Eur J Cancer Clin Oncol, Vol. 19, No. 5, pp. 577-582, 1983.
Printed in Great Britain.

0277-5379/83/050577-06$03.00/0

Improving Peritoneoscopic Staging of Patients with Solid Tumors

H. BLEIBERG

Service de Médecine et Laboratoire d'Investigation Clinique H. J. Tagnon, Unité de Gastroentérologie, Institut Jules Bordet, Centre des Tumeurs de l'Université Libre de Bruxelles, 1, rue Héger-Bordet, Brussels, Belgium

Abstract—*Peritoneoscopy and guided needle biopsy were carried out as the staging procedure in patients with solid tumors. The disease was disseminated in 379 patients with various tumor types and limited in 109 with breast cancer and malignant melanoma. Adequate liver biopsies were obtained in all cases. Macroscopic liver tumors were demonstrated in 96 patients. Eleven additional patients had peritoneal or mesenteric tumors with normal livers. Attempts were made to improve the yield of positive findings of the procedure. The cytologic examination of cells adhering to the needle after biopsy or optimizing visualization of the liver surface by using a fiberoptic gastroscope did not answer this purpose. A 7.2% increase in liver tumor detection was obtained by taking 4–6 biopsies at random or towards deep palpated nodules in macroscopically normal livers. The data, although difficult to interpret in terms of accuracy of the method, suggest that in solid tumors random samplings of normal livers could contribute to the diagnosis of otherwise undetectable liver metastases.*

INTRODUCTION

THE STAGING of carcinoma is of paramount importance in planning the treatment approaches for localized as well as advanced diseases. Precise assessment of tumor dissemination or regression in the liver and the abdomen is difficult. Clinical evaluation is often obscured by the structural heterogeneity of the liver, the presence of an inflammatory process or benign tumors, and the final diagnosis of metastatic liver involvement can only be determined by histological examination of biopsies.

Since 1971 the role of peritoneoscopy has been emphasized as a staging procedure in different cancer types [1–6]. This work summarizes the results of peritoneoscopy with guided needle biopsy in solid tumors. Attempts were made to improve the yield of positive examinations by systematic random biopsies when no tumor was seen at the surface of the liver by cytologic examination of cells adherent to the needle after biopsy and by optimizing visualization of the liver surface using a fiberoptic gastroscope.

Accepted 2 November 1982.

MATERIALS AND METHODS

Peritoneoscopy was performed in advanced and locoregional neoplastic diseases. Patients with lymphomas and hematologic malignancies were excluded from this report. Peritoneoscopy was more often performed under general anesthesia. The latter method did not exclude any patient eligible for peritoneoscopy nor did it prolong the duration of hospitalization. Peritoneoscopy with guided needle biopsy was performed following a classical technique described by others [7] using a Wildhirt operating peritoneoscope with a Hopkins forward-oblique telescope (Karl Storz KG, D 7200 Tutlingen, F.R.G.). Various manipulations are possible with this instrument, including biopsy, palpation with probes, section of adhesions, electrocoagulation and photography. Two to six biopsies were taken through the peritoneoscope with Menghini liver biopsy needles in macroscopically suspected areas.

When no lesion was seen on the surface of the liver the presence of deeply located nodules was investigated using a palpator probe inserted into the sheath of the peritoneoscope. Biopsy needles were then directed towards these lesions. If no nodule was palpated, two or three needle biopsies were taken at random in the anterior and posterior areas of both lobes. A different biopsy needle was

used for each lobe in order to avoid eventual dissemination of malignant cells from one lobe to the other. In all cases the abdominal cavity was explored and any suspected area was biopsied to rule out peritoneal neoplastic dissemination. Peritoneoscopy was classified as positive or negative according to the histological findings.

Advanced tumors

From September 1976 to November 1981 peritoneoscopy was carried out in 379 patients with histologically proven cancer. All had advanced disease. Six had a second primary tumor. One hundred and forty one patients were included in previously published series [8, 9]. In the vast majority of cases peritoneoscopy was performed because of abnormal physical examination, liver chemistries, liver scan, ultrasound (US) or computed tomography (CT). In the remaining cases it was performed in patients known to have rapidly proliferating malignancies.

In 52 previously operated patients the peritoneal cavity was entered through a small 2- to 3-cm surgical incision following visual examination and palpating exploration for adhesions [6].

In 37 patients with macroscopic liver metastases 2–6 biopsies were taken in the neoplastic tissue and all the specimens were examined.

