SPLENO-MYELOGENOUS LEUKÆMIA ;

WITH DISAPPEARANCE OF THE SPLEEN TUMOUR AND OF THE
MYELOCYTES FROM THE BLOOD.

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THIS case is reported on account of the unusual features shown in the course of the disease. So far as a search of the literature has shown no such case has been reported.

R. J., male, aged 28 years, white, stockfarmer, was first seen on September 28th, 1898, when he came complaining of weakness. His family history was negative, although he thought he came from a neurotic stock. He had had the ordinary diseases of childhood, and was always delicate as a child. His digestion had always been weak, and he was subject to frequent attacks of dyspepsia. His colour had always been sallow. He used neither tobacco nor alcohol, and denied syphilis. His occupation kept him out of doors a great deal, but did not involve any exposure. His present illness had no very easily determined time of onset. His previous attacks of weakness and indigestion had become more frequent and severe since August of 1897. He had had several acute attacks of stomach trouble with much pain but no vomiting. At times, after December, 1897, he had frequent attacks of herpes preputialis, and with these very troublesome erections lasting sometimes for several hours. In the spring of 1898 he became very weak and nervous, and went to the sanatorium at Clifton Springs, New York, where it was discovered that his spleen was enlarged. He had not noticed this himself until his attention was directed to it. Through the kindness of Dr. Lichty, of Clifton Springs, I am able to give the blood condition at that time. He was good enough to send the blood counts made at the time, and also his dried specimens of the blood. Dr. Lichty's note of June 21st, 1898, was: "The spleen is much enlarged, coming to within 2½ inches of the navel. The edge is rough." The blood examination at that time showed hæmoglobin 45 per cent., red corpuscles 2,680,000, and white corpuscles 584,000 per c.mm. The differential count, made from the dried specimens sent by Dr. Lichty, showed:

Polymorphonuclears	...	...	72 per cent.
Mononuclears, etc.	...	...	2 "
Eosinophiles	...	...	3 "
Myelocytes	...	...	23 "

In counting 600 white cells 6 nucleated reds were seen, all normoblasts.

Dr. Lichty made the diagnosis of "spleno-myelogenous leukæmia," and put the patient on arsenic with general hygienic treatment. On August 1st, 1898, the spleen was barely palpable, and the blood count was hæmoglobin 65 per cent., red cells 4,240,000, and white cells 184,000 per c.mm. A differential count, also made from the slides furnished by Dr. Lichty, showed:

Polymorphonuclears	...	...	90 per cent.
Mononuclears, etc.	...	...	2 "
Eosinophiles	...	...	3 "
Myelocytes	...	...	5 "

In counting 500 white cells, 7 nucleated reds were seen, of which 6 were normoblasts and 1 a megaloblast.

He left Clifton Springs in August, 1898, and had been gaining gradually until he was seen in Baltimore in September, 1898. Examination then showed a sparsely-nourished man, who had no difficulty in getting about, although rather easily fatigued. His colour was sallow but there was no yellow tint. The mucous membranes were of fair colour. The lymphatic glands were palpable but not specially enlarged. The thorax was negative. The spleen could just be felt on deep inspiration. The blood examination showed: Hæmoglobin 68 per cent., red cells 4,640,000, and white cells 9,250 per c.mm. The differential count of 1,000 whites showed:

Polymorphonuclears	...	...	84 per cent.
Small mononuclears	...	...	10 "
Large " and transitionals	...	...	4 "
Eosinophiles	...	...	2 "

The red cells showed very slight variation from the normal in shape and size. No nucleated red cells or myelocytes were found.

To recapitulate: The patient, in June of 1898, undoubtedly had "spleno myelogenous leukæmia," with a much enlarged spleen, and 584,000 white corpuscles per c.mm., of which 23 per cent. were myelocytes. In September of the same year the spleen was barely palpable and the blood count was practically a normal one. Until the account of Dr. Lichty's blood examination was forwarded considerable doubt was felt as to the existence of leukæmia in June. The patient was advised to continue the use of arsenic for about three weeks in each month, during each period increasing the dose of Fowler's solution from 3 to 10 drops three times a day.

