Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

19 were done including chest computed tomography and throat swab reverse transcriptase-polymerase chain reaction, which revealed negative results. Testing for serologic IgM and IgG antibodies for SARS-CoV-2 were also performed and were found to be positive, which suggested that the patient was an asymptomatic SARS-CoV-2 carrier (Fig. 1). On consideration that the positive IgM antibody might represent potential infectivity, the patient was placed in an isolation ward to prevent possible in-hospital transmission. Subsequent throat swabs tests performed on March 31, April 2, and April 3, 2020 were all negative. Further serologic IgM antibody results turned negative on April 3, 2020, confirming the patient had recovered from COVID-19. Meanwhile, as a close contact, his wife was required to undergo screening tests; she tested positive for serologic IgG antibody alone but was negative on throat swab assay and chest computed tomography. His wife denied any clinical symptoms and contact history. This familial transmission highlights that asymptomatic carriers are indeed contagious.

On April 7, 2020, after consulting COVID-19 specialists, the patient resumed his chemotherapy regimen to which he was confirmed to be responsive before the COVID-19 outbreak. Subsequently, a postchemotherapy diagnostic test was performed, which revealed that only serologic antibody IgG was positive.

In conclusion, this case suggests that we should be alert to suspicious symptoms in patients with lung cancer, which might overlap with those of asymptomatic COVID-19. To our knowledge, we are the first to report that chemotherapy might be safe for asymptomatic carriers after the serologic IgM antibody turns negative. However, further studies are urgently required.

Wen Ouyang, MD
Jing Yu, MD
Junhong Zhang, MD
Department of Radiation and Medical Oncology
Zhongnan Hospital
Wuhan University
Wuhan, People's Republic of China

Conghua Xie, MD
Department of Radiation and Medical Oncology
Zhongnan Hospital
Wuhan University
Wuhan, People's Republic of China
Hubei Key Laboratory of Tumor Biological Behaviors
Zhongnan Hospital
Wuhan University
Wuhan, People's Republic of China
Hubei Clinical Cancer Study Center
Zhongnan Hospital
Wuhan University
Wuhan, People's Republic of China

References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395:497–506.
2. Hu Z, Song C, Xu C, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China [e-pub ahead of print]. *Sci China Life Sci*. https://doi.org/10.1007/s11427-020-1661-4, accessed April 7, 2020.
3. Yu J, Ouyang W, Chua MLK, Xie C. SARS-CoV-2 transmission in patients with cancer of a tertiary care hospital in Wuhan, China [e-pub ahead of print]. *JAMA Oncol*. https://doi.org/10.1001/jamaoncol.2020.0980, accessed April 7, 2020.

A Rapid Fatal Evolution of Coronavirus Disease-19 in a Patient With Advanced Lung Cancer With a Long-Time Response to Nivolumab

To the Editor:

Coronavirus disease-19 (COVID-19) is now a pandemic disease. In Italy, the first set of cases were documented at the end of January 2020 reporting a dramatic spread. Liang et al.[1] reported an increased risk of COVID-19 for patients with cancer, having poorer prognosis than those without cancer. We present a case of a rapid fatal evolution of COVID-19 in a patient with metastatic lung cancer in partial remission with immunotherapy since 2013.

On March 4, 2020, a 65-year-old male patient presented in the emergency department for shortness of breath, fever, and mental confusion. The hemogasanalysis revealed hypoxia; laboratory tests revealed normal leukocytes with lymphopenia, and elevation of C-reactive protein, transaminases, and lactate dehydrogenase. Chest radiograph showed reticular interstitial addensative findings (Fig. 1). Nasal swab was positive for COVID-19.

His medical history was positive for emphysema and lung adenocarcinoma diagnosed in August 2012. At that time, the patient underwent cerebral metastasectomy,

Address for correspondence: Lucia Bonomi, MD, Oncology Unit, Azienda Socia Sanitaria Territoriale Ospedale Papa Giovanni XXIII Bergamo, Lombardia, Italy. E-mail: lbonomi@asst-pg23.it

ISSN: 1556-0864
https://doi.org/10.1016/j.jtho.2020.03.021

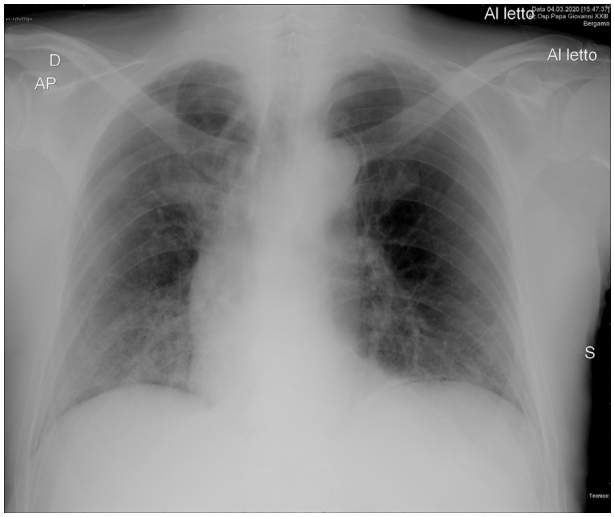

Figure 1. March 4 2020 Chest X-ray.

