Diffuse Malignant Epithelial Mesotheliomas of the Peritoneum in Women

A Clinicopathologic Study of 25 Patients

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BACKGROUND. The behavior of diffuse peritoneal mesotheliomas in women and the possible relation between tumor morphology and outcome are uncertain. Reported survival has ranged from < 1 month to > 14 years, and a previous study found that tumor morphology could not be used reliably for predicting outcome. The authors examined the behavior of diffuse epithelial peritoneal mesotheliomas in women and the possible relation between pathologic features and outcome.

METHODS. Twenty-five female patients with diffuse peritoneal epithelial malignant mesotheliomas were divided into two groups: those who survived for < 4 years (60%) and those who survived for > 4 years (40%). Both groups were compared in terms of age, presentation, treatment, survival, tumor architecture, mitotic rate, necrosis, nuclear grade, and immunohistochemical profile.

RESULTS. Patients in the two groups were similar in terms of age at diagnosis (median ages, 50.7 years and 49.9 years), presentation, initial tumor burden, and treatment. In both groups, the most common initial clinical presenting features were ascites and abdominal pain. The tumors typically took the form of multiple nodules measuring < 1.5 cm in greatest dimension. Slightly less than 50% of patients in both groups received some form of chemotherapy or radiation therapy after undergoing tumor-reductive surgery or biopsy. Overall survival ranged from 1 month to 15 years. The median survival was 12 months in the group of women who survived for < 4 years and 7 years in the group of women who survived for > 4 years. Overall, 10 of 25 patients survived for ≥ 5 years. One patient was alive with disease 15 years after diagnosis. Although there was a suggestion that the tumors in patients with short survival more often had solid architecture and high-grade nuclei, these findings were not significant statistically. The frequency of necrosis and the mitotic activity were the same in both groups.

CONCLUSIONS. The spectrum of diffuse epithelial peritoneal mesotheliomas in women includes tumors that are highly aggressive and behave much like pleural mesotheliomas, although a sizeable number of tumors, unlike the pleural tumors, are relatively indolent. However, because there do not appear to be morphologic features that reliably identify favorable tumors versus unfavorable tumors, aggressive therapy for all women with diffuse peritoneal mesotheliomas may be warranted. ***Cancer* 2002;94:378–85.** © *2002 American Cancer Society.*

KEYWORDS: peritoneum, female, mesothelioma, epithelial mesotheliomas.

Diffuse malignant mesotheliomas are rare tumors, with an incidence of about 2500 per year in the United States.[1] Peritoneal mesotheliomas account for 17–32% of mesotheliomas in females,[2–5] and the majority of lesions are epithelial forms.[3,6] Diffuse malignant mesotheliomas must be separated from well-differentiated papillary mesotheliomas, which usually are solitary and indicate an excellent

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prognosis.[7–9] The prognosis for most patients with diffuse peritoneal epithelial mesotheliomas is less clear. Survival data reported in the literature have ranged from < 1 month to > 14 years, observations that contrast with the uniformly dismal survival reported in patients with pleural mesotheliomas.

Many of the studies that have evaluated prognostic factors in patients with peritoneal mesotheliomas have focused on clinical factors;[10–12] however, in a series of 19 women with peritoneal mesothelioma, Goldblum and Hart[13] found that tumors with pure epithelial growth and particularly those with a predominately tubulopapillary pattern and low-grade nuclei tended to behave in a benign manner. However, there was considerable overlap in the histologic features of the benign and malignant tumors, suggesting that histology was not a reliable prognostic factor. Indeed, those investigators found that the most reliable predictor of survival was the distribution of the tumor. Patients with solitary tumors had an excellent prognosis, whereas patients with diffuse tumors (with more than one site involved) had a poor prognosis. Our study of 25 women with diffuse peritoneal epithelial mesothelioma compares the histologic features of short-term and long-term survivors in an attempt to elucidate useful prognostic features.

