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Non-small cell lung cancer with a single metastasis, the new stage M1b; does the site matter?

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ABSTRACT

Non-small cell lung cancer (NSCLC) patients with a solitary metastasis are considered to have a more favourable prognosis compared to those with multiple metastases. This is also shown in the 8th tumor, node, metastases edition for lung cancer (TNM8): patients with M1b (single extrapulmonary metastasis) have a superior prognosis than those with M1c disease (multiple metastases). Although not described in the TNM8, site of single metastatic disease may reflect tumour biology and may be of important prognostic value. We report a case of a patient with squamous cell NSCLC and a single skeletal muscle metastasis with a remarkably aggressive disease course.

Main text

Case description

A 62-year-old woman, former smoker (50 pack years), without other medical history, was referred because of a painful lump in the left upper arm. Her World Health Organisation performance status (WHO-PS) was 0. Except for a palpable ill-defined lump, firmly attached to the proximal biceps muscle underneath, physical examination was normal. Laboratory results were normal. A work-up with imaging and biopsy revealed an irresectable squamous cell carcinoma originating from the biceps muscle. Staging with 18-fluodeoxyglucose positron emission tomography-computed tomography (^{18}FDG-PET-CT) revealed two suspicious nodules in the right lower lobe, but no lymphadenopathy or other distant metastases (Fig. 1). CT-guided biopsy of the cavitating pulmonary nodule showed squamous cell NSCLC with comparable morphological features. Endobrochial ultrasound was not performed in absence of enlarged or ^{18}FDG-avid lymph nodes and peripheral pulmonary tumour sites in according to the ESMO guideline [1]. In our multidisciplinary team the cancer was staged as cT3N0M1b, stage IVA (TNM8) NSCLC with a single muscle metastasis and it was decided to treat both the lung lesion and the muscle metastasis with curative intent. Concurrent instead of sequential chemoradiation was chosen because of the very painful metastasis and the planned pain-reducing effect of the radiotherapy. However, the patient's clinical condition deteriorated rapidly to WHO-PS 4 in three weeks from diagnosis due to development of a deep venous thrombosis and a grade 4 hypercalcemia caused by bone invasion. Appropriate treatment could not improve her performance status. A second ^{18}FDG-PET-CT for radiation planning, performed four weeks after the staging ^{18}FDG-PET-CT, showed an impressive rapid progressive disease with extensive invasion of the soft tissue of the chest wall and humerus (Fig. 2). Six weeks after staging ^{18}FDG-PET-CT and only ten weeks after her first presentation to her general practitioner, the patient died.

Discussion

In the last decade, there is an increasing interest in the field of radical treatment of oligometastatic disease. In TNM8, patients with M1b are considered a separate entity with a superior prognosis than those with M1c disease [2]. Low local disease burden (especially N0 disease) is associated with a superior prognosis in radically treated oligometastatic NSCLC [3]. Nevertheless, disease course in our patient with ^{18}FDG-PET-CT staged N0 disease and a solitary metastasis was very aggressive. According to the seed and soil hypothesis, tumor cells must acquire the ability to disseminate hematogenously by accumulating specific genetic mutations and, in turn, the microenvironment of the target organ must be permissive to tumor growth [4]. The muscle resistance for metastatic disease may therefore be indicative for an aggressive subtype of NSCLC [4,5]. Although not shown in TNM8, due to small patient numbers per organ, site of single metastatic disease may reflect tumour biology and may be of important prognostic value [2,6].

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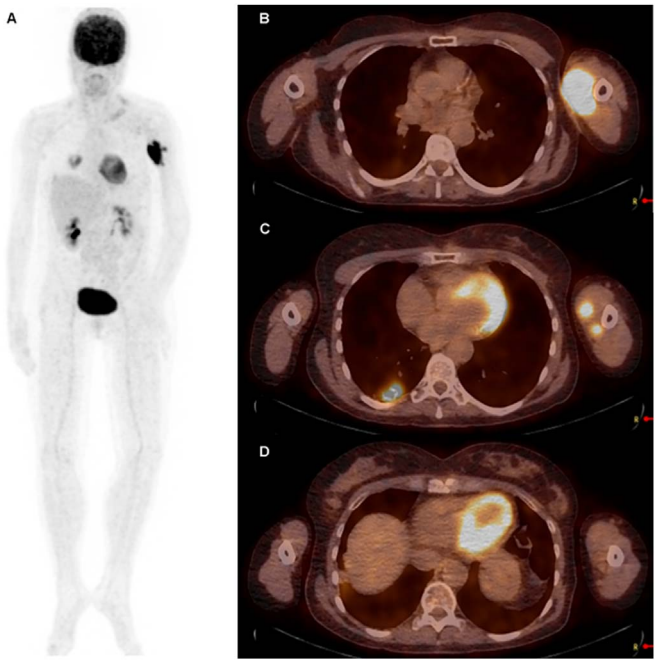

Fig. 1. A. Attenuation-Corrected Positron Emission Tomography shows a mass in the left upper arm and a cavitating pulmonary nodule in right lower lobe. B. Fusion ^{18}FDG-PET-CT shows an intense ^{18}FDG-avid mass (6.0 cm diameter) in the soft tissue of the left arm. C. Fusion ^{18}FDG-PET-CT showing a cavitating pulmonary nodule with PET-positive margins (2.9 cm diameter) and the lower part of the muscle metastasis. D. Fusion ^{18}FDG-PET-CT shows a slight ^{18}FDG-avid pulmonary nodule in the right lower lobe (7 mm diameter).

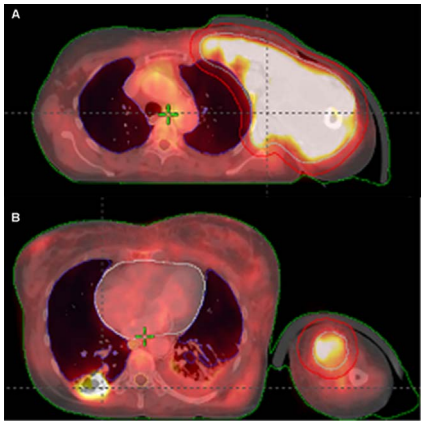

Fig. 2. A. Fusion ^{18}FDG-PET-CT four weeks after the staging ^{18}FDG-PET-CT showing extensive growth and invasion of the solitary metastasis in the chest wall and humerus. B. Fusion ^{18}FDG-PET-CT four weeks after the staging ^{18}FDG-PET-CT showing growth of pulmonary cavitating tumour and the lower part of the muscle metastasis.

More prospective data on this topic are needed and the site of metastasis should be incorporated in the next TNM classification in order to better identify subgroups with favourable prognosis in whom treatment with curative intent should be considered and tested.

Conclusions

Stage IV NSCLC, presenting with a single metastasis, especially with N0 disease, is considered to have a good prognosis. However, some metastatic sites may represent aggressive disease with poor prognosis. Prospective data are needed to further elucidate the importance of the site of single metastatic disease and potentially identify patient subgroups with more favorable prognosis.

Clinical practice points

In case of NSCLC with a single extrathoracic metastasis, the new TNM8 M1b, no hard evidence exist for significant differences in prognosis according to the organ site of metastasis [2,6]. However, this case illustrates that metastatic site may be of important prognostic value. This issue should be addressed in the next TNM classification in order to better identify subgroups with favourable prognosis in whom treatment with curative intent should be considered and tested.

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Conflict of interest

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