In 23 livers with nodular metastases 1 or 2 biopsies were taken in macroscopically normal areas near the metastatic nodules (19 breast-, 3 small cell- and 1 epidermoid cancer of unknown origin).

In 42 patients cells adherent to the needle after biopsy were collected from the outer and inner surface of the needle, spread out on a slide, fixed in 95% alcohol, stained by the Papanicolaou technique and submitted to cytological examination.

A fibroscopic Pan-Endoscope Olympus type GIF-P2 (Olympus Optical Co. Europe GmbH, Hamburg 1, Steindamm 105, F.R.G.) was used in 23 patients to explore the posterior face of the right lobe and the adjacent peritoneum. The instrument was inserted through the sheath of the trocar used for the Wildhirt peritoneoscope and exploration performed before starting standard peritoneoscopy.

Locoregional tumors

Peritoneoscopy was carried out as a staging procedure prior to treatment in 109 patients with clinically locoregional disease. Forty-nine had breast cancer (32 stage I, 17 stage II) and 60 had melanoma (24 stage I, 36 stage II). In all cases peritoneoscopy was performed immediately before the surgical resection of the primary tumor. When dissemination was suspected at peritoneoscopy surgery was postponed until histology was available.

RESULTS

Liver samples suitable for pathological examination were obtained from the 379 patients with advanced solid tumors who underwent peritoneoscopy (Table 1). Peritoneal metastases without liver tumors were found in 9 patients (2.3%) and benign liver tumors in 15 (3.9%).

The liver samples were free of neoplastic disease in 281 cases (74.1%), but microscopic analysis revealed other abnormalities, including steatosis (21%), cirrhosis or hepatitis (7%).

Neoplastic invasion was demonstrated in 98 (25.8%) of the 379 biopsied livers. In 5 of these (5.1%) the surface of the liver was macroscopically free of metastases (4 bronchogenics, 1 breast cancer), but microscopic involvement was found by biopsying palpated nodules (2 cases) or by random sampling (3 cases). In these latter only 1 or 2 biopsies out of 4–6 were positive regarding tumor detection.

Multiple biopsies were taken from macroscopically invaded areas in 37 cases. For 29 patients all specimens were positive for malignant tissue, 1 or more specimens were negative in 7 and,

Table 1. *Peritoneoscopy findings in* 379 *patients with advanced solid tumors*

Tumor site	No. of patients by tumor site	No. of patients with liver metastases: Macroscopic and microscopic (%)	Microscopic only (%)	Total (%)	No. of patients with peritoneal metastases and normal liver (%)	No. of patients with benign liver tumors (%)
Breast	159	46	1	47(29.5)	1	5
Malignant melanoma	47	7	—	7(14.8)	—	6
Lung	61	18	4	22(36.0)	—	2
GI tract	39	10	—	10(25.6)	1	—
Genito-urinary	27	3	—	3(11.1)	6	—
Head and neck	19	1	—	1(5.2)	—	1
Miscellaneous	27	8	—	8(29.6)	1	1
Total	379	93(24.5)	5(1.3)	98(25.8)	9(2.3)	15(3.9)

*Table 2. Comparison of histological and cytological findings**

Histology	Cytology	No.
Positive	Positive	2
Positive	Negative	1
Negative	Positive	1
Negative	Negative	30
	Total	34

*Sampling was inadequate for cytological examination in 8 cases.

in 1 case of carcinoma of the kidney, the 2 specimens which were taken were negative.

In patients with macroscopic nodular dissemination biopsies taken from an apparently healthy area in the proximity of the tumor were positive in 2 out of 19 breast cancers, in 2 out of 3 small cell cancers and in 1 epidermoid cancer.

Cytology and histology were compared in 42 cases (Table 2). Smears were technically inadequate in 8 (19%). Of the remaining cases biopsy and cytology were both negative in 30 cases (73%), both positive in 2 cases (4.7%) and yielded opposite findings in 2 other positive cases. Cytological examination alone never allowed detection of malignant tissue which was not evident macroscopically.

Four patients out of 6 with 2 different primary tumours had liver metastases. In 3 the primary tumours were clinically apparent (gastric and breast, prostate and colon, lymphoma and bladder), but in the fourth, a carcinoma of the larynx, the liver biopsy revealed an unsuspected small cell carcinoma.