MATERIALS AND METHODS

All patients came from a group of 36 women from the authors' consultation files. Clinical information was obtained from the referring pathologists, clinicians, medical records, or a combination of these sources. Survival was calculated from the time of diagnosis to the time of death or last follow-up. The criteria for inclusion were 1) agreement among the authors that these were mesotheliomas, which required the presence of typical monotonous, cuboidal-to-flattened mesothelial cells arranged in a histologic pattern characteristic of mesothelioma accompanied by the proper histochemical and immunohistochemical profile (see below); 2) epithelial histology; 3) multifocal (two or more sites) peritoneal involvement; and 4) follow-up data extending either to the death of the patient or to at least 4 years after diagnosis. Twenty-five women satisfied our inclusion criteria. Two women (Patients 2 and 24) were reported previously in a series of nine patients with mesothelioma involving the ovary.[14] The excluded patients included four patients with epithelial tumors without at least 4 years of follow-up data, two patients with solitary epithelial mesotheliomas, four patients with well-differentiated papillary mesotheliomas, and one patient with sarcomatoid mesothelioma. No biphasic tumors were encountered. Well-differentiated papillary mesotheliomas consisted entirely of papillae lined by a layer of uniform cuboidal cells with bland cytologic features, no more than a rare mitotic figure (MF), and no evidence of invasion.

The number of sections from each tumor ranged from 1 section to 20 sections (mean, 10 sections). Nuclear grade was assessed using a previously reported grading scale,[13] with Grade 1 indicating tumors with small nuclei, a uniform chromatin pattern, and inconspicuous nucleoli; Grade 2 indicating tumors with larger nuclei, some chromatin irregularity, and more prominent nucleoli; and Grade 3 indicating tumors with large nuclei, an irregular chromatin pattern, and prominent macronucleoli. The number of MFs per 50 high-power microscopic fields (HPFs) was counted on a microscope for which the greatest dimension of the HPF was 0.35 mm. Sections stained by the periodic acid-Schiff (PAS) reaction before and after diastase and immunohistochemical methods were available for 21 tumors. Most of these tumors predated the introduction of immunohistochemical markers most useful for mesotheliomas, such as calretinin, thrombomodulin, and cytokeratins 5 and 6. Immunohistochemical staining employed the strepavidin-biotin method and antibodies directed against cytokeratin (Z622; Dako, Carpinteria, CA; 1:4000 dilution), epithelial membrane antigen (EMA) (M613; Dako; 1:400 dilution), carcinoembryonic antigen (CEA) (polyclonal; Dako; 1:1000 dilution), Ber-EP4 (Dako; 1:10 dilution), S100 (HSC; 1:8000 dilution), placental alkaline phosphatase (PLAP) (Zymed Laboratory, Inc., San Francisco, CA; 1:100 dilution), Leu-M1 (Becton Dickson, San Jose, CA; 1:10 dilution), TAG-72 (Signet; 1:100 dilution), and vimentin (BioGenex, San Ramon, CA; 1:1000 dilution). Statistical analysis was conducted using Fisher exact tests and chi-square tests.

RESULTS

Clinical Features

There were 15 short-term survivors and 10 long-term survivors. The mean ages of the short-term and long-term survivors were 50.7 years (range, 24–73 years) and 49.9 years (range, 21–85 years), respectively (Table 1). Details of clinical presentation were available for 10 of the short-term survivors, 6 of whom presented with ascites, 2 with abdominal or pelvic pain, 1 with fever and weight loss, and 1 with an incidental asymptomatic adnexal mass. Details of clinical presentation were available for 9 of the long-term survivors, 4 of whom presented with abdominal pain (including 1 with melena and 1 other with an autoimmune hemolytic anemia), 3 with ascites, 1 with fever and lymphadenopathy, and 1 who presented during the course of treatment for endometriosis. Twelve of 15 short-term survivors were known to have multiple foci of tumor at initial laparotomy; in

TABLE 1
Clinical Features, Therapy, and Follow-Up of 25 Female Patients with Peritoneal Mesothelioma

