Annals of Case Reports
Leite LM, et al. Ann Case Rep: 9: 101711
www.doi.org/10.29011/2574-7754.101711
www.gavinpublishers.com

OPEN ACCESS

Case Report

GAVIN PUBLISHERS

Ten Years Survival in a Patient with Brain and Meningeal Metastases from ALK-Positive Lung Cancer Treated with Five Lines of Therapy: A Case Report

Wanda Liguigli*, Roberto Barbieri, Rita Cengarle, Anita Rimanti, Giovanna Catania, Francesca Turina, Camilla Pesoni, Maurizio Cantore

Oncology Unit, Ospedale Carlo Poma, Strada Lago Paiolo, 10, 46100 Mantova, Italy

***Corresponding author**: Wanda Liguigli, Oncology Unit, Ospedale Carlo Poma, Strada Lago Paiolo, 10, 46100 Mantova, Italy

Citation: Liguigli W, Barbieri R, Cengarle R, Rimanti A, Catania G, et al (2024) Ten Years Survival in a Patient with Brain and Meningeal Metastases from ALK-Positive Lung Cancer Treated with Five Lines of Therapy: A Case Report. Ann Case Report. 9: 1711. DOI:10.29011/2574-7754.101711

Received: 24 February 2024, **Accepted:** 20 March 2024, **Published:** 25 March 2024

Abstract

Anaplastic lymphoma kinase (ALK) translocation is observed in 4–5% of lung adenocarcinoma patients. In October 2012, we diagnosed a translocated ALK lung adenocarcinoma with pleural and bone metastases in a 42-year-old woman. After 16 months of chemotherapy, due to progression of the abdominal lymph nodes, the patient started Crizotinib. After 28 months, brain MRI documented progression of brain disease and a CT scan showed lung progression. The patient underwent whole-brain radiotherapy and Ceritinib was started but discontinued after six months due to grade 3 gastrointestinal toxicity. In June 2017, progression of meningeal disease was documented and the patient started Brigatinib. After 41 months the brain CT scan showed multiple lesions and Lorlatinib was started. The patient is still continuing this therapy while maintaining a good quality of life. The advent of ALK inhibitors has changed the prognosis of these patients even in cases of cerebral and meningeal metastatic disease.

Keywords: Lung Cancer; ALK, Long-Term Survival; Brain and Meningeal Metastases

Introduction

The echinoderm microtubule-associated protein like-4-anaplastic lymphoma kinase (EML4-ALK) fusion gene is present in 4-5% of patients with metastatic Non-Small Cell Lung Cancer (NSCLC). The clinical characteristics most correlated with the presence of this fusion gene are: young age, adenocarcinoma histotype and non-smoking patient [1]. The presence of brain and meningeal metastases in NSCLC patients is associated with a worse prognosis and a shorter median survival compared to patients without brain disease [2]. The advent of ALK inhibitors, especially second and third-generation ones, has changed the prognosis of NSCLC patients even in cases of cerebral and meningeal metastatic disease [3,4]. We report the case of a long-term survivor patient treated with chemotherapy and four lines of ALK inhibitors.

