CASE OF SPLENIC ANÆMIA

(SPLÉNO-MÉGALIE PRIMITIVE)

WITH AN ACCOUNT OF THE DISEASE

BY

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WALTER D—, a horsekeeper, æt. 36, came to see me in the out-patient room at St. Bartholomew's Hospital, complaining of losing flesh and feeling very ill. He looked extremely feeble, was sallow and pallid, had a raised temperature, and a very large spleen. I thought the case might be one of leucocythæmia, but the hurried examination of the blood in the out-patient room did not reveal any increase of white blood cells. The patient was then admitted into the hospital. ✓

The patient gave the following history:—He was quite well until one year ago, when he was troubled with a severe cold and pain across the loins. In January, 1894, a tooth was extracted, and this was followed by profuse bleeding. The patient said he lost about a quart of blood, bleeding continually from 7.30 p.m. till noon of the following day. He was in bed for about a week after this hæmorrhage. From that time till now he had been getting weaker and weaker and losing flesh. When in health he weighed fifteen stone, and now weighs not much more than nine.

Shortly before the extraction of the tooth he began to suffer with bleeding from the nose. This occurred chiefly during attacks of coughing, and from that time till now his nose has bled occasionally, and he has been spitting blood from time to time, which comes, he thinks, from the nose. His wife says he has been getting weaker and thinner for the last twelve months.

There is nothing in the previous history of the patient, nor in the family history, which has any reference to the case.

The patient has been a temperate man, and has never had syphilis.

The patient looks sallow, cachectic, and very ill. He is extremely pale, but the cheeks are flushed. His temperature, on admission at 7 p.m., was 103°. The patient is constantly spitting some blood-stained fluid which looks like saliva, the fauces are congested, and the gums a little vascular. The bleeding probably comes from the nose or back of the pharynx.

An examination of the respiratory organs revealed nothing abnormal, but the voice was hoarse, and on laryngoscopic examination the cords were seen to be reddened, with a little blood on the upper surface, but nothing else abnormal was found. The cardiac dulness was slightly increased, and the heart somewhat dilated, but there was no other sign of disease. A blowing systolic murmur was heard all over the præcordium, especially over the pulmonary area. There was somewhat increased pulsation in the vessels of the neck. The pulse was 96, of normal tension and fair volume, the artery being a little thickened.

Examination of the abdomen showed that the liver was somewhat enlarged, the upper level being in its normal position, but the lower an inch or an inch and a half below the edge of the ribs in the right nipple line. On the left side of the abdomen was a hard tumour, extending downward in the direction of the right pubes, and reaching to the umbilicus in the middle line and to a point about one inch from the anterior superior spine of the ilium on the left side. It was continuous with the splenic dulness, which extended four inches or more above the costal arch. The tumour was not tender nor painful, it moved freely on respiration, was dull to percussion, smooth on the surface, and in its centre towards the middle line a deep notch was to be felt. It was evidently the spleen.

The urine was normal, 1020 specific gravity, containing no albumen and no blood. There was no tenderness of the bones, nor any defect in the neuro-muscular system. The left pupil was a little larger than the right; ophthalmoscopic examination showed the retinæ to be quite healthy although somewhat pale.

The extreme anæmia and illness, associated with the large spleen, suggested leucocythæmia, and the blood was examined from this point of

view, and although the white blood cells were somewhat increased, they were not sufficiently increased to justify that diagnosis. The following estimate was made; red corpuscles, 2,055,000; white corpuscles, 50,000; hæmoglobin, 25 per cent. of the normal.

The patient was put upon arsenic and quinine, and a chlorate of potash gargle was given him for the throat and mouth.

On December 3rd, a week later, the following note was taken:—The patient's general condition has not improved, the temperature remains high, reaching on some days 103°. He has had some trouble with sleep, but a little paraldehyde has been sufficient to give him rest, and he can now sleep without it. He complains of cutting pain across the abdomen, not specially localised. His hoarseness has increased, but there is nothing special to be observed in the larynx. The urine is rather high-coloured, but otherwise not abnormal. The bleeding from the gums has practically ceased, though the sputum is now and then somewhat tinged with blood. The gums are less vascular.

