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Role of Multislice CT in Diagnosis, Staging and Evaluation of Malignant Pleural Mesothelioma

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ABSTRACT

Background: Malignant mesothelioma is a rare but fatal disease that arises from the epithelial lining of the pleura, peritoneum, pericardium and tunica vaginalis. Malignant pleural mesothelioma (MPM) is the most common form, accounting for 80-90% of malignant mesotheliomas

Aim of the work: was to identify the value of CT in diagnosing malignant pleural mesothelioma and applying the AJCC and the IMIG staging system for MPM. At the time to identify the limitations of CT if any.

Patient and methods: This prospective study included a total of 20 patients with CT findings suggestive of malignant pleural mesothelioma, diagnosed at Radiology Department, Damanhur Oncology Center. All patients had undergone multislice CT chest with intravenous contrast for detection and staging of the tumor. This study was conducted between March 2018 and December 2018. The data collected were tabulated and analyzed statistically.

Results: CT study of the chest for cases of MPM was able to evaluate and diagnose the disease, with most of the important staging items being easily seen on CT yet this study also showed the limitations of CT in the staging MPM since CT alone was not able to prove the involvement of the chest wall, diaphragmatic muscle and trans diaphragmatic extension.

Conclusions: Chest CT alone is often sufficient for disease staging and treatment planning. Typical CT findings that suggest MPM include unilateral pleural effusion with nodular irregular pleural thickening which can be discrete or diffuse with or without inter lobar fissure thickening and nodal metastasis.

Keywords: Multislice CT – Malignant Pleural Mesothelioma.

INTRODUCTION

Malignant mesothelioma is a rare but fatal disease that arises from the epithelial lining of the pleura, peritoneum, pericardium and tunica vaginalis. MPM is the most common form, accounting for 80-90% of malignant mesotheliomas [(1)]. It is the most common primary malignant pleural neoplasm [(2)]. The majority of cases are associated with prior asbestos exposure [(3)].

The tumor can invade both visceral and parietal pleura and frequently extends to adjacent structures. MPM is locally aggressive with frequent invasion of the chest wall, mediastinum, and diaphragm [(4)].

The prognosis is poor, with a median survival time of 12 months after diagnosis. Several factors have been shown to correlate with reduced survival time which are intrathoracic lymph node metastases, distant metastatic disease, and extensive pleural involvement [(2)].

The primary role of imaging in malignant mesotheliomas lies in preoperative staging and assessment of treatment response, disease recurrence, or metastasis [(5)]. CT with contrast is the most frequently obtained examination owing to its easy accessibility [(5)].

It is the most frequently used modality in the preoperative assessment of patients being considered for surgical resection [(4)].

Low-dose CT has a greater sensibility than chest X-ray to detect tumor at early and treatable stage in screening population [(6)].

Key CT findings that suggest MPM include unilateral pleural effusion, nodular pleural thickening and inter lobar fissure thickening [(2)].

Chest wall invasion manifests as obliteration of fat planes or chest wall nodules. There is also frequent contraction of the affected hemithorax with associated ipsilateral mediastinal shift, narrowed intercostal spaces, and elevation of the ipsilateral hemidiaphragm [(4)]. FDG PET/CT which superimposes functional imaging over the anatomical mapping yields a more accurate presentation of mesothelioma [(7)].

FDG PET is generally good in differentiating benign lesions from malignant mesothelioma, which helps in detecting recurrence and provides prognosting information (staging, survival, mortality, etc) [(1)].

It is important to stress that a diagnosis of mesothelioma cannot be made exclusively with imaging studies. Biopsy is absolutely essential for the accurate diagnosis of mesothelioma [(2)].

The aim of the current study was to identify the value of CT in diagnosing malignant pleural mesothelioma and applying the AJCC and the IMIG staging system for MPM. At the time to identify the limitations of CT if any.

PATIENT AND METHODS

This prospective study included a total of 20 patients with CT findings suggestive of malignant pleural mesothelioma, diagnosed at Radiology Department, Damanhur Oncology Center.

Approval of the ethical committee of Al-Azhar Faculty of Medicine (girls) and a written informed consent from all the subjects were obtained. This study was conducted between March 2018 and December 2018.