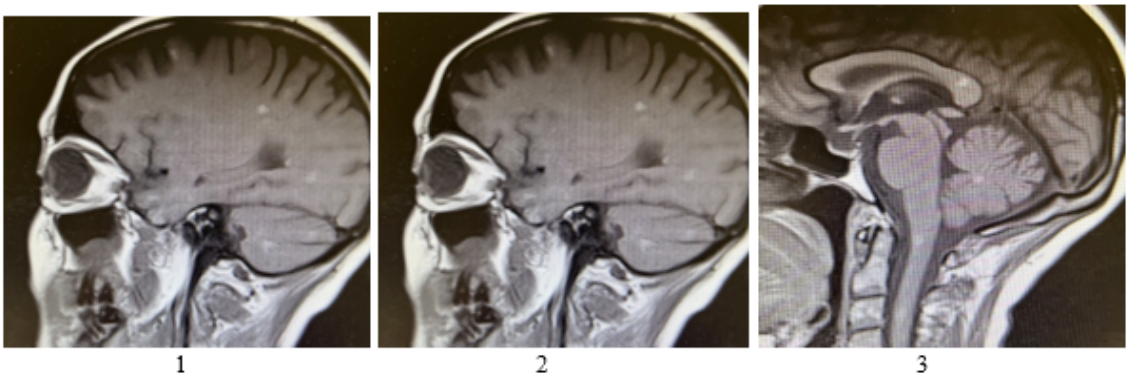

Figure 1-3: MRI brain June 2017.

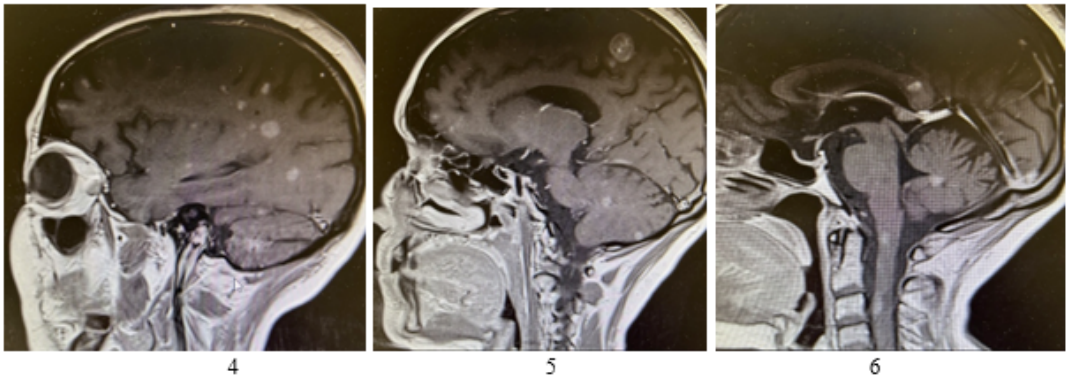

Figure 4-6: MRI brain November 2020.

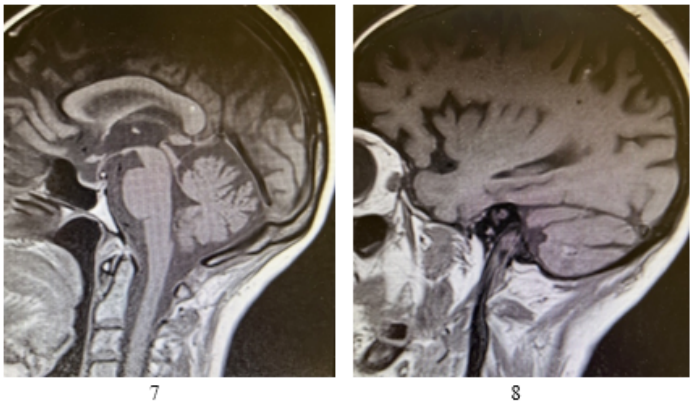

Figure 7,8: MRI brain December 2023.

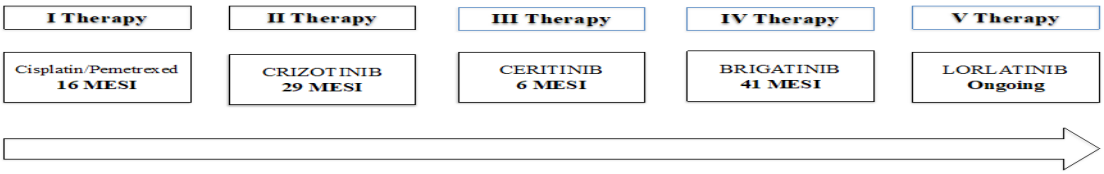

Figure 9: Timeline of treatments.

