Original Article

The role of computed tomography in characterization, diagnosis and staging of malignant pleural mesothelioma in a sample of Iraqi patients

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Abstract:

Background: malignant pleural mesothelioma (MPM) is uncommon neoplasm arising from mesothelial cells of the pleura. The most important etiologic agent is typically related to exposure to minerals fibers such as asbestos and erionite. Computed tomography (CT) plays essential role in characterization, diagnosis and staging of MPM.

Objectives: to determine the value of CT scan in characterization of MPM and its impact on diagnosis, and staging of the disease with histopathological correlation.

Patients and methods: the CT scan of 27 patients who had diagnosed of MPM were retrospectively evaluated, additionally CT findings of histopathological subtypes were compared and determine staging of the disease according to their documented CT findings. The study was performed at Medical City Teaching Hospitals and Hospital of Radiation & Nuclear Medicine in Baghdad from period of 2008 to 2014.

Results: Fifteen patients were male and twelve patients were female with percentage of (55.5%, 44.4%) respectively with age range of 36-66 years, 37% of patients were coming from area closed to asbestos manufacture in Baghdad, but only 14.8% of them had history of exposure to asbestos. histological subtypes analysis revealed that epitheliod types is the most frequent type occurred in 63% of patients, sarcomatoid type in 22.2% of patients and mixed (biphasic) type in 14.8% of patients. The statistical analysis of CT findings of different histological subtypes reveal that the interlobar fissure involved in 100% of patients, paranchymal lung involvement in 67%, chest wall involvement in 67%, pericardial involvement in 67%, mediastinal lymphadenopathy in 67% which are more significant with p-value <0.05 in sarcomatoid subtypes than alternate histological subtypes. Regarding the staging of MPM, the study show stage I in 11.1% of cases, stage II in 37.1, stage III in 25.9%, and stage IV in 25.9%.

Conclusion: This study show that contrast-enhanced CT of the chest and upper abdomen plays a fundamental role in characterization and categorization of key findings of malignant pleural mesothelioma and convert it into the updated staging system to guide appropriate evaluation and management.

Key Words: Mesothelioma, Computed tomography, asbestos exposure, pleural effusion.

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Introduction:

Malignant pleural mesothelioma is un common locally aggressive neoplasm that originate in the serosal membrane that line the thoracic cavity with invasion of the chest wall, mediastinum and diaphragm.1 The disease has become an important health issue over recent years since the incidence of malignant pleural mesothelioma has risen for some decades and is expected to peak sometimes between 2010 and 2020 due to the patterns of occupational exposure. The incidence per year of mesothelioma is currently of 3000 cases in united states.2 A strong association between malignant mesothelioma and asbestos exposure is observed3; however, reports suggest that radiotherapy may also cause mesothelioma4,5 and genetic factors may also play a role in MPM.6,7,8 So those employed in manufacture and industrial use of asbestos and those remotely connected with asbestos or living near asbestos plants are at risk of developing mesothelioma.9

MPM is not a simple disease to diagnose and most frequently achieved with careful review of clinical and radiological finding in addition to confirming tissue biopsy.10 Radiological modalities play a fundamental role in the assessment of malignant mesothelioma. CT scan is the primary imaging technique used for the diagnosis and staging of malignant mesothelioma and for guiding biopsy for tissue diagnosis.11 The International Mesothelioma Interest Group (IMIG) proposed a tumor-node-metastasis (TNM) staging system for MPM. This staging system is based on data suggesting that

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overall survival in MPM is related to the extent of the primary tumor (T status) and to lymph node involvement (N status), M (distant metastasis).12,13

The main purposes of the current study to determine the value of CT scan in characterization of MPM and its impact on diagnosis, and staging of the disease and to correlate CT findings with histopathological subtypes and to emphasize the possible risk factor of MPM in Baghdad governorate.

