Computed Tomographic Features of Malignant Peritoneal Mesothelioma

KATSUYA KATO[1§], KENICHI GEMBA[2], NOBUKAZU FUJIMOTO[2], KEISUKE AOE[4], YUKIO TAKESHIMA[5], KOUKI INAI[5] and TAKUMI KISHIMOTO[3]

[1]Department of Radiology, Okayama University Hospital, Shikatacho, Okayama, Japan; Departments of [2]Respiratory Medicine and [3]Internal Medicine, Okayama Rosai Hospital, Chikkomidorimachi, Okayama, Japan; [4]Department of Medical Oncology, National Hospital Organization Yamaguchi-Ube Medical Center, Higashikiwa, Ube, Japan; [5]Department of Pathology, Graduate School of Biomedical Sciences, Hiroshima University, Minamiku, Hiroshima, Japan

Abstract. *Aim: The objective of this study was to determine the computed tomographic (CT) features of malignant peritoneal mesothelioma (MPM). Patients and Methods: We analyzed CT features of MPM cases and compared them to those of other malignant conditions (non-MPM). Results: Multiple nodular lesions occurred more frequently in the MPM group compared to non-MPM cases (p=0.013). Thickening of the mesentery was detected more frequently in MPM cases than in non-MPM cases (56% vs. 18%, p=0.029). Pleural plaques were detected in 13 cases (45%) in the MPM group but were not detected in the non-MPM group. The MPM-CT index score, determined in each case as the sum of the findings which are potentially characteristic of MPM, was significantly higher in MPM than in non-MPM cases (p=0.001). Conclusion: MPM presented characteristic CT findings, and the MPM-CT index may be useful for differential diagnosis of MPM.*

Malignant mesothelioma (MM) is an aggressive tumor that develops from mesothelial cells of the pleura, peritoneum, pericardium, or testicular *tunica vaginalis*. It is generally associated with a history of asbestos exposure (1) and has a very poor prognosis (2). Once rare, the incidence of MM has increased worldwide as a result of past wide-spread exposure to asbestos. Malignant peritoneal mesothelioma (MPM) represents the second most common site of MM, accounting for 10-20% of MM (3, 4).

A diagnosis of MPM should be based on the histology of an adequate specimen of the peritoneum or cytological analyses of ascites, but this is often difficult. Paracentesis with fluid cytology has a variable sensitivity of 32-76%, with the major limitation being difficulty in distinguishing benign from malignant lesions (4, 5). In particular, the differential diagnosis between MPM and peritoneal carcinomatosis is a critical issue. Radiological analysis is essential for this differential diagnosis; computed tomographic (CT) imaging is the most common initial imaging modality and can reveal moderate to extensive ascites with peritoneal, visceral, or omental involvement. Magnetic resonance imaging may more accurately quantify the extent of disease; however, its routine use is not yet supported (6). The role of positron-emission tomography is not well defined in detection of this disease (7).

In the current study, we retrospectively examined the CT features for patients with MPM.

Patients and Methods

Study approval. All procedures performed in the current study were in accordance with the Helsinki declaration. This study was performed in accordance with the Ethical Guidelines for Epidemiological Research of the Japanese Ministry of Education, Culture, Sports, Science and Technology, and Ministry of Health, Labour and Welfare and was approved by the Japan Labour Health and Welfare Organization and the Institutional Review Boards of Okayama Rosai Hospital. Patient confidentiality was strictly maintained. As described below, informed consent was provided by the closest living relatives of each patient.

Patients. This study was a part of our previous nationwide survey of MM. Methods of the retrospective survey have been described

[§]*Present address:* Department of Diagnostic Radiology 2, Kawasaki Medical School, Nakasange, Kitaku, Okayama, Japan.

