SPLENIC LEUKAEMIA AND PHTHISIS COMBINED IN THE SAME PATIENT.*

BY G. PARKER, M.A., M.D.CANTAB.,

Physician to the General Hospital; Lecturer on Toxicology, University College, Bristol.

THIS patient presents a condition of which apparently no example has hitherto been reported in this country. Close as the connexion is between lymphadenoma or pseudo-leukaemia and pulmonary tuberculosis, the combination of true leukaemia with phthisis is exceedingly rare, and, though a few instances have been met with where the lymphatic form was present in this combination, no case of pure spleno-myelogenous leukaemia had till recently been recorded in which phthisis also existed. Of late some interest has been excited in the subject by the report of two undoubted instances by American observers, who failed to discover any others in the literature of the subject except a mixed case described by Quincke.[1] Cabot, Stengel, Osler, Janeway, and Prudden had never met with an instance, and neither Bramwell nor Muir mentions it. Indeed, there is some reason to think that an antagonism does exist between the two diseases, and that tuberculosis can rarely gain a foothold in the presence of the blood state which is characteristic of leukaemia. Another reason for interest is the effect which acute and chronic intercurrent diseases have upon this blood state. Thus, various infections make the blood again normal, at least for a time. I shall refer to many remarkable instances of this later on, though in none has a permanent cure resulted. Cabot has collected 17 such cases, and in nearly all there was a great reduction of the leucocytes, with often a relative increase of the polymorphonuclear ones.

History.—J. L., aged 34, a well-built man, an engine fitter by trade, came under my care in Febuary, 1900, complaining of severe pain in the left side. The right side of the chest was remarkably flattened and contracted, which he had noticed for some ten years, but he had no recollection of any illness preceding it. However, seven years ago he was troubled with hoarseness and attended the Royal Infirmary under Dr. P. Watson Williams, who diagnosed laryngeal phthisis and treated him with success. He remained in vigorous health, weighing about 11 stone, his height being 5 ft. 9 in., until May, 1899, when he fell from a platform and his left side came into collision with the corner of a table. This was followed by dragging pains on the same side, but lower down, together with a feeling of weakness, for which he was attended by his club doctor. The family history was good, all brothers and sisters and his mother were alive and well; his father died suddenly from supposed heart disease at 40. One grandfather had suffered from chronic "bronchitis," and died at 50, but no relations had been known to be phthisical.

State on Examination.—The right side of his chest showed strong evidence of old phthisis, and of a cavity extending under the first two or three intercostal spaces. The breath sounds were altered in character, too, over a large part of the lung and were feeble everywhere; nor did the disease seem to be altogether inactive, though evidently it did not much affect his general health or interfere with his work. In the splenic region I detected a rather hard mass extending a short distance below the ribs, which did not present the usual outlines of a spleen. There was no tenderness or enlarged glands, and the abdomen was otherwise normal. Mr. Morton saw him in consultation with me, and as the nature of the tumour was uncertain, he was admitted to the General Hospital on March 26th for an exploratory operation. He remained there for three weeks under observation, and his blood was repeatedly tested. The possibility of leukaemia was apparently negatived by the findings, though, of course, the state of the blood is not an infallible guide. The large lymphocytes seemed at first to be more numerous than usual, but on further investigation nothing abnormal could be detected. While in the hospital some of the submaxillary glands became enlarged on both sides, which he said had happened before. The lung condition made little or no progress, the kidneys and heart were normal, but the temperature often showed an evening rise to 100° or 101°.

Exploratory Operation.—Finally Mr. Morton made an exploratory incision, and found that the tumour was formed by the spleen slightly enlarged, bound down by adhesions, and rotated on its axis. In other respects nothing abnormal could be discovered. The patient made a quick recovery, and afterwards his pains were greatly relieved.

Progress.—A fortnight later the irregular temperature returned, and a blood count made on May 3rd showed red cells numbering 4,000,000, white cells 16,560, haemoglobin 76 per cent., but he rapidly improved and gained weight.