Patients and methods:

We retrospectively reviewed the CT scan of 27 patients with biopsy-proven MPM during period of study from 2008 to 2014, which evaluated at Medical City Teaching Hospitals and Hospital of Radiation & Nuclear Medicine. Age of the sample of the study ranges from 36-66 years. History of smoking, occupational hazard mainly exposure to the asbestos, and radiation therapy were obtained; family history and residency were also recorded. Thoracic CT scan was performed in all patients, using different brands of CT appliance, Toshiba (Aquilion) as definition of 64 multislice (120 KV, 250 mAs, slice thickness 5 mm), Siemens (Somatom) as definition of 64 multislice (120 KV, 200-300 mAs, slice thickness 6mm). CT evaluation was carried out from lower neck to lower abdomen with scan time of (12 sec). All sections (sagittal and coronal reformatted images were performed from initial axial CT data images), acquisition were taken in the supine position at the end of inspiration. Mediastinal, bone and lung window settings were used. Intravenous iodinated contrast medium (70 ml of omenipaque of 350 ml/mg concentration), the total dose of the contrast medium in adult injected by injector in the range (1-2 ml/kg) dose) was given to the patients with normal respiratory function, to further characterization of the lesion, and to determined mediastinal lymph node enlargement and/ or the relation of the lesion to adjacent vascular structures. Histopathological diagnosis of MPM was confirmed in all cases. All CT scan sections were reviewed by board-certified radiologist. On CT scan, pleural thickening was classified as diffuse, nodular/irregular, or mass; thickening of the pleura of 10 mm was defined as pleural thickening10-30 mm focal pleural thickening as" pleural nodule", pleural based soft tissue mass-like lesion with width of 30 mm or more was referred to as "pleural mass" and with using of contrast media the pattern of enhancement either heterogeneous, homogenous or peripheral. Localization of pleural effusion as ipsilateral and bilateral. Involvement of interlobar fissures, mediastinal pleura and pericardial involvement were noted. The presence of pleural calcifications was also recorded. Dislocation of the mediastinal structures due to pleural lesions was defined as mediastinal shift. Contraction of the involved hemithorax or mediastinal displacement, distortion of bronchovascular structures, elevation of the ipsilateral hemidiaphragm and compensatory hyperinflation of contralateral lung were evaluated as 'volume contraction ". Mediastinal lymph nodes were considered pathologically as enlarged, if they were greater than 10 mm in short-axis diameter in the transverse plane. Both hemi- thoraces were evaluated for pulmonary parenchymal abnormalities such as tumoral invasion or fibrosis and if there is pnemothorax, hemorrhagic changes, and cystic changes. Also the patients evaluated if they have chest wall invasion, peritoneal involvement. All patients were radiologically staged according to the International Mesothelioma Interest Group proposed a tumor-node-metastasis (TNM) staging system for MPM. Pleural biopsies were obtained and analyzed to determine the histopathological subtypes of MPM. Histopathologically, the MPM is classified into epitheliod, sarcomatoid, mixed subtypes and CT findings for each subtype are statistically analysed separately to determine the specific CT features of different subtypes. Collected clinical, radiological and histopathological data were statistically analyzed using SPPS software version 18.0. Grouped data were presented as mean+- SD unless otherwise specified, while Chi-square and Fishers Exact tests were used to evaluate the association among varying factors. A p-value equal or < 0.05 was considered significant, with confidence level of 95%. Finally all findings and results were presented in tables and figures with an explanatory paragraphs for each table and figure.

Results:

In our study, we evaluate the CT scan of 27 patients with biopsy–proven MPM (15 men and 12 female).Their mean age was 50.2+-9.3 years, with a range of 36-66 years. Nearly six of them were coming from AL–Zafaranya district, four of them from AL-Madaen region, the rest of patients distributed from different locations. We found that 4 patients (14.8%) have history of occupational hazard like asbestos, 11 patients (40.7%) were smokers, and one patient (3.7%) had history of radiation for her breast carcinoma. Two patients (7.4%) were sisters (positive family history). They presented with chest pain in 26 patients (96.3%), dyspnea in 20 patients (74.1%), and cough in 16 patients (55.6%), few patients presented with pallor, weight loss, and hemoptysis. We found MPM occurred in the right hemithorax in 19 patients (70.4%), as compared to the left hemithorax in 8 patients (29.6%). In all patients the pleural thickening showed homogenous enhancement in 9 patients (33.3%), heterogeneous in 17 patients (63%), peripheral enhancement in one patient (3.7%).The visceral and parital pleura could not be distinguished unless pleural fluid was present. The pleural fluid was present on the CT scan of 25 patients (92.6%) (One patient (3.7%) had effusion on both side, two patients (7.4%) had no effusion. The pleural thickening ranged from diffuse pleural thickening (pleural