Patient	Age (yrs)	Clinical presentation	Sites	Therapy	Survival
Short-term survivors					
1	24	Ascites	Omentum, liver, small bowel	N/A	12 months, DOD
2	31	Abdo pain, ascites	Bilateral ovaries, omentum	TAHBSO, oment	10 months, DOD
3	37	Abdo girth, ascites	Omentum, peritoneum	N/A	12 months, DOD
4	40	Abdo girth, ascites	Bowel, left adnexa	LSO, peritoneal BX	3 months, DOD
5	43	Abdo pain, ascites	Widespread implants	TAH, LSO, chemo	6 months, DOD
6	47	N/A	N/A	N/A	11 months, DOD
7	31	Ascites	Bowel, peritoneum	BX, chemo	30 months, DOD
8	56	N/A	Widespread implants	N/A	1 month, DOD
9	57	Asympt adnexal mass	Widespread implants	TAHBSO, oment, BX, rad	44 months, DOD
10	59	Abdo, pelvic pain	Widespread implants	TAHBSO, chemo, rad	24 months, DOD
11	59	N/A	Widespread implants	TAHBSO, oment	2 months, DOD
12	66	N/A	Widespread implants	BX, chemo	6 months, DOD
13	69	Abdo pain, constipation	Omentum	TAHBSO, oment, tamox	24 months, DOD
14	69	Fever, weight loss	Widespread implants	BX	12 months, DOD
15	73	N/A	N/A	N/A	19 months, DOD
Long-term survivors					
16	21	Abdo pain, melena	Widespread implants	TAHBSO, oment, chemo	13 yrs, CFOD
17	30	Abdo pain	Widespread implants	BX	12 yrs, CFOD
18	32	Laparoscopy for endo	Widespread implants	TAHBSO, oment, rad	14 yrs, CFOD
19	41	Abdo pain	Ladnexa, bladder, omentum	TAHBSO	13 yrs, CFOD
20	85	Ascites	Widespread implants	TAHBSO, oment, chemo Tamox, meg	7 yrs, DWD
21	61	Fever, lymphadenopathy	Ovaries, peritoneum	TAHBSO, oment	7 yrs, CFOD
22	64	Abdominal pain, AIHA	Ovaries, omentum	TAHBSO	5 yrs, CFOD
23	65	N/A	Widespread implants	TAHBSO, chemo	5 yrs, AWD
24	63	Ascites	Widespread implants	BX, chemo	7 yrs, AWD
25	37	Ascites	Widespread implants	BX, chemo	15 yrs, AWD

Abdo: abdominal; AIHA: autoimmune hemolytic anemia; Asympt: asymptomatic; AWD: alive with disease; BX: biopsy; CFOD: clinically free of disease; chemo: chemotherapy; DOD: died of disease; endo: endometriosis; LSO: left salpingoophorectomy; meg: megesterol; N/A: not available; oment: omentectomy; rad: radiation therapy; RSO: right salpingoophorectomy; TAHBSO: total abdominal hysterectomy bilateral salpingoophorectomy; tamox: tamoxifen.

the remaining 3 patients, this information was not available. All of the long-term survivors had multifocal tumors.

Surgical treatment was extremely variable. Some patients underwent limited peritoneal biopsy, and others underwent more extensive surgery. Generally, it was not clear from the information provided whether patients who underwent more extensive surgery, such as total abdominal hysterectomy and bilateral salpingoophorectomy, also underwent aggressive debulking of peritoneal tumors. The use of chemotherapy and radiotherapy also varied, and information on the duration of treatment was available for only one patient. In the group of short-term survivors, five patients had some form of postoperative chemotherapy, including two patients who also received abdominal radiation therapy and one patient who also received tamoxifen treatment. One patient was treated with intraperitoneal cisplatin and intravenous doxorubicin. A second patient was treated with paclitaxel. A third patient was treated with intravenous melphalan and abdominal radiotherapy. A fourth patient was treated with cisplatin, doxorubicin, cytarabine, and dexamethasone. A fifth patient was treated with intravenous cisplatin, doxorubicin, and cytarabine and also was on adjuvant tamoxifen treatment for a prior carcinoma of the breast. In the group of long-term survivors, five patients received some form of postoperative chemotherapy, including one patient who also received treatment with tamoxifen and megesterol. For one patient, we could not determine which chemotherapeutic agents were used. A second patient was treated with five cycles of cisplatin, cytarabine, and melphalan and also was on tamoxifen and megesterol. A third patient was treated with intravenous bleomycin, etoposide, and doxorubicin. A fourth patient was treated with cytarabine and carboplatin. A fifth patient was treated with intravenous doxorubicin.