Examination of the abdominal cavity using a fiberscope Pan-Endoscope Olympus Type GIF-P2 visualizes the superior surface of both lobes of the liver back to the triangular ligament and the inferior face. We could never detect lesions which were not subsequently observed with the Wildhirt operating peritoneoscope.

Peritoneoscopy findings in 61 patients with advanced bronchogenic carcinoma are given by cell type in Table 3. Among 36 with small cell carcinomas 12 had liver involvement. This was unsuspected in 5 prior to peritoneoscopy and neoplastic cells were found only at biopsy in 3 (1 in a deeply situated nodule, 2 by random biopsies). Liver metastases were detected by microscopy only in 1 adenocarcinoma. Clinical findings were negative whenever microscopic involvement was detected with no macroscopic invasion. In all cases with other cell types liver invasion was predicted by clinical tests and metastases were apparent on the surface.

Peritoneoscopy findings in patients with limited malignant melanoma are given in Table 4. Patients with stage I disease had normal peritoneoscopy and 3 out of 36 patients with stage II disease had liver metastases. Patients with metastases also had abnormal clinical findings. Two patients with normal liver had unsuspected peritoneal dissemination. Eight patients out of 60 were found to have benign tumors. This prevalence of benign lesions was also apparent in patients with disseminated malignant melanoma (6 out of 47).

The results of peritoneoscopy in patients with localized breast cancer are given in Table 5.

Table 3. Peritoneoscopy findings by cell type in patients with advanced bronchogenic carcinoma

Cell type	Total No. of patients	No. of patients with liver metastases		
		Total	Clinically unsuspected	Microscopic findings only
Small cell	36	12*	5	3
Epidermoid	17	6	0	0
Adenocarcinoma	5	1	1	1
Large cell	3	1	0	0
Total	61	18	6	4

*One additional patient had peritoneal invasion with a normal liver.

Table 4. Peritoneoscopy findings in clinical stages I and II malignant melanoma

Stage of disease	Total	No. of patients		
		Liver metastases	Mesenteric metastases and normal liver	Benign tumors
I	24	0	0	3
II	36	3	2	5
All stages	60	3	2	8

Table 5. Peritoneoscopy findings in clinical stages I and II breast cancer

Stage of disease	No. of patients	
	Total	Liver metastases
I	32	0
II	17	2
All stages	49	2

Thirty-two patients with stage I disease had no demonstrable liver tumors. Two patients out of 17 with stage II disease had malignant cells found only at biopsy (one in a deeply situated nodule, one by random biopsy). Clinical findings were abnormal in both.

Compared to previously published series [9] the rate of complications was low: one patient developed scrotal emphysema and biliary discharge after biopsy occurred in a woman submitted to staging peritoneoscopy before mastectomy. The opening was closed via the endoscope with gel-foam and electrocoagulation of the puncture site.

DISCUSSION

Misdiagnosing neoplastic dissemination may have major consequences on survival. The difficulties encountered in recognizing malignancies on macroscopic appearance only [8, 10] and the need of histological demonstration of the disease before treatment prescribes biopsy of any suspected malignant lesion. The negativity of some of our specimens indicates that tumor tissue suitable for pathological diagnosis may require more than two samplings.

If the biopsy of metastases definitely assures a positive diagnosis, negative peritoneoscopy and biopsy offers no certainty as to the lack of metastases. False negative results were reported in many series [2, 6, 11–13]. If the true status of the liver and the prevalence of metastases are not known, the number of metastatic livers missed by peritoneoscopy cannot be accurately determined and an undefinable number of neoplastic liver involvements will not be detected by peritoneoscopy [14]. Several approaches were developed to increase the yield of positive findings. Techniques which allow a more complete visualization of the hepatic surface have been proposed [15]. The use of the Pan-Endoscope Olympus Type GIF-P2 optimizes hepatic inspection [16]. In this work no additional liver involvement was disclosed. In fact, moving the patients adequately, in different positions, a complete exploration of the liver, including the posterior and inferior faces, could be performed using a standard rigid peritoneoscope which, moreover, offers the advantages of a better visualization of intra-abdominal organs and easier biopsy sampling.

Autopsy studies have shown that about 90% of hepatic metastases were present at the surface of the liver [17]. This might not be the case in patients at an earlier stage of the disease. Indeed, previous studies have shown that malignant lesions not visualized at peritoneoscopy were found in the depths of the liver parenchyma [6, 18]. Increasing the number of biopsies when the surface of the liver is macroscopically normal and searching deeply located nodules should allow the detection of at least some of the unsuspected neoplastic liver involvements. This approach has been shown to be useful in untreated patients with Hodgkin's and non-Hodgkin's lymphomas [2, 12, 13, 19, 20].

