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Contributors

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ON
ACUTE YELLOW ATROPHY
OF
THE LIVER.

BY

T. GRAINGER STEWART, M.D., F.R.C.P.,

PATHOLOGIST AND SPECIAL ASSISTANT-PHYSICIAN TO THE ROYAL INFIRMARY, AND LECTURER
ON GENERAL PATHOLOGY, SURGEONS' HALL, EDINBURGH.

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THE LIVER

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ON

ACUTE YELLOW ATROPHY OF THE LIVER.

THE following case is worthy of attention, both on account of its rarity and of the light which it seems fitted to throw upon the disputed question of the nature of the affection of which it affords an example.

Mrs H., æt. 35, was admitted to the Royal Infirmary, almost moribund, on 11th February 1865. She was sent to one of Dr Warburton Begbie's wards, but died very soon after admission. Her history was imperfectly ascertained, as she was comatose at the time of her admission; but from inquiry among her friends who had been with her before she went to the hospital, I have ascertained the following facts:—She was in the sixth month of her fifth pregnancy, and was leading an unhappy life, in consequence of domestic quarrels; but it was not known that any special disagreement had preceded her illness. She was in good health until a fortnight before her death, but then complained to her neighbours of a strange feeling of uneasiness which she felt and feared, but could not define. She gradually became worse, and began to vomit yellow matter like the yolk of an egg. She then also became jaundiced, and this gradually deepened. Her bowels were constipated. She never was drowsy or delirious, nor did she vomit blood nor pass it at stool until the morning of 11th February, when she became much worse, vomited a large quantity of blood, became very drowsy, and could not be roused. In the afternoon, Mr Furley was called to see her, and, by his direction, she was removed to the Infirmary. The movement roused her, and she became for a little time conscious. On admission to the Infirmary she was shivering, and complained of cold. She vomited blood almost incessantly. She passed her fæces in bed; they were dark-coloured and fluid. She made water, but it could not be collected for examination. About eight o'clock, she became delirious, violent, and very noisy. This continued until midnight, after which she was

comatose. Labour commenced about eight o'clock; the waters came away about nine. She was delivered of twins, just as she was dying, at seven o'clock on the morning of the 12th.

Autopsy.—The body was examined thirty-one hours after death. It was moderately well nourished. The *skin* was icteric and somewhat dusky. There was considerable hypostatic congestion, but no subcutaneous extravasation of blood. The *muscles* were dry; the blood dark and fluid. *All the internal organs* were jaundiced. There were *patches of extravasation* under the visceral layer of the pericardium, particularly over the left auricle, and towards the upper part of the left ventricle. The *heart* was moderately contracted, contained no clot, and very little blood. The muscular substance was somewhat pale; the valves were natural. The *aorta* was natural. The *lungs* were congested and somewhat œdematous, particularly at their lower and posterior parts. The *liver* was reduced to one-half its natural size; but, except being somewhat flattened, it retained its ordinary form. It weighed 1 lb. 7½ oz. Its surface was not shrivelled. Beneath its capsule and throughout its substance there were numerous ecchymoses, and small patches of an ochre yellow colour, but the mass of the organ was of a dark reddish brown hue. The outlines of the lobules were not recognisable. The *gall-bladder* was contracted, and contained a little grey inspissated mucus.

On *microscopic examination* of a scraping from a cut surface of the liver, a large quantity of debris and fatty matter, with cells in different stages of alteration, some full of oil globules, and containing a few bright ochre-yellow granules, and others full of dense granular matter, not fatty, were found. All the cells were considerably enlarged, and denser than natural. No natural cell was observed. The amount of bile pigment found both in the cells and debris was less than is usual in such cases.

On examining sections, it was found that the cells in the outer part of the lobules were almost completely destroyed, while those towards the centre were larger, denser, and more opaque than natural, and the amount of oil was greater towards the margins, where the destruction of cells was taking place. The system of vessels and the fibrous stroma of the organ were not destroyed. It was easy to make sections, and the sections were easily washed without their giving way. In the sections a considerable amount of bile pigment was seen scattered about.

Some demonstrations were made of the blood in the liver, but neither in it nor in the substance were any crystals or balls of tyrosin or leucine observed.

The *spleen* was enlarged, weighed 8 oz., was soft and pulpy. There were some points of extravasation in its substance and beneath its capsule.

The *suprarenal bodies* were somewhat enlarged and partially disorganized, but their microscopic structure was not ascertained.

