CLINICAL LECTURE

ON A

CASE OF EXTREME CIRRHOSIS OF THE LIVER IN EARLY LIFE.

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Progressive Emaciation and Debility in a Boy, aged 18.—Absence of any Drain to account for it.—Slight Enlargement of Liver and Spleen.—Gradual Aggravation of all Symptoms.—Ascites.—Wild Delirium.—Partial Paralysis.—Death by Coma.—Post Mortem Examination.—Remarks.

FREDERICK B., whom you will remember as an out-patient under my care, and subsequently in the Albert Ward, first came to me five months ago, complaining of gradual wasting and increasing debility, accompanied by a constant dull aching pain across the loins. He was a tall, ill-made lad, eighteen years of age, so emaciated that each rib stood out distinctly; the bony framework of the thorax seemed encased in skin alone. What struck one most, next to the loss of flesh, was the strange, dull look and manner of the boy. It was not the effect of mere languor and weakness; his intellectual faculties worked with difficulty. He answered questions intelligently, but very slowly, after an interval, as if it took him some time to comprehend what was said to him. Partly from himself, but chiefly from his mother who accompanied him, I learnt that he had suffered from large abscesses in the back five years previously; and that a year ago his feet had swelled a little, the swelling, however, quickly disappearing on his going away into the country. His principal complaint was of pain in the loins, which had troubled him constantly for the last two years. This had become worse latterly, and he had wasted rapidly. A careful examination of the chest disclosed no morbid signs of any kind. The abdomen was found considerably distended by flatus; no fluid could be detected there. There was slightly increased dullness over the region of the liver, and still more over the spleen, but no distinct tumour could be made out. The distension of the abdomen, however, prevented satisfactory examination in this respect. There was no tenderness anywhere. The urine was examined and found free from albumen, of normal specific gravity, and lithatic; under the microscope, it showed no casts or abnormal deposits of any kind. The boy was affirmed by his mother to be exceedingly industrious and steady, and the mainstay of the family. He had had no cough or expectoration, or diarrhoea, or acute disease—in a word, there had been no drain on the economy which could account for the extreme wasting. The tongue was clean, the pulse quiet, the skin cool, and the appetite moderately good. It was clear, at any rate, that the emaciation was due to defective supply, not to excessive consumption. The fault was that the tissues were not built up, not that they were too rapidly destroyed. The only deviation from the normal condition which could be detected in any organ was the slight enlargement of the liver and spleen; and the inference was that the interruption to nutrition was due to some fault there. The history of lumbar abscesses and prolonged suppuration pointed to amyloid infiltration as the most probable morbid condition, and the slow progress of the disease, the malnutrition without loss of appetite or marked cachectic look, and the tympanitis, all tended to give support to this conclusion; while, on the other hand, cirrhosis and malignant disease seemed almost excluded by the age of the patient, and the general symptoms and history of the case.

The treatment adopted was the administration of cod-liver oil, and iodide of potassium with steel. In spite of medicine and nourishing diet, however, the patient gradually became more emaciated, and at the end of three months' time, he staggered in his walk, and was more vacant and dull. The belly had become more distended, the superficial veins very conspicuous, and fluctuation was distinctly perceptible in the flanks. The spleen was now greatly enlarged, but no increase of dullness or hardness could be detected in the hepatic region. The urine had been constantly examined, but was always found of normal specific gravity, free from albumen or sugar. No casts or abnormal bodies of

any kind could be seen under the microscope. At this stage, being quite unfit to attend longer as an out-patient, the boy was admitted into the hospital under the care of Dr. Sieveking. A few days after his admission, he twice passed a considerable quantity of blood with the urine, but this did not recur, and the urine remained clear, showing under the microscope only a few blood-cells and crystals of oxalate of lime. Three weeks later, he lay helplessly in bed, constantly moaning, and frequently moving the left arm and the head with a succession of spasmodic jerks. He occasionally answered questions correctly, but very slowly, and usually merely replied "yes, sir," "yes, sir," "yes, sir," which he would go on repeating again and again many times. He complained, however, of pain in the left hypochondrium, where was the large splenic tumour, and of excessive thirst. Then he went on, "Mayn't I get up, sir?" "Mayn't I get up, sir?" over and over again, quite regardless of the reply. The tongue had become dry and very red, and coated with brown fur in the centre, the pulse faster (118), and he passed his fæces under him, but his appetite still remained good, and he took food freely. The signs of obstruction to the portal circulation now became more marked, the abdomen being tightly distended with fluid, the superficial veins swollen and tortuous, and the lower extremities highly cedematous. The skeleton framework of the thorax and upper extremities, reduced to the last stage of emaciation, showed in strange contrast to the huge swollen body and legs. There was no trace of jaundice at any time. A thick crop of acne appeared on the face and remained throughout.

