Remarks

ON

THE GALL-BLADDER IN RELATION TO FOCAL INFECTION.*

BY

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GALL-BLADDER disease commands our attention from three aspects—namely: (1) As a cause of recurrent attacks of acute abdominal pain. (2) As a cause of persistent reflex flatulent dyspepsia. (3) As a focus from which infection spreads to various organs and tissues throughout the body.

With biliary colic and with gall-bladder dyspepsia we are all thoroughly familiar, and I do not propose to touch on these subjects, nor will I refer to complications such as obstructive jaundice and pancreatitis. Our concern to-day will be entirely with the infective aspect of gall-bladder disease and its relation to certain common ailments of obscure etiology.

The importance of the study of the "pathology of the living," which Moynihan has done so much to emphasize, is seen nowhere to such advantage as in the investigation of biliary disease. Post-mortem pathology taught us practically nothing in regard to the essential features of infection of the biliary passages. The gall-bladder is the organ above all others which suffers from early post-mortem changes which mask all the finer pathological features. Indeed, the frequency with which gall-stones were found at post-mortem examination tended to obscure the significance of gall-bladder disease and its relation to other morbid changes.

To surgery belongs the credit of disclosing the frequency of gall-bladder infection and of defining its essential characters. The study of the early stages of cholecystitis in the operating theatre and clinical laboratory has proved a fruitful field of observation during recent years, and the correlation of this study with experimental research has led to results which are fundamental in their bearing on pathology. The practice of extirpating the gall-bladder when it has shown clear evidence of disease has provided an experiment the results of which have been illuminating, and we are now in a position to speak with some assurance regarding the role which this organ plays as a seat of focal infection. We now know that gall-bladder infection, far from being merely the result of the straying of bacteria into its lumen by way of the bile, as was so long believed and taught, is a very definite specific blood-borne infection of the wall of the organ by a streptococcus which has a specific affinity for this tissue. This idea, which sprang from the pioneer work of Rosenow, has received ample confirmation in the Surgical Research Laboratory in Edinburgh, from the work of Illingworth, and of A. L. Wilkie. The latter was able to isolate a streptococcus from 84 out of 100 gall-bladders removed at operation for biliary disease. He showed that, whilst the bile was usually sterile, there could be isolated from the wall of the viscus, and still more readily from the cystic lymph gland, a streptococcus which had this peculiarity—that it was killed or its growth inhibited by the presence of bile. The customary method of making cultures from a snipping of the whole thickness of the gall-bladder wall had failed to obtain a growth because the mucous membrane, included in the section, had bile adhering to it.

Wilkie showed that intravenous injections of an emulsion of this streptococcus into rabbits produced with great regularity a chronic cholecystitis with gall-stone formation in every way similar to that found in the human subject. The *Streptococcus viridans*, which was isolated in these cases, resembled closely that found so frequently in pyorrhoea, in infected dead teeth, in chronic tonsillitis, in chronic gastric ulcer, in chronic appendicitis, and in the nodules in chronic muscular rheumatism. In a few cases, three or four in all, we have isolated *B. welchii* from the wall of the gall-bladder, and, although rare, this form of infection is peculiarly toxic, and in its acute phase may

prove fatal. The *B. coli*, although not infrequently found in acute obstructive cholecystitis, has proved in our experience to be a rare type of infection in chronic gall-bladder disease.

The conception of chronic cholecystitis as a blood-borne streptococcal infection situated within the wall of the gall-bladder, indolent, slow, tenacious, causing at first little interference with the bile storage and concentrating functions of the organ, but permitting of streptococcal invasion of the lymph stream, as evidenced by the frequent presence of the organism in the cystic lymph gland and thence possibly infection of the blood stream—this conception, now a proven reality, establishes the important role which the gall-bladder may play as a focus of infection. There is now a considerable body of proof that a chronic streptococcal infection may have an intimate etiological relationship to many of the so-called chronic rheumatic conditions of joints and of fascial planes, to myocardial degeneration, to certain renal conditions, and to some affections of the central nervous system.

Possessed of the knowledge that the gall-bladder is very frequently the seat of a chronic streptococcal infection, it would seem to be only natural that we should search for evidence of gall-bladder disease when casting about for a focus of infection in our investigation of cases of any of the above-mentioned maladies. I propose to refer to some cases in which such an etiological relationship appeared to be possible and in which the removal of an infected gall-bladder was followed by a notable amelioration in the secondary lesion.

Chronic Arthritis.

Miss S., aged 32, had suffered for almost two years from a chronic rheumatic affection of both knees which did not yield to local treatment or anti-rheumatic remedies, and which incapacitated her from all forms of active exercise. She also suffered from a mild flatulent dyspepsia, and on two occasions during the past six months had had an attack of severe pain in the upper abdomen, accompanied by vomiting and diarrhoea, and by marked tenderness under the right costal margin.

