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Peritoneoscopy in the Staging of Hodgkin's Disease

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Summary

Peritoneoscopy was performed in 38 previously untreated patients with Hodgkin's disease, who presented for staging, as an alternative to examination of the liver at laparotomy. The results indicate that the yield of positive biopsies is similar to the series reported from Stanford, and in both studies the patients at risk of having liver involvement are those with preoperative evidence of disease below the diaphragm. If careful study of the data evolving from staging laparotomies shows that the major therapeutic benefit of the procedure is the identification and exclusion from radiotherapeutic programs of those patients with evidence of liver involvement, then peritoneoscopy may be an alternative to laparotomy.

Introduction

A major problem in staging patients with Hodgkin's disease has been the identification of disease involving the liver. The distinction is an important one, since, as we shall see later in this Symposium, the finding of tumor in the liver radically changes the approach to treatment (2, 5, 6). It is abundantly clear by now that liver function studies alone can no longer be relied upon to indicate the risk of actual tumor being present in the liver. The results of the laparotomy studies from the Stanford group have indicated that percutaneous Menghini needle biopsies of the liver also often miss occult involvement with Hodgkin's disease (3, 4).

Since the identification of the spread of the cancer to the liver indicates metastatic spread and dictates the choice of systemic chemotherapy as the primary approach to treatment, the need for identification of disease in the spleen and confirmation of the status of the retroperitoneal lymph nodes may be obviated in such cases.

At institutions where total nodal X-irradiation is used routinely in patients with disease limited to lymph nodes, regardless of the extent of involvement, the results of laparotomy assume less importance except in those cases where the disease can be identified outside the potential radiation field in organs such as the liver. Since at the National Cancer Institute total nodal X-irradiation is the treatment of choice (5), we have elected to evaluate an alternative approach, peritoneoscopy, to attempt to examine the liver in patients with Hodgkin's disease.

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Patient Material

The population under discussion consists of 38 previously untreated patients with Hodgkin's disease who presented for initial staging either at the National Cancer Institute (33 patients) or the Walter Reed Army Hospital (5 patients). Patients were staged according to the Rye classification (10), as has been previously reported from this institution (1, 2). For evaluation of the liver, liver function studies and liver scans were performed routinely. All patients had biopsies of their livers performed routinely, either percutaneously, at the time of peritoneoscopy, or both; 21 patients first had a single Menghini percutaneous needle liver biopsy followed by peritoneoscopy for further study, if the percutaneous biopsy was negative.

Before peritoneoscopy, the liver was considered involved with Hodgkin's disease if both the sulfobromophthalein retention and serum alkaline phosphatase were abnormal or one of these tests was abnormal in the presence of hepatomegaly on physical examination or scan. The spleen was considered abnormal if clinically enlarged. At the time of peritoneoscopy, the spleen was considered abnormally enlarged if it was visible with the patient in the supine position, or if nodules of tumor were noted on the surface, or both. The original node biopsy was classified histologically according to the classification of Lukes and Butler (9).

Peritoneoscopy Procedure

The procedure is performed in the early morning, after an overnight fast, under local Xylocaine anesthesia, with preoperative medication with meperidine and atropine (14). The abdomen is cleaned with surgical soap and Betadine and draped with sterile coverings. The site for puncture is usually in the midline, 1 to 2 cm below the umbilicus. After local anesthesia is obtained, a 7- to 10-mm incision is created, and blunt dissection is carried to the fascia. A pneumoperitoneum needle is inserted while the patient tenses his stomach wall, and a pneumoperitoneum is created. An 11-mm trocar is inserted and through it a Menghini-Wildhert endoscope is introduced. Light is provided by a high-intensity external source through a fiber optic system.

Biopsies are performed either through the endoscope with a Menghini-type needle or a bite forceps, or alternatively by inserting a modified Vim needle through the abdominal wall, via a separate puncture site, and directing it to the area to be biopsied (11). In most cases 4 deep biopsies were performed, 2

in each lobe of the liver. If lesions were visualized, additional biopsies were performed as indicated.

After observing hemostasis and inspection of visible organs, the endoscope is removed, the air is evacuated, and the small wound is closed with 3 3–0 Dermalon sutures. The patient remains immobile for the remainder of the day but can eat lunch in bed, sit up for dinner, and be discharged from the hospital the next morning.

