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Review

Distant metastases from head and neck squamous cell carcinoma. Part II. Diagnosis ☆

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SUMMARY

The detection of distant metastases is critical for prognostication and for the choice of treatment in patients with head and neck squamous cell carcinoma (HNSCC). Pretreatment screening for distant metastases should be conducted particularly for patients with high risk factors, prior to locoregional treatment decisions. Different diagnostic techniques are discussed. Unfortunately, most studies lack sufficient follow-up to reliably assess false-negative results. Moreover, the designs of most studies vary substantially with regard to homogeneity of groups (tumor types and stages), timing (pretreatment, follow-up) and definition of risk factors (patient selection). Therefore, only a few studies are comparable. The combination of F-18 fluoro-D-glucose-positron emission tomography (FDG-PET) and a dedicated CT (at least of the chest) is the most important imaging protocol at the present time. Eventually, whole-body-MRI (WB-MRI) may possibly replace PET-CT for screening patients for distant metastases.

Introduction

A usual feature of head and neck squamous cell carcinoma (HNSCC) is that distant metastases tend to occur late in the course of the disease.[1,2] The incidence of distant metastases at presentation varies from 4.2% to 23.8%, while at autopsy incidences up to 57% have been reported.[3] If distant metastases are present, in general no curative options are currently available. Once distant metastases have been detected, the prognosis is dismal. The median time to death from the diagnosis of distant metastases ranges from 1 to 12 months.[1–6] About 88% of patients with distant metastases will die within 12 months.[1] Thus, the detection of distant metastases is critical for prognostication and for the choice of treatment in patients with HNSCC.[3] Patients with known distant metastatic disease can possibly be spared the toxicities of aggressive and often unnecessary locoregional therapy. The currently available techniques and new developments in the assessment of distant metastasis will be discussed.

Diagnostic tests for different sites of distant metastasis

Various tests have been used to detect distant metastases. Some of these are not primarily screening tests, but if abnormal warrant additional examinations to rule out or detect distant metastases. During the last decade, advancements in imaging techniques have improved the detection of distant metastases. In order of frequency, metastases occur in the lungs, bone and liver.[3]

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Computed tomography (CT) is more sensitive for detection of pulmonary nodules than plain chest radiography, because of the superiority of CT in detecting small nodules (see below). Plain films detect only 28–60% of all malignant pulmonary lesions detected by CT.[4,7–9]

Bone scintigraphy is non-specific because any bone disease leading to increased turn-over of bone, regardless of etiology and histology, will cause increased uptake of the radioisotope. Thus fractures, arthritis, degenerative disease of the spine and osteoporosis will cause false positive results.[10] Consequently, bone scintigraphy lacks specificity for metastatic disease, particularly in the older HNSCC population.

Several diagnostic imaging techniques are available for detection of liver metastases, including ultrasound, CT, magnetic resonance imaging (MRI) and positron emission tomography (PET). Ultrasonography is often the first choice because of its widespread availability, repeatability, lack of ionizing radiation and low costs.[11] Combining ultrasound with contrast medium (CEUS), which is virtually risk-free, can significantly increase the sensitivity and specificity of this test to detect liver metastases. If further certainty as to the cytology or the histology of the lesion is wanted, ultrasound may be combined with fine needle aspiration or automatic cutting biopsy needle.

If the initial ultrasound examination is not adequate, contrast-enhanced CT should be used.[12] The (combination of) investigation(s) of choice will usually depend on availability and experience and be based on consultation with the radiologist who interprets the studies.[12]

F-18 fluoro-D-glucose-positron emission tomography (FDG-PET) is most useful for detection of distant metastases in HNSCC patients, both before and after treatment. Because in most cases conventional imaging techniques are needed to confirm and evaluate PET findings, whole-body-FDG-PET is more often used for screening than for detailed information on distant metastases of HNSCC. FDG-PET scanning combined with CT (PET-CT) may more accurately localize the lesions, as will be discussed below.