During the next three weeks all the symptoms became intensified. The patient no longer answered questions, but seemed dimly to comprehend them, and pointed to the right side of his head as if he had pain there. He was constantly muttering, moaning, and calling out, and jerking his head and left arm; his tongue became perfectly dry and brown; sordes accumulated on the lips and teeth. At length he became so wildly delirious that his shrieks and groans disturbed patients even in the next ward, and he was removed into a separate room in a secluded part of the hospital. A few days later, he was lying on his back, unconscious, moaning faintly, the right side paralysed, and the left arm and leg moving with slight spasmodic jerks. The pupils were widely dilated, and insensible to light. This condition deepened until he died comatose a day or two afterwards.

At the *post mortem* examination, the liver was found in a state of the most extreme cirrhosis, contracted, small, and its surface studded over with projections from the size of a No. 4 shot to a marble. The prominent tubercles were soft, consisting of the proper liver-substance more or less altered, the shrunken part between being whitish, semi-translucent, and almost cartilaginous in appearance. On section, the cut surface exhibited a curious spotted look, small islands of yellowish-coloured liver-substance implanted in a mass of whitish glistening tissue, which formed the great bulk of the organ. When examined first under the microscope, the liver-cells were seen to be fatty, and loaded with bile-pigment. A thin section, hardened in chromic acid, showed a very advanced condition of cirrhosis; the fibrous tissue was seen passing in broad massive bands between the compressed lobules, or groups of lobules, while from these larger bands branched smaller ones, spreading into the lobules, and forming areolæ of various sizes. Some of those enclosed in the broadest bands contained numerous cells; others in the finer portion of the network one or two only; and others, again, the mere granular debris of cells. The spleen was enormously enlarged, congested, and hard, but free from any morbid deposit. The kidneys were congested, and the capsules rather adherent, but otherwise healthy. There was an unusual quantity of dark pigment over the surface of the parietal peritoneum about the pubic region. The pancreas was dark-coloured, and unusually hard. The bladder was greatly congested near the urethral orifice, probably marking the site of the former hemorrhage. The abdominal cavity was full of reddish serum free from lymph or pus. The base of the right lung was in a state of red hepatisation, and the left congested. There was no tubercle anywhere. A few minute ecchymoses were observed under the arachnoid, which was slightly opaque. But there was no other lesion of the brain, and no trace of amyloid changes in any organ.

REMARKS.—The interest of this case lies chiefly in the obscurity in which it was involved during life, and in the fact that so extreme a degree of cirrhosis was developed at such an early age; but there are several points in addition which illustrate with unusual clearness the pathology of interstitial hepatitis, and especially as to the mode in which death is produced. The mystery which enveloped the exciting cause was eventually cleared up. The mother confessed that her son took regularly a considerable quantity of drink when in work, and especially gin. It appeared, from her statement, that the labourers in the brick-fields share the popular delusion, and believe that a large quantity of stimulant is necessary to enable them to encounter the fatigue and damp