thickness of 10 mm) in 15 patients (55.6%), nodular (focal pleural thickness of 10-30 mm) in 6 patients (22.2%), pleural mass (lesions of 30 mm or more in diameter) in 5 patients (18.5%), only one of these 5 patients had chest wall invasion. One patient (3.7%) showed hemorrhagic changes, and also one patient (3.7%) showed cavitation. We found mediastinal pleural involvement in 22 patients (81.5%), the tumor extend to involve the interlobar fissure in 18 patients (66.7%) and involved lung paranchymal in 8 patients (29.6%). Additionally, pleural calcification was found in one patients (3.7%). Atelectasis was found in 8 patients (29.6%). Contraction of involved hemithorax was noted in 13 patients (48.1%), those 13 patients showed ipsilateral mediastinal shift. We found contralateral mediastinal shift in 4 patients (14.8%) due to either large effusion in two patients and tumoral masses in two another patients. MPM spreads primarily by local extension throughout pleural cavity, so we found chest wall invasion in 8 patients (29.6%), pericardial involvement in 9 patients (33.3%), and mediastinal lymphadenopathy in 9 patients (33.3%). Also we found that the MPM extend beyond the thoracic cavity inform of peritoneal involvement in 6 patients (22.2%), hepatic metastasis in 2 patients (7.4%). CT findings of patients are summarized in table (1).

Biopsy was performed to all patients, histopathological subtypes analysis revealed that epitheliod types is the most frequent type occurred in 17 patients (63%), sarcomatoid type in 6 patients (22.2%) and mixed (biphasic) type in 4 patients (14.8%).

The statistical analysis of CT findings seen in histopathological subtypes show that the interlobar fissure (100%), paranchymal lung involvement (67%), chest wall involvement (67%), pericardial involvement (67%), mediastinal lymphadenopathy (67%) are more significant with p- value <0.05 in sarcomatoid type than alternate histopathological subtypes. CT finding in all histological types are shown in table (2). Finally, in our results, regarding staging of MPM, we found that our patient were more at stage I (11.1%), stage II (37.1), stage III (25.9%), stage IV (25.9%).

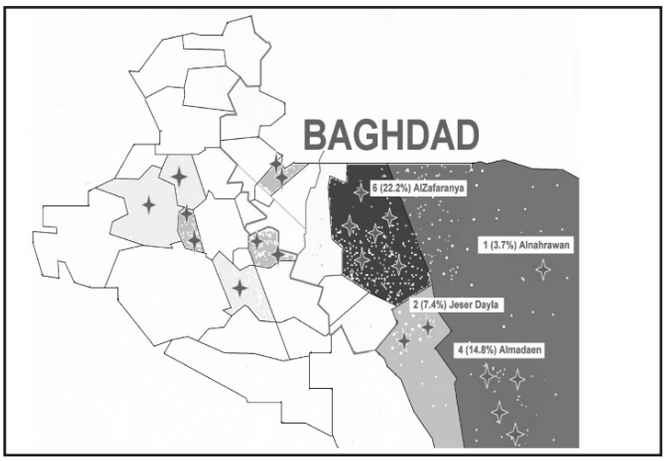

Figure (1) distribution of the patients in districts of Baghdad governorate

Table (1) distribution of the patients according to CT findings.

