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ACUTE APLASTIC ANÆMIA FOLLOWING ANTISYPHILITIC TREATMENT

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THIS paper records a fatal case of acute anæmia of aplastic type, arising in the course of antisyphilitic therapy.

History.—The patient, a woman aged 56, was first seen in June, 1931, suffering from a vulvar chancre and generalised papular secondary eruption, the Wassermann reaction being strongly positive. Three intravenous injections of stabilarsan (0·3 gm., 0·45 gm., 0·45 gm.) were administered, but the patient developed a generalised arsenical dermatitis in July, and treatment was discontinued. Therapy was resumed in December, and a total of 2·85 gm. of stabilarsan was administered until April, 1932. The patient then ceased attending, and was not seen again for ten years (June, 1942), when she was found to have a left third nerve paralysis; the blood Wassermann reaction was weak positive (+) and the Kahn positive +2. From June to August, 1942, she attended for treatment regularly and received 3·15 gm. stabilarsan intravenously and 6 c.c. chlorostab intramuscularly. The patient went away for a short holiday in August feeling well, but returned at the end of the month looking extremely ill and showing a widespread purpuric eruption. Hospital treatment was then recommended.

Clinical Features on Admission to Hospital.—On examination (5.9.42) the patient was very pale and breathless. Both pupils were irregular, the left being enlarged and failing to react to light and accommodation; the right pupil reacted to light sluggishly. There was a left-sided ptosis. Physical signs indicated the presence of chronic bronchitis. There was a profuse purpuric eruption over the chest and both arms, with a more discrete eruption in the flanks and on the thighs. The temperature was 99° F. on admission, but during her stay in hospital varied from 98° to 104·6° F.

Hæmatological Findings.—Results of various blood examinations are shown in Table I.

TABLE I

Date of Examination.	7.9.42.	14.9.42.	24.9.42.
Hæmoglobin per cent.	31	25	37
Red blood cells (millions per c.mm.)	1·59	1·14	2·11
Colour index	1	1·1	·9
Reticulocytes per cent.	Under 1	Under 1	Under 1
R.B.C. mean diameter (μ)	—	—	7·6
Mean corpuscular volume (cubic microns)	97	100	—
Blood sedimentation rate (corrected, mm. fall in 1 hr.)	22	—	—
W.B.C. per c.mm.	3000	488	866
Polymorphs per cent.	28	12	60
Lymphocytes per cent.	72	88	40
Platelets per c.mm.	Under 10,000	—	Under 5000
Coagulation time (minutes)	8	—	—
Bleeding time (minutes)	Over 15	—	—
Hess's capillary resistance test	Strongly positive	—	—

Serological Findings.—The blood Wassermann reaction was found to be weak positive (+) and the Kahn positive +2 (10.9.42).

Biopsies of Sternal Marrow.—Sternal puncture was carried out on two occasions, and the cellularity was found to be definitely low. The differential counts of 400 nucleated cells in each case are shown in Table II. The terminology used to describe the red cell precursors is that of Israëls (1939).

TABLE II

Sternal Marrow Biopsies

Date of Examination.	8.9.42.	24.9.42.
Myeloblasts	2·5	3·5
Premyelocytes	28·5	17·0
Neutrophil myelocytes	30·25	39·0
Neutrophil metamyelocytes	4·75	8
Basophils	Nil	Nil
Eosinophils	1·75	0·5
Neutrophil polymorphs	0·25	3·0
Lymphocytes	22·75	19·0
Plasma cells	4·75	4·0
Pro-erythroblasts	Nil.	0·5
Early normoblasts	1·75	1
Intermediate normoblasts	2·0	1·5
Late normoblasts	0·75	3

Treatment and Progress in Hospital.—From these various examinations a diagnosis was made of acute aplastic anæmia following antisyphilitic therapy, and the following treatment was administered :

(*a*) colliron, 45 minims t.d.s. ;
(*b*) pernaemon forte, 2 c.c. daily intramuscularly ;
(*c*) sodium pentose nucleotide, 25 c.c. twice daily intramuscularly ;
(*d*) blood transfusions were given on 10.9.42 (1 pint), 15.9.42 (3 pints) and 24.9.42 (1 pint); 40 c.c. sodium pentose nucleotide was administered intravenously along with the last transfusion.

