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A rapid fatal evolution of Coronavirus Disease-19 (COVID-19) in an advanced lung cancer patient with a long time response to nivolumab

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Declaration of conflicting interest

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Coronavirus Disease-19 (COVID-19) is now a pandemic disease, in Italy first cases were documented at the end of January showing a dramatic spread. Liang and colleagues reported an increased risk of COVID-19 for cancer patients and a poorer prognosis than those without cancer [1]. 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 showed hypoxia, laboratory tests revealed a normal leukocytes with a lymphopenia, an elevation of C-reactive protein, transaminases and lactate deidrogenease. Chest x-ray showed reticular-interstitial addensative findings, a nasal swab was positive for COVID-19.

His medical history was positive for emphysema and lung adenocarcinoma diagnosed on August 2012. At that time the patient underwent cerebral metastasectomy, panencefalic radiotherapy and chemotherapy (carboplatinum and pemetrexed) until July 2013. After six cycles of chemotherapy brain MRI and CT scan showed progression of disease. He was then enrolled in CA209-057 clinical trial and treated, from August 2013 until February 14, 2020, with nivolumab, a PD-1 checkpoint inhibitor, without adverse event and with a hold partial response. The last CT scan was performed on February 2,2020, and described stable disease.

On March 5, 2020, he was admitted in infectious disease unit and started empiric antibiotic treatment and oxygen therapy with reservoir mask at 15 L/min. He was sedated for agitation and, for this reason, he never received prescribed lopinavir+ritornavir and hydroxychloroquine. The patient had a rapid worsening of condition and died on March 9.

There are no specific therapeutic agents for coronavirus infections: as World Health Organization suggests in its guidance for the management of severe COVID-19, our patient was treated with empiric antimicrobial, oxygen therapy and symptomatic treatment [2]. Emerging evidences suggest that same patients with a severe course may respond to the infection with a "cytokine storm", [3]. In the biopsy samples at autopsy from a patient who died from severe COVID-19, histological examination showed bilateral diffuse alveolar damage with cellular fibromyxoid exudates, mononuclear inflammatory lymphocytes were seen in both lungs [4]. Our patient had a history of long exposure to immunotherapy: a kind of paradoxical immunological response to influenza infection/vaccination during immune checkpoint inhibitors have been described [5], but we have no data regarding immune checkpoint inhibitors and the

risk of COVID-19. Our patient presented a rapid evolution of respiratory failure and wasn't treated with more invasive procedures, probably due to his cancer and emphysema history. We don't know if treatment with steroids, not routinely recommended in COVID-19 but very useful to contrast side effects of immunotherapy, could help to control pneumonitis in these patients.