In our patients 2 or 3 biopsies were taken in each liver lobe when the surface had a normal aspect. A number of patients suitable for analysis was obtained in breast cancers (159 advanced, 49 localized), malignant melanomas (47 advanced, 60 localized) and lung cancers (61 advanced). Microscopic liver involvement was found in breast and in lung cancers. None was found in malignant melanomas, although the abdominal exploration disclosed unsuspected peritoneal metastases in 2 out of 36 stage II patients (Table 4).

An increased probability of false negative findings was observed in series with a high prevalence of liver metastases and a selection of more advanced cases [6]. This could partly explain the lack of microscopic involvement in malignant melanomas since the prevalence of metastases was half that observed in the other tumors (14 vs 29%). However, in breast cancer more positive biopsies in normal liver were found in localized than in advanced tumors (1 out of 113 advanced, 2 out of 17 stage II).

In our series it could not be specified whether the difference observed between tumor types or sub-types were based on different patterns of dissemination or on artefacts due to selection. Small cell carcinomas are said to have a diffuse pattern of dissemination [3]. The fact that 5 out of 12 patients with liver metastases had negative clinical findings favours that hypothesis but does not exclude a bias based on selection since 60% of lung cancers were small carcinomas (Table 3).

In other tumor types the number of cases are too few to be conclusive. However, 23 patients with proven nodular tumor dissemination had biopsies taken in normal areas close to the metastases. They were positive in 6. This suggests that systematic sampling of normal livers should be further investigated in all tumor types whenever neoplastic dissemination is suspected.

Most positive peritoneoscopies were found among patients with abnormal clinical findings.

In breast cancer the procedure should not be performed without clinical tests suggestive of liver metastases, even when patients have localized tumors. However, small cell carcinomas and stage II malignant melanomas deserve special attention considering the rather high rate of unsuspected abdominal malignancies.

None of the cytologic examinations led to the discovery of metastatic involvement which was not macroscopically apparent. This difference, compared to the results obtained with percutaneous liver biopsy [21, 22], could be related to the biopsy method itself. In fact, biopsy under visual control immediately allowed the detection of twice as many lesions as percutaneous liver biopsy [1, 2, 23, 24]. All visualized or palpated lesions can readily be biopsied and the probability of positive cytology when the surface of the liver and the biopsies are normal must be very low. Since it can be accomplished with relatively little effort and at no additional risk for the patient, the evaluation of the technique could be further pursued, particularly in those tumors with a diffuse pattern of dissemination. Cytological examination could also be useful in necrotic metastases, and when the risk of multiple biopsies seems too high.

Findings in this and other series suggest that peritoneoscopy and liver biopsies play a major role whenever liver and abdominal staging is required. In an undefinable number of cases neoplastic involvement will not be detected. Procedures aimed to ensure a more complete visualization of the liver surface or cytology have not increased the yield of positive findings. Overall, a 7.2% increase in liver metastases detection has been obtained by multiple biopsies at random or guided toward deep palpated nodules in macroscopically normal livers. This was found only in breast and lung cancers. It cannot be said whether this was due to some bias in selecting patients or to a different mode of dissemination. Since hemorrhagic complications related to the procedure were not observed, we think that further investigations should be undertaken to assess this approach in other tumor types.

Acknowledgements—The author wishes to thank Dr. F. Lejeune and W. Mattheiem for their help in investigating malignant melanomas (L.F.) and breast cancers (M.W.), and Mrs J. Collette for typing this manuscript.

