

Successful Management of an Oligometastatic Nsclc Patient with Multimodal Therapy

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ABSTRACT

Non-small cell lung cancer (NSCLC) is more often diagnosed at an advanced stage and carries a poor prognosis. Recently, according to the new version of AJCC staging system published in 2018, oligometastatic disease has been integrated as an intermediate stage between non-metastatic and metastatic forms. The prognosis of oligometastatic NSCLC was significantly improved by the use of multimodal therapy, including chemotherapy, targeted therapies, immunotherapy, surgery and stereotactic radiotherapy. However, there is little evidence regarding the optimal sequence of these modalities in the management of patients with oligometastatic disease. We describe here a case study of a patient diagnosed with metachronous oligometastatic NSCLC, successfully managed by multimodal therapy based on stereotactic radiotherapy, chemotherapy, immunotherapy and standard radiotherapy for local control. Furthermore, randomized prospective studies would be of capital interest, including multi-centre patient studies and evaluation of several treatment strategies.

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Dear Editor

We would like to share a rare case study of a patient diagnosed with metachronous oligometastatic non-small cell lung cancer (NSCLC), successfully managed by multimodal therapy based on stereotactic radiotherapy, chemotherapy, immunotherapy and standard radiotherapy for local control.

The patient was 62 years old and had a medical history of only 17 P-Y chronic smoking that had been withdrawn 26 years ago. The patient's disease history goes back to two months before his first consultation by the installation of a cough with a worsening of his general condition.

A Chest-Abdomen-Pelvis CT scan (CT scan of CAP) was requested and revealed a right upper lobe parenchymal lesion process, classified as T4N0M0, stage IIIA (TNM 8th edition 2017) (Figure 1a). The CT-guided biopsy showed a poorly differentiated non-small cell carcinoma, more of an adenocarcinoma type. The immunohistochemical study favored an adenocarcinoma of pulmonary origin (CK7+, CK20-, TTF1-).

During the extension work-up, PET scan revealed a metabolically active right pulmonary neoplastic process and homolateral hilar lymph node hypermetabolism suspected of malignancy. Cerebral MRI was normal and the pre-therapeutic work-up did not contraindicate surgery.

The patient then received neoadjuvant therapy with three cycles of chemotherapy according to the Cisplatin 75 mg/m² plus Pemetrexed 500 mg/m² protocol, which is among the neoadjuvant protocols in the NCCN 2018 recommendations. Tolerance to

treatment was good, except for grade one nausea and asthenia.

Evaluation by CT scan of CAP was performed and showed an estimated partial response of 36% compared to the initial CT scan (Figure 1b.).

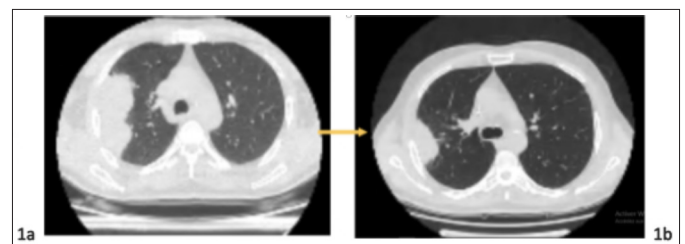


Figure 1: Chest, abdomen and pelvis scan:

1a: Right upper lobar parenchymal lesion process with broad contact with the chest wall on the axillary side of a 9*5 cm long axis, without thoracic or bony extension, without hilar and mediastinal lymphadenopathies

1b: Estimated partial response of 36% compared to the scanner in figure 1a

Four months after diagnosis, the patient underwent lobectomy and lymph node dissection. Pathologic examination showed lobectomy with a morphological appearance of a poorly differentiated invasive necrotic and inflammatory (non-small cell) carcinoma. It measures 8*5*4cm with vascular embolisms and invasion of the visceral and parietal pleura with a negative parietal border of 3 mm. It was then classified as pT3N0R0. Monitoring was envisaged.

Seven months later, we had the appearance on the CT scan of CAP of a right axillary adenopathy, associated with fat infiltration at the axillary level. The PET scan showed a single right cerebellar localization with right upper retro pectoral and right axillary adenopathies (figure 2a.). Cerebral MRI identified a right cerebellar metastasis (figure 3a.).

The patient was at this stage asymptomatic with a performance status of zero at the time of consultation. He had no EGFR mutation and there was no rearrangement of the EML4-ALK. His PDL1 expression was less than 10%.

Stereotactic radiotherapy was then given for brain metastasis, chemotherapy (Pemetrexed Cisplatin) plus immunotherapy (Pembrolizumab) every 3 weeks for three courses followed by evaluation and treatment with local radiotherapy for right axillary lymph node relapse.

Evaluation after three courses of treatment showed intolerance to the treatment, manifested by disturbed liver function tests (GOT 89 IU/L vs 22 IU initially), neutropenia, severe asthenia for twelve days and nausea.

PET showed a disappearance of secondary hypermetabolisms, previously described in the brain and lymph nodes, and an absence of new suspect hypermetabolisms over the whole volume explored. Thus, a complete metabolic response to the initiated treatment was achieved (figure 2b.). Progressive cerebral MRI showed a reduction in the size of the right cerebellar lesion of around 65%, indicating a partial response (figure 3b.).