A sixth patient received postoperative abdominal radiotherapy without chemotherapy.

Survival Data

The overall median survival for both groups combined was 30 months (mean, 56 months) and ranged from 1 month to 15 years. The median survival for the group of short-term survivors was 12 months (mean, 16.2 months; range, 1–44 months). All of these patients died of disease. Ten patients (67%) survived for 1 year, but only two patients (13%) survived for > 2 years. The median survival for the group of long-term survivors was 7 years (mean, 10.3 years; range, 5–15 years). None of these patients died of disease, although one patient died with disease at 7 years. Two patients were alive with disease at 7 years and 15 years after diagnosis. The patient who was alive at 15 years had recurrent pleural effusions with positive cytology. At the time of last follow-up, seven patients were alive and clinically free of disease, including one patient at 14 years after diagnosis.

Macroscopic Pathology

There was limited information concerning the macroscopic appearance of these tumors, and some information on these features was available for only half of the patients. Most tumors were described as white, tan, pink, or brown nodules varying in size from 0.5 cm to 1.5 cm. In one patient, the tumor nodules measured up to 5 cm. In another patient, the peritoneum was studded with minute foci of tumor resembling grains of sand. In two patients, the tumors were more plaque-like and encased portions of viscera. In the two patients with significant ovarian involvement, tumor enlarged the ovaries up to 9 cm in maximum dimension. Some of the tumors were papillary, and one tumor was cystic. The tumors most often were firm, but several were soft. None was necrotic macroscopically.

Microscopic Findings

Seven tumors in the group of short-term survivors and three tumors in the group of long-term survivors had a predominantly solid architecture. None of the tumors had a deciduoid morphology (Table 2).[9,15] The remaining tumors in both groups had tubulopapillary architecture (Figs. 1, 2). The difference in architecture between the two groups was not statistically significant ($P = 0.68$). In the group of short-term survivors, one tumor was Grade 1, eight tumors were Grade 2, and six tumors were Grade 3. None of the tumors in the group of long-term survivors had Grade 1 nuclei, seven tumors were Grade 2 and three tumors were Grade 3. The nuclear grades of the tumors in the two groups were not statistically different (chi-square value, 1.11; $P = 0.57$). The mean mitotic rates for the groups of short-term and long-term survivors were 1.47 MFs per 50 HPFs (range, 0–11 MFs per 50 HPFs) and 0.67 MFs per 50 HPFs (range, 0–5 MFs per 50 HPFs), respectively. The mitotic rate for short-term survivors was inflated by a single patient who had 11 MFs per 50 HPFs; if this patient is excluded, then the mean mitotic rate for this group becomes 0.79 MFs per 50 HPFs (range, 0–5 MFs per 50 HPFs). In nine tumors from the short-term survivors and in 7 tumors from the long-term survivors, no MFs were seen. The remaining two tumors in the latter group had mitotic counts of 1 MFs per 50 HPFs and 5 MFs per 50 HPFs, respectively (in one tumor that was not included in the mitotic rate calculation for this group because < 50 HPFs were available for assessment, no mitoses were seen). Only one tumor from each group showed necrosis. Multiple foci of necrosis were seen in the tumor of a patient who died of disease at 10 months, and a single microscopic focus was found in a patient who was clinically free of disease 7 years after diagnosis. Most tumors in both groups showed mild-to-moderate inflammatory responses. Almost all tumors showed lymphocytic infiltration, some with germinal center formation. However, the inflammatory infiltrate in one patient in the group of short-term survivors consisted predominantly of foamy macrophages, and, in one patient in the group of long-term survivors, the infiltrate consisted predominantly of neutrophils.