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

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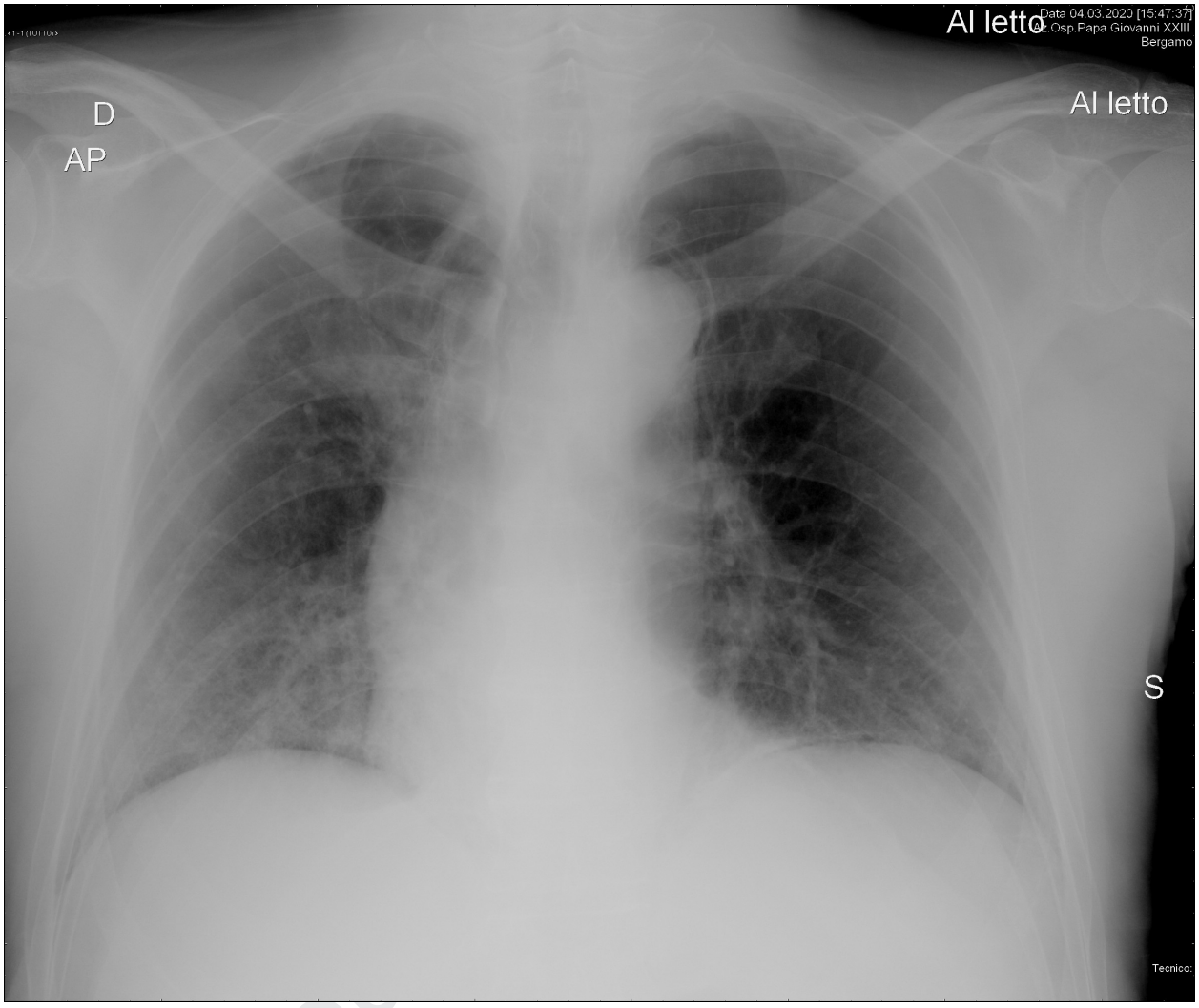
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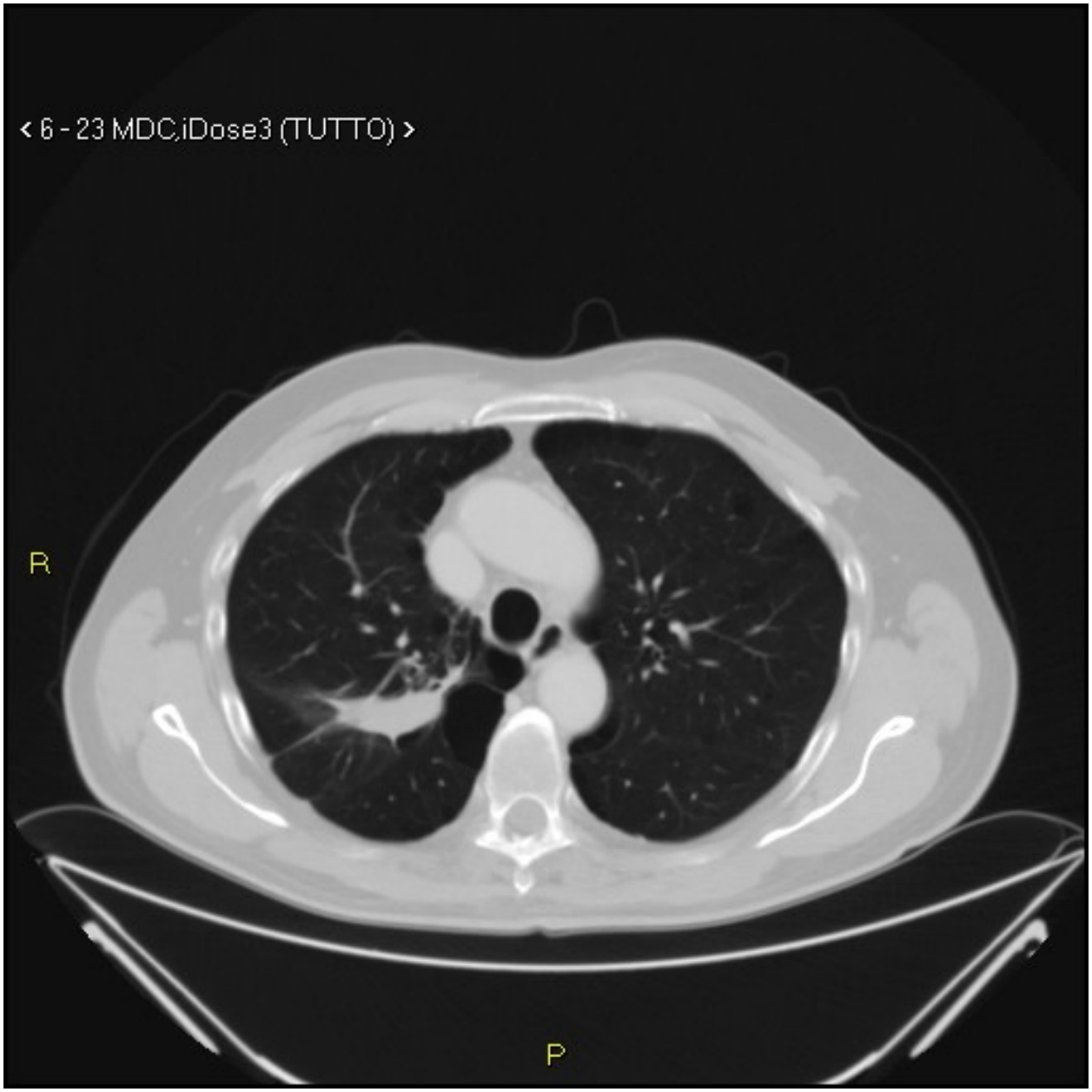
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