The *kidneys* were somewhat enlarged, weighed together $10\frac{1}{2}$ oz. Their cortical substance was dense and pale. The capsule was easily stripped off. On microscopic examination, the tubules, both straight and convoluted, were seen to be full of exudation,¹ and presented the appearance of having been very successfully injected with some dark matter. The Malpighian bodies and vessels stood out clear and transparent among the tubules. With a higher power the vascular structures appeared natural. The dark matter occupying the tubules was found to be composed of exudation into and between the cells. Very few tubules remained healthy; in some the epithelium was swelled, thickened, in a state of cloudy swelling, and here and there it was loaded with fat granules. In some parts the outlines of the renal cells could not be made out; the tubules were full of a dense homogeneous granular matter, containing numerous oil globules.

The *oesophagus* was natural; the *stomach* was distended, and contained a good deal of dark uncoagulated blood. Its inner surface was coated with slimy mucus; its walls were thickened, and in the mucous coat there were numerous catarrhal ulcers, mostly along the greater curvature, and on the anterior and posterior walls. Extravasation of blood existed about the bases of some of the ulcers.

The *intestine* contained almost no bile, but some altered blood, and a good deal of hard nearly clay-coloured faeces. The Peyerian patches and solitary glands were swelled and prominent, particularly those about three feet from the lower end of the ilium. The large intestine was natural.

The *pancreas* was natural.

The *mesenteric glands* were somewhat enlarged.

The *uterus* was large, about seven inches in length, moderately contracted; the cervix was long, and a plug of bloody mucus projected from the os.

Both *ovaries* were much scarred, and each contained a distinct corpus luteum.

The *Fallopian tubes*, particularly their fimbriated extremities, were congested.

The *skull* was natural. There was a little subarachnoid effusion. The brain was firm, somewhat congested throughout; it weighed 2 lb. $6\frac{1}{2}$ oz. The ventricles were not dilated. There were a few small cysts in the choroid plexus.

¹ *Exudation*.—I employ this convenient term as one which is in general use, and generally understood as describing the condition referred to in the text, but do not regard it as an accurate term. The idea upon which it was originally founded, viz., that certain elements of the blood were poured or sweated out of the vessels, in consequence of changes in the vessels or in the blood, is quite untenable. The view now generally held, and which I have adopted, is, that the tissues attract to themselves certain elements, and in this way the appearance referred to is produced. But though the theory of its production be altered, the descriptive term need not be changed; I think, therefore, that we may continue to call this matter exudation.

The *bladder* contained almost 16 oz. of dark amber-coloured urine, which was carefully removed and sent to Dr Arthur Gamgee who kindly analyzed it, with the following result:—

“The urine was of an intensely jaundiced hue, and exhibited in a very characteristic manner the reaction of bile pigment. Its reaction was acid. It was divided into two portions—A and B.

“The portion A, measuring 200 c. c., was precipitated with neutral and basic acetate of lead, and the fluid filtered. The lead precipitate was reserved for the analysis of the bile acids.

“The filtrate was treated with a stream of sulphuretted hydrogen gas, in order to precipitate the excess of lead, and the clear and almost colourless filtrate thus occasioned was concentrated at a very gentle water-bath heat, and then placed aside in a cool place. At the end of twenty-four hours an abundant crystallization had taken place. The crystals, when examined under the microscope, were found to consist of the most characteristic needles and tufts of tyrosin tinged of a light yellow colour; they were separated by filtration, and dissolved in boiling water. On cooling, the water deposited a nearly snow-white mass, composed of beautiful needles of tyrosin; these were again crystallized from a solution in boiling water, and then dried. In the process of drying they contracted very much. When strongly heated they burned away completely, without leaving a trace of ash; they exhibited in a most characteristic manner the chemical reactions of tyrosin.

“The fluid from which the tyrosin had been separated was evaporated to a syrupy consistence, and set aside for some days. When examined, it was found to contain, in addition to much tyrosin which had separated, most characteristic masses of leucine.

“The precipitate which had been obtained by precipitating the urine with acetate of lead was suspended in water, and a stream of sulphuretted hydrogen passed through it. The fluid was filtered and evaporated at a gentle heat. The residue was dissolved in water, and tested by Pettenkoffer's test for bile acids, but none were found.

“The smaller portion of urine, B, was employed to determine the presence and quantity of the more usual urinary constituents, and the results of the analysis are tabulated below.

