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Case Report

***Pneumocystis jirovecii* Pneumonia in a Patient with Lung Adenocarcinoma and EGFR Mutation Treated with Afatinib During the Coronavirus Pandemic 2019**

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ABSTRACT

The novel coronavirus (SARS-CoV-2) or COVID-19 pneumonia is a new global pandemic that can be a challenge for the oncologists. Cancer patients are at high risk of contracting this infection and to develop severe respiratory complications. We present the case of a young patient with a metastatic EGFR positive lung adenocarcinoma in complete remission with afatinib therapy, who developed fever, dyspnea, dry cough, widespread pain and weakness during COVID-19 pandemic in Italy. The thorax computed tomography scan showed suspected pneumonia. Empiric antibiotic therapy was initiated without significant improvement in symptoms. The differential diagnosis included COVID-19 or other pneumonia, mycotic infection, disease progression or afatinib related pneumonia. A SARS-CoV-2 test on a nasopharyngeal swab was repeated twice, and it was negative. Tests for pneumobacteria, cytomegalovirus, tuberculosis bacteria and *Legionella* were also negative. We further performed a bronchoscopy with bronchoalveolar lavage, and a *Pneumocystis jirovecii* was microscopically identified. Treatment with trimethoprim-sulfamethoxazole was initiated, with regression of all symptoms. This case confirms the growing difficulties for oncologists during COVID-19 pandemic in the proper management of cancer patients, showing the challenges due to differential diagnoses. In this context, a multidisciplinary approach is crucial to define the best diagnostic and therapeutic strategy.

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Introduction

The Coronavirus Disease 2019 (COVID-19) was first described in China at the end of 2019, and then it rapidly spread all the world, causing fever, pneumonia, respiratory failure and death [1, 2]. During COVID-19

pandemic, cancer patients are at high risk of contracting the infection and to develop severe respiratory symptoms [3]. In patients with advanced lung cancer, a further issue is excluding disease progression or treatment-related complications. We present the case of a young woman with a metastatic EGFR positive lung adenocarcinoma in treatment with afatinib, who developed pneumonia during the COVID-19 pandemic.

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Case Report

In October 2018, a 35-year-old, never smoker woman without comorbidities underwent a left pneumonectomy with lymphadenectomy for lung adenocarcinoma (stage IIIA) with EGFR activating mutation (exon 19 deletion). After surgery, the multidisciplinary team (MDT) proposed 4 cycles of adjuvant chemotherapy with cisplatin and vinorelbine, followed by thoracic radiotherapy (50Gy). After 6 months, a computed tomography (CT) scan showed a metastatic lesion in the upper lobe of the right lung: the patient started first-line treatment with afatinib 40 mg/day, achieving a complete response on February 2020. On 4th April 2020, during the COVID-19 pandemic in Italy, the patient was admitted to Emergency Room for 38°C fever, dyspnea, dry cough, widespread pain and weakness. She had tachycardia with 104 bpm, normal arterial pressure and a SpO₂ of 98%. Laboratory tests showed normal white blood counts with neutrophilia ($7.17 \times 10^3/uL$) and lymphopenia ($0.77 \times 10^3/uL$), elevated LDH (368 UI/L) and CRP (3.07). A chest X-ray showed no alterations. The patient refused admission to the Hospital.

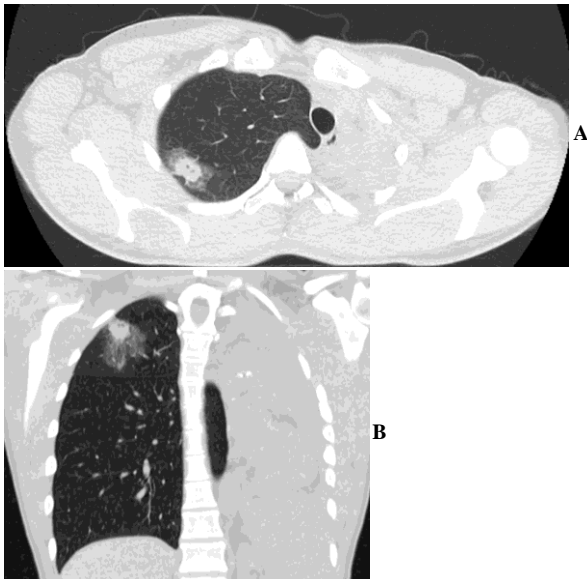


Figure 1: HRCT scan showing a solid lesion of 2 centimeters surrounded by diffuse ground glass opacities (GGO) on the right upper lobe.