REFERENCES

1. BAGLEY CM, ROTH JA, THOMAS LB *et al.* Liver biopsy in Hodgkin's disease. Clinicopathologic correlations in 127 patients. *Ann Intern Med* 1972, **76**, 219–225.
2. CHABNER BA, JOHNSON RE, CHRETIEN IB *et al.* Percutaneous liver biopsy, peritoneoscopy and laparotomy: an assessment of relative merits in the lymphomatoma. *Br J Cancer* 1975, **31**, 242–247.
3. HANSEN HH, MUGGIA FM. Staging of inoperable patients with bronchogenic carcinoma with special reference to bone marrow examination and peritoneoscopy. *Cancer* 1972, **30**, 1394–1401.
4. OZOLS R, FISHER RI, ANDERSON T *et al.* Peritoneoscopy in ovarian cancer: a safe and valuable procedure for staging and follow-up. *Proc Am Assoc Cancer Res* 1979, **20**, 408.
5. ROSENOFF SH, DEVITA VT, HUBBARD S *et al.* Peritoneoscopy in the staging and follow-up of ovarian cancer. *Semin Oncol* 1975, **2**, 223–228.
6. BLEIBERG H, ROZENCWEIG M, LONGEVAL E *et al.* Peritoneoscopy as a diagnostic supplement to liver function tests and liver scan in patients with carcinoma. *Surg Gynecol Obstet* 1977, **145**, 821–825.
7. RUDDOCK JC. Peritoneoscopy, a critical clinical review. *Surg Clin North Am* 1957, **37**, 1249–1260.
8. BLEIBERG H, LA MEIR E, LEJEUNE F. Laparoscopy in the diagnosis of liver metastases in 80 cases of malignant melanoma. *Endoscopy* 1980, **12**, 215–218.
9. BLEIBERG H, ROZENCWEIG M, MATHIEU M *et al.* The use of peritoneoscopy in the detection of liver metastases. *Cancer* 1978, **41**, 863–867.
10. JORI GP. Peritoneoscopy in the diagnosis of liver metastases. *Am J Roentgenol* 1979, **133**, 977.
11. SAUER R, FAHRLANDER H, FRIDRICH R. Comparison of the accuracy of liver scans and peritoneoscopy in benign and malignant primary and metastatic tumours of the liver. 222 confirmed cases examined by both methods simultaneously. *Scand J Gastroenterol* 1973, **8**, 389–394.
12. VERONESI V, SPINELLI P, BONADONNA G *et al.* Laparoscopy and laparotomy in staging Hodgkin's and non Hodgkin's lymphoma. *Am J Roentgenol* 1976, **127**, 501–503.

13. BERETTA G, SPINELLI P, RILKE F *et al.* Sequential laparoscopy and laparotomy combined with bone marrow biopsy in staging Hodgkin's disease. *Cancer Treat Rep* 1976, **60**, 1231–1237.
14. STAQUET M, ROZENCWEIG M, LEE YJ *et al.* Methodology for the assessment of new dichotomous diagnostic tests. *J Chronic Dis* 1981, **34**, 599–610.
15. SUGARBAKER PH. Optimizing peritoneoscopy visualisation of the liver utilizing a double telescope technique. *Surg Gynecol Obstet* 1981, **152**, 655–657.
16. BLEIBERG H, ROZENCWEIG M, MATHIEU M *et al.* Peritoneoscopy in the detection of liver metastases: limitations and expectations. *Digestion* 1977, **16**, 231.
17. OZARDA A, PICKREN J. The topographic distribution of liver metastases, its relation to surgical and isotope diagnosis. *J Nucl Biol Med* 1962, **3**, 149–152.
18. BLEIBERG H, OSTEAUX M, PETROONS PH. Laparoscopic evaluation of computed tomography (CT) and ultrasonography (US) in liver and abdominal tumor dissemination. *Acta Endoscop* 1982, **72**, 51–60.
19. DEVITA VT, BAGLEY CM, GOODELL B *et al.* Peritoneoscopy in the staging of Hodgkin's disease. *Cancer Res* 1971, **31**, 1746–1750.
20. SPINELLI P, BERETTA G, BAJETTA E *et al.* Laparoscopy and laparotomy combined with bone marrow biopsy in staging Hodgkin's disease. *Br Med J* 1975, **4**, 554–556.
21. ATTERBURY CE, ENRIQUEZ RE, DESUTONAGY GJ *et al.* Comparison of the histologic and cytologic diagnosis of liver biopsies in hepatic cancer. *Gastroenterology* 1979, **76**, 1352–1357.
22. GROSSMAN E, GOLDSTEIN MJ, KOSS LG *et al.* Cytological examinations as an adjuvant of liver biopsy in the diagnosis of hepatic metastases. *Gastroenterology* 1972, **62**, 56–60.
23. CUSCHIERI A. Value of laparoscopy in hepatobiliary disease. *Br J Surg* 1974, **61**, 318–319.
24. JORI GP, PESCHLE C. Combined peritoneoscopy and liver biopsy in the diagnosis of hepatic neoplasm. *Gastroenterology* 1972, **63**, 1016–1019.