Correspondence to: Nobukazu Fujimoto, MD, Ph.D., Department of Respiratory Medicine, Okayama Rosai Hospital, 1-10-25 Chikkomidorimachi, Okayama 7028055, Japan. Tel: 81-86-2620131, Fax: 81-86-2623391, e-mail: nobufujimot@gmail.com

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previously (1, 8). In brief, we requested and received authorization to view the death records from the Vital Statistics database in Japan. We then extracted all cases of death due to MM between 2003 and 2005. There were 2,742 deaths due to MM (Figure 1). We contacted the closest living relatives of each patient to obtain consent for our study by postal mail. As a result, informed consent was obtained by postal mail for 1,153 cases. Based on authorization from relatives, we contacted the patients' medical institutions to obtain medical information, including medical records, X-ray and CT images by postal mail. These data were obtained in 743 cases. Among them, we found 105 cases in which the clinical diagnosis of MPM had been made. Pathological specimens were provided in 53 out of the 105 cases. We reviewed the pathological specimen of these cases according to World Health Organization criteria (9), and analyzed the radiological features of the cases.

CT analysis of MPM. The items examined on the CT images were as follows: (i) degree of accumulation of ascites, (ii) location of the lesion, (iii) maximum dimensions of the nodular lesion, (iv) number of tumor masses, (v) extent of peritoneal thickening, (vi) extent of thickening of the mesentery, (vii) stellate pattern findings in the mesentery, and (viii) pleural plaques. These items were examined according to the criteria listed in Table I.

Statistical analysis. Comparisons between independent groups were performed using the Chi-square test and non-parametric analysis was performed with the Mann–Whitney *U*-test. Average values were compared by *t*-test. Areas under the receiver operating characteristic (ROC) curves (AUCs) were calculated using standard techniques. Statistical calculations were performed with SPSS statistical package, version 11.0 (SPSS Inc., Chicago, IL, USA).

Results

Pathological review of the cases. As shown in Figure 2, pathological diagnosis of MPM was confirmed in 34 cases. Among the 34 cases, there were 27 (79.0%) cases of epithelioid, four (12.0%) cases of biphasic, and three (9%) cases of sarcomatous sub-types. There were 16 cases ultimately diagnosed as other conditions (non-MPM), including six cases of serous papillary adenocarcinoma, four cases of adenocarcinoma, two cases each of carcinosarcoma and unclassified sarcoma, and one case each of peritoneal metastasis of renal cell carcinoma and rhabdomyosarcoma. Differentiation between the epithelioid sub-type of mesothelioma and poorly differentiated adenocarcinoma was impossible in one case. In another case, a confirmed pathological diagnosis could not be made as to whether it was an epithelioid sub-type of mesothelioma, another malignant condition, or reactive mesothelium. In addition, there was one case in which a malignant condition was highly suspected from CT images, but only reactive mesothelium was demonstrated in the pathological specimen. These three cases were finally categorized as "diagnosis could not be made," and they were excluded from further analyses. The MPM group included 30 (88.2%) males and 4 (11.8%) females and the non-MPM group included two (12.5%) males and 14 (87.5%) females.

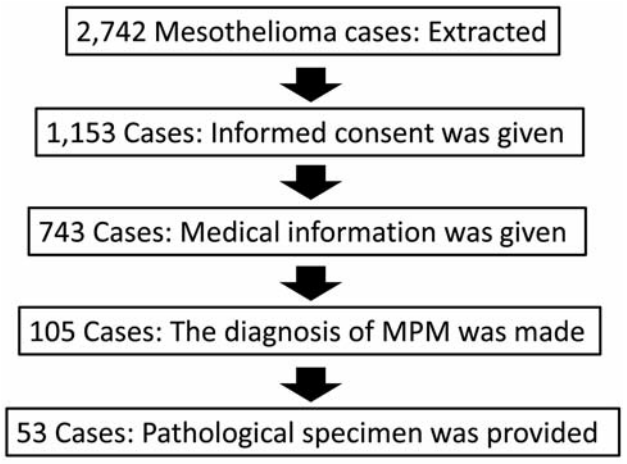

Figure 1. *The schema of the case collection of this study.*

Radiological analyses. Among the 50 cases, abdominal and pelvic CT scans were available in 32 MPM cases and 11 non-MPM cases (three cases of serous papillary adenocarcinoma, two cases each of adenocarcinoma, carcinosarcoma and unclassified sarcoma, and one case each of peritoneal metastasis of renal cell carcinoma and rhabdomyosarcoma). Chest CT images were available in 40 cases (29 MPM and 11 non-MPM). CT findings of the MPM and non-MPM groups are shown in Table I.