TABLE 2
Microscopic Features of Tumors

Microscopic feature	Short-term survivors (%)	Long-term survivors (%)
Predominantly tubulopapillary	8 of 15 (53)	7 of 10 (70)
Predominantly solid	7 of 15 (47)	3 of 10 (30)
Necrosis	1 of 15	1 of 10
Nuclear grade		
1	1 of 15	0 of 10
2	8 of 15	7 of 10
3	6 of 15	3 of 10

Special Stains and Immunohistochemistry

PAS with (PAS/D) and without diastase staining and immunohistochemistry were available for 13 short-term survivors and for 8 long-term survivors (Table 3). All tumors for which PAS and PAS/D staining was available were PAS/D negative. All tumors were strongly positive for keratin. Vimentin was at least focally positive in 12 short-term survivors and 4 long-term survivors. S100 was weakly positive in four short-

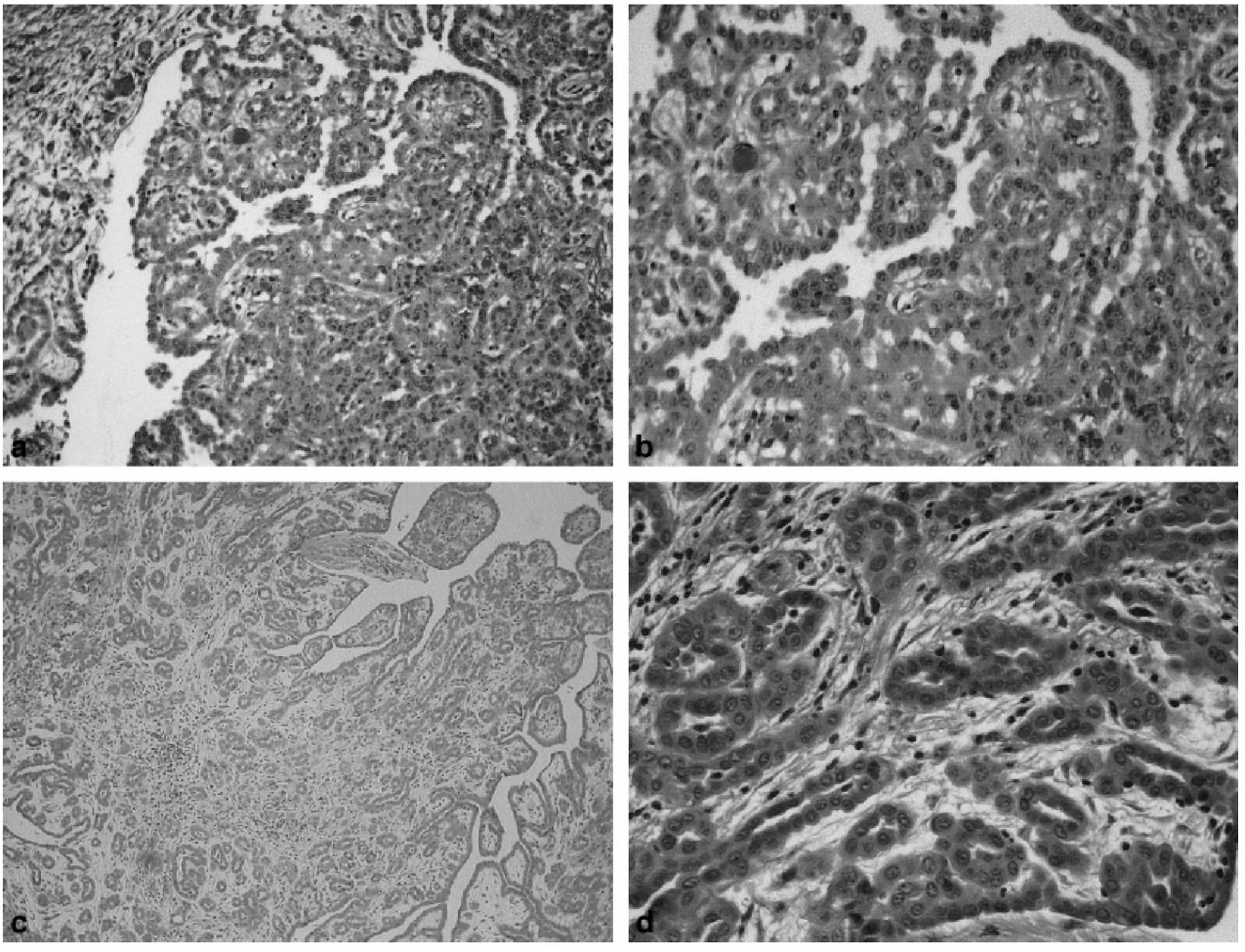

FIGURE 1. Tubulopapillary architecture. (a) Low-power view of tumor tissue from a short-term survivor (original magnification, ×160). (b) High-power view of tumor tissue from a short-term survivor (original magnification, ×320). (c) Low-power view of tumor tissue from a long-term survivor (original magnification, ×80). (d) High-power view of tumor tissue from a long-term survivor (original magnification, ×320). Note the extensive tumor invasion in both short-term and long-term survivors.

term survivors and two long-term survivors. EMA was positive in nine and two of the patients, respectively, with no consistent differences in membranous or cytoplasmic distribution. All tumors were negative for Leu-M1, CEA, B72.3, and Ber-EP4.