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Patients were referred for CT chest examination from the Medical and Surgical Oncology Clinic, Damanhur Oncology Center, Damanhur Chest Hospital and Alexandria University Hospital.

All patients had undergone multislice CT chest with intravenous contrast for detection and staging of the tumor.

Inclusion criteria

Patients with CT chest findings suggestive of malignant pleural mesothelioma.

Exclusion criteria

Patients who had contraindication to radiation exposure as pregnant women or contra indication to contrast media as patient who have hypersensitivity or renal failure.

All patients were subjected to:

A. **History taking including:** Age, residence, occupational exposure of asbestos and local chest symptoms and symptoms of distant metastasis.

B. **Clinical general and chest examination.**

C. **Laboratory tests:** mostly complete blood picture and bleeding profile.

D. **Plain Chest X-ray in PA view.**

E. **Multislice CT with IV noniodinated contrast medium examination** with multi-detector row CT scanner which will be performed in the craniocaudally direction as follows:

1) Employment of a contrast medium is mandatory. The CT scanning delay should be also set at 60-80 seconds to optimize the maximum pleural tumor uptake.
2) Dose of contrast medium: 100 ml intravenous just before the examination.
3) The field-of- view (FOV) due to the tumor growth through the diaphragmatic pillars had to cover a wide area from the lung apex to L3.
4) Slice thickness: 10 mm contiguous sections.
5) Radiation factors: kv: 120-140 and mAmp: 200.
6) Window-level: lung window 1200-600, mediastinal window 300-30, and bone window 1500-250.

F. **Histopathological assessment** was done either by U/S guided or CT guided True-Cut biopsy. U/S guided biopsy is the preferred method if the thickening is seen by U/S. If the thickening wasn't visible or accessible via U/S, CT guided biopsy was performed.

Statistics

The data collected were tabulated and analyzed by SPSS (Statistical package for the social science software) statistical package version IBM compatible computer.

RESULTS

This study was carried out on 20 malignant pleural mesothelioma patients. Their ages were ranged between 30 to 82 years.

Age: Table 1 shows the age groups between the studied patients.

Table (1): The age groups of the studied patients.

	Age groups					
	30-	**40-**	**50-**	**60-**	**70-**	**80-**
Count	3	2	5	5	4	1
%	15.0%	10.0%	25.0%	25.0%	20.0%	5.0%

- **Gender:** The study group consisted of 13 males and7 females, Table 2.

Table (2): Gender variation among the MPM patients.

	Sex	
	Male	**Female**
Count	13	7
%	65.0%	35.0%

- **Laterality:** Ten (50%) of the cases showed right sided disease equal to ten (50%) showed left sided disease, Table 3.

Table (3): Laterality among the studied patients.

	Side	
	Right	**Left**
Count	10	10
%	50.0%	50.0%

- **History of asbestos exposure**, Table 4.

Table (4): History of asbestos exposure among the studied cases

	History of asbestos exposure	
	Positive	**Negative**
Count	8	12
%	40.0%	60.0%

- **Fissural involvement:** Lung fissures showed a high percentage of involvement in 13 (65.0%) cases, Table 5.

Table (5): Fissural involvement among the studied cases.

	Fissural involvement	
	Positive	**Negative**
Count	13	7
%	65.0%	35.0%

- **Pleural effusion:** Most cases are associated with pleural effusion in about 11 cases including one case with hydropneumothorax, Table 6.

Table (6): Pleural effusion among the studied MPM cases.

	Pleural effusion		
	Positive	**Hydro-pneumothorax**	**Negative**
Count	10	1	9
%	50.0%	5.0%	45.0%

- **Circumferential pleural involvement**, Table 7.

Table (7): Circumferential distribution among the studied patients.

	Pleural affection			
	Localized costal mass	Costal and diaphragmatic pleura	Costal and Mediastinal pleura	All-circumferential
Count	2	2	3	13
%	10.0%	10.0%	15.0%	65.0%

- **Hemi thorax volume:** It is decreased in in about 12 (60.0%) cases, Table 8.

Table (8): The hemi thorax volume in MPM patients.

	Hemi-thorax volume	
	Not affected	**Decreased**
Count	8	12
%	40.0%	60.0%

- **Lung affection**, Table 9.