There were 19/32 (59%) cases of moderate to massive accumulation of ascites in the MPM group, and 3/11 (27%) cases in the non-MPM group. Although the proportion was higher in the MPM compared to non-MPM group, the difference did not reach statistical significance (p=0.066). We analyzed the location of MPM. For this purpose, the existence or non-existence of MPM in the parahepatic space, great omentum, paracolic gutter, mesentery proper, rectovesical pouch, and perisplenic space was determined. There was no difference concerning the location of the disease between the MPM and non-MPM groups.

We next categorized the maximum dimension of the nodular lesion as <1 cm, 1-3 cm, >3-5 cm, or >5 cm based on the abdominal CT images (Figure 3A). As shown in Table I, the proportion of cases with a maximum dimension of <1 cm was higher in the MPM group than in the non-MPM group, but this difference was not statistically significant (47% *vs*. 18%, p=0.097).

In the MPM group, there were multiple nodular lesions in 30 cases (94%), which was significantly more frequent in MPM than in non-MPM cases (p=0.013).

Thickening of the peritoneum was categorized as none, mild, irregular, or massive (defined as ≥1 cm, Figure 3B). As shown in Table I, MPM cases had a higher proportion of irregular or massive thickening compared to non-MPM cases, although this

Table I. *Computed tomographic findings of malignant peritoneal mesothelioma (MPM) and finding of cases ultimately diagnosed as other conditions (non-MPM).*

Characteristic		Proportion of cases with the finding (%)		
	Findings	MPM	Non-MPM	*p*-Value
Ascites accumulation	None	2 (6.3)	2 (18.2)	
	Small	11 (34.4)	6 (54.5)	
	Moderate	12 (37.5)	2 (18.2)	
	Massive	7 (21.9)	1 (9.1)	0.066
Maximum dimension of nodular lesion	<1 cm	15 (46.9)	2 (18.2)	
	1-3 cm	6 (18.8)	2 (18.2)	
	>3-5 cm	2 (6.3)	3 (27.3)	
	>5 cm	9 (28.1)	4 (36.4)	0.097
Location of MPM				
Parahepatic space	Yes	18 (56.3)	5 (45.5)	
	No	14 (43.8)	6 (54.5)	0.536
Great omentum	Yes	29 (90.6)	8 (72.7)	
	No	3 (9.4)	3 (27.3)	0.139
Paracolic gutter	Yes	18 (56.3)	5 (45.5)	
	No	14 (43.8)	6 (54.5)	0.536
Mesentery proper	Yes	25 (78.1)	8 (72.7)	
	No	7 (21.9)	3 (27.3)	0.715
Rectovesical pouch	Yes	18 (56.3)	9 (81.8)	
	No	14 (43.8)	2 (18.2)	0.13
Perisplenic space	Yes	14 (43.8)	3 (27.3)	
	No	18 (56.3)	8 (72.7)	0.668
Nodular lesions	Solitary	2 (6.3)	4 (36.4)	
	Multiple	30 (93.8)	7 (63.6)	0.013
Thickening of the peritoneum	None	3 (9.4)	3 (27.3)	
	Slight thickening	15 (46.9)	6 (54.5)	
	Irregular thickening	6 (18.8)	2 (18.2)	
	Massive thickening	8 (25.0)	0 (0.0)	0.066
Thickening of the mesentery	None	14 (43.8)	9 (81.8)	
	Slight thickening	12 (37.5)	2 (18.2)	
	Irregular thickening	4 (12.5)	0 (0.0)	
	massive thickening	2 (6.3)	0 (0.0)	0.029
Stellate pattern findings	Yes	11(34.4)	3 (27.3)	
	No	21(65.6)	8 (72.7)	0.665
Pleural plaques	Yes	13 (44.8)	0 (0.0)	
	No	16 (55.2)	11(100.0)	0.007

difference was not statistically significant (44% *vs*. 18%, p=0.066).