The chest was carefully re-examined and nothing fresh found, but the pulsation in the carotids seemed to be somewhat more marked, and the pulse was now of low tension. A few crepitations were heard at the base of the lungs, probably due to position.

The arsenic had been gradually increased, so that now the patient was taking about 10 minims three times a day. This did not in any way disturb the digestion.

December 14th.—The general condition of the patient had considerably improved during the last few days, his voice was less hoarse, but he had begun again to spit blood or blood-stained saliva, and was now spitting up as much as when he was admitted. The temperature had been lower during the last few days by nearly a couple of degrees on the average. It was still markedly hectic, falling considerably towards morning and rising to its maximum in the evening. Another examination of the blood was made with the following result: red cells, 2,226,000; white cells, 75,000; hæmoglobin, 35 per cent. of the normal. The proportion of red cells to white was as 29 to 1. There were also many masses of blood platelets, resembling in colour the red blood cells though much smaller.

On the 17th another examination of the blood was made: red cells, 1,900,000. Leucocytes 58,300, stained deeply with Toison's fluid. The maximum temperature last night was 103°.

On the 18th the patient had some more bleeding from the nose, which came evidently from the right nostril. No bleeding point could be seen either on the turbinate bone or on the septum when the nose was examined with the speculum. The nostrils were syringed with cold water, and then with Liq. Ferri Perchlor., after which the bleeding stopped.

On December 27th the eyes were examined again, and in the left fundus oculi a very large hæmorrhage was found just outside the disc. The patient had lately become very hoarse. His general condition had in no way improved, he was extremely pale and ill, and was obviously losing ground. The fever remained much as before.

On January 3rd, as the hoarseness still continued and seemed to get worse, the larynx was examined, and the ary-tænoids were found somewhat swollen; two days later, on the 5th, the patient's breathing became very laboured, with marked inspiratory stridor and some recession of the soft parts of the chest. The patient was placed in a steam tent, but the stridor and recession increased until the dyspnœa became so extreme that at six o'clock on the morning of the 5th tracheotomy was performed under chloroform. The operation gave considerable but not complete relief, though towards evening the breathing became much less difficult, and the patient more comfortable. Later, however, the temperature reached 105°, and the patient became much worse.

The examination of the larynx made shortly before the operation showed that the patient had an acute swelling of all the parts about the larynx, viz. the ary-tænoid cartilages on both sides, the epiglottis, and the epiglottic folds, as well as the false chords. The condition was regarded as one of acute œdema of the glottis. After the operation the œdema greatly subsided, but the patient was not able to do without the tube. The tracheotomy wound was very deep, and took on an unhealthy character from the first, becoming foul and sloughing, especially in its deeper parts. There was also at times a good deal of venous bleeding from the wound. On the 8th the tube was left out and remained out all night, the wound in the meanwhile being cleansed as much as possible, and fomentations applied. The patient was able to breathe fairly through the mouth, and could speak without much hoarseness, but it was thought right the next day to replace the tube, and the parts around were packed closely with gauze on account of hæmorrhage, the exact source of which could not be ascertained, and it seemed to be a general oozing from the surface. There was no hæmorrhage, however, on that night, and the patient slept well after an injection of morphia.

On the afternoon of the 10th there was a sudden return of bleeding, the patient coughed violently, and expelled the plugs round the tube. He then seemed to suck blood into his trachea, and died suddenly.

The patient had been treated with arsenic throughout, the dose being gradually increased until it reached 12 minims of *Liquor Arsenicalis* three times a day; this was combined with iron. Ergot was also administered from time to time with the object of controlling the hæmorrhage, but without much result. The diet consisted of such light food as the patient was able to take, and he had stimulants to the extent of four or five oz.

[illegible]

Temperature chart giving the maximum (evening) and minimum (morning) temperature daily.

daily of brandy, though just at the last, on account of his extreme feebleness, the amount was increased to 8 oz.

