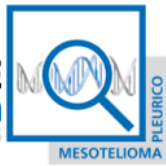

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The role of radiology in MPM

Introduction

Like most neoplastic diseases, malignant pleural mesothelioma (MPM) requires a great deal of radiological evaluation both at the time of diagnosis and for monitoring patient response during therapy.

For this reason, the FBU also wished to be involved in this area of diagnosis and treatment of MPM and has initiated a project to fund a radiologist specializing in this field, currently under way at the UFIM of Alessandria / Casale Monferrato.

This month's bibliography review provides an informative and simplified overview of the use of radiology in this disease.

(Please see the bibliography for further information or for the "experts in the field".)

Use of radiology

Chest X-rays

Radiological techniques allow us to determine pleural alterations and their characteristics, such as the presence of thickening and pleural plaques, their pattern of distribution, and the eventual presence of pleural effusion.

Radiological analysis can be used to arrive at the diagnosis as well as for staging the disease (1).

The initial examination is usually a standard chest X-ray, but this is not always conclusive, especially if the presence of pleural lesions is suspected.

Computed tomography

Because a chest X-Ray does not allow for a detailed examination of suspected pleural lesions, the first real in-depth examination for this disease should be computed tomography (CT). According to the AIOM national guidelines, the data obtained by CT analysis have demonstrated a specificity of 78% (95% CI, 72%-84%), but a sensitivity of only 68% (CI 95%, 62%-75%). This is necessary particularly in the differential diagnosis of pleural effusion with a negative CT scan that is negative for pleural lesions, in case you want to exclude the diagnosis of malignant disease.

Consequently, this often means subjecting the patient to an invasive diagnostic procedure, such as thoracentesis or a pleural biopsy. In these cases, the decision should be based on the clinical data rather than the negative CT scan (2).

If the thoracic CT scan shows evidence of MPM, the examination should be extended to the abdomen to exclude any secondary disease in the abdominal organs and the peritoneum in particular.

Ultrasonography

A simple ultrasound is one of the possible ultrasonography approaches to MPM, allowing us to analyze both the presence of pleural fluid and any parietal lesions. Ultrasound may also be used together with color Doppler or contrast media (CEUS). As such, ultrasonography allows us to easily identify pleurisy and pleural thickening and also determine any suspicious lesions due to malignancy based on their vascularization (3).

Magnetic resonance

Several studies have shown that nuclear magnetic resonance imaging (MRI) appears to be superior to CT in differentiating between benign and malignant pleural thickening, and particularly in assessing the possible infiltration of the chest wall and diaphragm (4). However, it is important to point out that the introduction of new generation and increasingly sophisticated TC equipment has greatly reduced this discrepancy. MRI could therefore be useful mainly to further the CT findings, particularly as an additional examination before

performing an intervention. Preliminary studies also suggest the possibility of using MRI with special techniques, such as diffusion-weighted imaging (DWI), to assess the histology of patients with pleural mesothelioma using the apparent diffusion coefficient (ADC) (5). However, although the results are promising these methods are currently experimental.

Positron emission tomography

18-FDG PET-CT has been studied because it is a technique that helps to distinguish between benign and malignant pleural lesions (6). It is also used in the clinic for staging, in other words to identify metastatic sites not shown by other radiological procedures.

This metabolic method has demonstrated greater sensitivity, specificity and accuracy in lymph node staging (7). However, the reliability of the method is limited due to the possibility of false negatives (especially in the presence of micrometastases <4 mm) and false positives (very often related to non-necrotizing granulomatous reactions) (8). However, the gold standard for the most accurate pleural staging remains the thoracoscopy, as suggested by at least one study which compared metabolic imaging with this procedure (9).