On examination she looked healthy and was well nourished. Her knees were slightly swollen and were painful on movement. Definite tenderness was elicited over the gall-bladder. A cholecystogram showed a fairly well-defined gall-bladder shadow.

At operation, in January, 1928, the gall-bladder was found to be small, was slightly opaque, but not appreciably thickened. There were no gall-stones; the other abdominal organs showed no abnormality. The gall-bladder was removed and cultures were taken from the bile, from the gall-bladder wall, and from the cystic lymph gland. Those from the bile and gland were negative, that from the wall of the gall-bladder gave a pure growth of a streptococcus which, on injection into rabbits, produced cholecystitis.

Progress.—One year after operation the patient reported that within a few months of the operation the rheumatic condition of the knees had cleared up completely, and that she could skate and play badminton for hours on end without ill effect.

Comment.—The above case is one of a number in which so-called rheumatoid joint conditions have shown lasting improvement following cholecystectomy.

Toxic Myocarditis.

Mrs. A., aged 45, complained that for two and a half years she had suffered from increasing breathlessness and palpitation on slight exertion. She had been subject to persistent flatulence after meals for at least seven years, and on several occasions had been laid up with attacks of severe pain in the epigastric region and the right side of the chest, and had been treated for "congestion of the lungs" in two of these attacks. Owing to her inability to take exercise without distressing breathlessness she had got much stouter during the past year.

On examination the patient was rather stout, pale, and of poor muscular tone. Moderate exercise induced breathlessness and rapid heart action. There were no cardiac murmurs, but the heart sounds were feeble. There was very definite tenderness on pressure below the right costal margin. A cholecystogram showed a definite gall-bladder shadow with a few negative areas indicating calculi.

A diagnosis of cholecystitis with gall-stones and myocarditis was made and operation was recommended.

Operation (June, 1926).—Owing to the heart condition gas and oxygen and ether were chosen as anaesthetics. A greatly thickened gall-bladder, containing numerous calculi, was removed. A pure growth of a streptococcus was obtained from the wall of the gall-bladder; the bile was sterile. Apart from having a rapid pulse rate for several days following operation the patient made a

* Part of an address (with lantern demonstration) to the South Wales and Monmouthshire Branch at Porthcawl on May 16th, 1929.

satisfactory recovery, and on leaving hospital was instructed to take graduated exercises.

Progress.—Two and a half years later the patient reported, looking thinner, with a healthy complexion, and obviously in good physical condition. She stated that during the year following the operation she gradually increased her physical exercise and was now able to walk and to climb stairs without any of her former distress.

Comment.—The “cholecystitic heart,” as it has been termed, is, in my experience, a very common condition. It would appear to result from chronic toxæmia, probably first a slight myocardial degeneration, later complicated by fatty infiltration owing to the patient’s inability to take exercise without distress, and the consequent obesity so common in these cases. It is the myocardial change which presents the chief risk of operation in old-standing and neglected cases, and which makes acute infective complications, when they supervene, so dangerous.

Toxic Nephritis.

The following case, although standing by itself, was perhaps the most dramatic in the series, and the credit for the successful result rests with the physician who advised, rather than with the surgeon who, with considerable trepidation, carried out the operation.

Mrs. B., aged 63, had for some years suffered from a chronic flatulent dyspepsia. In August, 1927, she had an acute attack of obstructive cholecystitis with great pain and fever, associated with a large palpable gall-bladder. As this was subsiding she developed the signs of nephritis—namely, marked generalized oedema and urine loaded with albumin. This persisted week after week and had several distinctive features. The oedema would vary greatly, even in the course of one day. As a rule there was a state of complete generalized anasarca, the conjunctivæ hanging out as oedematous sacs. Twenty-four hours later, without apparent reason, the oedema would be much less. The excretion of urea was normal, as was the blood urea. There were no retinal changes. It was thought that the nephritis, or perhaps more accurately the nephrosis, must be toxic in origin and the diseased gall-bladder the most likely focus.

When first seen by me in October, 1927, the patient showed complete anasarca, the abdominal wall was oedematous, the abdomen contained much free fluid, and the limbs were tense and shiny with oedema. The risk of operative intervention appeared to me to be unjustified, and an expectant attitude was advised. The renal condition, however, showed no signs of improvement, and on November 21st, 1927, operation was undertaken.

Operation.—Twilight sleep and local anaesthesia, supplemented by gas and oxygen, was used. A Kocher incision was made through the extremely oedematous abdominal wall. A considerable quantity of free fluid escaped from the abdomen on opening the peritoneum. A very large, inflamed, and greatly thickened gall-bladder was exposed and tapped, muco-pus being drawn off. The gall-bladder, which contained one stone blocking the neck, was removed. Owing to the great oedema of the retroperitoneal tissues palpation of the kidneys was impossible. From the cystic gland a pure growth of *Streptococcus viridans* was obtained, and emulsion of this injected into a rabbit produced typical cholecystitis. Cultures from the muco-purulent content of the gall-bladder gave no growth.

