Sarcomatoid non-small cell lung cancer responding to sunitinib

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Introduction

Sarcomatoid NSCLC is a rare subtype of lung cancer, accounting for less than 1% of all lung cancers [1]. Apart from the inhibition of angiogenesis [2], targeted therapy for lung cancer has so far been restricted to those patients bearing EGFR and ALK mutations. Despite recent progress describing the use of tyrosine kinase inhibitors (TKI) in the treatment of lung cancer, this treatment approach has not yet become the standard of care, but is rather restricted to those patients bearing tumors with specific molecular aberrations in the EGFR or ALK genes [3]. For sarcomatoid NSCLC, a platinum-based doublet of conventional cytotoxic drugs is the first-line treatment of choice, especially since recent reports critically discuss the presence of EGFR mutations in this specific tumor entity [4, 5]. However, this entity might be another type of NSCLC responding to targeted therapies.

Case report

A 77-year-old Caucasian female presented with thoracic pain after heavy physical work. Her medical history included a thyroidectomy for benign reasons years ago, but no neoplasias nor cardiovascular or pulmonary conditions. A CT scan revealed pleural lesions, which by local biopsy could be confirmed as malignant, combined with a carcinomatous pleural effusion, staining positive for CD10 and vimentine. Suspecting renal cell cancer, the patient was referred to our hospital. After staging procedures, nothing but pulmonary lesions adjacent to the costal pleura could be found, particularly no renal cell cancer. Cancer of unknown primary (CUP) versus metastases of a sarcomatoid/spindle cell carcinoma was discussed after another biopsy, showing positivity of CK MNF 116 and CD10, while calretinin and CK5/6 were negative.

Despite only lesions adjacent to the pleura found, both pathologists involved favored the kidney as the organ of origin, so treatment decisions were made accordingly. The patient was started on sunitinib, for reasons of age; the initial dose was reduced to 37.5 mg on a 4-week on/2-week off regimen. Interim staging after one cycle revealed a partial remission, with only small tumor residues being left (Figure 1). During the following weeks, the sunitinib dose had to be reduced due to taste alterations affecting the patient’s quality of life. On a tolerable dose of 25 mg (4-weeks on/2-weeks off), the tumor still could be controlled for 1 year in total before pleural lesions progressed again. Since no further tumors have occurred in the meantime, the final diagnosis of a pleurally localized sarcomatoid non-small cell lung cancer is preferred. When disease progression occurred 1 year after diagnosis, we changed to everolimus at a standard dosage of 10 mg daily. Unfortunately, this treatment was not tolerated and had to be stopped after a few weeks. A standard doublet of cisplatin and gemcitabine therapy was subsequently administered, with no effect but further tumor progression. At present, 1.5 years after diagnosis, the patient is still alive and independent in her daily activities. She asked for therapy to be paused in order to recover from chemotherapy, however, we are considering another line of targeted therapy if the patient wishes to pursue further tumor-specific treatment.
Discussion

For sarcomatoid NSCLC, a platinum-based doublet of conventional cytotoxic drugs is the first-line treatment of choice. However, in our case, for reasons of uncertainty whether to name this tumor NSCLC versus CUP with renal cell differentiation, a primary TKI therapy was chosen, similarly to treatment of renal cell cancer. This discussion was entirely based on the histological subtype, but not on the pleural localization of the tumor. Eventually, this approach proved to be very successful, reaching a progression-free survival even slightly longer than has been reported for renal cell cancer [6]. Since we could demonstrate an initial partial reduction of tumor size, following by disease stabilization, we continued treatment according to current guidelines for renal cell cancer. Even when the diagnosis of a sarcomatoid NSCLC had become more likely because no renal lesions occurred, we stuck to the therapeutic regimen as long as the disease remained stable.

A standard doublet of cisplatin and gemcitabine therapy was administered upon progression of the disease after second line TKI therapy with everolimus had not been tolerated; quite surprisingly, this conventional therapeutic approach had no effect at all on tumor growth. This finding underlines the aggressive character of a sarcomatoid lung cancer known to bear a worse prognosis than other subtypes of NSCLC [1, 7]. Moreover, it emphasizes the fact that molecular analyses of supposedly “uniform” cancer types are gaining importance for the identification of those (rare) subgroups which respond to specific drugs or therapies. To conclude, off-label targeted therapy may be an option in the treatment of rare subtypes of NSCLC, when conventional chemotherapy fails.

References