A total body 18-FDG PET-CT is recommended for the staging of patients eligible for multimodal treatment due to its greater accuracy in extra-thoracic and lymphatic staging compared to a CT scan. The optimal timing for performing this procedure is before conducting any invasive procedures such as pleurodesis due to the risk of subsequent false positive results due to the procedure (10, 11). Precisely because of the above limitations, the use of this method for evaluating response to treatment is still being studied and it is not recommended for routine use (12).

Metabolic assessments could be used not only in the diagnosis and staging of the disease but also for monitoring the malignant lesions during antineoplastic therapy. In fact, a recent study suggests that there is a possible role for metabolic imaging to identify the non-responders among patients with stable disease according to mRECIST criteria. In this subgroup of patients, a $\geq 25\%$ increase of SUVmax compared to baseline was associated with a statistically significant reduction in median time to progression (10.0 vs 13.7 months, $p < 0.001$) (13).

RECIST criteria

The radiological criteria usually evaluated are known as RECIST (Response Evaluation Criteria in Solid Tumor), which were updated and published in 2004 ("modified RECIST"). However, the use of these criteria for evaluating response in mesothelioma is rather complex. The modified RECIST1 system published in 2004 allows for more accurate measurements. Even though this has led to an improvement over the initial RECIST criteria, the rate of variability and inaccuracy of the measures remains very high. It is important to point out that compliance of the radiology specialists with the correct method greatly influences the evaluation of disease response to treatment.

Currently the modified RECIST criteria are based on the CT measurement of the thickness of the neoplasm perpendicular to the chest wall or the mediastinum at three different levels, so as to take into account the irregularity of the tumor (Tables 1 and 2) (14). These criteria are the diagnostic standard, since the response evaluated with these tools has shown a statistically significant correlation with overall survival and respiratory function.

Tabella 1: Misurazione secondo i criteri RECIST modificati (14)

- A) Lesioni pleuriche:
 1) misurare lo spessore della neoplasia in 2 punti perpendicolarmente alla parete toracica o ad una struttura mediastinica; effettuare tale misurazione a 3 livelli diversi;
 2) sommare le 6 misure ottenute; tale risultato rappresenta una misurazione pleurica unidimensionale.
- B) Lesioni non-pleuriche: misurare come per RECIST
- C) Sommare le varie misurazioni per ottenere la misurazione globale del tumore (total tumor measurement; TTM).

Tabella tratta dalle linee guida AIOM

Tabella 2: Valutazione della risposta secondo i criteri RECIST modificati (14)

Risposta	Definizione
Risposta completa	Scomparsa di tutte le lesioni target in assenza di evidenza di neoplasia in altre sedi
Risposta parziale	Riduzione maggiore o uguale al 30% del TTM
Progressione di malattia	Incremento maggiore o uguale al 20% del TTM rispetto al nadir o comparsa di nuove lesioni
Stabilità di malattia	Pazienti che non soddisfino né i criteri per definire una risposta parziale né per definire una progressione di malattia
TTM: total tumor measurement	

Tabella tratta dalle linee guida AIOM

Studying volumetric variation using CT is a promising approach in this area, considering also the potential correlation with survival, if analyzed together with several clinical parameters (15).

An article was also recently published proposing further modifications to the modified RECIST version 1.0, with a recommendation to adopt a new RECIST version 1.1 (16). Specifically, the continuous updating of the RECIST criteria evaluates different approaches that are reflected in clinical practice. The main ones are as follows:

- Definition of measurable lesions
- Evaluation of non-pleural lesions
- Characterization of non-measurable pleural disease
- Definition of pathological lymph nodes
- Definition of disease progression

Conclusions

Radiology plays a fundamental role for malignant pleural mesothelioma and is useful for diagnosing, staging and, more importantly, for monitoring the disease during specific antineoplastic treatment.

However, continuous updates are needed specifically in this area and the role of the radiology specialist in this field is increasingly necessary.

The FBU, which has always been involved in the diagnosis and treatment of MPM, also wished to contribute to this sector by funding a radiology specialist dedicated to this neoplasm.

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