Table (9): Lung affection in MPM patients.

	Lunge affection		
	Hematognous spread	Lymphangitis carcinomatosis	Direct affection
Count	6	2	12
%	30.0%	10.0%	60.0%

- **Chest wall invasion** Table 10.

Table (10): Chest wall invasion in the studied MPM patients.

	Chest wall invasion	
	yes	**no**
Count	2	18
%	10.0%	90.0%

- **Pattern of mediastinal affection** Table 11.

Table (11): Describes pattern of mediastinal affection

	Mediastinal affection			
	Transmural pericardial invasion	Non-transmural pericardial invasion	Tracheal or esophageal encasement	no
Count	1	6	3	10
%	5.0%	30.0%	15.0%	50.0%

- **Mediastinal nodal involvement:**
  In the form of ipsilateral bronchopulmonary /hilar lymph nodes (N1), ipsilateral mediastinal (N2) and contralateral mediastinal or supraclavicular lymph nodes on either side (N3) Table 12.

Table (12): Mediastinal lymph nodes involvement in MPM patients.

	Nodal metastasis			
	Ipsilateral hilar/bronchopulmonary lymph nodes	Ipsilateral mediastinal	Contralateral mediastinal	No
Count	3	5	4	8
%	15.00%	25.00%	20.00%	40.00%

- **Diaphragmatic affection:** Trans diaphragmatic spread upstages the disease to T4. About 4 cases (25%) that showed suspected CT evidence of diaphragmatic muscle infiltration, only one case showed definite trans diaphragmatic extension Table 13.

Table (13): Showing diaphragmatic affection in the studied MPM patients.

	Diaphragmatic affection		
	Trans diaphragmatic invasion	Suspected diaphragmatic muscle invasion	No
Count	1	4	15
%	5.0%	20.0%	75.0%

- **Distant metastasis:** Distant metastasis in MPM is infrequent. 15 (75.0%) of cases had no distant metastasis while 5 (25.0%) of cases had distant metastasis Table 14.

Table (14): Showing distant metastasis in MPM patient.

	Distant metastasis				
	Multiple Peritoneal nodules	Hepatic deposits	Hepatic, both adrenals, and posterior abdominal wall	Both adrenal glands	Negative
Count	1	2	1	1	15
%	5.0%	10.0%	5.0%	5.0%	75.0%

- **Pathological variation** Table 15.

Table (15): Shows the pathological variation of malignant pleural mesothelioma in this study proving the predominance of epithelioid type.

	Pathological variant		
	Sarcomatoid	Epithelial type	Biphasic type
Count	4	14	2
%	20.0%	70.0%	10.0%

CASES

CASE 1

A 38 years old male patient who presented with chest pain and dyspnea.

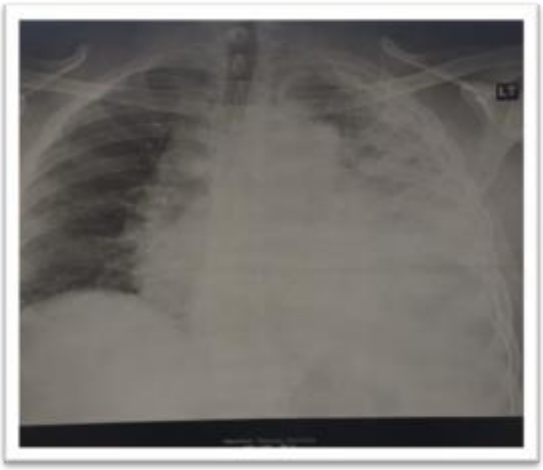

Figure1: PA chest X-Ray showing: near total left lung collapse and left pleural effusion. Also widened mediastinum??Lymphadenopathy

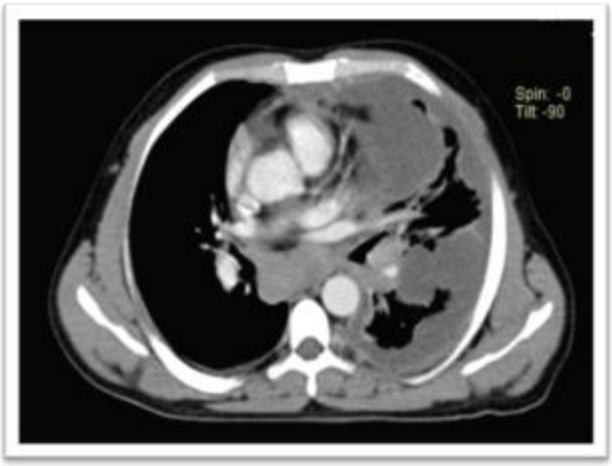

Figure 2: Axial contrast enhanced CT showing Lt sided circumferential pleural thickening involving all pleural surfaces with fissural extension and abutting the aorta.