Case Report

In October 2012, a 42-year-old woman, non-smoking, presented to our hospital with widespread pain and dyspnea. A total-body CT scan revealed a lung tumour with pleural, mediastinal lymph node and bone metastases (whole spine and pelvis). A bronchoscopy was then performed and made the histological diagnosis of lung adenocarcinoma. The molecular profile by immunohistochemistry and then confirmed with Fluorescent In Situ Hybridization (FISH) highlighted the presence of the ALK translocation. The patient was started first-line chemotherapy treatment with Cisplatin and Pemetrexed for 6 cycles and subsequent maintenance with Pemetrexed. In February 2014, CT scan highlighted disease progression at the abdominal lymph node. Crizotinib (500mg/day) started as second-line treatment. Treatment for 29 months was well tolerated. The first re-evaluation PET scan, showed no uptake, highlighting a complete metabolic response. In July 2016, the total-body CT scan showed lung and brain progression of the disease, the latter confirmed with a brain MRI which showed multiple lesions. The patient underwent whole-brain radiotherapy (30 Gy in ten fractions) and was started Ceritinib (450mg/day) as a third line of therapy. After the first month of treatment, the dosage of Ceritinib was reduced (300mg/day) due to grade 3 gastro-intestinal toxicity. At the first re-evaluation of disease (3 months after whole-brain radiotherapy and the start of therapy with Ceritinib) the CT scan showed a complete lung disease response and the brain MRI a partial response. In January 2017, due to the reappearance of grade 3 gastro-intestinal toxicity, especially diarrhea, the patient withdrew her consent to treatment and continued only with CT and MRI checks until May 2017. In June 2017 the patient presented with ataxia and vomiting. After urgent neurological evaluation she was hospitalized and brain MRI showed meningeal progression (Figures 1,2,3). The patient started fourth line therapy with Brigatinib (90mg/day the first week and then 180mg/day). After 2 months from the start of treatment, the neurological symptoms disappeared and the MRI showed a good partial response of the brain disease, the CT scan confirmed stable disease and the PET scan still showed a complete metabolic response. After 41 months of therapy with Brigatinib, in November 2020, the patient was hospitalized for dizziness, balance disorders and headache. The CT scan showed no new lesions but the brain MRI confirmed disease progression with multiple brain metastases (Figures 4,5,6). Even though the patient presented significant clinical deterioration and a performance status of 3, we prescribed the fifth line of treatment with Lorlatinib (100mg/day). The patient was then transferred from the Oncology department to a rehabilitation facility. One month after starting therapy with Lorlatinib, the patient progressively improved until complete regression of neurological symptoms. After 3 months, PET scan confirmed the complete response and brain MRI confirmed an excellent partial response of the brain disease with a significant reduction in the number of multiple brain lesions (Figure 7,8). In June 2023 the MRI showed the progression of a single symptomatic brain lesion in the right parieto-mesial area, it caused weakness in the left lower limb. The patient continued Lorlatinib, started steroid therapy and was treated with stereotactic radiotherapy (24 Gy in three fractions). In December 2023, the patient was re-evaluated with PET scan and MRI which confirmed, respectively, the complete metabolic response and the stability of brain disease. More than 11 years after the diagnosis, the patient is alive, continues an active therapy and leads a good quality of life, working and carrying out her daily activities independently (Figure 9).