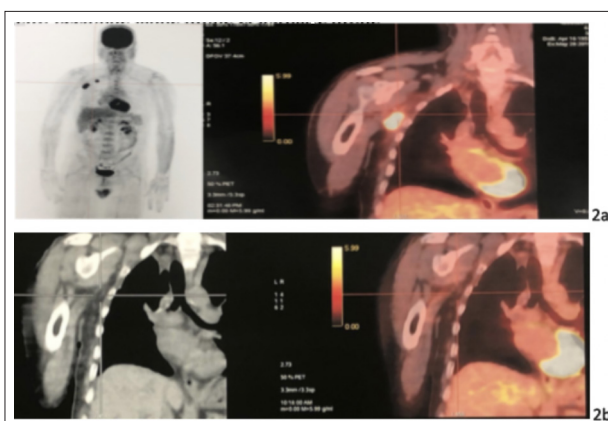


Figure 2: PET CT scan:

2a: Single right cerebellar localization with right upper retropectoral and right axillary adenopathies

2b: Disappearance of the secondary hypermetabolisms, previously described in the brain and lymph nodes, and absence of new suspect hypermetabolisms over the whole volume explored

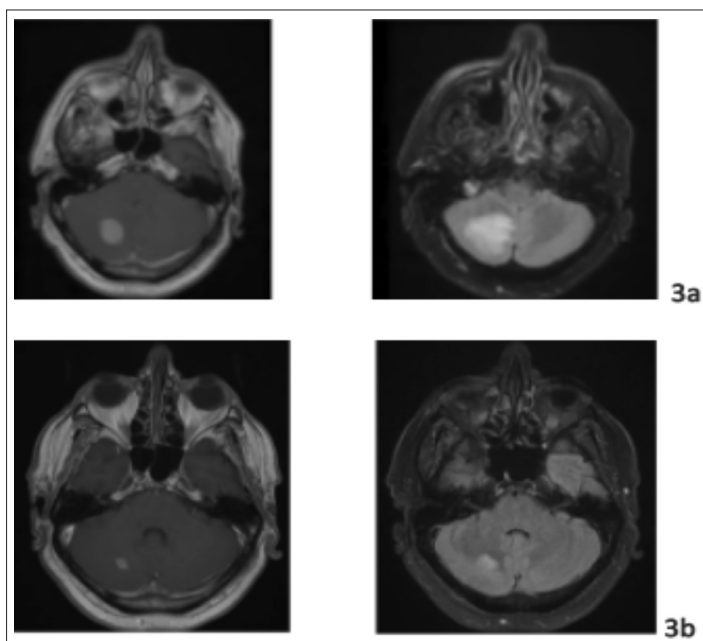


Figure 3: Cerebral MRI:

3a: Right cerebellar metastasis measuring 23*17mm

3b: Reduction in the size of the right cerebellar lesion by approximately 65% (measuring 10*7 mm versus 23*17 mm) with no perilesional edema or mass effect on ventricle four, indicating a partial response

The patient is currently in good general condition. He has received radiation therapy and chemotherapy concurrently with three courses of Pembrolizumab – Pemetrexed - Cisplatin then he has received two courses of Pemetrexed – Pembrolizumab then Pembrolizumab alone. Finally, he received ten courses of Pembrolizumab (the latest one in February 2020). Good tolerance to treatment was observed apart from lower limb edema. The latest comparative CT scan of CAP to date shows a complete regression of right axillary adenopathy with a stable aspect of mid-lobar parenchymal condensation (complete response). In addition, cerebral MRI shows an almost total disappearance of the right cerebellar lesion showing a complete response according to RECIST V1.1 criterion.

To date, the patient has survived 23 months since the diagnosis of the disease. However, treatment was not continued because of CoViD-19 and because the patient had a complete response.

Although we cannot conclude due to the case report being based on a single patient, it illustrates the benefit of a multimodal strategy in the management of metastatic cancers.

Overall, although the presence of brain metastases has always been considered a poor prognostic factor, the development and large-scale implementation of stereotactic brain radiotherapy has proven to be a powerful tool in the arsenal of radiation oncologists for the treatment of oligometastatic NSCLC in the brain, which was confirmed by our optimal outcome with an almost complete disappearance of our patient’s cerebellar lesion [1].

Radiotherapy allowed us to locally control the relapse of lymph nodes and chemotherapy plus immunotherapy were already known to be the reference protocol. In fact, several studies have already been conducted, including Keynote 021, which suggests that the combination of Pembrolizumab, Carboplatin and Pemetrexed gives better results compared to chemotherapy alone for patients with advanced non-squamous NSCLC [2]. Another study, Keynote-189, confirmed that adding pembrolizumab to the standard chemotherapy regimen of Pemetrexed and a platinum-based drug resulted in significantly longer overall survival and progression-free survival than chemotherapy alone [3].

The ETOP NICOLAS trial demonstrates the tolerability of a combination of radiochemotherapy and nivolumab in unresectable stage III NSCLC with no unexpected adverse events or increased risk of severe pneumonia [4]. This is consistent with our patient’s case of minimal and reversible adverse events.

However, we cannot judge whether it was the multimodal strategy or immunotherapy plus chemotherapy that made this patient’s treatment successful. Thus, the case of this patient shows us the interest of multi-modal management in the treatment of oligo-metastatic disease; especially immunotherapy which is revolutionizing first-line treatment of metastatic NSCLC without oncogenic addiction.

The emergence of combination therapies has changed the therapeutic algorithm and will increase the proportion of patients benefiting from immunotherapy, since patients with high PDL1 expression account for 20% of NSCLC without oncogenic addiction. The best treatment option is the combination of chemotherapy plus immunotherapy for patients with PDL1 less than 50%. Furthermore, randomized prospective studies would be of capital interest, including multicenter patient studies and

evaluation of several treatment strategies. Written consent was obtained from the patient to allow for the publication of this report and any relevant accompanying images.

Disclosure

The authors declare there are no conflicts of interest.

Consent

Written consent was obtained from the patient to allow for the publication of this report and any relevant accompanying images.

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