Malignant pleural mesothelioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

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incidence

Malignant pleural mesothelioma (MPM) is a rare tumour. The incidence is 1.25/100 000 in Great Britain and 1.1/100 000 in Germany. Within the next 20 years the incidence is estimated to double in many countries. Exposure to asbestos is a well-established aetiological factor for MPM, with occupational exposure being documented in 70%–80% of those affected.

diagnosis

Patients typically present with shortness of breath due to pleural effusion or chest pain in a more advanced stage. The diagnosis is usually suggested by imaging studies (unilateral pleural thickening; pleural effusion). An occupational history must be obtained.

Cytological examination of the effusion can be diagnostic, but often shows equivocal results. Therefore, histology, including immunohistochemistry, is the gold standard. Pleuroscopy, a video-assisted surgical procedure or open pleural biopsy in a fused pleural space may be necessary to provide sufficient material for accurate histological diagnosis. There are three main histological types (epithelial, sarcomatous and mixed) with ~60% being epithelial.

Data suggest the possible contribution of serum mesothelin-related proteins and osteopontin as useful markers to support the diagnosis of mesothelioma; however, the precise role of these markers is yet to be defined.

staging and risk assessment

Clinical staging is based on the CT scan of the chest. However, the translation of the images into TNM stages is often not conclusive. Mediastinoscopy and video-assisted thoracoscopy may be useful in determining the stage. Accurate initial staging is essential to provide both prognostic information and guidance on the most appropriate therapeutic options. Several different staging systems exist, among them the international IMIG staging system for MPM which emphasizes the extent of disease post-surgery in a traditional TNM system and stratifies patients into prognostic categories similar to those shown in Table 1.

The European Organization for Research and Treatment of Cancer prognostic scores may be used. They include performance status, gender, certainty of histology, histological type and white blood count.

MPM rarely metastasizes to distant sites but most patients present with locally advanced disease. The use of PET scan to rule out extra-thoracic metastasis in patients considered for radical treatment is under investigation and findings seem promising.

treatment

surgery

Various surgical procedures have been studied with varying degrees of success.

Extra-pleural pneumonectomy (EPP) with resection of the hemi-diaphragm and the pericardium en bloc has the potential for a radical treatment and this approach is generally combined with neoadjuvant or adjuvant chemotherapy and/or adjuvant radiotherapy. Surgery, the appropriateness of which is still under consideration, should only be performed on selected patients by experienced thoracic surgeons in the context of a multidisciplinary team and preferably as part of a clinical trial [II, A]. Selection criteria include good performance status, and earlier stage disease with not more than localized involvement of the thoracic wall, and adequate cardiopulmonary function. The inclusion of
Table 1. TNM staging system for MPM

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Ia</td>
<td>T1a N0 M0</td>
<td>Primary tumour limited to ipsilateral parietal pleura</td>
</tr>
<tr>
<td>Ib</td>
<td>T1b N0 M0</td>
<td>As stage Ia plus focal involvement of visceral pleura</td>
</tr>
<tr>
<td>IIA</td>
<td>T2 N0 M0</td>
<td>As stage Ia or Ib plus confluent involvement of diaphragm or visceral pleura or involvement of the lung</td>
</tr>
<tr>
<td>III</td>
<td>Any T3 M0</td>
<td>Locally advanced tumour</td>
</tr>
<tr>
<td></td>
<td>Any N1 M0</td>
<td>Ipsilateral, bronchopulmonary or hilar lymph node involvement</td>
</tr>
<tr>
<td></td>
<td>Any N2 M0</td>
<td>Subcarinal or ipsilateral mediastinal lymph node involvement</td>
</tr>
<tr>
<td>IV</td>
<td>Any T4</td>
<td>Locally advanced technically unresectable tumour</td>
</tr>
<tr>
<td></td>
<td>Any N3</td>
<td>Contralateral mediastinal, internal mammary, and ipsilateral or contralateral suprACLavicular lymph node involvement</td>
</tr>
<tr>
<td></td>
<td>Any M1</td>
<td>Distant metastases</td>
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</table>

Platinoids, doxorubicin, and some antimitabolites (methotrexate, raltitrexed, pemetrexed) have shown modest single-agent activity [III, B].

The combination of both pemetrexed/cisplatin, and to a smaller extent raltitrexed/cisplatin, have been shown to improve survival as well as lung function and symptom control in comparison with cisplatin alone in randomized trials [II, A]. The combination of pemetrexed/carboplatin is an alternative effective therapy [III, A].

A phase III trial evaluated second-line pemetrexed versus best supportive care in patients not previously exposed to this agent and found a longer time to disease progression in the chemotherapy arm. Since vinorelbine or gemcitabine have first-line activity they might be a reasonable choice in second-line therapy. One study on 63 patients treated with vinorelbine reported a 16% response rate and median survival of 9.6 months [III, A].

If extrapleural pneumonectomy is planned, platinum-based neoadjuvant or adjuvant combination chemotherapy should be considered.

**response evaluation**

Response evaluation using CT scan is recommended after two to three chemotherapy cycles and the modified RECIST criteria should be applied. Volumetric measurements are under investigation.

**follow-up**

Follow-up consists of clinical evaluation, with particular attention to symptoms or chest wall recurrence, and chest CT as needed.

**note**

Levels of Evidence [I–V] and Grades of Recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the expert authors and the ESMO faculty.

**literature**