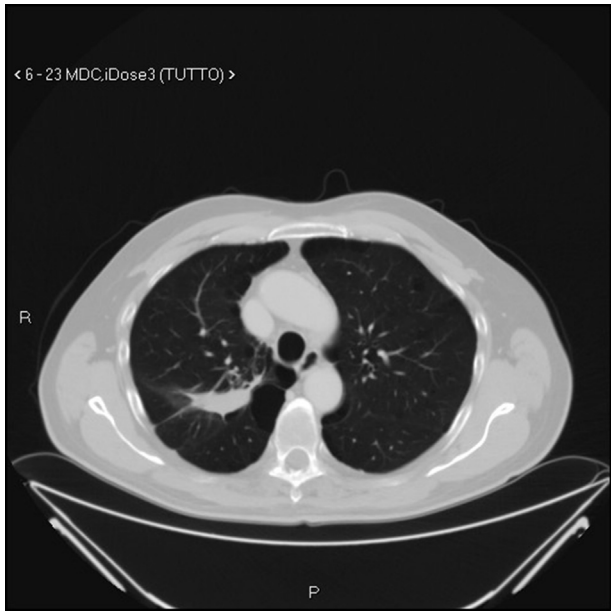

Figure 2. February 4 2020 CT scan.

panencephalic radiotherapy, and chemotherapy (carboplatin and pemetrexed) until July 2013. After six cycles of chemotherapy, brain magnetic resonance imaging and computed tomography scan revealed progression of the disease. He was then enrolled in CA209-057 clinical trial and treated from August 2013 to February 14, 2020 with nivolumab, a programmed cell death protein-1 checkpoint inhibitor, in which there was partial response without adverse events reported. The last computed tomography scan was performed on February 2, 2020, which described stable disease (Fig. 2).

On March 5, 2020, he was admitted to the infectious disease unit and started empiric antibiotic treatment and oxygen therapy with a reservoir mask at 15 L/minute. He was sedated because of agitation; because of this, he never received prescribed lopinavir plus ritonavir and hydroxychloroquine. The patient had a rapid worsening of the condition and died on March 9, 2020.

There are no specific therapeutic agents for coronavirus infections. As per WHO's guidelines in the management of severe COVID-19, our patient was treated with an empiric antimicrobial, oxygen therapy, and other symptomatic treatment.[2] Emerging evidence suggests that the same patient with a severe course may respond to the infection with a "cytokine storm."[3] Histologic examination of the biopsy samples at autopsy from a patient who died from severe COVID-19 revealed the presence of bilateral diffuse alveolar damage with cellular fibromyxoid exudates and mononuclear inflammatory lymphocytes in both lungs.[4] Our patient had a history of long exposure to immunotherapy; and although a kind of paradoxical immunologic response to influenza infection or vaccination during the use of immune checkpoint inhibitors has been previously described,[5] we have no data regarding immune checkpoint inhibitors and the risk of COVID-19. Our patient presented a rapid evolution of respiratory failure and was not treated with more invasive procedures, probably owing to his cancer and emphysema history. We do not know whether treatment with steroids, not routinely recommended in COVID-19 (but very useful against side effects of immunotherapy), could help to control pneumonitis in these patients.

This case emphasized the importance of a multidisciplinary approach, even in the presence of a severe outbreak like the pandemic COVID-19, because the knowledge of underlying disease and concomitant treatments is important to take the best individual therapeutic decision.

Lucia Bonomi, MD
Laura Ghilardi, MD
Ermenegildo Arnoldi, MD
Carlo Alberto Tondini, MD
Anna Cecilia Bettini, MD
Oncology Unit
Azienda Socia Sanitaria Territoriale Ospedale Papa Giovanni XXIII
Bergamo, Lombardia, Italy

References

1. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol*. 2020;21:335-337.
2. WHO. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance version 1.2; 2020. https://apps.who.int/iris/rest/bitstreams/1272156/retrieve. Accessed March 13, 2020.

3. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395:507-513.
4. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome [e-pub ahead of print]. *Lancet Respir Med*. https://doi.org/10.1016/S2213-2600(20)30076-X, accessed February 17, 2020.
5. Bersanelli M, Scala S, Affanni P, et al. Immunological insights on influenza infection and vaccination during immune checkpoint blockade in cancer patients. *Immunotherapy*. 2020;12:105-110.

KEAP1-NFE2L2–Mutant NSCLC and Immune Checkpoint Inhibitors: A Large Database Analysis

To the Editor:

In the study by Goeman et al.,[1] it was stated that *KEAP1-NFE2L2* mutation defines a subset of rapidly progressing lung adenocarcinoma in which chemotherapy and targeted therapies could be of little utility. They suggested that patients with lung adenocarcinoma carrying *KEAP1-NFE2L2* mutation could benefit from immune checkpoint inhibitors (ICIs).

KEAP1-NFE2L2 pathway plays a central role in protecting cells from oxidative and electrophilic stress in NSCLC. Evidence has revealed that *KEAP1-NFE2L2* mutation is associated with poor prognosis and chemotherapeutic resistance in NSCLC.[2] Yang et al.[3] found that patients with stage IV disease exhibited higher *NFE2L2* expression than patients with stage IIIB disease. Solis et al.[4] established an association of nuclear NFE2L2 abundance with worse progression-free survival. In clinical practice, the deregulation of the KEAP1-NFE2L2 pathway serves as a negative prognostic factor for patients with NSCLC, as manifested in the reduced overall survival (OS).

Despite numerous studies on *KEAP1-NFE2L2* in NSCLC, the response of patients with NSCLC harboring *KEAP1-NFE2L2* mutation to ICIs has never been documented. Therefore, we have used the tumor mutational burden (TMB) and immunotherapy database[5] to ascertain the responses of patients with *KEAP1-NFE2L2* mutational NSCLC to ICIs. This database contains genomic and survival data of 1661 tumor-normal pairs from 1661 patients with various cancer types sequenced with the Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets assay. We first analyzed the TMB in patients with either *KEAP1* or *NFE2L2* mutation and their wild-type counterparts. The TMB varied significantly between patients with wild-type and mutational *KEAP1* NSCLC ($p = 0.009$) (Fig. 1*A*). For patients with NFE2L2 wild-type and

Drs. Chenyue Zhang and Chenxing Zhang equally contributed to this work.

Address for correspondence: Haiyong Wang, MD, Department of Internal Medicine Oncology, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Number 440, Ji Yan Road, Jinan 250117, People's Republic of China. E-mail: wanghaiyong6688@126.com

ISSN: 1556-0864

https://doi.org/10.1016/j.jtho.2020.02.027

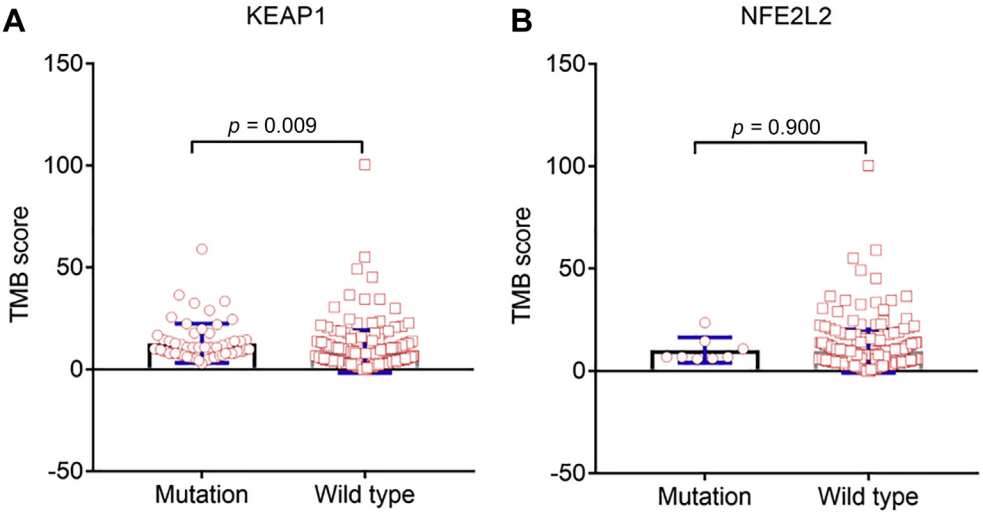

Figure 1. TMB in patients with NSCLC harboring (*A*) *KEAP1* and (*B*) *NFE2L2* mutation and their wild-type counterparts. TMB, tumor mutational burden.