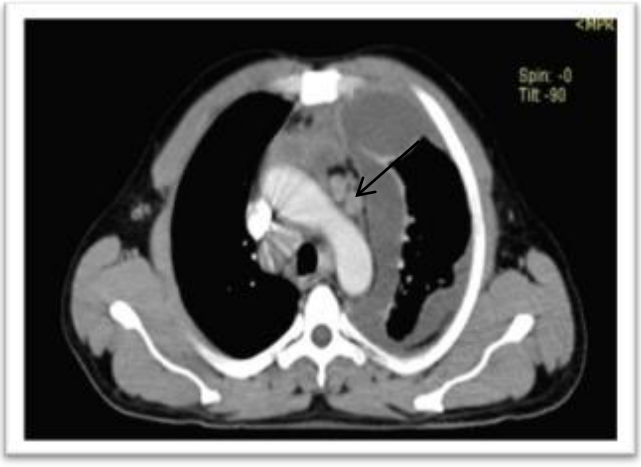

Figure 3: Axial CT scan of the chest with contrast showing: perivascular and retro-caval lymphadenopathy and pleural effusion.

CASE 2

A80 years old male patient presenting with dyspnea and weight loss.

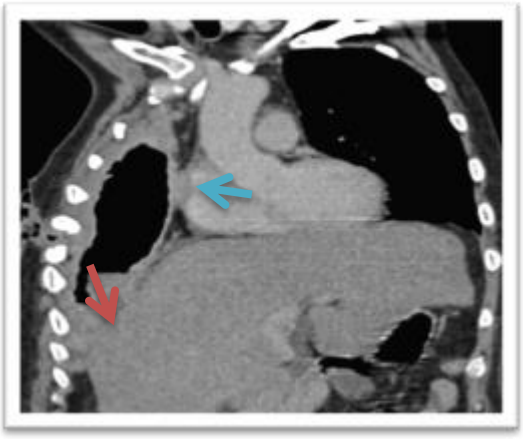

Figure 4: Coronal reformatted image of the chest showing: indistinct diaphragm with suspected diaphragmatic muscle extension and pericardial thickening (arrows).

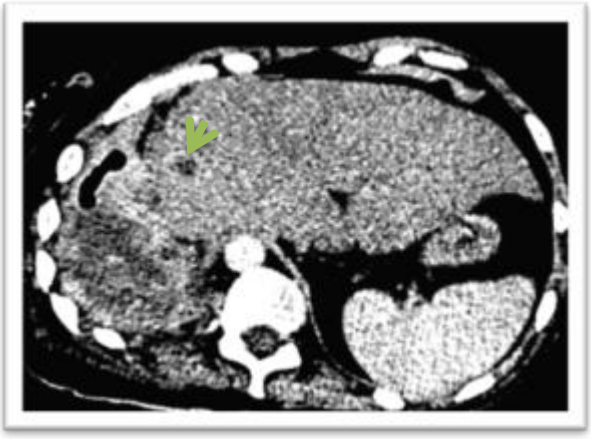

figure 5: Axial contrast enhanced CT of upper abdomen showing: hypodense marginally enhanced hepatic focal lesion.

