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Mesothelioma Diagnosis: A Comprehensive Guideline-based Approach

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Abstract

English:

Mesothelioma is a rare and aggressive cancer that affects the lining of the lungs, abdomen, or heart. Early diagnosis and treatment are essential for optimizing survival and quality of life for patients with mesothelioma. The article aims to offer a clear and practical perspective on the guidelines for diagnosing mesothelioma. Our goal is to provide clinicians with a comprehensive guide on how to diagnose and manage this condition effectively. We will examine key aspects such as the prompt acquisition of tissue samples, the significance of imaging and biopsy techniques in the diagnostic process, and the utilization of biomarkers to raise suspicion of mesothelioma. Additionally, we emphasize the essentiality of adopting a multidisciplinary approach to patient care, encompassing holistic support for both patients and their families. The paper aims to offer a comprehensive overview for clinicians working in general hospitals who are required to diagnose mesothelioma. The suggestions provided are based on current international guidelines, which should be adapted to suit local clinical practices. By addressing this need, we hope to assist clinicians in effectively diagnosing mesothelioma within their specific healthcare settings.

Keywords

mesothelioma • diagnosis • clinical guidelines • multidisciplinary care • general hospitals • local clinical practice

Diagnosticul mezoteliomului: O abordare comprehensivă bazată pe ghiduri

Rezumat

Romanian:

Mezoteliomul este un cancer rar și agresiv care poate afecta pleura, peritoneul sau pericardul. Diagnosticul și tratamentul precoce sunt esențiale pentru optimizarea supraviețuirii și a calității vieții pacienților cu mezoteliom. Articolul își propune să ofere o perspectivă clară și practică asupra liniilor directoare pentru diagnosticarea mezoteliomului. Scopul articolului este de a oferi clinicienilor informații din ghidurile actuale despre cum să diagnosticăm și să gestionăm eficient această afecțiune. Articolul examinează aspecte cheie, precum achiziția promptă a probelor de țesut, importanța tehnicilor imagistice și de biopsie în procesul de diagnosticare și utilizarea biomarkerilor pentru a ridica suspiciunea de mezoteliom. În plus, se subliniază importanța adoptării unei abordări multidisciplinare a îngrijirii pacienților, care să cuprindă sprijinul holistic atât pentru pacienți, cât și pentru familiile acestora. Lucrarea oferă o imagine de ansamblu utilă pentru clinicienii care lucrează în spitalele generale, care uneori trebuie să ridice suspiciunea sau să pună diagnosticul de mezoteliom. Informațiile discutate se bazează pe ghidurile internaționale actuale, care ar trebui adaptate pentru a se potrivi practicilor clinice locale. Prin abordarea acestei nevoi, se dorește ajutarea clinicienilor în diagnosticarea eficientă a mezoteliomului în cadrul condițiilor lor specifice de asistență medicală.

Cuvinte-cheie

mezoteliom • diagnostic • ghiduri clinice • îngrijire multidisciplinară • spitale generale • practică clinică locală

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Mesothelioma is a rare and aggressive cancer that affects the lining of the lungs, chest, abdomen, and heart. It is primarily caused by exposure to asbestos, a mineral fibre used in construction, insulation, and other industries. Once inhaled, asbestos fibres can become lodged in the lining of the lungs, causing irritation and inflammation that can lead to the development of mesothelioma (1).

Diagnosing mesothelioma poses challenges due to the nonspecific symptoms and the absence of specific biomarkers. Patients commonly experience symptoms which can mimic other respiratory disorders, leading to delayed suspicion of mesothelioma. This delay in diagnosis is not exclusive to mesothelioma but is a recurrent issue in rare conditions. The field of internal medicine primarily focuses on more prevalent conditions during the differential diagnosis process. However, certain distinct characteristics, such as persistent or recurring pleural exudate, should raise additional suspicions and prompt further investigations.