“The points which specially call for notice are the following:—*1st*, The urea was determined by Liebig's method. As tyrosin is equally with urea precipitated by nitrate of mercury, the results of the analysis are obviously not perfectly correct, the urea and tyrosin having in fact been estimated together. As the tyrosin appears to have been present in very large quantity, it may be assumed that the amount of urea was actually very small. *2d*, The amount of uric acid could not, from the excessively small quantity of urine which was obtained, be estimated; only traces of it, however, existed. *3d*, The urine contained absolutely no chlorides, only the faintest trace of sulphates, and the earthy phosphates were

absent. The only salts present were in fact alkaline phosphates. This fact, which was brought out by the qualitative analysis, was also borne out by the quantitative; for the amount of phosphoric acid which was found, when calculated as phosphate of potash, is almost identical with the amount of ash as found by direct ignition."

Table showing the Result of Analysis of Urine.

Specific gravity of urine at 60° Fahr.,	1018·82	
Reaction acid.		
Total solids in 100 c. c.,	2·194	
Urea and tyrosin in 100 c. c.,	1·80	gramme.
Leucine, uric acid, and colouring matter in 100 c. c.,	·1415	...
Albumen,	·0116	...
Salts,	·2525	...
Phosphoric acid,	·204	...

This case affords a very good example of the acute yellow atrophy of the liver. But there are three points which I should like to bring under the notice of the Society:—1st, The state of the urine as ascertained by Dr Gamgee; 2d, The peculiar affection of the kidneys; and, 3d, The evidence which the case affords as to the nature of the disease.

I. *The State of the Urine.*—The points which appear to be most important are,—1st, That notwithstanding the presence of a large amount of abnormal ingredients, the *total solids* were considerably below the natural quantity, and thus the functional activity of the kidneys was shown to be diminished; 2d, That *leucine and tyrosin* were the chief abnormal ingredients, as is usual in this disease; 3d, That a little *albumen* was present; 4th, That notwithstanding the extreme jaundice, *no bile acids* were found,—a fact which, at first sight, seems to confirm Dr Harley's view that these constituents are wanting in cases of jaundice from suppression; but this point cannot be deemed important, when we consider that only Pettenkoffer's test was employed, a test which chemists do not now consider satisfactory; 5th, That the *urea* was probably much diminished in quantity, and only traces of *uric acid* were found, while in most febrile and hepatic affections these elements are found in excess; 6th, That the *chlorides and earthy phosphates* were entirely absent, and that only the faintest trace of *sulphates* was found.

It is evident that some of these altered conditions of the urine depended upon the state of the kidneys and some upon that of the liver and the system generally. There can be little doubt that the leucine and tyrosin resulted from changes in the liver, and that they were eliminated from the kidneys along with the water, at a time when the renal epithelium had become incapable of separating from the blood the natural solids of the urine. The absence or diminution of some of the elements—as the chlorides, earthy phosphates, and sulphates—may have depended upon the state of the system generally, but almost certainly the diminution of the urea

depended upon the peculiar condition of the kidneys, for Frerichs has found that in this disease its quantity is rather increased than diminished.

It is to be regretted that the only urine obtained for analysis was that found in the bladder after death. During the time that she was in the Infirmary she made water, but in bed and involuntarily, and it could not be collected. It is very probable that, had we been able to examine the urine for some days before death, we might have found, as did Frerichs in some of his cases, a progressive diminution of the urinary solids, coincident with changes in the kidneys. It seemed impossible that kidneys in the state in which this woman's were found could be capable of any secretion at all; and, from this consideration, I think that the urine which was in the bladder had been secreted some time before, but retained in consequence of the torpid state of the nervous system. I have seen at least one case in which suppression of urine had occurred, in the course of pyæmia, and in which the kidneys were much less affected than they were in this instance.

But though we cannot in the meantime speak positively upon these points, it is evident that in every case of this disease the urine should be carefully examined, and that in treatment constant attention should be paid to the state of the kidneys.

II. *The Affection of the Kidneys.*—The state in which we found the kidneys specially deserves attention. A very copious exudation occupied the uriniferous tubules, and the epithelium was affected in the same way as the cells of the liver. Some were swelled, dense, opaque, granular, some extremely fatty, and some had broken down and disappeared,—a series of changes exactly corresponding with those of the liver. But for the firmer support which the stroma of the kidney and the walls of the tubules affords, we might expect a rapid wasting of the kidney like that which occurs in the liver.

The complete identity of the appearances met with in the two organs satisfies me that they were really affected in the same manner, that the morbid processes were identical, and that we cannot regard the renal affection as a consequence of the hepatic.