Thickening of the mesentery was categorized as none, mild, irregular thickening, or massive thickening (defined as ≥3 mm, Figure 3C). Thickening of the mesentery was detected more frequently in MPM cases than in non-MPM cases (56% *vs*. 18%, p=0.029).

We examined stellate pattern findings as an indicator of mesenteric vascular enlargement (Figure 3D). Stellate patterns were detected in 11 cases (34%) in the MPM group and in three cases (27%) in the non-MPM group. This difference was not statistically significant (p=0.665).

Finally, pleural plaques were examined in chest CT images, which were available for 29 out of the 32 MPM

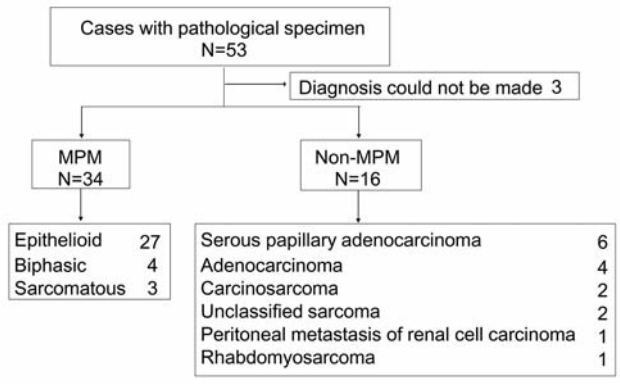

Figure 2. *The breakdown of the confirmed pathological diagnosis of enrolled patients.*