CT finding		Frequency	Percentage
Pleural Involvement	Normal Pleural Appearance	1	3.7
	Diffuse	15	55.6
	Nodular or Irregular	6	22.2
	Mass	5	18.5
Side	Right	19	70.4
	Left	8	29.6
Pleural Effusion	No Effusion	2	7.4
	Unilateral	24	88.9
	Bilateral	1	3.7
Mediastinal Pleural Involvement		22	81.5
Interlobar Fissure Involvement		18	66.7
Pericardial Involvement		9	33.3
Pleural Calcification		1	3.7
Lung Volume	Normal	14	51.9
	Reduced	13	48.1
Atelectasis		8	29.6
Mediastinal Lymphadenopathy		9	33.3
Ipsilateral Mediastinal Shift		13	48.1
Chest Wall Invasion		8	29.6
Parenchymal Lung Involvement		8	29.6
Peritoneal Involvement		6	22.2
Haemorrhagic Changes		1	3.7
Cavitation		1	3.7
Pattern of Enhancement	Homogenous	9	33.3
	Heterogenous	17	63
	Peripheral	1	3.7

Table (2) CT finding of different histopathological subtypes of MPM.

CT finding		Histopathology (%)					
		Epitheloid		Sarcomatoid		Mixed	
		(n=17)	%	(n=6)	%	(n=4)	%
Pleural Involvement	Normal	1	5	0	0	0	0
	Diffuse	10	59	4	66	1	25
	Nodular or Irregular	3	18	1	17	2	50
	Mass	3	18	1	17	1	25
Side	Right	12	71	4	67	3	75
	Left	5	30	2	33	1	25
Mediastinal Pleural Involvement		13	77	6	100	3	75
Interlobar Fissure Involvement*		10	59	6	100	2	50
Pericardial Involvement*		5	29	4	67	0	0
Pleural Calcification		0	0	0	0	1	25
Lung Volume	Normal	10	59	1	17	3	75
	Reduced	7	41	5	83	1	25
Atelectasis		5	29	2	33	1	25
Mediastinal Lymphadenopathy*		4	24	4	67	1	25
Mediastinal Shift		8	47	4	67	1	25
Chest Wall Invasion*		3	18	4	67	1	25
Parenchymal Lung Involvement*		3	18	4	67	1	25
Peritoneal Involvement		3	18	2	33	1	25
Haemorrhagic Changes		1	6	0	0	0	0
Cavitation		1	6	0	0	0	0
Pattern of Enhancement	Homogenous	7	41	0	0	2	50
	Heterogenous	10	59	6	100	1	25
	Peripheral	0	0	0	0	1	25

*: p-value < 0.05 for sarcomatoid group versus alternate groups.

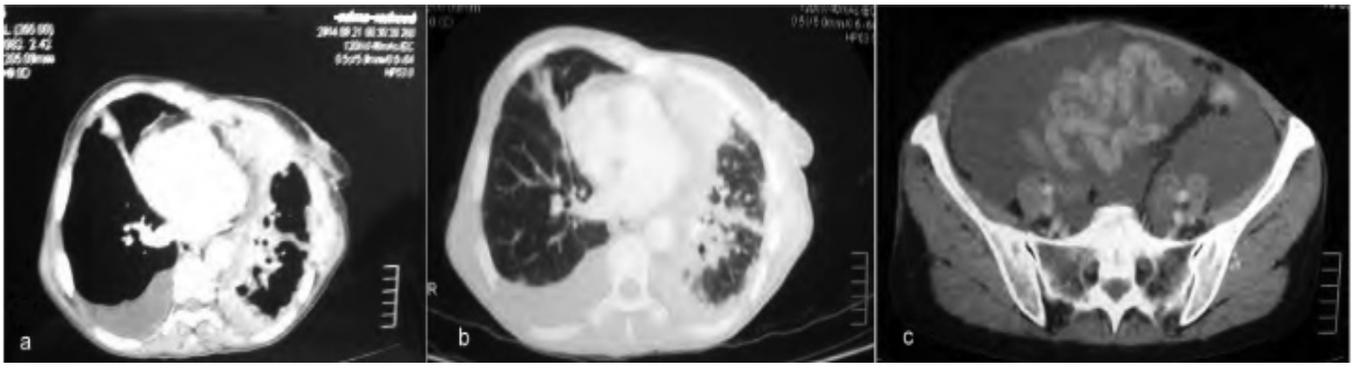

Figure (2) 54 years-old female presented with chest pain and dyspnea. Axial contrast-enhanced CT paranchymal (a) and mediastinal sections (b) shows irregular and circumferential left-sided pleural thickening, involvement of interlobar fissure and pericardial involvement with left lung volume contracture. Right sided pleural effusion also noted. (C) axial contrast enhanced CT abdomen shows abdominal involvement inform of ascites proved as malignant ascites by cytological study.

