

PRIMARY CARCINOMA OF THE FIRST PART OF THE DUODENUM WITH SECONDARY INVOLVEMENT OF THE COMMON BILE-DUCT.

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PRIMARY carcinoma of the duodenum is a rare disease. Its actual frequency, as estimated by Brill¹ from the post-mortem records of Maydl, Nothnagel, Müller, and Lubarsch, is 0·3 per cent. of all cases of carcinoma (15 cases in 4675 deaths from carcinoma). In a majority of the recorded cases the disease has involved the second part of the duodenum, and in not a few of these the opening of the common bile-duct has been implicated. The case here recorded appears to be unique in that a carcinoma arising primarily in the first part has, by direct extension, come to involve the common bile-duct in the middle of its course, leading finally to a clinical picture in which the outstanding phenomena were those of obstruction in this latter situation.

On July 14th, 1913, a man, aged 61, was admitted to the wards of the General Infirmary at Leeds, under the care of Dr. A. G. Barrs. The appearance of the patient was striking. He was deeply jaundiced, the jaundice being remarkable for its ruddiness. He was feeble, wasted, and lethargic, obviously suffering from a dire disease. His complaints were three—yellowness of the skin, abdominal discomfort, and hiccough. The history obtained was marked by its brevity and was barren of assistance in accurate localisation of the primary condition. Three months seemed to cover the time that he was sensible of change in himself. For that period he had been troubled with indigestion of the flatulent variety, discomfort being almost continuous, though occasionally he was disturbed by paroxysms of pain coming on half an hour after food. Water-brash was not infrequent, whilst less often he vomited a trifling amount of what he called "darkish-coloured fluid." From the outset he had lost weight steadily, though more rapidly latterly. A month ago he noticed his urine getting darker, his motions paler, and then his skin became yellow, deepening rapidly in hue, and without remission. His past personal history revealed little, and for the last 12 years he had apparently been rigidly temperate in all things. His wife, however, told us that three years ago he had suffered from an attack of somewhat severe abdominal pain, localised to the upper part of the abdomen, not specially to one side, colicky in nature, unaccompanied by jaundice, and he had not passed anything abnormal by the rectum.

On admission the temperature was 100° F., but rapidly fell to normal, and remained so until the end. The pulse was 80 per minute, regular, though feeble. Frequent hiccough disturbed the patient and the examination. The abdomen was hollow, the skin of the lower part striated, and there was no distension of veins. There was some slight tenderness in the right hypochondrium; clinically the liver was neither enlarged nor diminished. The gall-bladder was not palpable, nor were there

signs of fluid in the peritoneal cavity. The stomach was not dilated, and peristaltic action of this organ or of the intestines was not seen. Rectal examination was negative. Examination of the urine revealed the presence of bile, some albumin, and numerous granular and epithelial casts. Leucin and tyrosin were not found. Neither the fæces nor the urine gave evidence of pancreatic insufficiency.

A diagnosis of "obstruction of the common bile-duct by malignant disease" was made, there being insufficient evidence to implicate any organ as the primary seat. Dr. Barrs hesitated in making a diagnosis of either primary disease in the duct itself or of the duodenum. From the moment of admission the patient rapidly got worse, and the illness ended fatally four days later, on July 18th.

Post-mortem examination.—External appearances: The integuments and conjunctivæ were stained an intense golden-yellow colour. The little toes were markedly dorsiflexed and adducted, so that they came to overlap the next digit in each instance.

Internal examination: On laying open the intestine a tumour was found in the first part of the duodenum, commencing 1½ inches from the pylorus and extending along the gut for a distance of about 2 inches. The growth was 3 inches in length, and almost completely encircled the viscus, leaving only ½ inch of the anterior wall uninvolved. It was ulcerated in the centre, while the rest of the surface presented a honeycombed necrotic appearance, save at the extreme margin. The bile papilla and opening of the common duct were situated about an inch below the tumour, and appeared normal. Between the papilla and the lower margin of the growth, and immediately abutting on the latter, there was a diverticulum about ¾ inch in depth, and just wide enough to admit the tip of the little finger. The common duct, where it lay in relation to the duodenal tumour—that is, about an inch below the junction of the cystic and hepatic ducts—was itself the seat of an annular new growth completely encircling the lumen, and apparently directly continuous on its deep aspect with the duodenal growth. Above the tumour there was marked dilatation of all the bile passages, gall-bladder, common duct, cystic and hepatic ducts, but that the obstruction was anatomically incomplete was shown by the ease with which a probe could be passed through the stenosed portion of the tube, and so through the remaining portion of the common duct to the intestine. The dilated bile passages, both intra- and extra-hepatic, were filled with a thin, slightly bile-stained, mucoid fluid, while their walls presented a curiously pitted appearance.

The liver on section was soft and fatty looking, and showed a considerable degree of bile-staining, especially around the dilated hepatic ducts. There were several secondary deposits of new growth, of which the largest, about the size of a hazel-nut, was necrotic and bile-stained in the centre. The pancreas presented no evidence of new growth, but several of the lymph glands in relation to it were the seat of secondary deposits. The spleen was fibrous but of normal size. There was an accessory spleen the size of a hazel-nut immediately above and in front of the left adrenal. The latter glands were of very large size, and the brown zona reticularis was unusually prominent. The kidneys, which were markedly bile-stained, were of small size, and were embedded in a very large amount of

¹ American Journal of the Medical Sciences, 1904, vol. cxxviii, p. 824 (Bibliography)

fat. On section, cortex and medulla were badly differentiated, although the former was not unduly narrow. There were several small puckered depressions on the surface of both organs, clearly the result of a starvation fibrosis.