DISCUSSION

This is the largest study of diffuse peritoneal epithelial mesotheliomas in women reported to date. An arbitrary cut-off value of 4 years was chosen to separate short-term and long-term survivors, because almost all patients with pleural mesotheliomas are dead at 4 years; thus, this cut-off time should show whether epithelial peritoneal mesotheliomas behave differently. Our results indicate that, unlike their pleural counterparts, a substantial proportion of diffuse peritoneal epithelial mesotheliomas in women behave indolently. In our series, 40% of patients survived for at least 4 years, with one patient alive with disease 15 years after diagnosis and another patient alive and clinically free of disease at 14 years. The 15-year survival is the longest reported to date. In contrast, the 67% 1-year survival rate and the 13% 2-year survival rate in the group of short-term survivors are similar to the survival rates reported for patients with pleural mesothelioma: approximately 50% at 1 year with few patients surviving for 2 years.[2,3]

Could our results be an artifact of how patients were selected? One could argue that patient selection was compromised by a failure to match clinical features, such as tumor bulk and treatment, that appear to be of some importance in the clinical literature.[10–12] The most recent and largest series of peritoneal mesotheliomas reported on 33 patients, 10 of whom were

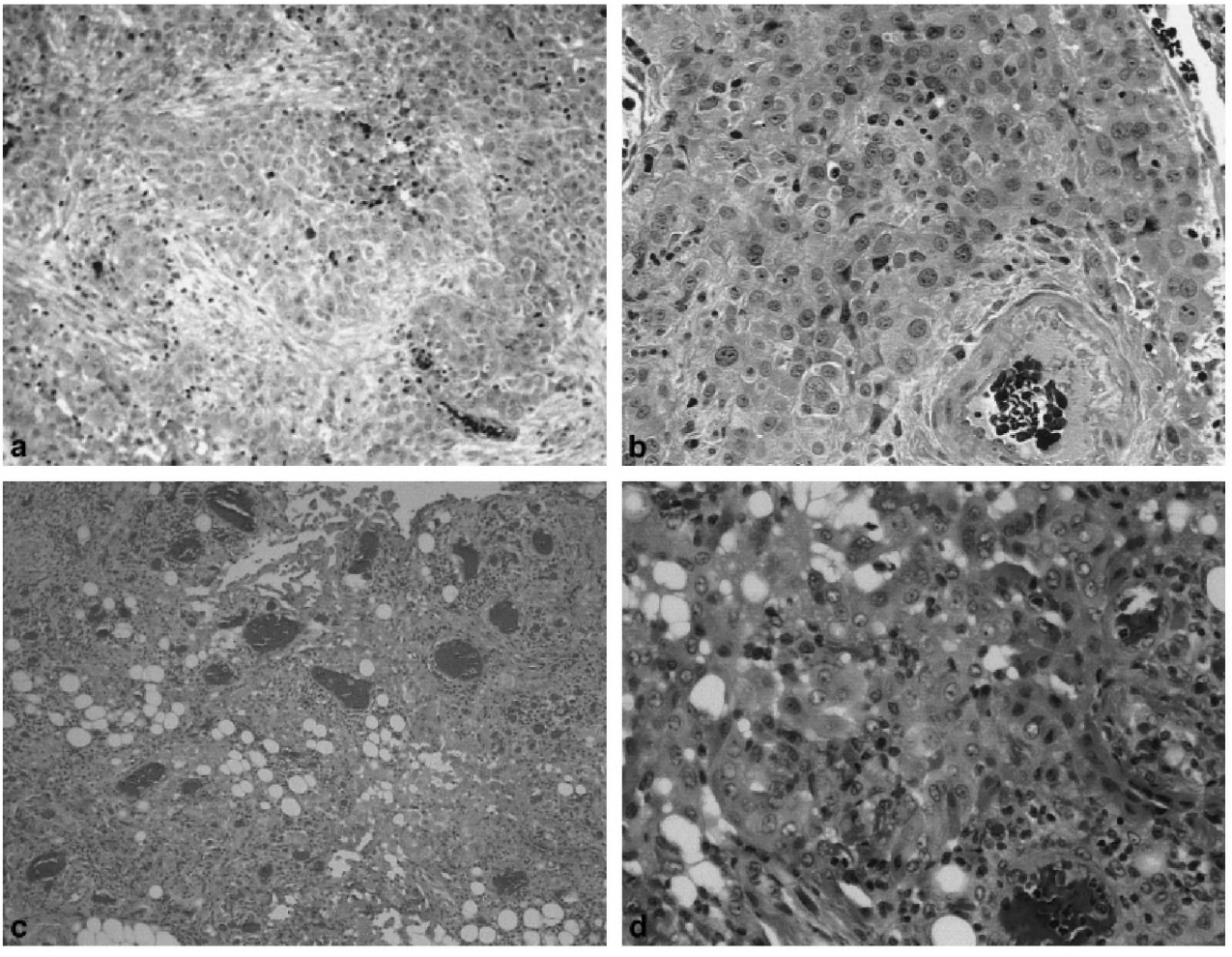

FIGURE 2. Solid architecture with large sheets of tumor. (a) Low-power view of tumor tissue from a short-term survivor (original magnification, ×160). (b) High-power view of tumor tissue from a short-term survivor (original magnification, ×320). (c) Low-power view of tumor tissue from a long-term survivor (original magnification, ×80). (d) High-power view of tumor tissue from a long-term survivor (original magnification, ×320).