incident to heavy work amongst the wet clay. Accordingly, it has become the recognised custom for each man to put aside a certain proportion of his wages every week for the purchase of this necessary; gin being the favourite liquor, taken, as a rule, without any dilution. Hence, after all, the case turned out to be one of genuine alcoholic cirrhosis—true gin-drinker's liver; and when these circumstances are known, there is nothing extraordinary in the fact itself that a youth of eighteen should have extreme cirrhosis. The reason why it is so rare in early life is no doubt because spirit-drinking is a vice which is naturally also rare in youth. If the cause were in operation, the effect would be as readily produced upon the liver of a child as upon that of an adult. The case affords further proof that it is not so much the quantity of alcohol imbibed which determines cirrhosis, as its degree of concentration. The experiments of Dr. Percy showed that alcohol poured into the stomach is instantly absorbed, and is found abundantly in the liver in the course of a few seconds; and Dr. Budd pointed out that cirrhosis is usually the result of drinking neat spirits on an empty stomach. We constantly meet with men who imbibe large quantities of wine and beer, and spirits freely diluted, who, although they suffer from other consequences of intemperance, never have cirrhosis. The truth is, I believe, that *dilute* alcohol, although a fruitful source of general fibroid degeneration and other morbid changes, dependent upon its constant presence and influence in the blood, does not cause genuine cirrhosis of the liver. Wine- and beer-drinkers escape the disease, because the solution of alcohol they take is never above a certain strength. It is stronger alcohol which excites active congestion around the portal vessels in the liver by direct contact, just as it excites congestion of the stomach; the dilution of it to a certain degree removes its irritant character. Now, Sir William Jenner has shewn that mechanical congestion of any organ produces induration of its substance as a regular and constant result; interstitial exudation of lymph takes place, which is converted into fibrous tissue. And I think this proposition might be extended to long-continued chronic congestion of any kind. We see this increase of fibrous tissue as a result of chronic congestion produced by an irritant, and not mechanically, in the case of gout, where the gouty poison causes fibroid degeneration of the kidney, and fibrous thickening round the joints and in the tendons and ligaments. And we may have similar results from the poison of alcohol acting on the liver, the kidneys, and even the lungs. Whether the congestion thus set up gives rise to fibroid growth by causing interstitial effusion of lymph, or whether the presence of vitiated blood in excess stimulates the connective tissue to increased proliferation, is yet uncertain. One point, however, seems to me clear, and that is, that in this case of hepatic cirrhosis, as in cirrhosis of other organs, there is an actual increase of the fibrous element. In the instance before us, the amount of connective tissue was far too great to allow the conclusion that it was merely the aggregate resulting from the compression of the normal fibrous network, by the destruction of the true liver-tissue between the interlobular sheaths which are thus massed together, as suggested by Dr. Lionel Beale. Fresh material must have been added to make up the massive bands pervading the whole structure.

Another feature of interest exhibited by this in common with most cases of cirrhosis was the complete absence of jaundice throughout.

The fact that nearly the whole of the secreting tissue of the liver may be destroyed, and yet no trace of bile appear in the blood, attested as it is by innumerable instances, affords conclusive proof that the colouring matter of the bile, at any rate, is elaborated in the liver, and that the office of that organ is to *make* it, not merely to eliminate it from the blood in which it pre-exists; otherwise the most intense jaundice would follow the destruction of its active tissue. Jaundice, then, must be a consequence of some error in the chain of physiological action later than the formation of bile in the liver. The bile must first be manufactured; it appears in the blood because it is not disposed of in the normal manner. This may be due to one of two causes; either the passage out by the biliary ducts into the duodenum may be prevented by mechanical obstruction and the bile therefore absorbed into the blood, or bile may be secreted in such excess that a portion of it is absorbed by the hepatic capillaries under the increased pressure. The former we see constantly in operation in the case of tumours pressing upon the ductus choledochus, or in occlusion of the ducts by calculi. The latter is probably the mode by which jaundice is produced by fright and anxiety. A third cause may come into action in some cases, viz., diminished metamorphosis, or consumption of bile-acids normally absorbed into the blood, either in the liver or in the intestine, and transformed into pigment to be cast out as colouring matter of the urine. This view is forcibly advocated by Frerichs, but can hardly be accepted as established; and there is one circumstance which is sometimes observed in certain diseases of the liver which shews that it is not the sole cause in ordinary cases, viz., that, although nearly the whole