He again came under observation in November, 1898, when he was admitted to the service of Professor Osler in the Johns Hopkins Hospital. His general condition was much the same as on the last note. He looked rather sallow, and complained especially of his digestion. During the interval he had taken arsenic fairly regularly. Examination showed that the spleen was somewhat enlarged. Its edge was hard and firm, and palpable 2½ cm. below the costal margin. There was slight dilatation of the stomach. The edge of the liver could be felt. The blood examination: Hæmoglobin 67 per cent., red corpuscles 4,160,000, and white corpuscles 178,000 per c.mm. The differential count of 1,000 whites showed:

Polymorphonuclears	...	...	67 per cent.
"Doubtful" forms	...	...	0 "
Mononuclears	...	...	2 "
Eosinophiles	...	...	1 "
Mastzellen	...	...	1 "
Myelocytes	...	...	20 "

The red cells showed but little variation from normal in either shape, size, or staining. In counting 1,000 white cells, 18 nucleated reds were seen, of which 12 were normoblasts and 6 intermediate forms between normoblasts and megaloblasts. The white cells classed as "doubtful" were between myelocytes and multinuclear neutrophils. They were smaller than the average neutrophile, and had a single eccentric nicked nucleus with a neutrophilic granulation. The myelocytes varied much in size, the majority being smaller than usual.

The patient remained in the hospital until December 10th, 1898, when Dr. Osler noted: "The edge of the spleen on quiet respiration cannot be felt. On deep inspiration it is just palpable." The blood then showed 98,000 white corpuscles per c.mm. The differential count showed 81 per cent. of polymorphonuclears and only 8 per cent. of myelocytes. In counting 1,000 white corpuscles, 16 nucleated reds were seen.

He was advised to continue the arsenic as before. During his stay in the hospital, he took 10 drops of Fowler's solution three times a day. He spent the winter in Florida, and was again seen in April, 1899. He had continued the arsenic during the interval. His general condition was excellent; he had gained weight, and his digestion was good. The area of stomach tympany was normal, and the spleen could not be felt even on the deepest inspiration. The blood examination was practically normal. Hæmoglobin 70 per cent., red corpuscles 5,328,000, and white corpuscles 5,000 per c.mm. The differential count was normal. There were no myelocytes or nucleated reds found.

This patient therefore came twice under observation with the typical condition of spleno-myelogenous leukæmia. On each occasion, under the use of arsenic, the leukæmic condition disappeared. The spleen became reduced to normal size, and the myelocytes disappeared from the blood. At these periods his health was good, and there was not any intercurrent affection present. The main blood counts of the white cells and the differential counts may be tabulated:

Date.	June, 1898.	Sept., 1898.	Nov., 1898.	April, 1899.
Leucocytes...	584,000	9,250	178,000	5,000
Polymorphonuclears	72.0	84.0	67 + 9.0 (?)	66.0
Small mononuclears	0.30	10.0	0.20	13.0
Large mononuclears and transitionals	0.60	4.0	1.80	16.0
Eosinophiles	3.0	2.0	1.0	2.0
Myelocytes...	23.0	0.0	20.0	0.0
Nucleated reds	6	0	18	0

His subsequent history was unfortunately not obtained in any detail. He went to California, and died there some months later. His death was sudden, and considered by his physician to be due to cerebral hæmorrhage.

As already stated, no similar case has been found in the literature. It is impossible to know how long the patient had been suffering from leukæmia when he first came under observation. The occurrence of priapism in December of 1897 suggests the existence of the disease at that date. Twice during the space of less than twelve months he showed typical features of spleno-myelogenous leukæmia, and twice was his condition a normal one. Emphasis may be laid on the fact that at neither of these times was there any intercurrent disease. He seemed in ordinary good health.