III. *The Evidence which this Case affords as to the Nature of the Disease.*—Various opinions have been held as to the nature of this affection. They may be referred to three classes:—

1. Some conceive that from an increase in the amount, and perhaps a change in the quality of bile, the hepatic cells are dissolved, and so the acute atrophy is induced. This condition has been referred by Rokitansky to an excess of bile in the portal system, by Hensch and Van Dusch to changes in the bile ducts. But I think that this view has been disposed of by Frerichs, who points out,—1st, That no accumulation of bile precedes the acute atrophy; 2d, That even if such an accumulation did precede, it could not occasion the atrophy, because in cases in which bile is retained no solution of the cells of the liver takes place, and he has

found by experiments that hepatic cells may be immersed in bile for whole days without undergoing solution.

2. Others conceive that the acute yellow atrophy is a result of a blood disease, and that the destruction of the hepatic cells, as well as the hæmorrhages which are often associated with it, depend upon the marked weakening of the heart's action and the rapid increase of the peripheric metamorphosis of matter.

This theory is, I think, right in so far; but before entering upon it, let me refer to the third.

3. It has been held by some to depend upon a diffuse inflammation of the gland: the wasting of the gland elements being a result of fatty degeneration consequent upon exudation into this substance.

This view has been maintained by Bright, Engel, Wedl, and Bamberger, and has been supported also by the eminent Professor of Clinical Medicine in Berlin, Professor Frerichs, but with a certain reservation; for while he says that, "according to his experience, an exudation process constitutes the starting-point of the disease," yet "he has some hesitation in identifying the destruction of the hepatic cells with fatty degeneration; because in the case of other glands, such as the kidneys, fatty degeneration of the epithelium does not produce such a rapid and general destruction of the cells, and especially because in acute atrophy of the liver the fat can only be seen deposited in the circumference of the lobules, whilst the destruction of the cells is found to extend so far as the central vein."¹

Of the fact that the destruction of the hepatic cells is a result of exudation, and that through a rapid fatty degeneration, I have no doubt. The state of the cells in different parts of the lobules put this beyond question; for in the centres they were dense, solid, and full of exudation, at the margins they had completely disappeared, leaving only the vascular network and the stroma, and between those two zones there was an intermediate ring of extreme fatty degeneration.

The first part of Frerichs' difficulty is very well met by the facts observed in the case under consideration, for the epithelial cells of the kidney were in the same state as those of the liver. It thus appears that a similar exudation thrown out into the cells of those two organs leads to the same destruction in both. And his second difficulty seems to me to disappear, when we observe that a regular series of changes existed from the centre to the periphery of the lobules.

It is interesting to observe, that while in most cases the disintegration of cells commences at the margins and spreads towards the centre of the lobule, Dr Handfield Jones² observed one in which the destruction commenced around the hepatic venous radicle and

¹ A Clinical Treatise on the Diseases of the Liver, by Professor Frerichs. Syd. Soc. Translation. Vol. i. p. 229.

² Diseases of the Liver, by George Budd, M.D. 2d Edition, p. 256.

spread outwards; and in his case it would appear that the destruction of the cells also resulted from an exudation process. We may assume, then, that the destruction of the cells is a result of an exudation process, but we have further to inquire as to the origin of this process. Is it a local affection, commencing in the liver and secondarily affecting the kidneys, the spleen, the intestine, and the blood? or is it a blood disease independently operating on all these organs?

The latter view seems distinctly indicated by the case which we have recorded, as well as by many others already on record.

The following considerations seem to me to point distinctly to this conclusion:—1. The blood was dark and fluid, and the muscles were dry as they are in typhus fever and other blood diseases. 2. The spleen was soft and pulpy as it is in many febrile blood diseases. 3. The fact that the kidneys and the liver were affected by a peculiar and identical morbid process indicates that they were influenced by a common cause, that cause situated in the blood, and a form of fever poison. 4. The appearance, amount, and effects of the exudation being different from what we see in simple inflammation, either of the liver or kidneys, indicates that some peculiar matter was present in the system altering the ordinary processes. 5. The facts that this disease occurs so often during pregnancy, and that it seems to be induced by depressing mental emotions, indicate that it is of a constitutional origin. From these considerations, I think that we cannot avoid concluding *that this peculiar affection is a blood disease, and that it leads to atrophy of the liver, by diffuse exudation into the hepatic cells, which is followed by a rapid fatty degeneration.*

This case is also fitted to draw special attention to the fact, that the blood poison may act on the cells of the kidneys as well as those of the liver, may destroy their structure, and arrest their functional activity as it does to those of the liver. There are very few cases of the disease on record in which the kidneys were so seriously involved as in the present; but Frerichs mentions that a granular state of the renal epithelium is by no means uncommon in cases which, like the present, occurred during pregnancy. What may be the import of the renal complication we cannot in the meantime determine, but it is evident that it must seriously increase the dangers of the disease.