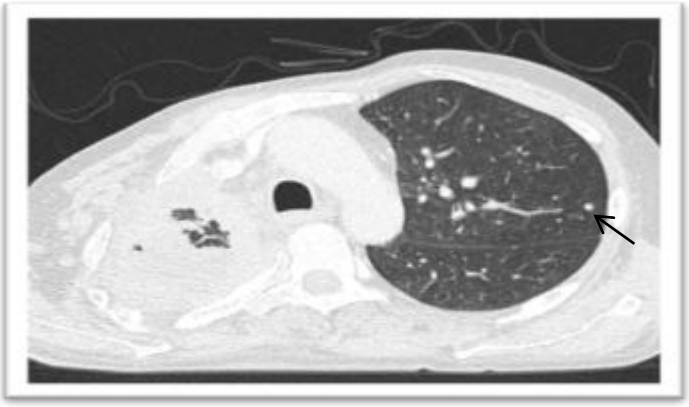

Figure 6: Axial CT chest (lung window) showing solitary left pulmonary nodule (arrow).

CASE 3

A 49 years old male patient presenting with chest pain.

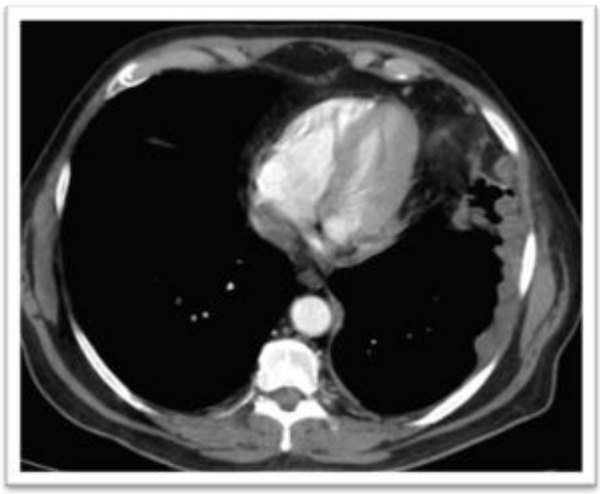

Figure 7: Axial contrast enhanced CT scan of the chest showing costal non uniform nodular left pleural thickening with nodular thickening of the left diaphragmatic crus.

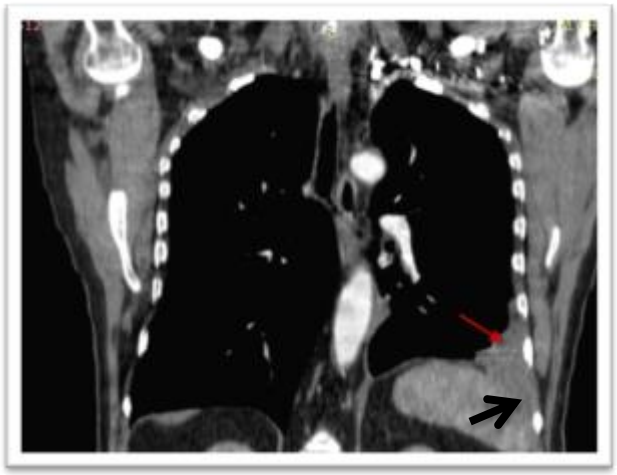

Figure 8: Coronal reformatted image of the chest showing obliteration of the left costo-phrenic recess (red arrow) and indistinct diaphragm suspecting involvement of the diaphragmatic muscle (black arrow).

DISSCUSION

Malignant pleural mesothelioma (MPM), the commonest pleural malignancy, is a rare malignant disease yet recent studies have proven its increased incidence worldwide, **(8).**

MPM is known for its aggressive nature regarding local disease extent, local spread and distant metastases. Its survival lies somewhere between 12-18 months even with treatment since it has shown resistance to different treatment options **(4).**

All the latter lead to the importance of early detection and diagnosis of MPM with proper staging in order to give the patient a better chance at early treatment and a better survival time **(5).**

CT is the most widely used investigation for diagnosing MPM. Other modalities can be used as well like MRI and PET CT**(2).**

This study showed prevalence of the disease between males which agrees with **Wolf *et al.* (9)** who state that MPM has a higher incidence in men than women and also with **Nickel *et al.* (2)** and **Truong *et al.* (4)** who state that it is more common in men than in women, with a ratio of 4:1.

This study also showed that the most prevalence of the disease is in the 6^{th} and 7^{th} decades.

Agreeing with **Truong *et al.* (4)** that MPM has a peak incidence in the sixth and seventh decades of life and **Nickel *et al.* (2)** that MPM most commonly occurs in patients aged 50–70 years.

This study showed the prevalence of the epitheliod variant of the three subtypes of malignant pleural mesothelioma.

