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SCLEROSING CHOLANGITIS†

WILLIAM S. HAUBRICH, M.D.,* RICHARD DEW, M.D.,* PHILIP WILLIAMS, M.D.,** AND MELVIN A. BLOCK, M.D.***

A Case Report

Dr. Haubrich. The case we share with you this morning is representative of a condition really rather rare although it is interesting that, just within the past 12 months, reports of this condition have appeared in at least four major medical and surgical journals. I think the importance of this case is not only in one's ability to recognize it, but perhaps more so in the differential diagnosis. The subject of our presentation is usually called "primary sclerosing cholangitis", a chronic proliferation of connective tissue affecting the biliary duct system in any or all of its segments from the distal common bile duct to the finest ramifications of the small bile channels within the liver itself. I would hasten to point out that this condition is distinguished from posttraumatic or postsurgical stricture of the extrahepatic ducts and, also, from fibrosis limited to the ampullary or sphincteric structures at the duodenum.

Dr. Dew. Our patient is a 64-year old gentleman, retired owner of a foundry. He recalls a transient episode of jaundice with no associated symptoms or disability in 1925. In 1953, he had brief epigastric pain; a cholecystogram at that time was reported to show a "cloudy" gallbladder. In 1957, cholecystography was repeated twice, presumably because of a suspicion of gallbladder disease, each time with non-visualization. In March 1964 the patient was admitted to another hospital because of an abrupt onset of midepigastric ache, chills, fever, jaundice, dark urine, and light stools. The diagnosis was hepatitis. In January 1965 the same picture recurred briefly. Since then he has had four similar, acute, isolated episodes, each with abrupt chills, fever, and variable jaundice of short duration. Among numerous determinations of transaminase activity, no level exceeded 118 units. He felt quite well between these episodes. During this period, his activity and diet were rather severely restricted because of the diagnosis of hepatitis, and it was probably more because of these restrictions rather than the symptoms themselves that he sought consultation here.

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The physical examination was unremarkable except for a smooth, nontender liver edge 5 cm below the right costal margin. The sequence of laboratory studies is listed (Table I). During 18 months before the patient was admitted here, the results of numerous bromsulfalein tests varied from 4 to 23%. When the patient was readmitted for operation, all symptoms had remitted and his liver was no longer palpable.

Dr. Haubrich. Thank you very much, Dr. Dew. (The patient is introduced.) Did you ever see a more friendly group of faces, Mr. C......................?

Patient. (Looking over the audience) I don't know if they're friendly or just resting.

Dr. Haubrich. Our patient is perceptive, too.

Mr. C......................, when did your present symptoms first appear?


Dr. Haubrich. And the onset was rather abrupt?

Patient. Right.

Dr. Haubrich. How did you feel between spells?

Patient. Quite well.

Dr. Haubrich. Actually, the patient's appetite between the acute episodes was good, and there has been comparatively little net change in his weight. Are there any questions for Mr. C......................?

Dr. Raymond Monto. Had the patient taken any icterogenic drugs? Was he aware of any factor precipitating his acute episodes?

Dr. Haubrich. We could not elicit his having taken any medications to which we could ascribe jaundice. Mr. C......................, was there anything that seemed to bring on these spells?

Table I

Serial Representative Laboratory Data

<table>
<thead>
<tr>
<th></th>
<th>1st Admission</th>
<th>2nd Admission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12/15/65  12/18/65</td>
<td>1/3/66  Postop</td>
</tr>
<tr>
<td>Sr. bilirubin (mg)</td>
<td>2.08    5.4</td>
<td>1.6     0.96</td>
</tr>
<tr>
<td>Sr. alk. phosphatase (BU)</td>
<td>9.9     17.2</td>
<td>11.3    7.2</td>
</tr>
<tr>
<td>Sr. transaminase (U) 62</td>
<td>260</td>
<td>59      23</td>
</tr>
<tr>
<td>Sr. antinuclear factor</td>
<td>chills, fever</td>
<td>present</td>
</tr>
</tbody>
</table>

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Patient. As I would try to determine myself what might have created the spell, I couldn't think of a thing — neither food nor overactivity.

Dr. Laurie Dickson. Mr. C., what sort of actual distress or pain would you have with these spells?

Patient. Generally, each of these spells would start about the same way. I would begin to feel a bit of distress in this area (indicating his epigastrium), an ache as I call it, not a sharp pain. Then I would feel a chill lasting — well, one time I timed it, it was 5 minutes, and the longest was an hour or so; immediately after that, fever, and I would perspire. Then I would begin to come out of the situation in a couple of days.