Capabilities of the Procedure

The use of peritoneoscopy (7, 8, 11–14) has been improved immeasurably by the provision of brilliant lighting with fiber optic lighting systems, which allow clear visualization of intraabdominal structures.

The parietal peritoneum can be readily visualized and biopsied. The anterior and upper surfaces and much of the undersurface of the liver can be examined, and the interlobar fissure and falciform ligament are well visualized. In addition, the gallbladder can be easily inspected in most patients.

If the spleen is enlarged, it can be readily detected with the patient in the supine position, and a normal spleen can be brought into view by tilting the patient in a right lateral decubitus position. Splenic aspirations and cauterizations can be performed through the instrument. Other areas that can be visualized are the anterior wall and greater curvature of the stomach; the underside of the diaphragm; and the anterior surfaces of the omentum, colon, and small bowel. The pelvic organs, particularly the tubes and ovaries, can be easily brought into view by tilting the table in Trendelenburg position (14). In addition, small droplets of ascites fluid can be easily aspirated.

The diagnostic limitation of the procedure is primarily the inability to visualize the retroperitoneal area containing the lymph nodes, kidneys, and pancreas, and, in the case of staging for Hodgkin's disease, to remove and section the spleen serially.

Results

No mortality or significant morbidity resulted from the procedure in these 38 patients. Details of the extent of disease and findings at peritoneoscopy are shown in Table 1. Hodgkin's disease was found in the liver in 6 of 38, or 16%, of cases studied. Two patients with a positive liver biopsy did not have a lymphangiogram before peritoneoscopy, and the true extent of retroperitoneal disease could not be evaluated. The remaining 4 patients with positive liver biopsies at peritoneoscopy all had either a palpable spleen, a positive lymphangiogram, or both. The incidence of Hodgkin's disease in this group of 25 patients with subdiaphragmatic disease was 16%. Ten patients had a positive lymphangiogram and a palpable spleen, and 3 of these patients had biopsy-proven Hodgkin's disease in their liver. No patient without evidence of subdiaphragmatic disease had a positive biopsy.

The liver was assessed as positive preperitoneoscopy in 14 patients, and 2 (14%) had evidence of Hodgkin's disease at biopsy. On the other hand, 24 patients were not thought to have Hodgkin's disease involving the liver, on the basis of liver function tests and liver size, and 4 (16%) proved to have tumor in their liver at biopsy.

Twelve patients were thought to have an enlarged spleen, and in 10 this finding was confirmed at peritoneoscopy; in 1 case the spleen was not enlarged, and in the remaining patient the splenic area was obscured by prior surgical adhesions.

In 25 patients the spleen was thought to be normal on initial evaluation, and in 14 of these patients (54%) an enlarged spleen was noted at the time of the procedure. One of the patients with a positive liver biopsy did not have evidence of splenomegaly on initial evaluation or at peritoneoscopy.

DISCUSSION

One of the most desirable characteristics of peritoneoscopy is the low morbidity and mortality. With proper case selection, mortality should be negligible. In 11 large series, the mortality was 0.1% (12). However, the procedure can often be performed on very-poor-risk patients as an alternative to laparotomy, since general anesthesia is not required.

Absolute contraindications to the procedure are acute surgical conditions of the abdomen, infections of the anterior abdominal wall, and any acute medical condition which prohibits manipulation of any sort, such as acute myocardial infarction.

Previous surgical procedures with residual scars and adhesions increase the risk of perforation of a viscus and can preclude visualization of an organ if the previous procedure was performed in the area of the organ to be visualized.

Prior to the advent of the use of surgical intervention for staging of patients with Hodgkin's disease, liver involvement was diagnosed in the presence of 2 abnormal liver function tests (abnormal sulfobromophthalein retention and increased serum alkaline phosphatase) in the presence of a normal needle liver biopsy. The latter procedure in the above case was used to rule out other diseases as a cause of abnormal liver function studies.

The results of routine percutaneous Menghini liver biopsy for the purpose of staging in 73 previously untreated patients with Hodgkin's disease at our institution resulted in an extremely low yield (C. M. Bagley, Jr., J. A. Roth, L. B. Thomas, and V. T. DeVita, unpublished observations); only 5% of such biopsies were positive. The overall incidence of positive liver biopsies of 16% with peritoneoscopy is significantly higher.