Discussion:

Malignant pleural mesothelioma is uncommon, highly aggressive cancer that arise from mesothelial cells that line pleural cavity. Its incidence is 2.2/ million/year. MPM has a poor prognosis with a median survival from diagnosis of 9 to 12 months. In our study, mean age of patients is 50.2+-9.3 SD, being more in male than female, these results were comparable to Dogan et al15, while at Hussain WM16 the patients presented mainly in the 4th decade of life. There was a considerable association between malignant mesothelioma and asbestos exposure; nearly 10 patients (37%) were coming from south eastern of Baghdad (from AL-Zafaranyaa and AL-Madaen) where the risk of environmental exposure to asbestos is high due to asbestos manufacture in AL-Rasheed camp, but in those patients such exposure may be difficult to document because only four patients reported as asbestos worker. In Elizabith Alexander et al17 confirmed that those employed in asbestos manufacture and those remotely connected with asbestos (such as wives of asbestos workers) and those living in near asbestos plants are at risk of developing MPM. This may gave us an explanation for those who were living in south eastern of Baghdad, they were presented in the 4th decade of life (youngest than other patients who belong to other residents). In our study one female patient had history of breast cancer treated with radiotherapy, this goes with De Burin ML et al4 reported that radiotherapy may cause mesothelioma. Two patients with family history of mesothelioma, this also goes with Hussain WM.16 Testa JR et al8 reported that the genetic factor may play a role in MPM. Eleven patients (40.7%) had history of smoking but according to Mossman BT et al18 said that the smoking is not a risk factor for MPM, however patients with smoke and have exposed to asbestos are at increased risk factor for MPM. In addition patients who smoke should be encouraged to quit because smoking impedes treatment (delay wound healing after surgery).19 the patients were presented by chest pain, dyspnea and cough more than other symptoms. Nearly all patients with chest pain, two third patients with dyspnea. This confirmed by Hussain WM16 that dyspnea is the sign of advancement of disease and this comparable with our study results that most of our patients belong to advanced stages. Radiological imaging is important for diagnosis, staging and management of mesothelioma. After evaluation of CT scan of the sample of the study, we found that the most common CT finding is pleural thickening occurred in (96.3%), and more frequent in right hemithorax as compared to left hemithorax this confirmed by Elif Aktas et al20 and Dogan OT et al.15 In all patients the pleural thickening showed marked enhancement inform of heterogeneous in 63%, homogenous in 33.3% and peripheral in 3.7%. Although, contrast medium enhancement may be present in any pleural malignancy as well as an active benign process such as infection21, the tumor tissue of mesothelioma usually shows heterogeneous enhancement on post contrast scan22, at P.Maailta et al study reported in all but one patient the pleural thickening showed marked contrast medium enhancement.23