women, and found that female gender, more limited prior pelvic or abdominal surgery, complete tumor-reductive surgery, and the performance of a second-look surgery were positive predictive factors for survival.[10] The median survival was 31 months, but the relative survival rates for men and women were not specified. Antman et al.[11] reported long-term disease free survival with up to 36 months follow-up in six patients (three women) who were treated aggressively with tumor-reductive surgery, postoperative chemotherapy, and whole abdominal radiation. Those authors also found that age < 40 years conferred a much better prognosis. Eltabbahkh et al.[12] described 15 women with peritoneal tumors and noted that tumor-reductive surgery and chemotherapy both improved survival, but their median survival was still 12.5 months, and only 5 patients survived for > 1 year.

The amount of clinical information available to us varied greatly between patients, which often is the situation with consultation patients. However, the two groups of patients appear to be very similar in terms of patient age at presentation, initial tumor burden, and treatment, and there is no evidence that these clinical features accounted for the observed differences in survival. Furthermore, because some of the studies mentioned above have shown that treatment confers marginal improvement in survival at best, it seems unlikely that any unknown differences in treatment that may exist, such as extent of tumor debulking or duration of chemotherapy, would account for the observed survival difference between our two groups.

The unintentional inclusion of tumors other than mesotheliomas is another important source of potential bias. Mesotheliomas must be distinguished from far more common lesions in the differential diagnosis, such as atypical mesothelial hyperplasia, primary and meta-

TABLE 3
Immunohistochemical Staining Results

Immunohistochemical	Short-term survivors	Long-term survivors
Keratin	13 of 13	8 of 8
Vimentin	12 of 13	4 of 8
LeuM1	0 of 13	0 of 8
S100	4 of 13	2 of 8
CEA	0 of 13	0 of 8
EMA	9 of 13	2 of 8
B72.3	0 of 13	0 of 8
Ber-EP4	0 of 13	0 of 8

CEA: carcinoembryonic antigen; EMA: epithelial membrane antigen.