Despite all this treatment, directed towards causing regeneration of blood-forming tissue, the patient's condition became worse, and she died on 27.9.42.

Autopsy Findings.—Numerous petechial hæmorrhages were present in the skin and in the serous membranes. The mouth was ulcerated. Marrow from the middle of the right femur was examined by frozen section and found to consist of fatty tissue only. The lungs showed an acute terminal broncho-pneumonia. The liver was pale, and microscopically showed well-marked fatty degeneration, mainly of the cells at the peripheral part of the lobule. The kidneys were pale, and microscopically showed cloudy swelling of the tubular epithelium ; there was some evidence of extramedullary hæmopoietic tissue. The spleen was of normal size and consistence and gave a positive Prussian blue reaction ; microscopically, there was some infiltration with cells of myelocytic type. There were some enlarged lymph glands alongside the abdominal aorta ; microscopically the structure was that of numerous dilated vascular spaces surrounded by a pulp infiltrated by myelocytes.

Discussion.—Blood dyscrasias are well recognised, though fortunately rare, complications of antisyphilitic therapy, and can be divided into the following types (McCarthy and Wilson, 1932) : (1) thrombocytopenic ; (2) granulocytopenic ; (3) aplastic. Approximately 50 cases of anæmia of this third or aplastic type have been described, following arsenical therapy (see Kadin, 1938), and we now add a further. Anæmia of aplastic type has been recorded in patients who have received either small or large doses of arsenic (see, von Bonsdorff, 1937 ; Kadin, 1938 ; Bomford and Rhoads, 1941*b*), and in many cases this occurrence

can be regarded definitely as a manifestation of intolerance to arsenic. In support of this contention it is of interest to note in our case that, when the patient was first treated in 1931, dermatitis appeared after a very small quantity of arsenic had been given.

The clinical features of the other cases recorded in the literature seem to be similar to those in our patient, signs of profound anæmia, purpuric hæmorrhages, and ulceration of the mouth being the cardinal findings.

The previously recorded hæmatological results have likewise been similar to ours, severe anæmia, thrombocytopenia, and granulocytopenia being characteristic.

Biopsy of sternal or tibial marrow has been performed on cases of anæmia of aplastic type following antisyphilitic therapy (*e.g.* by Smith and Lyon, 1935; Bomford and Rhoads, 1941*b*). This examination is obviously indicated in these cases, first from a diagnostic point of view to exclude other conditions such as aleukæmic leukæmia and secondary carcinomatosis, which by interfering with normal erythropoiesis may produce such a clinical and hæmatological picture. Secondly, sternal puncture is of value from the point of view of prognosis by assessing the degree of aplasia. Thus in our case, although few segmented polymorphs were found, there were in fact numerous white cell precursors, and it seemed perfectly rational, therefore, to institute treatment designed to stimulate the production of granulocytes. Further, a few red cell precursors were also present, suggesting that red cell regeneration was theoretically possible, if only it could once be initiated. Unfortunately, however, in our case active measures to stimulate erythropoiesis entirely failed.

Concerning the autopsy findings, they also seem to resemble those previously described. Bomford and Rhoads (1941*a*), for example, state that extramedullary hæmopoiesis, hæmosiderosis, and liver necrosis were frequently found in their cases of refractory anæmia.

Finally, with regard to the terminology appropriate in this case, despite the fact that the sternal marrow was not by any means completely aplastic, but was hypoplastic, we use the term "aplastic anæmia." It would appear to be perfectly justifiable to employ this term because Bomford and Rhoads (1941*a*) in their monograph on refractory anæmia state that the term "aplastic anæmia" can reasonably be used to include any anæmia in which there is definite hypoplasia of the hæmopoietic marrow. An alternative term used by these authors is "refractory

anæmia with hypocellular marrow." According to Whitby and Britton (1942) our case would be classifiable as a "complete aplastic anæmia," in which failure of production of mature cells was due mainly to a maturation defect rather than to a complete absence of the necessary precursor cells.

Summary.—Full clinical, hæmatological, sternal biopsy, and autopsy findings are recorded in a case of general aplastic anæmia, associated with antisyphilitic therapy.

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