CT is also though to allow a precise characterization of different types of pleural thickenings. We detected that diffuse pleural thickening in 56% of the patients, the most common type in our study. In A. Senyigit et al24 reported that the diffuse pleural thickening is a manifestation of asbestos exposure, in this study only four patients documented to have asbestos exposure. Nodular pleural thickening seen in 22% while Leung et al25 reported 64%, it is possible that this discrepancy was result of the fact that our cases were in advanced stages at which diffuse pleural thickening had already developed. The last type is tumoral masses detected in 18.5% which is less than Dogan OT et al15 reported. We detected unilateral pleural effusion in 89% of our cases, bilateral in 4% as Ismail –Khan et al26 reported & A. Senyigit et al.24 However, in some cases, pleural effusion may be the only finding without pleural thickening confirming this Leung et al25 reported pleural effusion as a unique finding of neoplastic involvement in 7.6% of their cases and Yilmaz et al27 detected MPM in 1 of 46 cases with MPM have no pleural thickening. Hence, it has been proposed not to exclude a possible diagnosis of MPM in the absence of pleural thickening. Pleural calcification occurred in only one of our cases, this against other studies as Elif Aktas et al20 & Dogan OM et al15 that reported pleural calcification occurred in 20% but Senyigit A. et al24 reported that pleural plaques were infrequently encountered in mesothelioma by CT and suggested that this could be a result of absorption of the calcification by the tumor.25 We detected mediastinal pleural thickening occurred in 81% , interlobar fissure in 66.7% and atelectatic changes in 29% these were comparable with Senyigit A et al24 and Dogan OT et al15 reported these finding are the earliest finding of MPM detectable by CT. Volume contraction occurred in 48.1% and in those patients, all of them showed ipsilateral mediastinum shift, these were comparable with Senyigit A et al24 and Dogan OM et al15 and more than Elif Aktas et al.20 In this study, parenchymal lung involvement occurred in 29.6% as Dogan OM et al15 reported similarly, Rabinowitz et al28 reported that intra-parenchymal lesions histologically represented malignant mesothelioma in patients with mesothelioma. As the diseased advanced we see chest wall invasion, mediastinal lymphadenopathy and pericardial involvement. In our study we found these finding in 29.6%, 33.3% & 33.3% respectively. These findings are comparable with Dogan OM et al15 and Elif Aktas et al.20

In more advanced cases, we found peritoneal involvement in 22.2% and hepatic metastasis in 7.4%, these were comparable to Elif Aktas et al.20

In this study all patients proved their disease by biopsy revealed three histological types, epitheliod type was the most common type occurred in 63%, sarcomatoid type in 22.2%, mixed type in 14.8%, these were comparable with Akira Kawashima et al29, but against Hussain WM et al16 reported only 5% of epithelial type. Although the degree of therapeutic efficacy is reported to be closely related to the histological structure of the tumor, to our knowledge, these are limited studies investigating CT features of histologic subtypes of MPM.

In our study, however, the frequency of most CT finding detected in all three subtypes was not much different. The only significant differences were that interlobar fissure involvement, paranchymal lung involvement, chest wall involvement, pericardial involvement, mediastinal lymphadenopathy was more frequent in sarcomatoid type compared to other subtypes, these were comparable to A. Senyigit et al.24 Otherwise, we can not found any significant difference in epithelial type when compared with non epithelial types. Although the presence of extensive lesions suggested sarcomatous type, there was no significant difference in the localization and characteristic of the tumor (as being diffuse, nodular or mass type). Although CT scan is the primary imaging modality for staging of MPM, in our study we do CT staging according to their patients data (CT chest and abdomen), we found stage II most frequent isolated stage but more than half of our patients (51.8%) had advanced stages (stage III & stage VI). This comparable with S. Cicenas et al30 and Hussain WM16 reported that most of patients belong stage II of the disease.

Conclusion:

This study show that contrast-enhanced CT of the chest and upper abdomen plays a fundamental role in characterization and categorization of key findings of malignant pleural mesothelioma and convert it into the updated staging system to guide appropriate evaluation and management. This study try to pass a message to radiologists in favor of increase their awareness regarding early key findings of MPM on the first diagnostic workup by CT scan in view of the fact that diagnosis if made in the early stages of disease may improved the survival and decreased morbidity and mortality. Probable exposure to the asbestos, family history and radiation therapy may considered main risk factors for MPM in Baghdad governorate since AL-Zafaranya and AL-Madaen districts show highest incidence for disease in the Baghdad which are considered the main asbestos manufacture areas in the capital.

Author contributions:

Abdullateef Aliasghar Mustafa, Zainab Ismael Murad, : Authors make substantial contributions to conception and design, and/or acquisition of data, and/or analysis and interpretation of data.

Waleed Mustafa Hussain, Abdullateef Aliasghar Mustafa: Authors participate in drafting the article or revising it critically for important intellectual content; authors give final approval of the version to be submitted

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