Original Articles.

CLINICAL NOTES AND COMMENTS: CANCER OF THE EXTREMITY OF THE COMMON BILE DUCT.

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CASES of disease observed in the early anatomical stage, when few if any secondary lesions have developed, are the more instructive clinically and pathologically, as they are less impressive from their magnitude or intensity. This condition may be met with where a small initial lesion is so situated that a slight increase in bulk seriously interferes with some important function, and the consequences are as clear cut and decisive as in a laboratory experiment. In the following case the results cannot have been widely different from what would have come from an antiseptic ligature placed around the common bile duct.

A single woman, aged forty-eight, neither excessively stout nor the reverse, had enjoyed good health up to June, 1898. The appetite and digestion had been excellent. Repeated inquiries failed to disclose anything like attacks of gall stone. She had been in the country riding a bicycle and enjoying herself. One day she came home saying she was very tired and was going to bed. Within a day or two there was a loss of appetite, intense jaundice, and light-colored stools. Neither then nor at any other time was there any severe pain or tenderness on pressure. This condition lasted essentially unchanged until her death. In September there was some swelling of the legs, which later disappeared.

In February she had lost, say, 30 pounds of flesh, and was of a deep yellow color. The abdomen was much distended, and evidently contained considerable fluid. The liver was not to be felt below the edge of the ribs, nor could its dullness be detected there. Neither could the spleen be felt. The urine was scanty, although it had been increased somewhat after taking diuretics. The bowels were somewhat loose from the action of mild salines. The appetite was moderate but not absent, and so far, at least, as the absence of discomfort went, the patient enjoyed and apparently digested her food. The blood showed the red corpuscles a little less than 4,000,000, with the whites in normal proportion and normally distributed. There was no material change under any of the medications employed, including those of a clairvoyant, except that from the beginning of the ministrations of the latter the stools were described as becoming green and then black. That which I saw at this time was of a slaty grey, without any tinge of biliary color, and could have been described as green only under psychic stimulus. With nitric acid it yielded a reddish-yellow fluid, which in its turn gave a bluish precipitate with ferrocyanide of potassium, and was undoubtedly due to iron. The diagnosis received no light from supernatural sources. The pulse was usually in the neighborhood of 100, and the temperature at times a trifle above normal,

although it was not regularly taken and charted. There was nothing in the least resembling a biliary fever. The tongue was nearly clean and the breath not offensive.

On April 24th she was tapped, and about 12 quarts of serum removed, which contained a large amount of albumin (2.5% dry), and gave a strong reaction for biliary coloring matter. The legs were a good deal swelled. She had "distressed spells." There had been several times specks and streaks of blood in the stools and sputa, and also some epistaxis, but never any severe hemorrhage. After this first tapping it was noted that palpation through the relaxed abdominal walls revealed nothing, but after the second, sixteen days later, there was to be plainly felt below the ribs what was supposed to be (and was) the liver, with the rounded end of the gall bladder below it. The projection of the liver increased somewhat, and after successive tapplings its edge could be grasped through the relaxed abdominal wall by the hand for quite a distance without pain, and almost without the notice of the patient. There were in all eighteen tapplings, about 12 or 14 quarts being drawn each time, the intervals gradually decreasing.

In September, the patient was seen by Dr. Arthur Cabot, with a view to the (very remote) possibility of painless impaction of a gall stone, and an operation was decided against.

Death occurred on October 15th, after nearly a week of diminishing consciousness and, at the last, convulsions, that is, sixteen months after the first symptoms.

The urine throughout was very deeply colored with bile, of high specific gravity, containing either no albumin or a mere trace, with a few casts, hyaline and epithelial. There was at one time a deposit of rather unusual crystals, consisting, as I was informed by Dr. Wood, of phosphate of calcium. Its quantity used gradually to diminish until a tapping, when for a number of days it was more abundant.

Autopsy took place twenty hours after death. Body was extremely emaciated. A pailful of fluid was found in the abdominal cavity. There were no adhesions in the neighborhood of the punctures, but a few slight ones between the liver, spleen and diaphragm. The omentum was much emaciated. A few flocculi of recent lymph were on coils of intestines and abdominal walls. Kidneys were normal. Spleen was a little larger than the average, but not soft.

There was nothing abnormal in the external appearance of the stomach or intestines. The gall bladder was enlarged, containing many gall stones, pearly white, angular, with colored tips. The interior was yellowish brown in the centre, growing gradually lighter toward the outside. They were largely cholesterin. The fluid contents were greyish and viscid. The lower part of the gall bladder was adherent to the neighboring liver substance, and could not be separated from it except by cutting. The cystic duct was not followed down to the junction. The biliary passages were enormously dilated within the liver, and also the

hepatic and common ducts, down to a point 2 inches from the duodenum where there was an abrupt narrowing. Below this point there was some dilatation but much less extreme. At the point of narrowing there was a small rounded tumor, the size of a medium bean, in or closely attached to the wall of the gall bladder between it and the hepatic duct, and pressing upon the latter. Further down there were some dense portions of tissue seeming on section much like cicatricial. The substance of the liver after the emptying of the ducts was flabby, and very dark-greenish brown. Its firm rounded feeling during life was evidently due to its distension by bile in the dilated ducts. The duct and substance of the pancreas were healthy.

