

SARS-CoV-2 and Legionella Co-infection in a Person Returning from a Nile Cruise

Running title: SARS-CoV-2 and *Legionella pneumophila* Co-infection

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Highlight

We report a case of severe acute respiratory syndrome coronavirus 2 and *Legionella* co-infection manifesting as pneumonia with gastrointestinal symptoms. The case highlights the importance of differential diagnosis during the COVID-19 pandemic, so we do not miss the opportunity to diagnose other treatable causes of disease with similar symptoms.

Main Text

An 80-year-old Japanese male visited our hospital on March 11 for malaise, diarrhea, and cough (Figure 1). The patient had visited Egypt from February 26 to March 4. During his stay, he participated in a Nile cruise from February 28 to March 1. He was uncertain if he had contact with sick persons, but developed symptoms after returning to Japan. On day 1 of his illness, he experienced malaise and slight cough. On day 3, he experienced nausea without vomiting and had frequent watery diarrhea. On day 5, he went to a nearby clinic and was suspected to have gastroenteritis, and was prescribed probiotics and an antiemetic. On day 7, as malaise, diarrhea, and cough were worsening along with decreased appetite, he visited the emergency room at our hospital. He had not experienced rhinorrhea, sore throat, or dyspnea. He had history of dyslipidemia and benign prostatic hyperplasia. He had no smoking history. He was a construction worker and actively travelled both domestically and internationally in his spare time. On examination, his temperature was 38.4°C; blood pressure, 119/54 mmHg;

pulse, 92 bpm; respiration, 18 breaths/min; and oxygen saturation, 97% on ambient air. His throat was slightly red without exudates, lung auscultation was clear, and abdomen was soft and non-tender. Blood tests showed normal leukocyte count and alanine aminotransferase, but elevated aspartate aminotransferase, blood urea nitrogen, creatinine, lactate dehydrogenase, and C-reactive protein (Appendix Table 1). Urinary antigen test for *Legionella pneumophila* serotype 1 (BinaxNOW *Legionella*; Abbot, Lake Bluff, IL, USA), which has almost 100% specificity, was positive. Chest radiography was not clinically significant, but chest computed tomography showed bilateral, patchy, peripheral ground-glass opacity (Figure 2). 500 mg azithromycin and 2 g ceftriaxone were initiated. Although *Legionella* was suspected to be present, the history of the Nile cruise still strongly raised suspicion for COVID-19, so an upper respiratory sample was taken and sent to the Public Health Institute on day 8, where the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reverse transcription PCR test was positive. Unfortunately, the patient was intubated on day 13 and passed away on day 23 as he was 80 years old and had diabetes mellitus, which put him at extremely high risk. He and his family decided not to use extracorporeal membrane oxygenation, which could have possibly changed the outcome. For this patient, *Legionella* treatment was likely successful but COVID-19 may have determined the patient's outcome.

The World Health Organization declared that the global outbreak of 2019 novel coronavirus disease (COVID-19) constitutes a pandemic on March 11, 2020 (1). During the 2009 influenza A (H1N1) pandemic, many bacterial co-infections and secondary infections occurred, resulting in substantial morbidity and mortality (2). Also, misdiagnosis was a concern due to availability bias, and treatable bacterial/parasitic infections were mistakenly labeled as influenza (3). Our case, although fatal, highlights the importance of differential diagnosis during the current COVID-19 pandemic, so we do not miss the opportunity to

diagnose other treatable causes of disease with similar symptoms. In the present case, we found co-infection with *Legionella*, which can be fatal if untreated especially among the elderly. Although the exact source of exposure to *Legionella* is uncertain in this case, history of exposure to a contaminated water source is important for diagnosing *Legionella*, and cases of Legionnaires' disease associated with cruise ships have been reported previously (4). Gastrointestinal symptoms could have been caused by either or both pathogens, as both are known to cause them (5).

Author contributions

Takeshi A, SN, Takahiro A, and AN conceptualize the study. All authors contributed to acquisition and interpretation of the data. Takeshi A wrote the initial draft. All authors critically reviewed and approved the final manuscript.

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Conflict of Interest

The authors have declared no conflicts of interest.

Informed Consent

The patient provided written, informed consent to have his clinical details presented in this report.