On August 17th he reported that he had been at work for a month, and that there was still a little pain over the spleen, which now extended to the level of the umbilicus and to the linea alba. In the right lung there was bronchial breathing over the first right intercostal space and over the apex down to the level of the spine of the scapula with very few *râles*. Elsewhere the breath sounds, though weak, were normal. The last blood count showed 4,500,000 red cells, He was told to continue taking creosote and arsenic.

He remained well during the winter, but in March, 1901, a great change was found. The blood was completely altered. The red cells still numbered 4,000,000 but the white had gone up to 238,000, and a large number of myelocytes were present. The spleen was still more enlarged, and reached four fingerbreadths below the umbilicus, and three beyond the middle line. The cough became troublesome, and slight haemoptysis took place. Gastric disturbance made it difficult for him to take arsenic. This, however, subsided by April 18th, and he then took ½ gr. of sodium cacodylate three times a day. The spleen diminished, and extended only three fingerbreadths below the umbilicus, and two beyond the middle line.

April 26th. The cacodylate was increased to 1½ gr. daily, which was taken without difficulty. The spleen was slightly larger, but the patient felt fairly well and remained at work all the summer. The blood count in June showed the red cells were only 2,800,000, while the white reached the enormous number of 640,000. The arsenic had, however, about this time to be stopped for two months on account of a rash. A differential count of white cells for May is given below.

October 21st. Cough and hoarseness became troublesome, but the breath sounds in the right lung were nearly normal up to the first space. The spleen remained at the same size as in March, and he was taking a grain of cacodylate daily, which was now doubled. An effusion of blood under the conjunctiva of the right eye occurred about this date.

In November he had to give up work. Some heart failure came on with a rapid pulse and oedema of the legs. The red cells dropped again to 2,640,000, but the white were much improved, numbering only 100,000. He remained in bed a few days from a bronchial attack and cardiac weakness.

January 17th, 1902. He was now taking 3 gr. of cacodylate daily, but had occasional attacks of dyspepsia as before. The heart was normal and the oedema had disappeared. The spleen was unaltered in size. The cough continued troublesome, and at the left apex there was prolonged expiration and a few *râles*. At the right apex the signs were as before, in the second intercostal space prolonged expiration with a few *râles* were noted, and a few scattered *râles* were heard at times below this. The blood count showed 3,430,000 red and only 130,000 white cells. Some tenderness was found over the lower part of the sternum. No marked enlargement of the liver was recorded at any time. The sputa showed numerous tubercle bacilli.

Differential Blood Counts.—For the following differential counts I am indebted to Dr. J. Odery Symes, Bacteriologist to the General Hospital.

May, 1901—		
Polymorphonuclear	70.8	per cent.
Eosinophile ditto	3.6	,,
Large lymphocytes	2.5	,,
Small ditto	5.5	,,
Myelocytes	14.0	,,
Eosin ditto	2.0	,,
Nucleated red	1.6	,,
January, 1902—		
Polymorphonuclear	57.2	per cent.
Eosinophile ditto	3.9	,,
Large lymphocytes	6.6	,,
Small ditto	4.0	,,
Myelocytes	23.6	,,
Eosin ditto	1.2	,,
Nucleated red	1.0	,,
Basophile	1.0	,,

Thus during the period February, 1900, to January, 1902, the red cells varied in number from 2,640,000 to 4,500,000; and the white, having been approximately normal till March, 1901, varied from 100,000 to 640,000 for the last eleven months. The differential counts show clearly that we had to do with splenomyelogenous leukaemia, if we note the great number of myelocytes, the normoblasts, and even the number of eosinophiles and mast cells; while the evidence of phthisis is also unquestionable. It seems also clear that the phthisis preceded the onset of leukaemia, and made very little progress. This prevents us drawing any very definite conclusion as to the effect of phthisis in modifying the blood state. During the last few months, indeed, the lungs became worse, and the white cells fell to 100,000, but the myelocytes do not seem to have shared in this decrease, and moreover the patient was under the influence of large doses of arsenic. Where acute phthisis or other infections have supervened the results have usually been marked.