She discontinued afatinib and started at home treatment with steroids, azithromycin and amoxicillin plus clavulanic acid. A SARS-CoV-2 RT PCR test on a nasopharyngeal swab was negative. A high-resolution CT (HRCT) scan showed a solid lesion of 2 centimeters surrounded by diffuse ground glass opacities (GGO) on the right upper lobe, without mediastinal lymphadenopathy, pleural or pericardial effusion (Figure 1). The radiologist proposed a differential diagnosis among COVID-19 pneumonia, other pneumonia, mycotic infection, disease progression or afatinib related pneumonitis. Meanwhile, the fever disappeared, but the weakness, the thoracic pain and the dry cough persisted. The pneumologist suggested to repeat the SARS-CoV-2 RT PCR on a nasopharyngeal swab as well as tests for other infectious agents and to perform bronchoscopy with bronchoalveolar lavage. A new HRCT after 10 days showed excavation of the lung lesion with a reduction of the GGO (Figure 2). The second swab and all tests for pneumobacteria,

cytomegalovirus, tuberculosis bacteria and *Legionella* were negative. However, a *Pneumocystis jirovecii* was microscopically identified in the bronchoalveolar lavage by direct fluorescent antibody staining. A treatment with trimethoprim-sulfamethoxazole was initiated on May 4th, with complete regression of all symptoms of the patient.

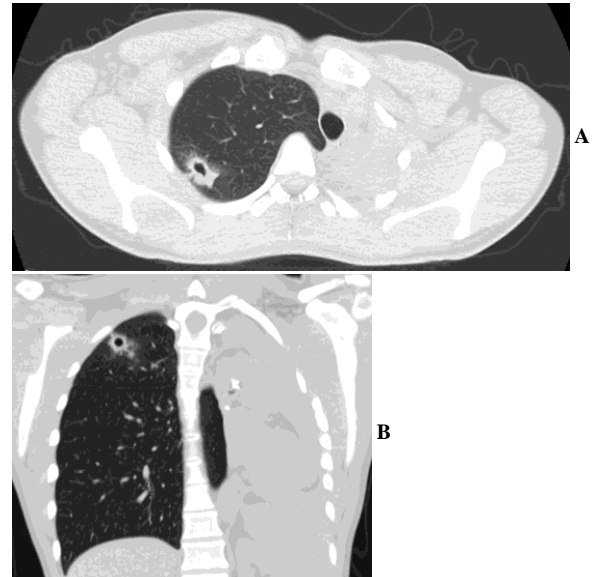


Figure 2: HRCT scan after 10 days showing excavation of the lung lesion with reduction of the GGO.

Discussion

We report the case of a young patient with a metastatic EGFR mutated lung cancer who developed pneumonia while she was in complete remission with afatinib treatment during the COVID-19 pandemic. Afatinib is a second-generation EGFR TKI [4]. In the Lux-Lung-3 and -6 trials, afatinib significantly increased progression-free survival (PFS) compared with chemotherapy in the first line treatment of advanced NSCLC patients with activating EGFR mutations [5, 6]. A pooled analysis of the two studies also showed a significant improvement of overall survival (OS) with afatinib versus chemotherapy in patients with common mutations (27.3 vs. 24.3 months; HR 0.81, 95% CI: 0.66-0.99, $p=0.037$) [7]. Finally, in the Lux-Lung-7 trial, afatinib improved PFS (HR: 0.73, 95% CI: 0.57-0.95; $p=0.017$) and time-to-treatment failure (HR: 0.73, 95% CI: 0.58-0.92; $p=0.0073$) in a head-to-head comparison with gefitinib.