The reports of the blood which have been given in the preceding report were made in the wards by Dr. Herringham and Mr. Lloyd. Dr. Kanthack was asked to examine the case in the laboratory, but his account differs from the preceding report. On January 4th, 1895, he reported that there was no leucocytosis; and of the few leucocytes present most were lymphocytes.

A post-mortem examination was made of the body twenty-four hours after death. The heart weighed 12 oz. All its cavities contained post-mortem clots. The endocardium of the left ventricle was thickened, the mitral valves competent, but the aortic valves slightly incompetent, a vegetation existing on one of them as large as a pea. The lungs were œdematous and somewhat emphysematous, but otherwise normal. The larynx was still in a condition of œdema, and there was a slight superficial ulceration of the vocal cords. The kidneys weighed 21 oz., and were not obviously abnormal. The liver weighed 93 oz.; it looked somewhat granular, suggesting an early condition of cirrhosis; no iron reaction was obtained. The spleen weighed 76 oz.; it was very soft and contained one small infarct; though so large, it did not present any abnormal appearance.

Portions of the different organs were retained and sent to the pathological laboratory for full report. The following account of the specimens has been given me by Dr. Kanthack.

The liver and spleen were hardened in a mixture of glycerine and spirit, and the heart in Müller's fluid.

Spleen.—The spleen shows slight increase in the trabecular tissue, *i.e.* slight fibrosis. The Malpighian bodies are much diminished in size and badly developed. The cellular elements are almost entirely lymphocytes. Only an occasional large cell with several nuclei, hardly worthy of the name giant-cell, can be detected. Iron reaction negative, both macroscopic and microscopic.

Liver.—Iron reaction negative, both macroscopically and microscopically. Liver-cells arranged in trabeculæ which are separated by an intercellular substance. This substance in many parts consists of connective tissue, in other parts there are round-cells. In many places red blood-corpuscles are found between the liver-cells. Where these collections of red blood-corpuscles are most evident, the liver-cells have atrophied. The liver presents thus: (1) intercellular or cirrhotic changes; (2) numerous capillary hæmorrhages; (3) cellular infiltration.

Heart.—There was no fat detected in the heart muscle.

Splenic Anæmia.

There is a form of profound anæmia, progressive in character, generally of no long duration, associated with great enlargement of the spleen, but without leucocytosis or enlarged glands. The disease is very rare and peculiar in its character, and therefore seems to deserve a special name.

Splenic Anæmia seems to be the name under which most cases are described in this country, but the disease has also been called *Splenic Cachexia*, *Splenic Pseudo-leukæmia*, *Lymphadenoma Splenica*, as well as *Splenomegalie Primitive*, under which name it is described chiefly in French literature.

Bruhl, though not the first to describe the disease, has given us the best account of it, and it is from this that the following description is chiefly derived.

There are three stages in the disease: the first the preliminary stage, in which there are no other symptoms except those of gradually increasing weakness, with perhaps occasional attacks of pain in the splenic region; the second where the anæmia becomes marked and the spleen greatly enlarged; and the final stage that of cachexia and death from asthenia.

The *initial symptoms* of the disease are those of great asthenia, similar to that which occurs in Addison's disease, and progressive anæmia. There are, at the same time, a good deal of wasting of muscle and loss of muscular power, usually without emaciation, the panniculus adiposus being well maintained.

Appetite and digestion are often preserved for some time, and other functions undisturbed. All the other symptoms in this stage are merely those common to all forms of profound anæmia, viz. shortness of breath, pain in the cardiac region, palpitation, and occasionally some swelling of the feet. There is at this stage nothing characteristic in the symptoms.

In the *second stage*, attacks of severe pain are complained of in the left hypochondriac region, with tenderness over the spleen, the pain radiating to the back, left shoulder, and especially to the lumbar region. It is intense enough to resemble colic, and except that it is felt on the left side, is very like hepatic-colic in character. There is generally a history to be obtained at this time of increasing pallor, loss of strength, and of attacks of epistaxis for some time previously. The temperature is now found to be raised, varying from 102° to 104° , and at the same time the digestive system is greatly disturbed. It is in this stage that most of the patients come under observation, or rather it is in this stage that the disease is first recognised.