static serous carcinomas, ectopic decidua, and malignant vascular tumors of the peritoneum.[16] A recent paper by the United States-Canadian Mesothelioma Reference Panel reviewed in detail the histologic features that are useful in distinguishing benign mesothelial reactions from malignant mesothelial neoplasms.[17] Histologic features that favor the diagnosis of mesothelioma over serous carcinoma include prominent tubulopapillary pattern, polygonal cells with eosinophilic cytoplasm, the absence of marked nuclear pleomorphism, the absence of high mitotic rate, and the presence of intracellular acid (PAS negative) mucin rather than neutral (PAS positive) mucin.[16] Several studies have reviewed the use of immunohistochemical markers in distinguishing mesotheliomas from serous adenocarcinomas.[18–20] Most of the patients in our series predated specific immunohistochemical markers for mesothelioma and were consultation patients from a large number of geographically dispersed sites. Therefore, it was not feasible to perform staining for newer markers, such as calretinin, thrombomodulin, and cytokeratins 5 and 6, which typically are positive in patients with mesotheliomas and negative in patients with serous carcinomas.[18] Some authors have used ultrastructural features, as determined by electron microscopy, to distinguish mesotheliomas from carcinomas[13,20]; however, given the availability of immunohistochemical methods and a general lack of suitable material on which to perform electron microscopy in our patients, this technique was not used in this study. Despite these considerations, we are confident that, among our patients, all tumors were mesotheliomas and not carcinomas based on their histologic appearance, lack of PAS staining, and the available immunohistochemistry.

Another potential source of bias may have been the unintentional inclusion of well-differentiated papillary mesotheliomas. Solitary, well-differentiated papillary mesotheliomas are benign,[13] whereas their behavior when multifocal is less certain, but at least some of these appear to be extremely indolent.[9] We avoided this source of bias by excluding tumors that consisted entirely of papillae lined by a layer of uniform cuboidal cells with bland cytologic features, no more than a rare MF, and no evidence of invasion. The tumors in our long-term survivors were Grade 2 or 3, which excluded well-differentiated papillary mesotheliomas by definition. Therefore, we believe that all of the tumors in our study, including those in the group of long-term survivors, were diffuse epithelial malignant mesotheliomas.

Some of our findings are consistent with those of Goldblum and Hart.[13] Their study of 19 patients with peritoneal mesothelioma included 17 purely epithelial tumors, 11 of which were diffuse. Those authors found that there was considerable overlap in the histologic features of the benign and malignant tumors but that tumors with a predominantly tubulopapillary pattern and low-grade nuclei tended to be less aggressive. Similarly, we found that the patients with short survival more often had tumors with solid architecture and high-grade nuclei, but there was considerable overlap between the two groups of patients, and the differences were not statistically significant. Necrosis, which correlates with an aggressive behavior in many types of tumors, was not useful, because only one tumor in each group showed any necrosis. Similarly, our mitotic counts, which were in keeping with others reported previously,[13,14] failed to provide any correlation with survival, an observation that has been made previously in patients with malignant mesothelioma in other sites.[17] A major difference between our study and that of Goldblum and Hart[13] was that, whereas they included solitary tumors, we limited ourselves to diffuse tumors. Perhaps not surprisingly, those authors found that the most reliable predictor of survival was the distribution of the tumor: Patients with solitary tumors had an excellent prognosis, and patients with diffuse tumors had a poor prognosis. By excluding patients with solitary tumors, we avoided this form of selection bias, because those patients would be expected to have longer survival than patients with diffuse tumors. Even so, survival in our group of long-term survivors was much better compared with the study by Goldblum and Hart.[13] In part, this may reflect differences in patient selection, because two of their patients had tumors with sarcomatous components, and sarcomatous tumors tend to be aggressive. However, for the most part, we cannot account for the differences in patient survival between the two studies.

In conclusion, we found that diffuse peritoneal epithelial mesotheliomas in women exhibit a varied spectrum with regard to outcome. Although many patients have a rapid course, a sizeable number have a

relatively prolonged survival and do not die of their disease. No difference in tumor morphology was clearly evident between groups of patients with poor and favorable outcomes. To us, this implies that all women with peritoneal mesotheliomas should be treated for long-term cure and long-term survival. The proper treatment for these women remains controversial: To date, there is no standardized therapy for patients with mesothelioma, although limited evidence suggests that tumor-reduction surgery and chemotherapy may improve survival.[11,12] Accordingly, given our inability to predict outcome with routine histology, it may be appropriate to proceed with treatment in all women with diffuse epithelial peritoneal mesotheliomas.

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