On the basis of these results, afatinib has been approved for the first line therapy of patients with metastatic NSCLC and EGFR mutations [8]. Pneumonitis during therapy with afatinib are uncommon (1-2% of cases), but they could be fatal for patients, if not correctly diagnosed [9]. Similarly, *Pneumocystis jirovecii* infections, often associated with high corticosteroid intake and immunosuppression, are rarely reported in patients with solid tumors, but they can lead to the death of the patients if not promptly treated [10]. They are characterized by lung infiltrations at chest radiography or computed tomography (CT) and severe respiratory symptoms, mimicking the clinical picture of COVID-19 pneumonia. This case confirms the growing difficulties for oncologists during the COVID-19 pandemic in the proper management of cancer patients, showing the challenges due to differential diagnosis, including

COVID-19 or other viral pneumonia, mycotic infection, disease progression or afatinib related pneumonia. In this difficult context, only a multidisciplinary approach can effectively define the best diagnostic and therapeutic strategies.

Author Contributions

All authors contributed equally.

Conflicts of Interest

A.M. declares the following speakers' bureau: Roche, Takeda, Pfizer, Boehringer Ingelheim, AstraZeneca, MSD Oncology, BMS. The other authors declare no conflicts of interest.

Consent

The patient signed an informed consent for participation.

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REFERENCES

- Dawei Wang, Bo Hu, Chang Hu, Fangfang Zhu, Xing Liu et al. (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 323: 1061-1069. [[Crossref](#)]
- Rajesh T Gandhi, John B Lynch, Carlos Del Rio (2020) Mild or moderate Covid-19. *N Engl J Med*. [[Crossref](#)]
- The Lancet Oncology (2020) COVID-19: global consequences for oncology. *Lancet Oncol* 21: 467. [[Crossref](#)]
- Pasqualina Giordano, Anna Manzo, Agnese Montanino, Raffaele Costanzo, Claudia Sandomenico (2016) Afatinib: An overview of its clinical development in non-small-cell lung cancer and other tumors. *Crit Rev Oncol Hematol* 97: 143-151. [[Crossref](#)]
- Lecia V Sequist, James Chih Hsin Yang, Nobuyuki Yamamoto, Kenneth O'Byrne, Vera Hirsh et al. (2013) Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. *J Clin Oncol* 31: 3327-3334. [[Crossref](#)]
- Yi Long Wu, Caicun Zhou, Cheng Ping Hu, Jifeng Feng, Shun Lu (2014) Afatinib versus cisplatin plus gemcitabine for first-line treatment of Asian patients with advanced non-small-cell lung cancer harbouring EGFR mutations (LUX-Lung 6): an open-label, randomised phase 3 trial. *Lancet Oncol* 15: 213-222. [[Crossref](#)]
- James Chih Hsin Yang, Yi Long Wu, Martin Schuler, Martin Sebastian, Sanjay Popat et al. (2015) Afatinib versus cisplatin-based chemotherapy for EGFR mutation-positive lung adenocarcinoma (LUX-Lung 3 and LUX-Lung 6): analysis of overall survival data from two randomised, phase 3 trials. *Lancet Oncol* 16: 141-151. [[Crossref](#)]
- Keunchil Park, Eng Huat Tan, Ken O'Byrne, Li Zhang, Michael Boyer et al. (2016) Afatinib versus gefitinib as first-line treatment of patients with EGFR mutation-positive non-small-cell lung cancer (LUX-Lung 7): a Phase 2B, open-label, randomised controlled trial. *Lancet Oncol* 17: 577-589. [[Crossref](#)]
- Chong Hyun Suh, Hye Sun Park, Kyung Won Kim, Junhee Pyo, Hiroto Hatabu et al. (2018) Pneumonitis in advanced non-small-cell lung cancer patients treated with EGFR tyrosine kinase inhibitor: Meta-analysis of 153 cohorts with 15,713 patients: Meta-analysis of incidence and risk factors of EGFR-TKI pneumonitis in NSCLC. *Lung Cancer* 123: 60-69. [[Crossref](#)]
- Eun Hye Lee, Eun Young Kim, Sang Hoon Lee, Yun Ho Roh, Ah Young Leem et al. (2019) Risk factors and clinical characteristics of Pneumocystis jirovecii pneumonia in lung cancer. *Sci Rep* 9: 2094. [[Crossref](#)]