The only two cases known of phthisis complicating myelogenous leukaemia are one of Elsner and Groat, and another of Sturmdorf. The former occurred in a male aged 40, and the leukaemic condition apparently began first; the leucocytes in the earlier stages reached 320,000, and the myelocytes 38 per cent. The second case was that of a female aged 35, who had had a splenic enlargement for two years, but the phthisis only appeared three months before the report. There is indeed an instance recorded by Quincke and referred to by Elsner, but the leukaemia was of a partly lymphatic type. In all these the effect of the phthisis was very interesting. Elsner and Groat,[2] from a study of the case they record, state that as the tuberculous process advanced there was a steady decrease in the total number of leucocytes, but an increase in the percentage of polynuclear neutrophiles, a decrease in the number of myelocytes, and an increase in the number of lymphocytes. In three cases of lymphatic leukaemia with

* Read at a meeting of the Bath and Bristol Branch of the British Medical Asscciation.

tuberculosis to which they refer, the effect of the tubercle on the leukaemia was seen in a reduction of the leucocytes. In Lichtheim's patient the numbers became normal, and he adds that no one would have dreamed from the state of the blood that there ever had been leukaemia. A. Sturmdorf[3] mentions that as febrile temperature from phthisis came on the myelocytes decreased and polynuclear cells multiplied. Baldwin, however, gives an instance where the advance of tuberculosis failed to check the increase of leucocytes in general. The addition of septic or other infection usually causes a marked reduction, though the improvement may only be temporary. Elsner and Groat refer to instances of typhoid, sepsis, and influenza where this has been seen. In Kraus's case of pneumonia as a complication there was a fall from 393,000 leucocytes to 4,000 in a few days' time,[4] and M'Crae[5] gives a list of similar instances. Thus a lymphatic case with staphylococcus infection showed a fall from 89,000 to 6,000, and a second from 220,000 to 6,000 in a few days, also an acute leukaemia under Muller in a child with staphylococcus infection, where 109,600 cells were reduced to 6,800. M'Crae notices also a similar fall, often seen before death, and probably owing to terminal affections, but he remarks that in all reported cases where the leucocytes have been reduced by a second infection the effect is only temporary, and the number has risen again if the patient has survived. Thus in Eisenlohre's patient an attack of typhoid reduced the numbers to normal, but only during the fever. In no instance has a permanent cure of leukaemia resulted.

During such a temporary suppression of the blood signs it may be impossible to recognize leukaemia, and the question naturally arises whether my own patient's leukaemia did not exist in this latent form at the time of his operation. It is clear that splenic trouble had existed for some time, and even if the phthisis had no definite effect, such periods of latency have been noted in other cases after taking medicine, or without any known cause. M'Crae's patient in a single twelve months twice showed typical blood symptoms of splenic leukaemia, and twice the blood appeared absolutely normal, without any superadded infection.

We can hardly regard the history of the injury J. L. received as a mere coincidence, though how the disease is caused by a blow is entirely unknown. The same effect of an injury as a determining cause occurs, however, both in malignant disease and in the infectious fevers such as pneumonia, and to one or other of these two classes leukaemia has been referred by most pathologists. Muir thinks that the occurrence of an injury as the starting point of the disease is quite exceptional, and apparently regards it as a mere coincidence, but this opinion is not shared by all authorities, Ewing and Ebstein for instance.

Looking at the above-mentioned results of a second infection, it is only natural to inquire whether any curative measures might not be based upon an imitation of the process. So far little success has attended such attempts. Henck[6] brought about a reduction of the leucocytes by injecting tuberculin, and Jacobs reported an improvement for a time after injecting splenic extract, and Richter after injections of spermin. A more rational method would seem to be W. Hunter's treatment of pernicious anaemia by vigorous intestinal antisepsis. There are noticeable periods of gastro-intestinal irritation in the course of the disease which were evident in the present case, and often a peculiar condition of the mouth, together with an increase of iron in the liver, which show some analogy to the symptoms of pernicious anaemia. Indeed, one disease has replaced or been substituted for the other after a time in one or two instances. Yet the differences are wide and important. In leukaemia there seems to be an over-stimulation of the cell-producing organs; in pernicious anaemia a destruction or paralysis of them, at least in the later stages. It would be interesting to trace the effects of acute intercurrent disease on this anaemia. Stengel finds that the sufferers react to fresh diseases in a most uncertain manner, but I find no histories of the effects on the blood count.