Comparison of the results of this study and a recent series from Stanford (4), in which laparotomy was used for staging of Hodgkin's disease, is given in Table 2. In both the Stanford series of unselected patients (4) and in the current group, no patients presenting with disease only above the diaphragm ultimately proved to have liver involvement at laparotomy or peritoneoscopy; liver involvement seems confined to those patients who, at the time of presentation, have some evidence of disease below the diaphragm, particularly those with symptoms. Of the 27 patients with disease confined to supradiaphragmatic areas preoperatively, in the Stanford series, 12 were, however, in Category B. Of the 23 patients with some evidence of disease below the diaphragm, 11 were

Table 1
Characteristics of the patient population in the present study

Patients	Age/sex	Symptoms	Supradiaphragmatic disease			Preperitoneoscopy impression			Previous closed biopsy	Peritoneoscopy results		Original histology[a]
			Neck	Mediastinum	Axilla	Liver	Spleen	Nodes		Liver	Spleen	
1. J. T.	24/M	B	–	–	–	–	–	+	No	–	–	NS
2. F. L.	38/M	B	+	–	+	–	–	–	Yes	–	–	LD
3. D. R.	19/M	B	+	+	–	–	+	+	No	–	+	MC
4. S. L.	16/F	B	+	+	+	–	–	–	Yes	–	+	NS
5. J. Tr.	27/M	A	–	–	–	–	–	+	No	–	–	MC
6. M. S.	14/M	B	+	+	+	+	–	+	Yes	–	+	NS
7. B. V.	23/M	B	–	–	+	–	–	+	No	–	–	NS
8. J. C.	58/M	B	+	–	+	+	–	+	Yes	–	+	MC
9. E. S.	22/M	B	+	–	–	–	+	+	Yes	–	+	MC
10. L. D.	19/M	B	+	–	+	+	+	+	No	+	+	LP
11. F. G.	37/M	B	+	+	+	–	–	+	No	–	+	MC
12. T. V.	16/M	B	+	+	–	–	+	±	No	–	+	MC
13. H. S.	27/M	B	+	+	–	+	–	±	Yes	–	–	MC
14. A. F.	23/M	A	+	–	+	–	+	+	No	+	+	MC
15. M. W.	36/F	A	+	+	+	+	–	–	No	–	+	NS
16. P. M.	16/M	B	+	+	+	+	+	+	No	–	+	NS
17. T. B.	23/M	B	–	–	–	–	0[b]	+	No	–	0	LD
18. S. L.	25/M	B	+	+	+	–	–	+	Yes	–	+	NS
19. B. B.	40/M	B	–	–	–	+	–	+	Yes	–	–	NS
20. B. N.	40/F	B	+	–	–	+	–	+	Yes	–	–	NS
21. J. R.	46/F	B	–	+	–	–	+	+	Yes	–	–[c]	LP
22. W. M.	60/F	B	–	–	+	+	–	+	Yes	–	+	MC
23. A. R.	16/F	A	+	–	+	–	–	–	Yes	–	+	MC
24. A. C.	27/M	B	+	–	–	+	+	+	No	–	+	MC
25. F. F.	23/M	B	+	+	+	–	+	+	Yes	+	+	MC
26. L. W.	19/F	B	+	+	+	–	–	+	Yes	–	–	U
27. R. H.	21/M	B	+	+	+	–	–	–	Yes	–	+	NS
28. S. H.	14/M	B	+	+	+	+	+	+	No	–	+	NS
29. J. F.	64/M	B	+	+	+	+	+	+	Yes	–	–	MC
30. D. Z.	41/M	B	+	–	+	–	–	+	Yes	+	–	LP
31. O. F.	16/M	B	+	+	–	+	–	+	Yes	–	+	U
32. J. S.	25/F	B	+	+	+	–	–	–	No	–	+	NS
33. M. M.	28/M	A	+	+	–	–	–	–	Yes	–	+	MC
34. J. T.	30/F	A	+	+	+	–	–	–	Yes	–	–	MC
35. M. B.	27/M	B	–	–	–	+	+	[d]	No	+	+	U
36. I. F.	25/F	A	+	–	+	–	–	–	Yes	–	+	NS
37. C. G.	23/M	B	+	+	–	–	–	[d]	No	+	+	MC

[a] Lukes and Butler classification: LP, lymphocyte predominant; LD, lymphocyte depleted; MC, mixed cellularity; NS, nodular sclerosis; U, unclassifiable.
[b] 0, previous splenectomy.
[c] Splenic area not visible due to surgical adhesions.
[d] These patients did not have a lymphangiogram performed.

symptomatic, and 3 of the 4 positive liver biopsies were in patients in this category. Only 1 positive liver biopsy was found in an asymptomatic patient. In the present study, 5 of 6 patients with positive liver biopsies were symptomatic. Thus, the incidence of proven liver involvement with Hodgkin's disease in the Stanford and National Cancer Institute series was 8 and 16%, respectively, for the entire group, and 17 and 20%, respectively, in those patients with preoperative evidence of disease below the diaphragm. The results are quite comparable and suggest that peritoneoscopic examination with multiple biopsies is adequate for evaluation of the status of the liver in patients with Hodgkin's disease.