liver-tissue may be destroyed by cirrhosis or malignant disease, and therefore a very small quantity only of bile be formed, yet, if any obstruction to the outflow arise by reason of increased pressure on the ducts from increase of morbid growth, jaundice at once follows. Now, why should jaundice follow the introduction of such a small quantity of bile-acid into the blood in these cases, when it does not follow the introduction of a larger quantity there in the normal condition? We know no reason why full transformation should not take place as well in one case as in the other. But to return to the example before us. A little bile was secreted, as shown by the yellow staining of the lobules, and the small quantity formed passed out by the ducts, which generally remain sufficiently pervious. If, however, as sometimes occurs in very advanced conditions of the disease, the ducts be compressed by the new connective tissue at their origin at the circumference of the lobules, slight jaundice ensues, provided the quantity of bile formed be sufficient to give a perceptible tinge to the tissues and secretions.

The curious condition of the parietal peritoneum has not, as far as I am aware, been recorded before in the case of cirrhosis. Deposit of pigment, in large quantity, in the liver, spleen, brain, kidneys, and other organs, is met with after death from intermittent fevers. It appears still further to be specially associated with congestion of the spleen. In the present instance, the deposit occurred in connection with the same condition of the spleen. The relation between the two is still obscure—but the fact of the coincidence is worthy of note.

The gradual loss of flesh, progressing to the most extreme emaciation, reached at the time of death, is more easily explicable by physiological laws. *The patient, in fact, died of starvation.* Even in temporary arrest of the function of the liver, as in simple jaundice, there is rapid loss of flesh, and often an intense craving after food. And where there is permanent and extensive destruction of liver-tissue, emaciation is always extreme. This seems to be due to several causes. First, there is the want of bile to mix with food in the intestine, and render certain portions of it fit for absorption and assimilation. Secondly, the nutriment which is absorbed and actually enters the portal veins, passes through the liver with great difficulty or not at all, owing to the obliteration of the lobular capillaries, and can only partially enter the general circulation by means of the few new direct channels developed between the portal and hepatic veins, and the normal pre-existing anastomoses between the portal system and the vena cava. But, perhaps, the most potent cause of all in producing wasting, is the arrest in the formation of glycogen. Whatever the special office performed by the animal sugar in the economy, whether it be burnt up in the lungs, evolve force in the muscles, or be consumed in other tissues, there can be no doubt whatever that the part it plays is one of the highest importance. The simple fact that the largest organ in the body is constantly engaged in preparing it, is a sufficient proof of this. Now, we know, in the case of diabetes, that if the sugar formed by the liver be of *imperfect quality*, and for this, or for some other reason, be not used up for its proper purpose, the fat of the body is rapidly absorbed to replace it as fuel, or to generate force in some form. And there can be little doubt that, in the same way, when the *quantity* of sugar is deficient, or when it is absent altogether, the fatty tissues are burnt up in the like manner. This result of the arrest of this function of the liver, and the important bearing which it must have upon the course of diseases such as cirrhosis, have not hitherto, I think, engaged sufficient attention. There were, then, three great causes for the emaciation; viz., the want of bile to digest certain food; the obstruction to transmission of nutriment from the portal vessels to the general circulation; and the non-production of glycogen, with the consequent absorption of fatty tissue to replace it. And we find, accordingly, that, in the present instance, the fat had entirely disappeared, just as it disappears in prolonged starvation.

I have shown how starvation practically did take place; and I wish to draw your attention to the identity of the symptoms with those observed in cases of starvation from want of food. The dullness of intellect, the indifference, the languor, the staggering gait which accompanied the gradual loss of flesh in the earliest stages, are exactly the symptoms met with in the early stages of privation from food. The delirium, the restless movements, the twitchings of the limbs, the hemiplegia, the paralysis of the sphincter, the brown dry tongue, the weak rapid pulse, and the death by *coma* at last, correspond with equal fidelity. Nothing was found in the brain after death to account for the cerebral symptoms. They were not due to cholæmia, since there was no bile in the blood, even if the experiments of Frerichs and the history of chronic jaundice did not throw extreme doubt upon the theory that it gives rise to evil effects on the nervous system. The delirium and paralysis, and convulsions, were due to deficient supply of nutriment to the brain and cord; the ultimate cause of death was starvation of the tissues.