Possibly the gastric troubles may lead to the origination of leukaemia in another way. As Mathes points out, there is a remarkable amount of deutero-albumose in the blood, and this may act by over-stimulating the cell-producing organs, but the attempts to produce the disease by injecting peptones have been against this, for they only resulted in a leucocytosis just as the superadded infections mentioned above may do, and not in an increase of the myelocytes.

One other point of interest must be referred to briefly. Phthisis is rarely found in gouty subjects. Can its rare occurrence in leukaemia be due to the excess of xanthin bodies in the blood, which several observers have held to be characteristic of the disease? This excess of xanthin bases is probably only secondary to the breaking up of the numerous white cells, but it may act, nevertheless, as a preservative against phthisis by rendering the ground less suitable for the growth of the bacillus. Where a chronic form of phthisis was in existence, as in this patient, very little inhibitory effect could be expected.

It is not necessary to discuss the pseudo-tuberculous lung affections sometimes found in leukaemia, for the previous existence of phthisis and the presence of bacilli suffice to prove the tuberculous origin of the lung trouble in the present case.

NOTE.—The patient appeared to be improving slowly till the second week in February, when cardiac symptoms reappeared, and death took place rather suddenly on February 15th.

REFERENCES.

[1] *Tageblatt der Naturforscher. u. Aerzte in Heidelberg*, 1889, p. 405. [2] *American Journ. of Med. Sci.*, 1901, vol. i. p. 275. [3] Ibid., vol. ii. p. 166. [4] Ewing, *Diseases of the Blood*. [5] BRITISH MEDICAL JOURNAL, March 31st, 1900. [6] *Deut. med. Woch.*, 1891, p. 747.

THE BLOOD IN CASES AFFECTED WITH FILARIASIS AND BILHARZIA HAEMATOBIA.

BY ALFRED C. COLES, M.D., B.Sc.,
Bournemouth.

I WAS particularly interested in Dr. Lovell Gulland's contribution to the BRITISH MEDICAL JOURNAL of April 5th, 1902, on the above subject.

Through the kindness of Dr. W. H. Best, medical officer to the Lagos Hospital, I have from time to time received dry blood films of malaria and on two occasions of filariasis. As the filaria can only be found in fairly thick film preparations, very little attention was paid to the variety of leucocytes present in the first set of specimens dated June 10th, 1901. In November of that year some more films containing filaria from a case of lymph scrotum arrived, and I was at once struck by the enormous proportion of eosinophile cells present. I looked up the literature on the subject, and found no mention of eosinophilia in the blood of this condition. As soon as I saw Dr. Gulland's paper I made a differential count of the leucocytes present in the specimen dated June 10th, and found a similar enormous increase in the number of these cells. In this, the earlier specimen, these leucocytes did not stain as conspicuously as in the last case, partly owing to the fact that they had been subjected to a prolonged staining with haematoxylin after treatment with eosine.

The following figures show the percentage of the leucocytes found in both cases, and also that found in normal blood:

	Case I. June, 1901.	Case II. Nov., 1901.	Normal.
	Per cent.	Per cent.	Per cent.
Multinucleated leucocytes... ...	34	43	60 to 75
Lymphocytes	44	33½	24 to 30
Large uninucleated	7	6½	3 to 6
Eosinophile cells	15	17	2 (not above 3)

It is interesting to note that Da Costa in his recent book on Haematology states that "the relative percentage of mononuclear non-granular leucocytes is somewhat higher than normal, with a consequent decrease in the proportion of polynuclear neutrophiles. The eosinophiles either remain at a maximum normal percentage or may be distinctly in excess of this figure." In three cases of filaria he found the eosino-