Dr. J. A. Rinaldo, Jr. Was there itching?

Patient. No, very little.

(The patient is dismissed.)

Dr. Haubrich. Again, as is so often the case, the radiologist made a significant contribution to our diagnosis. I'll ask Dr. Williams to show the intravenous cholangiograms.

Dr. Philip Williams. In this intravenous cholangiogram (Fig. 1) we can see the faint outline of a slightly dilated proximal common bile duct; its distal few centimeters are not seen. The larger intrahepatic ducts appear normal. The gallbladder is free of radiolucenties, but we cannot exclude possible defects in the lower common duct. Of significance is the observation that radiopaque material remains in the common duct for as long as 120 minutes; that is, the duct empties very slowly. This would indicate at least a partial obstruction of the extrahepatic duct.

Dr. Haubrich. With the history and the laboratory data we had, it seemed unlikely to us that the patient had hepatitis. Rather, the picture was that of any obstructive syndrome although we could not pinpoint the cause. Meanwhile, Doctor Block had seen the patient, and we both agreed that some sort of cholangitis was a distinct possibility. At this point, we fell back on the old dictum that if one can't make a precise diagnosis, then at least one should try to make a decision. A decision wasn't too difficult in this case; it seemed logical that the next step was a surgical exploration of the bile ducts.

Dr. Melvin A. Block. On entering the abdomen, we saw the gallbladder to be distended but otherwise normal. We did not encounter any stones in the gallbladder or in the biliary tract at any time during the procedure. The common bile duct appeared somewhat dilated as the intravenous cholangiogram had indicated. We opened the common duct just above a rather low entrance of the cystic duct. Proximally toward the hepatic ducts, we did not encounter anything abnormal. However,
Left, an intravenous cholangiogram outlines a slightly dilated common bile duct. Note the time of exposure following injection. Right, a cholangiogram taken of the catheterized common duct at operation; the arrow points to the abrupt constriction corresponding to the palpably sclerotic segment.

In this sketch of the operative dissection, the duodenum is depicted as mobilized and rotated toward the midline thus exposing the common bile duct. A slender probe encountered luminal obstruction where the duct wall was thickened and sclerotic. Aspirated bile was free of concrements. The liver was smooth and sharp-edged.
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on passing a fine probe downward, we did encounter obstruction in the distal portion of the common bile duct about 4 cm above the ampulla (Fig. 2). In this segment the duct wall was thickened and cordlike.

With the duodenum mobilized, I could find nothing suspicious of tumor. Curettings from the lumen of the involved duct showed only inflammatory change. We suspected then that this was probably a segmental sclerosing cholangitis. The question of occult malignancy was considered with some seriousness. However, in view of the duration of his illness and the gross findings, we elected not to do a pancreatoduodenectomy which would have been required had a cancer been present. Rather, we decided to relieve the obstruction mechanically at the point of choledochostomy, and therefore did a choledochoduodenostomy. Also, rather than remove the gallbladder with its somewhat low cystic duct closely approximating the common duct, we did a cholecystoduodenostomy to further assure adequate bile flow. An operative cholangiogram (Fig. 1) showed a sharp cutoff at the point where the palpable thickening and obstruction of the common duct was noted. The involved segment was estimated as 4 or 5 cm in length.

This is, of course, a rare situation. It is further unusual, in this case, in that it is segmentally distributed, for I have seen several examples of this condition in the past and they involved the entire bile duct. It was difficult surgically to do much about them. Fortunately, in the present case we have been able to relieve the situation mechanically at this time, at least. About six months ago we had a patient who had a segmental occlusion of the hepatic duct and we suspected a sclerosing cholangitis. Incidentally, this patient also had a positive antinuclear factor test.

Dr. Haubrich. Thank you, Dr. Block. We do have our own biopsy specimens which Dr. Block carefully took from both the right and the left liver lobes. The liver, you will recall, had receded and was no longer palpably enlarged when the patient returned in January. At operation this liver could very closely have passed for normal. Its surface was smooth and only faintly mottled. The first slide (Fig. 3) illustrates a very early stage of sclerosis surrounding a small bile duct. In the small and early lesions, there is perhaps a little more mononuclear cell infiltration than we see in the older lesions. Such mononuclear cell infiltration is nowhere prominent. Next is an example of a more advanced lesion (Fig. 3). In this section of liver the process was fairly uniform; that is, all portal spaces and duct structures had such surrounding sclerosis. The parenchymal architecture was intact in all sections. You might ask if that periductular fibrosis could be the sort seen in the liver following any extrahepatic duct obstruction, and I would say, possibly, at least to some degree. However, in such instances the intrahepatic changes are not quite so uniform as we see them here and the sclerosis is not so striking.