As has been shown by the Stanford group, the preoperative assessment of the status of the liver most often proved erroneous, since in our study more patients assessed as having normal livers proved to have liver involvement than the converse. Since the difficulty in detection of Hodgkin's disease in the liver seems to represent a sampling problem of a tumor that is erratically distributed through the liver, it seems likely that both approaches, laparotomy and peritoneoscopy, are still underdiagnosing the disease in the liver. We have recently modified our approach by increasing the number of routine biopsies to 6 deep needle insertions, in addition to those directed at suspicious lesions.

Splenomegaly is easily confirmed, or detected when previously unsuspected, through the peritoneoscope. It is of interest that of 25 patients whose spleen was thought to be normal prior to endoscopy, 14 (54%) proved to have

Table 2
Comparison of findings at peritoneoscopy in current series and findings reported at laparotomy by the Stanford group (4)

Preoperative impression		National Cancer Institute series		Stanford series	
Spleen	Abdominal nodes	No. of patients	Positive liver biopsies	No. of patients	Positive liver biopsies
+	+	10	3	7	4
+	− or ±	1	0	6	0
−	+	14	1	10	0
−	− or ±	11	0	27	0
+ or −	not done	2	2	0	0

splenomegaly by peritoneoscopic criteria. Since it has been shown that only 66% of such patients prove to have tumor in their spleen at the time of surgery (4), this finding is of limited value. Splenic aspiration and biopsy can be performed but were not done in this study. It was reasoned that random sampling by aspiration was not likely to yield enough results to warrant the risk involved.

Conclusions

Although the current series is small, the results of the endoscopic examination of the liver appear comparable to those obtained at laparotomy. It is the opinion of some radiotherapists that total nodal X-irradiation is the treatment of choice for all patients with Hodgkin's disease confined to lymph nodes, regardless of the extent of the disease (5). In such cases, the only findings at laparotomy that influence the selection of treatment are the presence of tumor in the liver, which dictates the use of chemotherapy, or the presence of positive lymph nodes outside the normal radiation fields. The latter example occurs rarely in patients with Hodgkin's disease (3, 4), and it appears that the former diagnostic problem may be handled as well through a peritoneoscope as through a surgical incision.

The lymphangiogram, when read as positive, is about 88% accurate in assessing the status of the retroperitoneal nodes (4). It has been known for some time that apparently normal lymphangiograms were falsely negative, particularly in patients with Stage IIB disease. Since lymph node biopsies at laparotomy represent, at best, a random sampling of potentially involved lymph nodes, little confidence should be placed on the finding of negative glands at surgery, particularly in symptomatic patients with disease otherwise limited to supradiaphragmatic regions. Such patients should receive therapy to lymph node bearing areas below the diaphragm. If such an approach is taken routinely, then laparotomy may not be justified solely to identify the presence or absence of disease in the retroperitoneal lymph nodes.

Splenectomy cannot be performed through a peritoneoscope, and many physicians feel that the benefit of splenectomy alone, in terms of reduction in the size of the radiation field, increased tolerance to radiotherapy, and perhaps chemotherapy, justifies the routine use of laparotomy. This opinion is not universally shared, however, and in the absence of existing data to confirm these opinions the answer to this question will have to await the results of some of the therapeutic trials now in progress.

The patients at highest risk of having liver involvement are those with preoperative evidence of disease below the diaphragm. Peritoneoscopy appears to be useful in identifying liver disease in such instances and, if available, can be used to spare these patients laparotomy. If, however, involvement cannot be demonstrated by this procedure and radiotherapy is indicated, then subsequent laparotomy may be useful in removing an excessively enlarged spleen, reducing the size of the radiation field, and preventing significant damage to the left kidney. At the moment there are no data that confidently militate toward routine splenectomy to facilitate the use of drugs in the treatment of Hodgkin's disease.

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