Changes in the condition of a leukæmic patient may be considered under two headings, (1) when an intercurrent malady is present, and (2) where improvement occurs, as in the present case. It has been recognised for some years that other conditions arising in a leukæmic patient may so alter the blood that the specific features are absent. This has been noted in connection with typhoid fever, influenza, erysipelas, septic infections, etc. Many of these cases have been tabulated by Marischler¹ in an article dealing especially with the influence of malignant growth on leukæmia. The most striking change, however, occurs with a septic infection. Fraenkel² has reported two cases of much interest. In one, on March 6th, the patient had 89,000 leucocytes per c.mm., the majority of which were lymphocytes. On March 21st there was a staphylococcus infection, and on March 26th the leucocytes had fallen to 6,000 per c.mm. In the second case the white cells fell in a few days from 220,000 per c.mm. to 1,200. The lymphocytes were 99 per cent. on the first date and 81 per cent. on the second. Death followed in both of these cases. Müller³ reports a case of acute leukæmia in a child with a staphylococcus infection in which the leucocytes fell from 109,600 to 6,800 per c.mm. In going over the records of a series of cases of leukæmia, it is striking to note the decrease in the number of leucocytes shortly before death in many of them. This is probably due to terminal infections. Fraenkel also refers to Eisenlohr's case, in which during an intercurrent

attack of typhoid fever the leucocytes fell to normal but returned to their previous condition after recovery.

In the second group are the cases in which, apart from any intercurrent affection, a marked change in the condition occurs. This, however, rarely goes to complete disappearance of all the special features of the disease. The spleen tumour may rapidly disappear, as in a case reported by Rensselaer,⁴ in which on November 21st there were 1,095,000 leucocytes per c.mm., and the spleen extended 4 inches to the right of and 1 inch below the umbilicus. There were many myelocytes present. The patient was given arsenic, and on December 23rd of the same year the white cells were 160,000 per c.mm., while the spleen had steadily reduced in size, and could not be felt. The patient died suddenly with convulsions soon after. Stengel⁵ refers to a case where the differential count was normal during improvement, but with characters not unlike a pernicious anæmia. Subsequently the blood picture of leukæmia returned, and the patient died.

Another class of cases show marked changes in the blood, but the enlarged spleen persists. Thus Osler⁶ has referred to a case of spleno-myelogenous leukæmia in which, the leucocytes fell to normal, but always showed a certain percentage of myelocytes. The enlarged spleen persisted. The case may be referred to in some detail. The patient was a coloured man, aged 24 years, who was first seen in the autumn of 1890, when he gave a history of having noticed a swelling in the abdomen about one year previously. He had frequent diarrhoea, and complained of having lost much strength. The spleen was much enlarged, and the blood showed 500,000 leucocytes per c.mm. In January, 1891, there were 714,000 leucocytes per c.mm., of which 23.5 per cent. were myelocytes. The spleen was still enlarged. He was put on arsenic, and in a month his blood condition was: hæmoglobin, 44 per cent.; red cells, 3,500,000, and white cells, 7,500, per c.mm. As Dr. Osler points out, were such a case seen for the first time with this blood count, a diagnosis of leukæmia would hardly be made, even with the enlarged spleen. The differential count, however, showed the presence of 4 per cent. of myelocytes. He was admitted to the Johns Hopkins Hospital in March of 1891. The spleen then extended to the right of the navel, and nearly to the crest of the left ilium. When discharged in May of 1891 the spleen was still enlarged, and the leucocytes were 9,500.

He was again admitted to the hospital in February of 1892. The spleen was much enlarged, reaching almost to the middle of Poupart's ligament on the right side. The hæmoglobin was 45 per cent., red cells 2,765,000, and white cells 230,000 per c.mm. Under treatment the leucocytes fell to 63,000. Myelocytes were found on every examination. This patient died in November of 1892. Although in this case the number of leucocytes at times fell to normal, marked enlargement of the spleen was always present and a certain percentage of myelocytes always found.

Bramwell⁷ reports a similar case coming under observation, with an enormously enlarged spleen and 210,000 leucocytes per c.mm., of which 29 per cent. were myelocytes. Under treatment the leucocytes fell to normal, although there were still myelocytes present. He also reports the case of a man seen in 1870, whose illness only dated back two or three weeks. The spleen half filled the abdomen; the lymph glands were not enlarged. On examining the blood, the white cells seemed almost as numerous as the red. Large doses of quinine and iron were given, and in a few weeks the enlargement of the spleen and the increase in the leucocytes had disappeared.

