a flexner dysentery present a leucopenia and others do not.

Bonemarrow examination, needed to exclude diseases as leucaemia and agranulocytosis, is of little help answering this question. The marrow is either normal or shows a "maturation arrest" at the promyelocyt level.

Signs of megaloblastosis cannot be found, which excludes a frank deficiency of Vit. B12 of folic acid. However, a borderline lack of folic acid could be demonstrated in our patient F. K. who had a positive Figlu-test.

A careful taken case-history is indispensable in search for factors inducing leucopenia. In our patients it appeared to be of little help in finding a common denominator.

Drugs capable of producing leucopenia were used by two of our patients, J. H. and P. M. The latter had been taking dilantin and phenobarbital during considerable time. This medication was not stopped and patient recovered in spite of this, making a possible relation between those drugs and leucopenia unlikely. Both patients had been given sulfaguanidine, a sulfa-drug theoretically capable of producing leucopenia, but being insoluble most likely harmless. The one day treatment with chloramphenicol of P. M. was instituted after the discovery of the leucopenia and as such was non-contributing but might have had its influence on the course of the leucopenia.

Alcohol, alone (SULLIVAN & HERBERT, 1964) or in combination with pneumonia (MCFARLAND & LIBRE, 1963) was recently stated to be a cause of leucopenia. It was, however, taken regularly by one patient (F. K.) only.

The only possibly leucopenia inducing factor which may be found by medical examination is an enlarged spleen. This was found in only one of these

patients, which argues against hypersplenism as a possible cause of the leucopenia. Chronic forms of leucopenia—f.e. the periodic or cyclic neutropenia (HATTERSLEY, 1947)—have been excluded by the follow up of our patients.

Not one of the usual leucopenia inducing factors has been observed in every one of our patients. For this reason the observed decrease of leucocytes, thrombocytes and possibly of the erythrocytes seems due to the flexner infection. This leaves, however, unanswered the problem if a flexner infection alone is capable of the described bloodchanges or if contributing factors are needed as old age, malnutrition, etc.

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