The lungs were emphysematous, congested, and somewhat œdematous, and there were old pleural adhesions on the left side. The aorta was bile stained and contained several atheromatous patches. The heart contained large agonal thrombi extending into the aorta and pulmonary artery on each side. The mitral valve showed marked thickening of the cusps and of the chordæ tendineæ, but there was no stenosis. The other viscera, including the stomach, presented no features worthy of note.

Microscopic examination.—Various portions of tissue were taken for histological investigation as follows: (1) Duodenal growth, (2) growth in common duct, (3) nodule in liver, (4) lymph gland deposits, and (5) pancreas. The general structure of the tumour is definitely cancerous, and for the most part the type is that of an adeno-carcinoma. This is best seen in the case of the lymph gland deposits and in the liver nodules, where the acini are large and well developed, being separated in the more central parts by a considerable amount of fibrous stroma. In the duodenal and common duct tumours, however, there is well-marked evidence of anaplasia, a reversion to a spheroidal cell and mixed cell type of growth without acinar formation. In these situations the cells show great variation in size and shape, and not a few are possessed of multiple nuclei, but mitotic figures are comparatively few in number. Many of the cancer cells, especially in the larger alveoli, show degenerative changes, both mucoid degeneration and varying degrees of necrosis. There are areas of massive necrosis in the centre of the duodenal tumour, in the larger liver nodules, and in the glands related to the pancreas. The duodenal tumour is fairly well defined at the margin, but it has extended through the whole thickness of the bowel wall, and is in direct continuity with the deep aspect of the common duct growth. The histological appearance of these two tumours is precisely similar, in our opinion strongly indicating that one is secondary to the other. The pancreatic tissue, while not actually invaded, is in direct contact with the lymph gland deposits. It presents a normal appearance, with large and prominent islets of Langerhans. The liver is the seat of advanced cloudy swelling, proceeding in parts to actual necrosis of the hepatic cells. Where it surrounds the carcinomatous nodules the liver tissue is compressed and infiltrated by the new growth.

Comment on the clinical diagnosis of this case need not be laboured by conjuring up fanciful possibilities, for the problem unravels itself up to a point, beyond which we enter upon the domain of pure speculation. That the trouble did not lie in the head of the pancreas was fairly obvious, for the gall-bladder was not distended, and signs of pancreatic insufficiency were wanting. A diagnosis of enlarged glands in the portal fissure secondary to disease in the stomach did not meet the facts of the case, owing to the absence of physical signs in that organ and absence of ascites. Primary malignant disease in the first part of the duodenum, a diagnosis of which is dependent upon the signs of pyloric obstruction, was equally unsatisfactory as a solution of the problem. Lastly, primary malignant disease of the common bile-duct as the

only cause revealed obvious shortcomings, and however impatient one might be of ignorance, the only logical outlet from the *impasse* was, as Dr. Barrs pointed out, to wait and see which of the two latter conditions post-mortem examination would show to be the cause of the man's death.

From the pathological standpoint the chief problem for solution was, Which was the primary growth—that in the duodenum or that in the common duct? The possibility that we had to deal with two separate tumours of independent origin was almost too remote to be worthy of consideration, but it may be pointed out here that not only were the tumours in this case precisely similar in histological structure, but they were directly continuous with one another. After careful consideration we have come to the conclusion that the duodenal tumour was the primary, and for the following reasons: 1. The gastric symptoms were of three months' standing, whereas the jaundice had only been in existence one month. 2. The type of tumour was very suggestive of a carcinoma of bowel origin. 3. There were secondary deposits in the liver and lymph glands, an event which occurs more frequently and earlier in duodenal cancers than in those of common duct origin. 4. The duodenal tumour was more extensive and the seat of more advanced degenerative changes than the common duct growth.

That the tumour was of a highly malignant character was shown both by the rapidity with which it killed the patient and by the presence of hepatic and glandular dissemination. The histological characters, showing reversion to a spheroidal cell and mixed cell type of growth, also bore this out.

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METHODS OF INCREASING THE ACCURACY AND DELICACY OF THE WASSERMANN REACTION.¹

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THE Wassermann reaction is not a complement fixation reaction brought about by the interaction of a true specific syphilitic antibody in the patient's serum with the syphilitic spirochaetes. The antigenic value of the antigen used in the original reaction has no relationship to the richness of the organ in spirochaetes—in fact, an emulsion of spirochaetes as antigen gives only very feeble complement fixation, if any, with a syphilitic serum. The only other possible way in which the original antigen as used by Wassermann might be superior to others derived from non-syphilitic sources might be that the organ from which the antigen is made contained products of the action of the spirochaete, which might cause complement fixation with a syphilitic serum. If this were so the antigenic value should be directly

¹ A paper read before the Pathological Section of the Royal Society of Medicine on Feb. 3rd, 1914.