Developments in diagnostic tests

Although imaging techniques such as CT and MRI have been used for decades, further technical improvements and developments have increased the sensitivity and specificity of detection of distant metastatic disease. With the continuous advancement of CT technology, multi-detector row computer tomography (MDCT) with thin collimation (0.5–0.75 mm) is now widely used in clinical practice. The sub-millimeter configuration of MDCT detector allows for multi-planar reformation with high spatial resolution. Moreover, multiple detector channels lead to a substantial increase in scanning speed and volume coverage.

MRI has improved both due to the introduction of faster MRI techniques and newer pulse sequences [short term inversion recovery (STIR) and diffusion-weighted-MRI (DW-MRI)]. The introduction of faster MRI pulse sequences and multi-channel receiver MRI substantially reduces examination times and improves signal-to-noise, respectively. Moreover, through these developments whole-body-MRI (WB-MRI) becomes possible. Using STIR-technique, MRI may better enable detection of pathological changes than may be done using T2-weighted MRI pulse-sequences.[13]

DW-MRI is used to measure differences in tissue microstructural changes that are based on random displacement of water molecules. These differences in water mobility are quantified by using the apparent diffusion coefficient (ADC). The ADC obtained by DW-MRI is a marker of cell density and potentially may distinguish malignant from benign lesions.[13]

FDG-PET scanning is a functional modality that has been used increasingly for staging head and neck cancer. Combined PET-CT studies, an imaging modality increasingly available to clinicians, offers anatomic and functional imaging, potentially providing more accurate diagnosis and improved patient management. The CT scan is used for attenuation correction of the PET images as well as for anatomic localization of lesions. Newer PET-CT scanners with multi-detector CT allow radiologists to obtain full diagnostic quality CT scans with intravenous contrast that can be combined with PET imaging. Modern equipment performs whole-body-PET in combination with a high quality CT scan within 30–40 min.[13]

Timing

Examinations to detect distant metastases in patients with HNSCC can be performed initially and during follow-up as screening if there are no symptoms or if symptoms suggestive of distant metastases occur during follow-up. In the latter situations the technique of choice depends on the type and localization of symptoms.

Screening may have different objectives and can be used in different ways. It is usually defined as routine testing of an at risk population who do not show any signs of the disease being tested. The aims of screening for distant metastases are twofold: (1) detection of occult disseminated disease without curative options may lead to the decision to withhold futile attempts at curative treatment and (2) to enable counseling patients about prognosis and to optimize quality of life. Routine screening of asymptomatic patients during follow-up is of limited clinical value since distant metastases from HNSCC cannot be treated with curative intent and asymptomatic distant metastases does usually not require immediate palliative treatment. The presence of distant metastases at pretreatment evaluation influences the prognosis and thus treatment selection. Detection of distant metastases will alter the treatment plan and may avoid futile extensive treatments with unnecessarily burden to the patient, affecting quality of life and use and costs of resources. These considerations affect therapeutic decision making at initial diagnosis as well as the management of locoregionally recurrent disease. However, in selected cases, depending on histology and natural history of the disease, treatment schedules used for curative treatment may be appropriate (please refer to Part III for discussion).

The overall survival of HNSCC patients with distant metastases detected by pretreatment screening using chest CT is significantly lower than patients with negative screening.[14,15] Brouwer et al.[14] found a significantly better overall survival (OS) in patients who showed no metastases at the time of pretreatment screening than in those who developed distant metastases during follow up. However, Haerle et al.[15] found no significant difference in OS with regard to the time of diagnosis of DM. A survey in The Netherlands revealed that the majority of head and neck surgeons would refrain from extensive treatment if a HNSCC patient would develop clinically manifest distant metastases within 12 months.[16]

Target group

The reported incidence of clinically identified distant metastases in HNSCC at presentation varies from 2% to 18%,[4,17,18] but this is generally considered too low to warrant routine screening for distant metastases in all HNSCC patients. Jäckel and Rausch[18] found that screening is particularly useful in patients with advanced stage disease, local and/or regional recurrences and second primary tumors below the clavicles. Loh et al.[19] found T4 and/or N2 or N3 oropharyngeal, hypopharyngeal and supraglottic squamous cell carcinoma to be risk factors for the development of distant metastases: 64% of the patients with T4 and 73% of the patients with N2 or N3 disease had distant metastases detected during