Discussion

This case report shows a survival of more than 11 years in a patient affected by metastatic NSCLC at diagnosis and treated with a first line of chemotherapy, four subsequent lines of ALK inhibitors and two brain radiotherapy treatments. Crizotinib was the first ALK inhibitor to demonstrate superior efficacy compared to chemotherapy in ALK-positive patients [5]. In our case, in addition to good tolerability, the treatment immediately led to a complete metabolic response with a progression free survival of 29 months. The advent of second generation ALK inhibitors have demonstrated good disease control even in patients pre-treated with chemotherapy and Crizotinib [6]. However, we know how much the toxicity profile of therapies and their management can influence the patient's compliance with treatment and therefore

the effectiveness of the therapy itself [7]. In fact, in our case the treatment with Ceritinib was suspended after just 6 months of therapy. When the disease appeared in the brain for the first time in our patient in 2016, the intracranial efficacy of ALK inhibitors was not yet well documented. Whole-brain radiotherapy treatment remains an indispensable therapy in patients with severe neurological symptoms not controlled by steroid therapy even if we know what the long-term side effects are [8]. From 2017 to today, our patient's disease has progressed "only" at the cerebral and meningeal level and treatments with Brigatinib first (41 months) and then Lorlatinib have allowed good local control of disease [3,4]. In our case it is highlighted how the third generation ALK inhibitor, Lorlatinib, was able to overcome the resistance mechanisms of previous ALK inhibitors at an intra- and extra-cranial level [9]. The sequence of ALK inhibitors allowed our young patient a long survival with a good quality of life and we expect research to soon show us equally effective results for fourth generation ALK inhibitors [10].

Acknowledgements: Not applicable.

Conflict of Interest: None declared.

Funding: No funding was obtained.

Ethical Approval: Ethical approval not required.

Consent: We had a written consent from the patient.

References

1. Soda M, Choi YL, Enomoto M, Takada S, Yamashita Y, et al. (2007) Identification of the transforming EML4-ALK fusion gene in non-small-cell lung cancer. Nature, 448:561-6.
2. Umemura S, Tsubouchi K, Yoshioka H,Hotta K, Takigawa N, et al. (2012) Clinical outcome in patients with leptomeningeal metastasis from non-small cell lung cancer: Okayama Lung Cancer Study Group. Lung Cancer 77:134–9.
3. Gaye E, Geier M, Bore P, Guilloïque M, Lucia F, Quéré G, et al. (2019) Intra-cranial efficacy of brigatinib in an ALK-positive non-small cell lung cancer patient presenting leptomeningeal carcinomatosis. Lung Cancer 133:1–3.
4. Chen W, Jin D, Shi Y, Zhang Y, Zhou H, et al (2020) The underlying mechanisms of lorlatinib penetration across the blood-brain barrier and the distribution characteristics of lorlatinib in the brain. Cancer Med 9:4350–9.
5. Solomon BJ, Mok T, Kim DW, Wu YL, Nakagawa K, et al. (2014) First-line crizotinib versus chemotherapy in ALK-positive lung cancer. N Engl J Med 371:2167-2177.
6. Shaw AT, Kim TM, Crinò L, Gridelli C, Kiura K, et al. (2017) Ceritinib versus chemotherapy in patients with ALK-rearranged non-small-cell lung cancer previously given chemotherapy and crizotinib (ASCEND-5): a randomized, controlled, open-label, phase 3 trial. Lancet Oncol 18:874-886.
7. Zhou F, Yang Y, Zhang L, Cheng Y, Han B, et al. (2023) Expert consensus of management of adverse drug reactions with anaplastic lymphoma kinase tyrosine kinase inhibitors. ESMO Open. 8:101560.
8. Warrington JP, Ashpole N, Csiszar A, Lee YW, Ungvari Z, et al (2013) Whole brain radiation-induced vascular cognitive impairment: mechanisms and implications. J Vasc Res 50:445-457.
9. Solomon BJ , Bauer TM , Mok TSK , Liu G, Mazieres J,et al.(2023) Efficacy and safety of first-line lorlatinib versus crizotinib in patients with advanced, ALK-positive non-small-cell lung cancer: updated analysis of data from the phase 3, randomised, open-label CROWN study. Lancet Respir Med 11:354-366.
10. Peng L, Zhu L, Sun Y, Stebbing J, Selvaggi G, et al. (2022) Targeting ALK Rearrangements in NSCLC: Current State of the Art. Front Oncol 6:12:863461.