Da Costa and Hershey⁸ report 2 cases of leukæmia treated by inhalations of oxygen, in one of which the leucocytes diminished from 320,000 to 12,000 per c.mm. The enlargement of the spleen persisted. There was no note as to myelocytes.

These cases show the rapid changes that may occur in the course of spleno-myelogenous leukæmia. Thus in the cases reported by Osler and Bramwell enormous reduction of the white corpuscles took place in a period of about a month. In the present case, in less than three months, the leucocytes fell from 584,000 per c.mm. to normal, and again in two months they had risen to 178,000. In all the cases reported, in which an intercurrent infection has brought the blood to normal, there was a return to the leukæmic condition if the patient

survived. The cases of the second group show the occurrence of a return of the leucocytes to a normal number, but with usually a percentage of abnormal elements present and the persistence of the enlarged spleen. The present case shows the possibility of the disappearance of all these symptoms, but also shows that, in spite of the temporary improvement, the essentially fatal character of the disease is not altered.

REFERENCES.

- ¹ Marischler, *Wien. klin. Woch.*, 1896, p. 686. ² Fraenkel, *Deut. med. Woch.*, 1895, xxi, p. 639 *et seq.* ³ Müller, *Jahrb. f. Kinderheilk.*, 1896, xliii, p. 130. ⁴ Rensselaer, *Albany M. Ann.*, 1897, xviii, p. 530. ⁵ Stengel, *Progressive Medicine*, June, 1899. ⁶ Osler, *Textbook of Medicine*. ⁷ Bramwell, *Anæmia*, 1899. ⁸ Da Costa and Hershey, *Amer. Journ. of Med. Sci.*, 1889.

MEMORANDA : MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, Etc.

PIECE OF AMBER IN A BRONCHUS FOR TEN WEEKS.

F. R. consulted me first on August 12th. He stated that on the previous evening, while smoking, a lad accidentally stumbled against him and broke the amber of his pipe. The roof of his mouth was cut, and he believed he must have swallowed a portion of the mouthpiece which could not be found. Immediately afterwards he spat out a large quantity of blood, and continued to spit blood at intervals all night, probably from the wound in the mouth. He also began to be troubled with slight dyspnoea and a frequent short cough. On examination, twenty-four hours after the accident, there were found slight dulness and diminished expansion at the base of the left lung, and a few moist râles, otherwise the chest was normal.

A sedative cough mixture was prescribed, and for the next two months he continued at his work as a coachman. At the end of that time he had to take to bed. The diminished expansion and dulness at the left base were now more apparent, and all over the left lung numerous sibilant rhonchi could be heard. There was frequent expectoration of a dark-coloured stringy mucus which was at no time purulent. Rest in bed was the only treatment that did any good though the rhonchi never entirely disappeared.

Finally, on November 10th, or more than ten weeks after the accident, he coughed up without any trouble, when sitting up in bed to take his breakfast, the end of an amber mouthpiece. It measured $1\frac{1}{2}$ inch long, $\frac{3}{8}$ inch broad, and $\frac{1}{8}$ inch thick. The rhonchi, cough, and other symptoms disappeared at once.

On examination a month later nothing abnormal could be discovered in the chest. I attribute the very slight dyspnoea in this case to the fact that there was a fairly large hole in the centre of the amber, and as it would lie lengthways in one of the larger bronchi, a limited amount of air would be able to pass.

I am indebted to my friend, Dr. Richardson, for the accompanying photograph.

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AMPUTATION WITHOUT ANÆSTHESIA.

LIKE Mr. Christopher Heath, I am not old enough to have practised surgery in the ante-anæsthesia days, but on one occasion, some years ago, I was compelled by circumstances to amputate a leg without chloroform. I have amputated many legs since with chloroform, but the case I now relate left a lasting impression on my memory, because I felt nearly as bad as the poor patient did; indeed, she seemed less concerned during the ordeal than I was.

A black woman, between 30 and 40 years old, was admitted to my hospital in one of the country districts of Jamaica with an incurable ulcer involving the bones of the foot, for