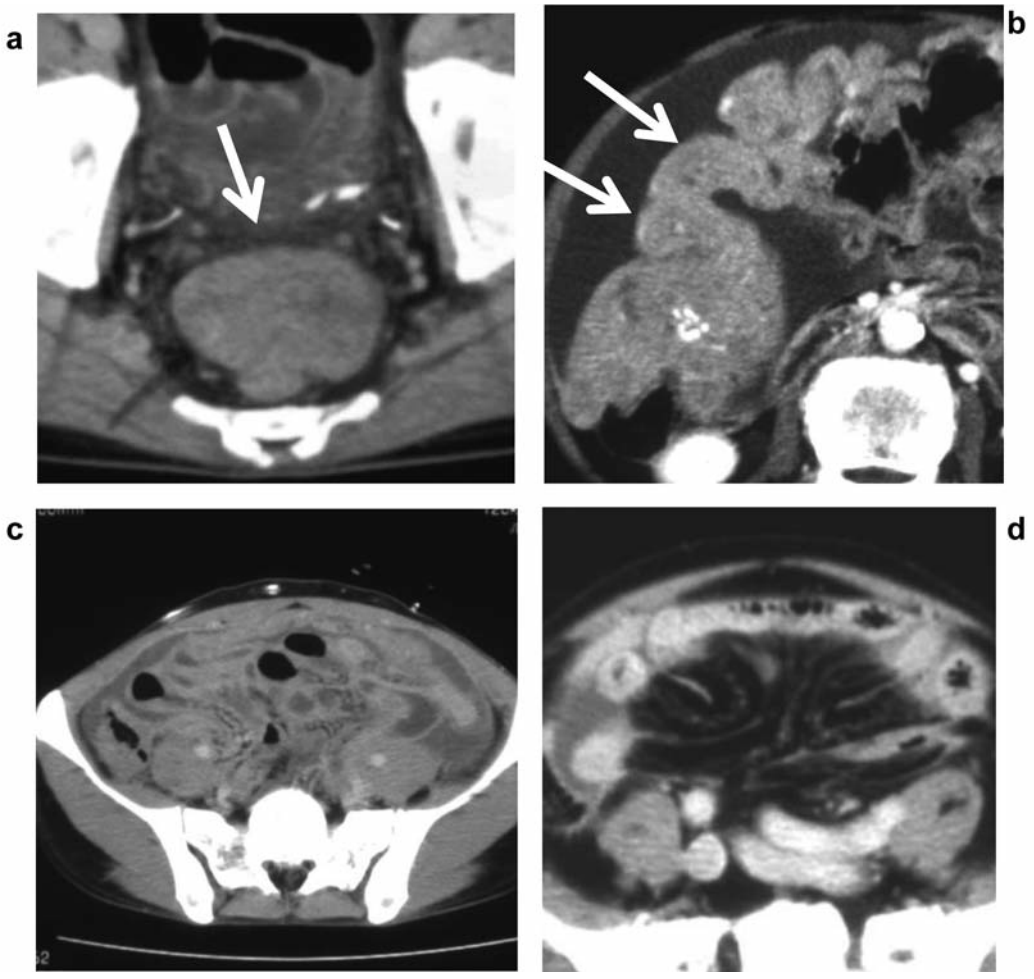

Figure 3. *Examples of computed tomographic images of malignant peritoneal mesothelioma with maximum dimension of the nodular lesion >5 cm (A), massive thickening of the peritoneum (B), massive thickening of the mesentery (C), and stellate structure findings (D).*

cases and 11 of the non-MPM cases. Pleural plaques were detected in 13 cases (45%) in the MPM group. None were detected among the non-MPM cases.

Proposal of an MPM-CT index. Among the findings analyzed above, we selected six findings that were detected more frequently in MPM than in non-MPM with a *p*-value of <0.100: degree of accumulation of ascites, maximum dimension of the nodular lesion, number of tumor masses, extent of peritoneal thickening, extent of thickening of the mesentery, and pleural plaques. In each case, CT findings were scored as 1 in the case of (i) moderate to massive accumulation of ascites, (ii) maximum dimension of nodular lesion <1 cm, (iii) multiple nodular lesions, (iv) irregular to massive thickening of the peritoneum, and (v) mild to massive thickening of the mesentery. The MPM-CT index was determined in each case as the sum of these six findings. As shown in Figure 4A, the index was significantly higher in MPM than in non-MPM cases (p=0.001). To evaluate the utility of the index for differentiation between MPM and non-MPM cases, we performed an ROC analysis. The AUC value for the differential diagnosis between the two groups was 0.821 (95% confidence interval=0.694-0.945) (Figure 4B). Based on a cutoff value of 3, sensitivity was 53% and specificity was 100%.

Discussion

MPM is poorly described and the knowledge of its natural history is very limited. In previous reports, at least 70% of cases of MPM were associated with chronic exposure to asbestos (10, 11); however, it is not clear how inhaled asbestos induces peritoneal neoplasms.

It is often difficult to make a pathological distinction between MPM and peritoneal metastatic adenocarcinoma (12, 13), although some immunohistochemical markers, such