The spleen is then found to be considerably enlarged, and tender; though usually smooth, it may be somewhat irregular on the surface. Signs of local peritonitis in the splenic region may be present, or those of left basilar pleurisy,—in both cases due to an inflammation spreading from the spleen; and sometimes there may be found some general peritoneal effusion.

The heart may be dilated, and blowing murmurs may sometimes be heard, as in other forms of anæmia.

The blood shows no characteristic pathological changes; the condition is simply that which is met with in all extreme anæmias of simple origin. The red cells are diminished to one half, one fourth, or less; their form is preserved, but they are a little reduced in size. There is no poikilocytosis, but the cells are poor in hæmoglobin, this being reduced to one half or one sixth, and this loss is in excess of the diminution in the number of blood cells. Occasionally there is a slight increase in the white cells, but not more than the fever or some intercurrent malady would account for, and there is nothing at all similar to what is found in leucocythæmia. No micro-organisms have been discovered on microscopical examination or by cultivation.

The spleen is observed gradually to increase in size,

but occasionally between the attacks it seems to become for the time smaller. The recurrent attacks of pain in the splenic region, apparently due to perisplenitis, often cause very great suffering.

The liver is also often somewhat enlarged, and is sometimes associated with slight jaundice.

The digestion is considerably disturbed, and the appetite is lost ; there is a good deal of nausea, and sometimes obstinate vomiting, which occurs in such paroxysmal attacks as almost to constitute crises, and they often coincide with attacks of abdominal pain. There is usually troublesome constipation, but occasionally diarrhœa, almost dysenteric in character, with tenesmus and discharge of bloody mucus.

Hæmorrhages are common, usually in slight degree, and of the nature of oozing ; this may be difficult to control and add greatly to the anæmia. Profuse hæmorrhage from any part is uncommon.

Epistaxis is very frequent, and is often one of the earliest symptoms, and usually slight ; it is of importance chiefly on account of its frequent occurrence. It is sometimes severe, and may even require plugging of the nostril.

Oozing from the gums, again, is not uncommon, and is very difficult to control.

From the gastro-intestinal organs, hæmorrhage is rare, and if in any large amount, is probably associated with some secondary lesion ; a case is recorded by Douglas Stanley, in which profuse and fatal hæmatemesis took place, and no ulceration of the stomach was found ; but in other cases gastric ulcers have been described, and Williamson records a case of fatal hæmorrhage from the bowels, in which an ulcer was found in the small intestine.

Hæmaturia and hæmoptysis are also met with, but these are rarer than other forms of hæmorrhage.

In the skin small petechiæ on the lower limbs are common, especially in patients who are not in bed, but they are of no special significance. A purpuric eruption of greater degree than this is not described.

Urinary changes are indefinite, and vary much, but sometimes there is albumen present.

No doubt hæmorrhages may occur into the retina, as they do in other forms of anæmia, but I do not know that they are recorded except in the case I have described.

Bruhl states that fever is unusual, but in some of the cases recorded the temperature reached a considerable height, and was of the nature of an irregular hectic, rising to 103° or 104° every evening.

The last stage of the disease is characterised by progressive asthenia ending in death, but there is nothing characteristic nor different from what is usually met with in cases of profound anæmia, except that the hæmophilic symptoms may be unusually pronounced.

The course of the disease is continuously progressive, though there appear to be periods of temporary arrest.

The duration of the disease is short, from six months to two years, but it is occasionally more prolonged; thus, Müller records one of which the duration was four years and a half.

It is possible that cases may be of even shorter duration than six months; thus Erbstein records one of this kind under the name of Pseudoleucæmia Acuta.

Complications may hasten the end; for example, pneumonia, bronchitis, abscess or peritonitis in connection with the spleen, and as described, sometimes severe hæmorrhage from the stomach or intestines, possibly connected with an ulcer there. In some cases death is sudden, from cardiac failure.