The epithelioid variant was diagnosed in 14 cases representing 70% of cases. According to **Anttila and Boffetta (10),** epithelioid and biphasic are the most common subtypes of malignant pleural mesothelioma where together they constitute approximately 70–90 % of all MPM and also describes the importance to differentiate the different subtypes in the pathology report of MPM since epithelioid MPM is known to have the best prognosis and it helps in leading the oncologist to the right treatment guidelines.

This also agrees with **Nickel *et al.* (2)** that epithelioid MPM is the most common type, representing 55%–65% of cases. This also agrees with **Inai (11)** who states that the proportion of each is approximately 60% for epitheliod variant, 20% for the biphasic variant and 20% for the sarcomatoid variant and with **Allen (5)** who confirms that the epitheliod variant is the most common histologic variant as well as.

50% of the cases in this study showed right sided disease which disagrees with **Allen (5)** who states that MPM is more common on the right than on the left side, in a ratio of 3:2 and with **Nickel *et al.* (2)** who state that the right hemi thorax is often more involved than the left.

26 cases (65%) presented with circumferential nodular irregular pleural thickening this agrees with **Cardinale *et al.* (12)** explain that CT features highly suggestive of the MPM include nodular or lobular circumferential pleural thickening with mediastinal pleural thickening seen in 90%-92% of patients.

According to **Nickell *et al.* (2),** 92% of cases show lobular/nodular pleural thickening.

Fissural involvement in this study was evident in 13 patients (65%) which agrees with **Allen (5)** who states that involvement of the inter lobar fissural pleura is characteristic of mesothelioma which can be sometimes more apparent on reformatted sagittal or coronal views compared to the conventional axial views.

Cardinale *et al.* (12) also demonstrated the high incident of fissural involvement and explain that the next most common feature found in MPM after the circumferential pleural thickening is the involvement of the fissures which is seen in 73-86% of cases.

Bagheri *et al.* (13) showed that the involvement of the inter lobar fissures is an important differentiating finding since it occurs in 40–86% of patients with mesothelioma.

In a recent study by **Karam *et al.* (14)** comparing MPM with metastatic disease, thickening of the inter lobar fissures involvement was seen in 47.1% of cases diagnosed as MPM making it an important diagnostic clue to the disease.

Dogan *et al.* (15) showed that only 12% of cases had lung parenchymal involvement disagreeing with this study that showed a high percentage of lung involvement in the form of direct invasion (60%) or parenchymal metastatic nodules (30%) and lymphangitic spread (10%).

Nickel et al. (2) whom say that invasion of endothoracic fascia or a single chest wall focus is better assessed by MRI and that chest wall involvement wither at sites of previous biopsy, thoracotomy, or chest tube tracts are also relatively more easily seen on MRI than on CT.

This study was able to stage the different nodal groups in the currently used staging system of MPM with 75% of cases showing affection of the ipsilateral mediastinal lymph nodes, yet **Wang *et al.* (16)** clearly states that the CT accuracy is suboptimal in proving nodal involvement

because size only does not prove nodal involvement and that PET CT has increased accuracy when it comes to detecting mediastinal lymph nodes involvement.

Wang *et al.* [16] state that trans diaphragmatic extension of MPM is suggested in CT by a soft-tissue mass that encases the hemi diaphragm and once a clear fat plane between the diaphragm and adjacent abdominal organs with a smooth diaphragmatic contour is seen by CT, this indicates that the tumor is limited to the thorax. This also agrees with **Ismail-Khan *et al.* [17]** that trans diaphragmatic spread of tumor may be visible or suspected on chest CT scans yet MRI of the chest is more sensitive in illustrating this.

CONCLUSION

CT with contrast is the most frequently obtained examination owing to its easy accessibility. Chest CT alone is often sufficient for disease staging and treatment planning.

Typical CT findings that suggest MPM include unilateral pleural effusion with nodular irregular pleural thickening which can be discrete or diffuse with or without inter lobar fissure thickening and nodal metastasis.

The most important differential diagnosis of diffuse nodular pleural thickening includes metastatic disease.

FDG PET/CT is useful to monitor the follow-up and assess the metabolic response to chemo and radiotherapy.

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