Guidelines have been developed to address the challenges of timely diagnosis in mesothelioma and provide a standardized diagnostic protocol. In the United Kingdom, the widely used guideline is published by the British Thoracic Society in 2018 (2). However, it should be acknowledged that there are slightly more recent guidelines available, such as those from the European Respiratory Society (ERS) or European Society for Medical Oncology (ESMO) (3,4). While there may be variations in the diagnostic aspects among these guidelines, it is important to clarify that this discussion does not focus on treatment-related issues. Treatment matters fall under the purview of oncologists, and the author's involvement in this area is peripheral.

The clinical presentation and history of patients with this condition often lack specificity. Common symptoms include cough, severe chest pain, breathlessness, and potential weight loss. In primary care, an initial investigation typically involves a prompt chest X-ray, particularly if symptoms persist or reocur (2). However, patients may initially receive antibiotics for a presumed respiratory infection. Suspicions should be increased when unilateral, persistent, or recurring pleurisy is observed, warranting an urgent referral to a pulmonologist for specialized evaluation. This proactive approach helps prevent disease progression and averts emergency admissions. It is crucial to gather a comprehensive history, encompassing not only the patient's occupational exposures but also those of individuals in their immediate environment, including partners and family members (2–4). While some patients may have obvious asbestos exposure, documentation of exposure may be lacking. Furthermore, certain professions not traditionally associated with asbestos exposure, such as teaching in the UK, may entail regular but minimal exposure due to activities like hanging items using pins or tacks on walls covered with asbestos-containing paint (5).

Point-of-care pleural ultrasonography has become the preferred initial imaging modality for patients presenting with pleural effusion following a chest radiograph. Despite its widespread use, it is important to note that this specific technique is not explicitly mentioned in the existing guidelines for mesothelioma (6). The British guideline recommends using chest computed tomography (CT) with contrast substance as the preferred imaging modality for diagnosing and staging pleural mesothelioma (2,7). To effectively visualize pleural thickening, it is advisable to perform the CT before complete aspiration of pleural fluid. In cases where the patient experiences dyspnoea and there is a substantial amount of pleural fluid, simple drainage can be performed to obtain fluid for cytology, with the extraction of 1.5-2 litres. Subsequent imaging investigations can be conducted as needed. However, if the patient is not experiencing dyspnoea and the pleural fluid is in small to moderate quantities, it is recommended to proceed with imaging first, specifically a CT with contrast substance for the pleura, before considering biopsy or thoracoscopy.

PET-CT may not always contribute significantly to diagnosis and can yield false positive or negative results, especially in patients who have undergone talc pleurodesis or in areas with high prevalence of tuberculous pleurisy. Magnetic resonance imaging (MRI) can be valuable for assessing tumour thickness and invasion of the diaphragm or chest wall in mesothelioma cases. However, it is important to note that the evidence supporting these imaging recommendations is limited, with a low level of grading (D) in the British guideline (2).

While pleural aspirate is commonly performed in cases of persistent or recurrent unilateral pleurisy, relying solely on cytology is inadequate for diagnosing mesothelioma or determining its histological type. Patients presenting with recurrent pleurisy or suspected of mesothelioma require immediate biopsy. The European guideline recommends obtaining a minimum of three biopsies from different pleural locations to establish a definitive diagnosis. It is crucial that these biopsies are examined by a pathologist with expertise in mesothelioma, and a second opinion should also be sought to ensure accurate interpretation of the results.

The British guideline suggests two techniques for obtaining biopsy samples: CT-guided biopsy and thoracoscopy. However, the European guideline prioritizes biopsy methods based on diagnostic success rates. Thoracoscopy is regarded as the preferred approach since it allows for direct visual guidance during the biopsy procedure. Nevertheless, not all pulmonology services have immediate access to thoracoscopy, which is often performed by surgeons in many UK centres. In such instances, CT-guided biopsy using a true-cut needle has significantly improved diagnostic capabilities (8). Additionally, the more recent option of pulmonologist-performed ultrasound guided biopsy is also available. It is important to highlight that

the use of Abrams or Cope needle biopsy is less common in most Western countries, but it remains utilized in low-income countries.