The diagnosis is as a rule easy, though the cases themselves are very rare. The diagnosis has to be made from leucocythæmia, from Hodgkin's disease, from other grave anæmias, from the cachexia of malignant disease, from pernicious anæmia, and lastly, from other forms of splenic

enlargement. In all other pernicious anæmias except this, splenic enlargement is very rare.

The ætiology of the disease.—The affection may occur at any age, but it is commonest in the adult, and most frequent by far in males, only two or three cases being recorded at all in the female.

The causes are unknown, but the ordinary causes of splenic enlargement are absent.

Morbid anatomy.—The spleen may be twelve inches long, and weigh from two to seven pounds. It is firm, with notches which are well marked, and there are occasionally irregularities on the surface. It is reddish-brown in colour, and it is often surrounded by a thickened capsule, which may be adherent either to the diaphragm or to the parts near. On section it looks as if there were a general hypertrophy of the organ, but occasionally there are hæmorrhagic infarcts in it. The surface of the section is dry and yields little juice, and it shows greyish streaks or fine granulations. The former prove on microscopical examination to be thickened trabeculæ, the latter fibrotic Malpighian corpuscles. The central artery is much thickened, and occasionally the whole corpuscle seems to have undergone complete sclerosis and atrophy. With the thickening of the trabeculæ there has been great disappearance of the spleen-cells and dilatation of the veins.

The characteristic changes are: (1) fibrosis of the organ; (2) the disappearance of the pulp; and (3) especially the cirrhosis and atrophy of the Malpighian bodies.

In leucocythæmia the Malpighian bodies as a rule are hypertrophied, that is to say, the condition of the spleen is one of hypertrophy; on the other hand, in this disease the condition is one of atrophy and has been called cirrhosis.

The liver is slightly cirrhotic, with much pigmentation. The cells are misshapen, atrophied, and often granular. But, as far as one knows, there is no iron reaction.

The pancreas also is occasionally indurated, it is stated, but this is by no means constant.

The lymphatic glands are normal.

The bone marrow is also usually normal, but in one or two cases it is described as red and infiltrated with leucocytes.

There are no definite changes in any other organ besides those which occur as the result of anæmia.

Bruhl argues in favour of the splenic change being primary and the cause of the disease, attributing the cachexia to the loss of function of the spleen and its interference with the chemical composition of the blood.

The treatment must be systematic, and does not differ from that of other anæmias, but so far nothing has been found to check the progress of the disease.

The following points of interest deserve attention in the case which I have described. (1) The acute onset and short duration of the disease, for the patient believed himself to be well until one year before his death. (2) The hæmophilic condition which developed so early, for epistaxis was one of the first symptoms, and profuse bleeding after the extraction of a tooth occurred soon after; later, the bleeding from the gums was troublesome, while in the last few weeks of life there was frequent hæmoptysis, the blood coming probably from the trachea, and possibly the larger air tubes; and at last came the hæmorrhage into the retina, and also from the tracheotomy wound. (3) The œdematous condition of the larynx and the necessity for tracheotomy, which operation, with the bleeding which took place from the tracheotomy wound, was no doubt the immediate cause of death. (4) The elevation of temperature, which was continuous as long as long as the patient was under observation.

The number of cases hitherto recorded is small, for in 1891 Bruhl could only collect fourteen cases, and two of

these only were in the female sex. Since then a few others have been published, but the total number is probably still under twenty.

The claim that these cases form a definite clinical group of anæmia must, I think, be regarded as fully established.

They appear to me to resemble most closely some cases of severe malarial ague, and if this be so it would suggest that a blood parasite was probably the cause of the disease, but careful examinations of the blood have hitherto proved negative.

On the other hand, it may be true, as Bruhl has suggested, that the symptoms are to be referred primarily to the changes in the spleen, and to perverted nutrition caused by the atrophy of the organ. Still, the acuteness of the symptoms, and the rapidity with which the anæmia develops, seems to be somewhat inconsistent with its reference to a chronic disease like cirrhosis.

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(For report of the discussion on this paper, see 'Proceedings of the Royal Medical and Chirurgical Society,' Third Series, vol. viii, p. 263.)