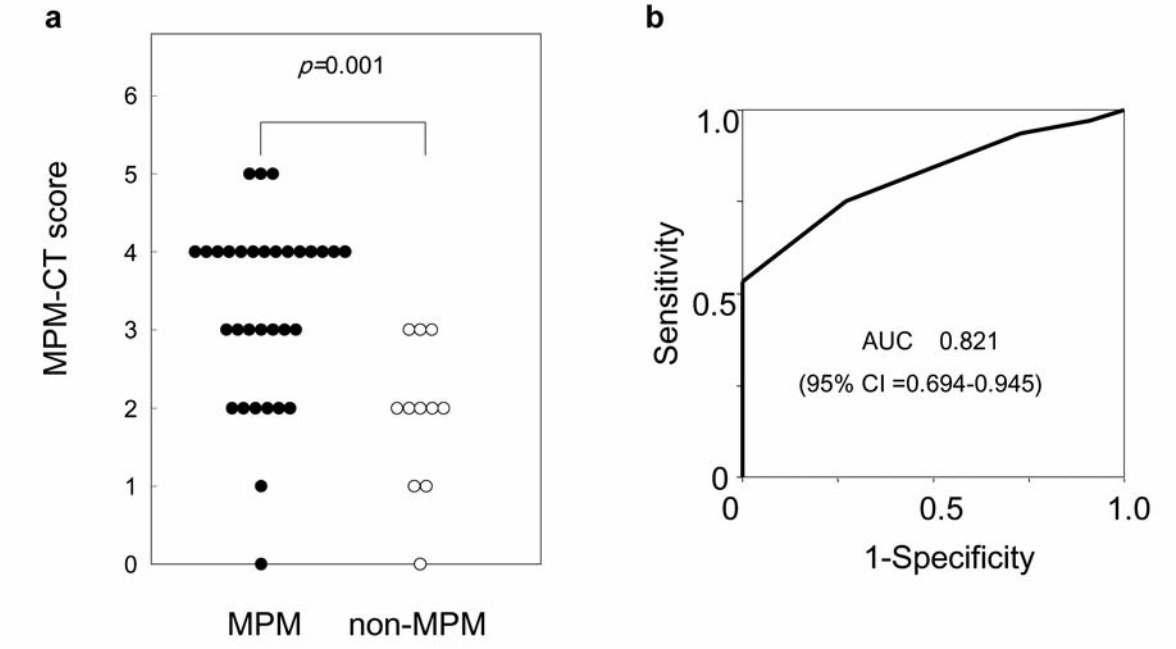

Figure 4. *A: Comparison of malignant peritoneal mesothelioma (MPM)–computed tomography (CT) index between MPM and non-MPM groups. B: Receiver operating characteristic curves to evaluate the usefulness of the MPM-CT index for the differentiation between MPM and non-MPM.*

as calretinin, thrombomodulin, and cytokeratin 5/6, could facilitate this (14, 15). In the current study, we reviewed the pathological specimens of 53 cases that had been diagnosed as MPM, and confirmed a diagnosis of MPM in only 34 cases (64.2%). The difficulty involved in making a clinical and pathological differential diagnosis often results in a diagnostic delay. Factors contributing to the diagnostic delay include the rarity of this entity, the long latent period from the exposure to asbestos, and the non-specific clinical features of the disease. Biochemistry and tumor markers are of limited assistance in this regard.

In the current study, we analyzed CT features of MPM. For this purpose, we extracted all cases of death due to MM between 2003 and 2005 based on death records from the Vital Statistics in Japan. A strength of our study is that it contained many cases of MPM. To the best of our knowledge, this is the largest study of radiological analysis of MPM. We tried to analyze 105 cases in which the clinical diagnosis of MPM had been made, and after the pathological review of the provided specimens, we determined there were 34 MPM cases. We had to accept the low collection rate of the study based on the postal mail method. However, there is no selection bias throughout the process of data collection.

There is a wide spectrum of imaging findings in MPM, the most common of which include a thickening of the mesentery and peritoneum. Findings on CT images are highly variable; therefore differentiating MPM from other intra-abdominal malignancies is difficult (12, 16-18). Based on the results of the current study, we proposed the use of an MPM-CT index that comprises accumulation of ascites, maximum dimension of the nodular lesion, number of tumor masses, extent of peritoneal thickening, extent of mesenteric thickening, and pleural plaques. We found marked differences in these findings between the MPM and non-MPM groups. With a cut-off score of 3, diagnostic sensitivity was 53% and specificity of 100%, while ROC analysis revealed an AUC value of 0.821. These results indicate the clinical utility of this MPM-CT index for the differential diagnosis of MPM. In fact, the sensitivity is around 50%; however, the high specificity would contribute to the differentiation.

A limitation of the current study is that this was a retrospective analysis. A validation study to confirm the utility of the index is warranted, with a new patient cohort that includes pathologically confirmed MPM cases and other peritoneal malignant conditions.

Conclusion

MPM is a rare tumor that is difficult to diagnose and treat. An accurate diagnosis of MPM is essential in order to determine the prognosis, and occupation-related compensation claims following asbestos exposure. MPM demonstrates characteristic radiological findings, and the MPM-CT index may be useful for the differential diagnosis of MPM.

Conflicts of Interest

None.

Acknowledgements

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