It is noteworthy that the British guideline does not recommend radiation therapy following biopsy to mitigate the risk of malignant cells spreading along the biopsy tract (2).

Accurate characterization of mesothelioma type and subtype requires biopsies and an adequate tissue volume for immunohistochemistry analysis. Guidelines recommend the use of at least two specific immunohistochemical markers for mesothelioma and two negative markers for adenocarcinoma (2). This approach aids in clearly distinguishing between these two types of tumours and achieving an accurate diagnosis.

The European guideline provides a broader perspective on biomarkers (4). They should only be utilized to raise suspicion of a diagnosis in cases where patients have suspected cytology but are unable to undergo multiple invasive tests. Biomarkers should not be employed for treatment selection, prognosis prediction, or screening purposes (2,4).

In cases where pleurisy reoccurs, the guidelines suggest two options based on patient preference: talc slurry or indwelling catheter placement. Surgery, on the other hand, does not have a well-established role in managing recurrent pleurisy (2,4,9). Despite a few recent studies, surgery plays a limited role in the multimodal treatment of these patients and is generally not recommended for controlling the disease or managing its complications (9).

The first-line treatment for mesothelioma involves a combination of cytostatics and immunomodulators. However, treatment recommendations may evolve as new findings emerge from ongoing oncological studies.

The British guideline emphasizes the importance of multidisciplinary care, holistic treatment approaches, and effective communication with patients and their families (2). Specialized nurses play a critical role in achieving these objectives. Considering the current limited 5-year survival rate of 10%, the period following diagnosis remains challenging for patients and their families. Therefore, it is crucial to approach this time with wisdom and expertise to provide appropriate care and support.

In recent developments, there have been advancements in the diagnosis and treatment of mesothelioma which are not yet included in the guidelines.

One notable change is the recognition and diagnosis of mesothelioma in situ, which refers to the early stages of the disease (10). This allows for timely intervention and management.

Another noteworthy development is the utilization of deep learning-based classification techniques to enhance the accuracy of histological typing of mesothelioma (11). This improvement in classification has demonstrated the potential to better predict patient outcomes, aiding in treatment planning and prognosis assessment.

In terms of new treatment strategies, there have been important advancements. Immune checkpoint inhibitors, a type of immunotherapy, have emerged as a promising treatment option for mesothelioma. These inhibitors work by boosting the immune system's ability to recognize and attack cancer cells. Additionally, the use of oncolytic adenoviruses, which are engineered viruses that selectively target and destroy cancer cells, has shown promise in mesothelioma treatment. Excitingly, studies are exploring the combination of immune checkpoint inhibitors with oncolytic adenoviruses, aiming to leverage their synergistic effects and enhance treatment outcomes (12).

These new developments in diagnosis and treatment strategies present promising opportunities to improve patient outcomes and enhance the management of mesothelioma. As research and clinical trials continue, further advancements and refinements are expected to occur in the field of mesothelioma diagnosis and treatment.

In conclusion, mesothelioma, a rare and aggressive cancer, presents diagnostic challenges due to nonspecific symptoms and the lack of definitive markers. However, early, and accurate tissue diagnosis following current guidelines and a standardized local protocol of investigation is crucial for initiating appropriate treatment. Additionally, early referral for a multidisciplinary approach involving healthcare professionals experienced in mesothelioma management is needed. This collaborative effort aims to achieve timely diagnosis, implement appropriate therapeutic strategies, and optimize survival outcomes while prioritizing the quality of life for affected patients, regardless of where they initially sought medical attention.

Disclaimer

This article was prepared and written by the author using Microsoft Word 2023. It was initially written as a draft in Romanian, then translated into English using the automatic translator in Word. The flow and accuracy of the information of the English translation was manually verified by the author. The English version was further refined for cohesion and coherence with the assistance of ChatGPT v3.5. No text generated only by artificial intelligence was included in the article. The final version presented here has been subsequently edited by the author. The references were managed using the Mendeley program.

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