The specimen was given to Dr. R. M. Pearce, at that time of the Harvard Medical School, for microscopic examination. He reported that there was a carcinoma of the papilla at the orifice of the common duct, and a lymph node in the immediate neighborhood. The cancer was very slight in amount, and might easily have been overlooked or mistaken without the microscope. In fact, the primary growth was overlooked at the autopsy and the lymph node supposed to be the primary. The whole amount of tissue involved was hardly as much as the last joint of one's finger.

Although this location of cancer is stated by many monographists to be very rare, a number of cases have been collected from the more easily accessible medical literature, periodicals, and especially from inaugural theses.

There is but little doubt, however, that cancer of the bile ducts is in reality somewhat more common than would appear from the older statements, and that many cases which would have been described as "obstruction" even so lately as fifteen or twenty years ago, have been brought by more careful microscopic methods under the head of carcinoma. This is rather interestingly shown by a comparison of titles in the earlier and later series of the "Index Catalogue" of the Surgeon-General's Library.

TITLES.	1ST SERIES UP TO 1881.	2D SERIES, 1881 TO 1897.
Bile ducts, obstruction and dilatation of.	7 dissertations, 2½ column references.	6 dissertations, 1 column references.
Bile ducts, cancer of.	1 dissertation, ½ column references.	7 dissertations, 1½ column references.

In a case which I saw some sixteen years ago, a man aged seventy-six, of simple habits but (supposed) gouty diathesis, had jaundice for forty-five days, with very dark urine and clay-colored stools. The liver and gall bladder were felt below the ribs. My diagnosis was, "probably cancer of the liver with a possibility of simple jaundice (that is catarrhal)."

At the autopsy the bile ducts were all enlarged down to a point about $\frac{3}{4}$ inch from the opening into the duodenum, where there was a sudden narrowing, and the duct was very small for the remainder of its course. In the neighborhood of

the stricture the tissues, adipose and fatty, were somewhat consolidated and nodulated. There was no distinct new growth, either here or in the liver. There is no record of a microscopical examination, but it is quite as likely that this was an unrecognized cancer as that it was a piece of cicatricial tissue, for the existence of which no cause could be found. Cicatricial stenoses have been found in other cases, but usually with them an indication of the causative lesion in the form of an old ulcer.

There are three points at which the bile ducts are especially liable to be affected by cancer, although it may occur in the intervals between them. These are the union of the ducts from the two lobes of the liver, the union of the cystic and hepatic ducts, and the entrance of the hepatic duct into the duodenum. Of cases in which the lesion has been found in the last-named region, that is, at the papilla or a very short distance above it, I have looked up 22, including a number also given in Musser's table.

As to the frequency of cancer in the ducts and of the papilla in particular, the following figures may be of interest. Musser gives 18 cases, of which 9 were in or near the papilla, as against 100 of the gall bladder. In Villard's monograph (1871) are collected 24 cases of cancer of the ducts, of which 1 may have been in this position. Dieckmann¹ says that in the reports of the Munich Pathological Institute, from 1854 to 1884, he finds only 1 case of gall bladder cancer recognized as primary, but 71 of cancer of the liver. Howald² says that in the last fifteen years, at the Pathological Institute at Bern, there were 10 cases of primary gall bladder cancer. As both of these last theses were upon "cancer of the common duct," it is fair to suppose that if the authors had found accounts of any cases beside those upon which they based their theses they would have been reported. Kelynaek (1897), after the remark that primary malignant disease of the bile passages "although far from common, can hardly be considered rare," states that, "in an extensive search through our pathological records (Manchester Royal Infirmary) of 4,578 cases, I can only find details of 8 clear cases of primary cancer of the gall bladder and 2 undoubted cases of primary cancer of the common bile duct."

The presence of gall stones in connection with primary cancer of the bile ducts and gall bladder is very interesting, in connection both with diagnosis and etiology, and as having a bearing on the origin of cancer in general. Considering the great frequency of gall stones, it is certainly fair to assume that in a certain number of cases their occurrence with cancer is a coincidence. In others, of which the one just reported is one, the deposition of the concretion is much more probably the result of the retention in the gall bladder of what is at first bile, but afterwards becomes considerably altered by a partial absorption and the secretion of mucus.

In this case the stones were small and angular,

¹ Inaug., Thesis, Munich, 1889.