Dr. Block also took a culture from this man's proximal bile duct, and coliform organisms were recovered. Free-flowing bile is usually devoid of culturable organisms. The positive culture in this case indicates a result of the ductal obstruction rather
Figure 3

Photomicrographs illustrating early (left) and more advanced (right) lesions of periadventitial inflammation and sclerosis (see text). H & E, x390.
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than a cause of the cholangitis. The frequency of organisms in bile rises sharply in any instance of extrahepatic obstruction. Stagnant bile fosters bacterial growth.

Smith and Loe, in a report appearing in the American Journal of Surgery, collected 21 cases and added 4 of their own. This series remarked a more frequent occurrence in males and covered a considerable age range, although children and the very elderly were absent from the series. Dr. Block mentioned that our case is extraordinary in that only the most distal portion of the common duct was involved. In Smith and Loe's series, most of the cases showed sclerosis in all the extrahepatic ducts. Today's case is one of the few in which a preoperative diagnosis has been made. Hence, it may represent an earlier stage of the disease.

A feature which has been emphasized by others is the high frequency of associated diseases. In the series just cited, 15 out of 25 patients had what were considered to be significant associated diseases. Now, occurrence of pancreatitis (in 8 cases) does not impress me from a pathogenetic standpoint because we often see pancreatitis complicating extrahepatic biliary tract disease of any sort. Therefore, I would be inclined to interpret pancreatitis as a secondary complication rather than as part and parcel of the whole disease.

However, it does seem extraordinary, in a series of 25 patients, to have 6 patients with ulcerative colitis. Also remarkable is the association with retroperitoneal fibrosis (at least one variant of which was described a number of years ago by our own Dr. Ormond here at the Henry Ford Hospital) and with Riedel's struma, regional ileitis, Banti's syndrome, and esophageal stricture. The idea here is that possibly the change occurring in the bile ducts may be only part of a more profound systemic disease. I would estimate that it took no more than 30 seconds for somebody to come up with the idea that sclerosing cholangitis might be a manifestation of an autoimmune phenomenon. The concept of autoimmunity has lost a little of its luster lately through overuse, but still I cannot deny that it is an attractive idea. You will recall that this patient and another recently seen here were found to have a positive test for antinuclear factor in the serum.

In passing, I should mention that a condition possibly similar to this has been described with extraordinary frequency in Asia among Cantonese Chinese. Then, finally, there is an indication that in the southwestern United States among the Indian population a noncalculous biliary tract disease is fairly frequent.

The best treatment of sclerosing cholangitis is surgical, when feasible, as Dr. Block has pursued it here. Bypassing the obstruction and freeing the flow of bile often is highly effective if only in a palliative sense. I would point out, too, that surgery provides the only sure means for establishing the diagnosis.

Even with an effective bypass for the bile, the disease, of course, remains. We have done nothing to change its possible course, and I suppose we would have to say that the ductular sclerosis may progress both within the liver and in the
extrahepatic ducts. What else can be done for this man meanwhile? Because of the frequent bacterial invasion, appropriate antibiotics have been used effectively to combat infection. Corticosteroids have been used empirically in these patients with greater benefit than one would expect by chance alone. Probably we'll not impose on our patient any additional treatment at this time. We'll see how well he does. But if he should have recurrent symptoms, then I think we would have little hesitancy in advising both antibiotics and corticosteroids. Prognosis is a bit uncertain because there have been too few cases of this sort recognized for a sufficient time to permit a meaningful follow-up. Are there any questions or comments?

From the Audience. Has this patient shown any evidence of pancreatitis or pancreatic insufficiency?

Dr. Haubrich. No, he has not.

From the Audience. How will you follow this patient's course? What tests will you use?

Dr. Haubrich. We are going to try to follow him closely and be on the alert for any further damage to his duct or to his liver. Whether the periductular sclerosis within the liver is primary or secondary is important. I'm inclined to believe intrahepatic sclerosis is part of the process and may progress, even though we have relieved the obstruction beyond; also, it will be important to apprehend any early sign of cholestasis. The serum alkaline phosphatase activity will be our chief guide. Others have reported that the alkaline phosphatase may remain somewhat elevated over a considerable period of time even with apparent clinical remission. The observation that the alkaline phosphatase already has declined to 7 Bodansky units seems encouraging.

Addendum: At follow-up examination 6 months after operation, the patient felt entirely well and had had no recurrent symptoms. The serum alkaline phosphatase activity was within the normal range.

REFERENCES