Progress.—The patient was upset but little by the operation; within a week the oedema was seen to be disappearing rapidly and the albumin in the urine was diminishing. At the end of a month all oedema had gone and but a trace of albumin remained. Three months after operation the patient had resumed her normal life, and now, eighteen months after, she is enjoying better health than for many years past.

Comment.—This most striking case of immediate recovery in a waterlogged patient on removal of an infected gall-bladder confirmed our opinion that focal infection in this viscus has wide clinical bearings.

Toxic Hepatic Cirrhosis.

It has been held by many that an infective hepatitis may be the precursor of cholecystitis, the gall-bladder being infected through the lymphatics which reach it from the liver. The experiments of A. L. Wilkie showed that this is probably not the case. On the other hand, an infected gall-bladder usually leads to a local hepatitis, and may, as in the following case, have an etiological bearing in a true general hepatic cirrhosis.

Mr. A., aged 62, complained of flatulent dyspepsia, occasional attacks of dull pain in the region of the liver, of lassitude, loss

of energy, and shortness of breath. He was not a heavy drinker, but had taken alcohol in strict moderation.

On examination he was seen to be of a high colour with a slightly cyanotic tint. The conjunctivæ showed a definite icteric tinge. The liver was enlarged, its lower border being readily palpable one and a half inches below the right costal margin. There was very definite tenderness localized over the gall-bladder region. There was no free fluid in the abdomen and no swelling of the legs. A diagnosis of chronic cholecystitis was made, but operation was deemed to involve a risk in view of the cyanosis and hepatic enlargement. Persistence of pain and tenderness in the gall-bladder region, however, led ultimately to a decision in favour of operation.

Operation (June 6th, 1927).—On opening the abdomen the liver was seen to show the typical appearance of a hypertrophic cirrhosis involving the whole organ. The gall-bladder was not enlarged, but was greatly thickened, evidently from long-standing chronic inflammation. There were no gall-stones. The gall-bladder was removed, and from its wall and the cystic gland a pure culture of streptococcus was obtained.

Progress.—The immediate recovery was uneventful, but a guarded prognosis was given. One year later the patient reported, looking extremely well, with a fresh complexion and no trace of cyanosis. He stated that he had now no dyspepsia, was able to take active exercise, and was never breathless. On examination his liver was not palpable.

Comment.—Whilst this case is, in my experience, quite exceptional, it serves to show that the infection of the gall-bladder may occasionally be the determining cause of hepatic cirrhosis.

Toxic Mental Derangement.

The following case, for the notes of which I am indebted to Mr. J. J. M. Shaw, under whose care the patient was, illustrates the part which cholecystitis may play in relation to some forms of insanity.

J. C., aged 44, wounded in 1916 and taken prisoner. Gas gangrene developed in a flesh wound of the thigh and the patient became insane. He was kept in an asylum for nine months, and it was noted that his insanity returned at the same time as his thigh wound finally healed. He enjoyed good health from 1917 to 1928, when he began to be troubled with symptoms diagnosed as those of mild cholecystitis. In October, 1928, he had an acute attack of cholecystitis with definite tenderness over the gall-bladder and faint jaundice. The day following the onset of acute symptoms he was admitted to a nursing home and the same evening developed acute confusional insanity with a marked tendency to violence, necessitating his removal to an asylum. One month later his mental state was one of complete mental confusion with inability to recognize his relatives.

On examination, under light anaesthesia, a resistance could be felt in the gall-bladder region.

The diagnosis of the alienist was “confusional insanity probably from a toxic focus.”

Operation (November 19th, 1928, by Mr. Shaw).—A moderately distended and much thickened gall-bladder, containing one stone impacted in Hartmann’s pouch, was removed.

Bacteriological examination of the gall-bladder gave a growth of a large Gram-positive bacillus. Unfortunately this was regarded as a contamination and the cultures were not preserved.

Progress.—After a few days of marked improvement in the patient’s mental condition there was a period of three months during which it remained uncertain. This was followed by steady improvement, and he was discharged from the asylum four months after the operation and returned to work. He is now, six months after operation, able to transact legal business without effort.

Comment.—The onset of insanity in this case with the development of gas gangrene in his war wound; the return to sanity coincidentally with the healing of the wound; the later attack of insanity along with the development of an acute cholecystitis; the regain of sanity following the removal of the inflamed gall-bladder, from the wall of which a Gram-positive bacillus was grown—these facts all point to an intimate relationship between the focus of infection and the mental derangement.

The cases recorded above have been selected as offering striking evidence of the importance of intramural infection of the gall-bladder in relation to certain chronic ailments. It is not suggested that in these diseases the gall-bladder will always be found at fault, but it is claimed that biliary infection has more than a local significance, and that it is the infection in the wall of the organ, and not its content, be that bile, pus, or calculi, which is the essential factor in its pathology.