² Inaug., Diss., Bern, 1890.

without being faceted, as if they had never been disturbed or subjected to friction. Their color in the interior was dark brown, with thin successive layers of lighter yellow, and externally a pearly white, as if they had been deposited from a menstruum, at first dark, becoming lighter, and at last white, like the fluid in which they were found. This undoubtedly took place after the duct was occluded, the bile originally contained therein having undergone the usual changes. Had they been the cause of the cancer and the stoppage, there was no reason why they should not have been throughout of the usual dark color. There was no stone in the common duct nor in the immediate neighborhood of the new growth.

The theory of the origin of cancer in a local irritation certainly receives support from many cases where gall stones are found in the midst of malignant growths, where they may have been the source of that long-continued but not very intense mechanical irritation, which seems, if any, to be the kind necessary to the formation of a neoplasm. This, however, is far more common in the gall bladder than in the bile ducts. Thus Musser, in 100 cases of cancer of the gall bladder, found stone mentioned 69 times and supposes that it may have been overlooked in many more. On the contrary, in 22 cases mentioned above of cancer of the papilla, or a very little above it, including some of those already tabulated by Musser, gall stones are mentioned 4 times, 3 at least of these being in the gall bladder. The possibility has been suggested that a stone may find a lodgment long enough to set up the necessary irritation, and then escape, without leaving behind definite traces. One case of Leith² lends some support to this view. A patient had had definite symptoms of gall stones. None were found at the autopsy, but there was a malignant adenoma, and the walls of the duct were roughened and thickened as if from catarrhal inflammation resulting therefrom. Quinlan (quoted by Kelynack) mentions a case of cancerous disease of the liver where the duct was imbedded in a mass of malignant growth, but its opening into the duodenum was four times the normal size, and suggested the likelihood of passing of gall stones.

To suppose, however, that this is an adequate explanation of the origin of cancer in the papilla or higher up, in any considerable number of cases, is working a mere hypothesis very hard in the face of a large number of cases, in fact in nearly all, where there have been no symptoms whatever of the presence or the passage of gall stone.

The further assumption of a painless passage to cover this gap involves the contradiction of an almost universal rule that the movement of a gall stone through a previously undilated duct is one of the most painful processes which ever takes place in the body. The records of the Dorchester Medical Club mention 2 cases where, death having apparently taken place from the pain and shock, a gall stone was found protruding from the papilla into the duodenum, that is, at the very point where this theory demands that they should escape with-

out pain, but leaving behind them a neoplasm. The observation of Musser that, unlike cancer of the gall bladder which, as well as gall stones, is more frequent in the female, that of the bile ducts occurs with equal frequency in both sexes, also points to the conclusion that while it is very probable that gall stones play an important part in the etiology of cancer of the gall bladder we must look elsewhere for the local irritation necessary to set up a similar growth in the ducts.

The diagnosis of these small neoplasms, lying as they do in a region where they are inaccessible to palpation, is stated by some authors to be almost impossible. This is undoubtedly true as regards their exact size and location, but an approximate diagnosis, such as can in many cases be made with some accuracy, is not without its practical value. I think that every one of the several physicians who saw this case, even in the early stage, formed at least a mental diagnosis not far from the truth as regards the nature of the disease, but I think also that all of them, including myself, would have expected a more extensive lesion to be found at the autopsy after more than a year's growth.

A rapid, complete, non-febrile jaundice in a person over forty or forty-five, preceded and accompanied by no severe and painful paroxysms, and succeeded, if by any, only by a moderate amount of diffuse pain and tenderness, especially after it has lasted long enough to exclude catarrhal jaundice, is an adequate basis for a highly probable diagnosis of cancer of the ducts; and if later the smooth non-nodular edge of the liver, with the gall bladder tense but not tender, presents below the ribs, it is also highly probable that the lesion of the ducts was the primary.

Unfortunately the presence of painful paroxysms is not so decisive in one direction as their complete absence is in the other, for even if significant of gall stones this does not exclude carcinoma.

The distinction between a growth originating in the walls of the duct itself and a small malignant or other tumor in the head of the pancreas pressing upon it, and producing total occlusion there before giving rise to symptoms elsewhere, would certainly be very difficult to make. When the pancreatic disease is more advanced, many of the symptoms are likely to resemble those arising from the bile ducts. The presence of such a tumor must be an extremely rare condition, much more so even than any we have been considering, and when the disease is more advanced the deep seated pain and tenderness, the gradual onset of the jaundice, a hard immovable tumor in the median line, would be likely in most cases to decide the matter. The presence of fatty stools would of course have great diagnostic value, but as this is usually insisted on rather from physiological theory than from clinical observation, its absence throws no light upon a doubtful case, and the same may be said of sugar in the urine.

Of course the important point is to determine as early as possible the exact location of the growth, and this certainly cannot be done without an operation. This has, of course, often been done and

² Transactions Medical Chirurgical Society, Edinburgh, 1895-96.

successfully for the diagnosis and relief of gall stone.

Musser in his last case⁴ had in contemplation an operation for cancer which was for special reasons postponed a few days, during which the patient was suddenly attacked by a fatal hemorrhage. Had this operation been performed it would have been the first to be based upon a distinct diagnosis of cancer of the biliary ducts. It can hardly be doubted that in the future exploratory operations will be undertaken with the object distinctly in view of dealing with a cancer, if such shall be found, either by removal or by circumventing the obstruction in such a way as to give a more or less extended relief.

So far as I am aware the only operation as yet done for the removal of a cancer of a bile duct was that reported by Dr. Halsted,⁵ and doubtless familiar to readers. Although not successful as to its ultimate result, it shows the feasibility of such an operation, and the return of the disease after the very careful removal only emphasises the fact, already only too well known, that it is almost impossible to cut wide enough of any focus of cancer to be sure of having included the utmost limits of the infected region.

At the time when the question of operation was formally considered in the present case, it certainly could not have been successful, but had it been possible a year before to have known exactly the condition, it might perhaps have been feasible as in Dr. Halsted's case, and either relief or permanent cure obtained according to the presence or absence of cells of carcinoma beyond the limits of the operation. Considering, however, what must have been the very slow growth, when even after sixteen months the primary and secondary growths together were so small, and yet, as it seems, so far beyond the bounds of a possible thorough removal, it is by no means improbable that even when the first symptoms appeared there must have been a wider diffusion of the new growth than would have been apparent or accessible to the knife.

This case exhibits without any complication the effects of suppression of the bile flow, and does not show the effects usually attributed to its reabsorption, which so far as coloring matter is concerned evidently took place freely. It is to be regretted that no examination of the urine for bile acids was made. I have not found any statement of such an examination having been made in any of the cases closely resembling this. There was not the slow pulse supposed to follow the ingestion of cholic acid, it having been usually not far from 100. There was no delirium until the last few days, no disturbance of the intellect nor excessive depression. It would appear from this and similar cases that the evil effects of long-continued obstruction to the flow of bile are due not so much to its presence in the circulation, as to its absence from the intestine and a consequent steady and fatal impairment of nutrition. Hence

the inutility, so far as promoting recovery, of tapping the gall bladder and establishing a fistula, although such a procedure would in cases where the cystic duct remains permeable, remove the effects of reabsorption such as the liability to hemorrhage and to sepsis, which is likely to take place if any ulceration occurs.

In case the only obstruction should be situated near the mouth of the duct, the cholecystenterostomy suggested by Mr. Robson would relieve both sets of symptoms until the growth of the neoplasm made another invasion higher up, and in the case of a very slow growth, such as there may be, such a temporary relief might add a considerable time to life.

An operation for establishing an anastomosis between the common bile duct and the duodenum is reported by Dr. J. E. Summers, Jr., of Omaha,⁶ but without details as to the anatomical condition before operating, especially the nature of the stricture. He speaks as if the getting rid of the bile were the chief object in making the communication, and as if it were to be undertaken only when the discharge cannot be secured through the gall bladder. The supply of this digestive fluid in the intestines, which cannot be supplemented by any other, is of equal importance, and more details as to this case would certainly be very interesting.

The bibliography of the subject may be found largely in the "Index Catalogue" of the Surgeon-General's library, but it is useful to call attention to four important articles not to be found there. The elaborate study by Dr. Musser in the *Transactions of the Association of American Physicians* for 1894 is not there, probably for the reason that it is to be indexed under the title "Gall Bladder," although it is equally complete on the subject now under consideration. There is a subsequent paper of his in the *Philadelphia Medical Journal* for October 6th of last year. The largely statistical article by Kelynaek is to be found in the *Medical Chronicle* (Manchester), and is a very important one. Fourthly, come the article⁷ and book (1897) of Mr. Robson on the "Surgery of the Biliary Passages."

THE INTERPRETATION OF BACTERIOLOGICAL FINDINGS IN DIPHTHERIA DIAGNOSIS.

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IN May, 1898, the examination of diphtheria cultures for the city of Boston was transferred from the Harvard Medical School to the laboratory then just established by the Board of Health in the Sudbury Building. For about three years prior to that date this work had been under the direction of Prof. H. C. Ernst. On him fell the trials and difficulties always inseparable from the introduction of new methods and procedures. Having successfully met and conquered these, he

⁴ University Medical Magazine, September, 1899.

⁵ Boston Medical and Surgical Journal, vol. cxli, No. 26, vol. 2, 1899, p. 646.

⁶ Journal American Medical Association, December 1, 1900, p. 1403.

⁷ British Medical Journal, April 28, 1894. Lancet, May 27, 1897.