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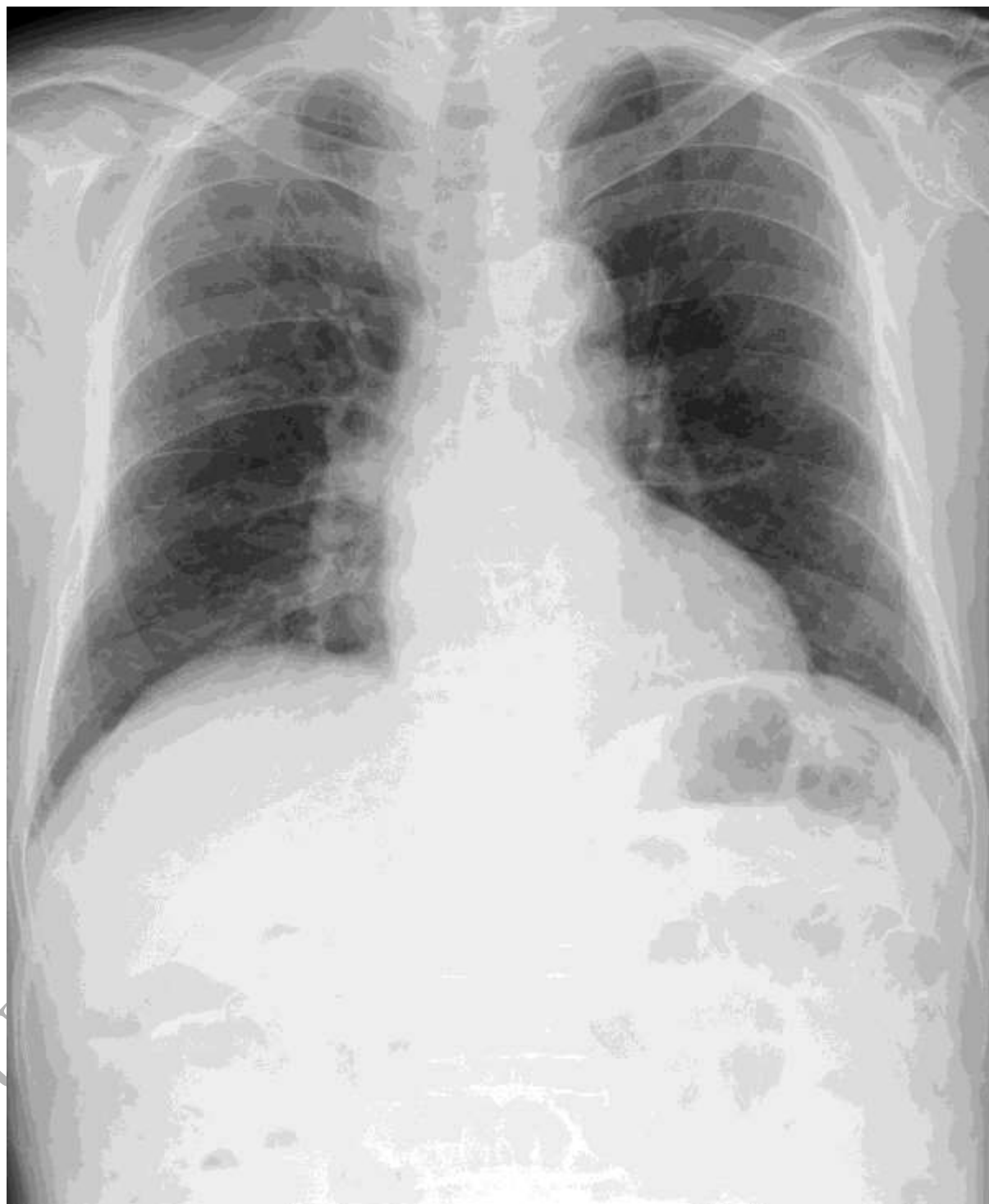
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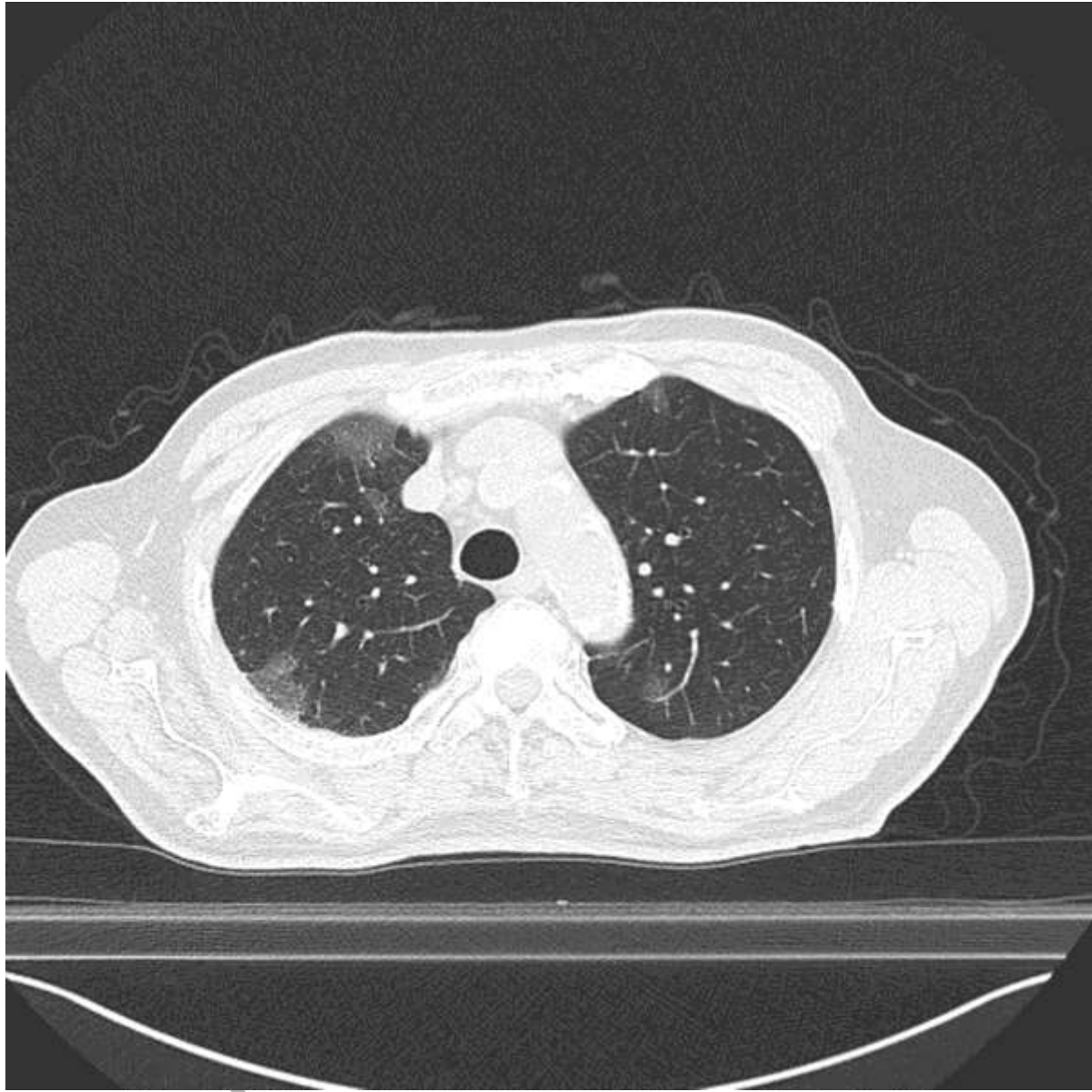
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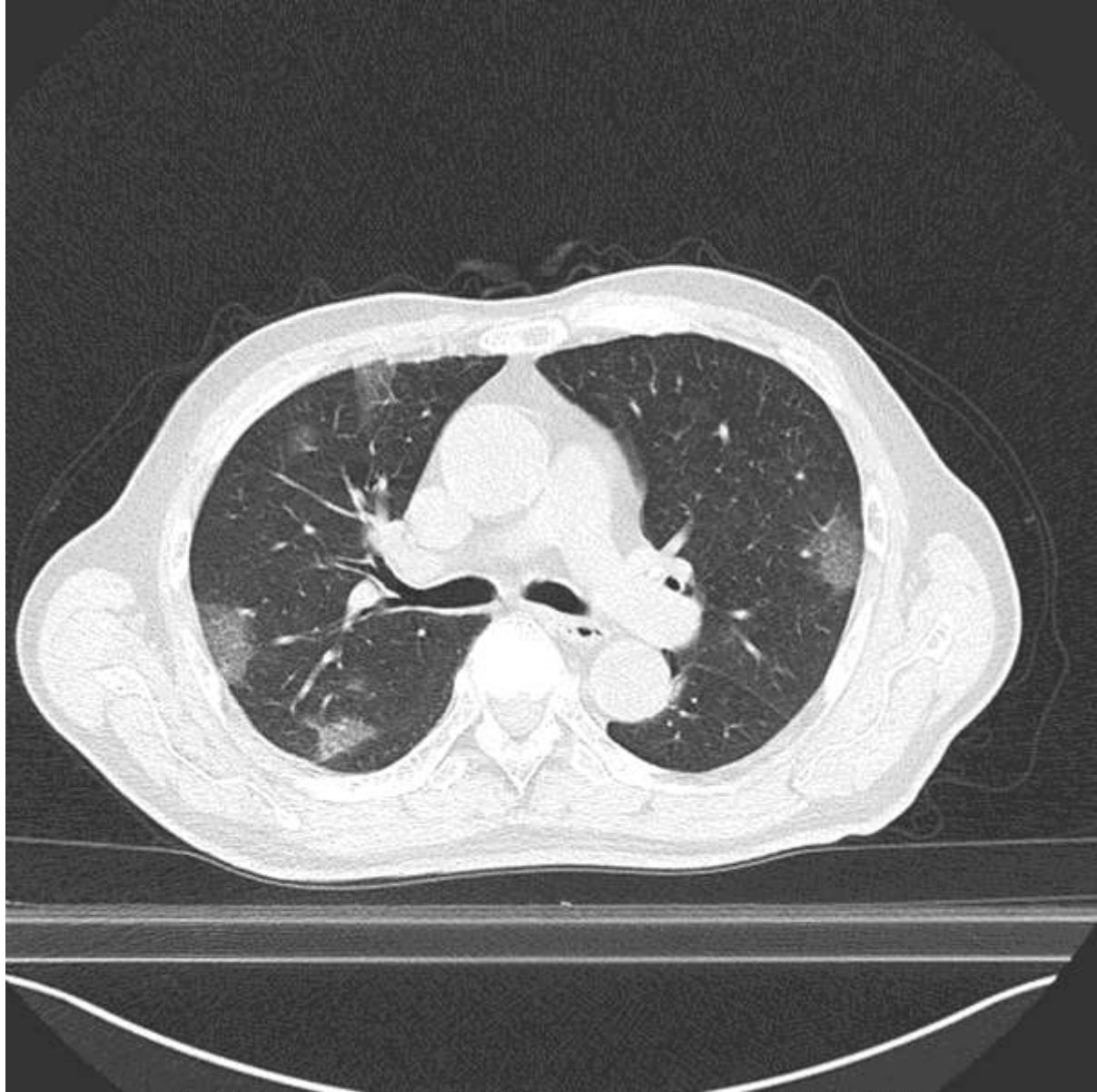
Figure 1. Clinical course of a patient with co-infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and *Legionella*. ER, emergency room; SpO₂, oxygen saturation; PaO₂, arterial partial pressure of oxygen; RT-PCR, reverse transcription-polymerase chain reaction.

Date	Egypt								Return to Japan		Work		Clinic visit	ER visit and admission		
	Feb 26	Feb 27	Feb 28	Feb 29	Mar 1	Mar 2	Mar 3	Mar 4	Mar 5	Mar 6	Mar 7	Mar 8	Mar 9	Mar 10	Mar 11	Mar 12
Illness day									1	2	3	4	5	6	7	8
Hospital day															1	2
Fever (°C)	?	?	?	?	?	?	?	?	?	?	?	?	?	?	39.4	37.7
SpO ₂ (%)															98	93
PaO ₂																63.7
Malaise																
Dry cough																
Nausea																
Diarrhea																
<i>Legionella</i> antigen															+	
SARS-CoV-2 RT-PCR															+	

Figure 2. Radiographs of a patient with co-infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and *Legionella*. (A) Chest radiograph. (B-E) Chest computed tomography of the patient (Illness Day 7).

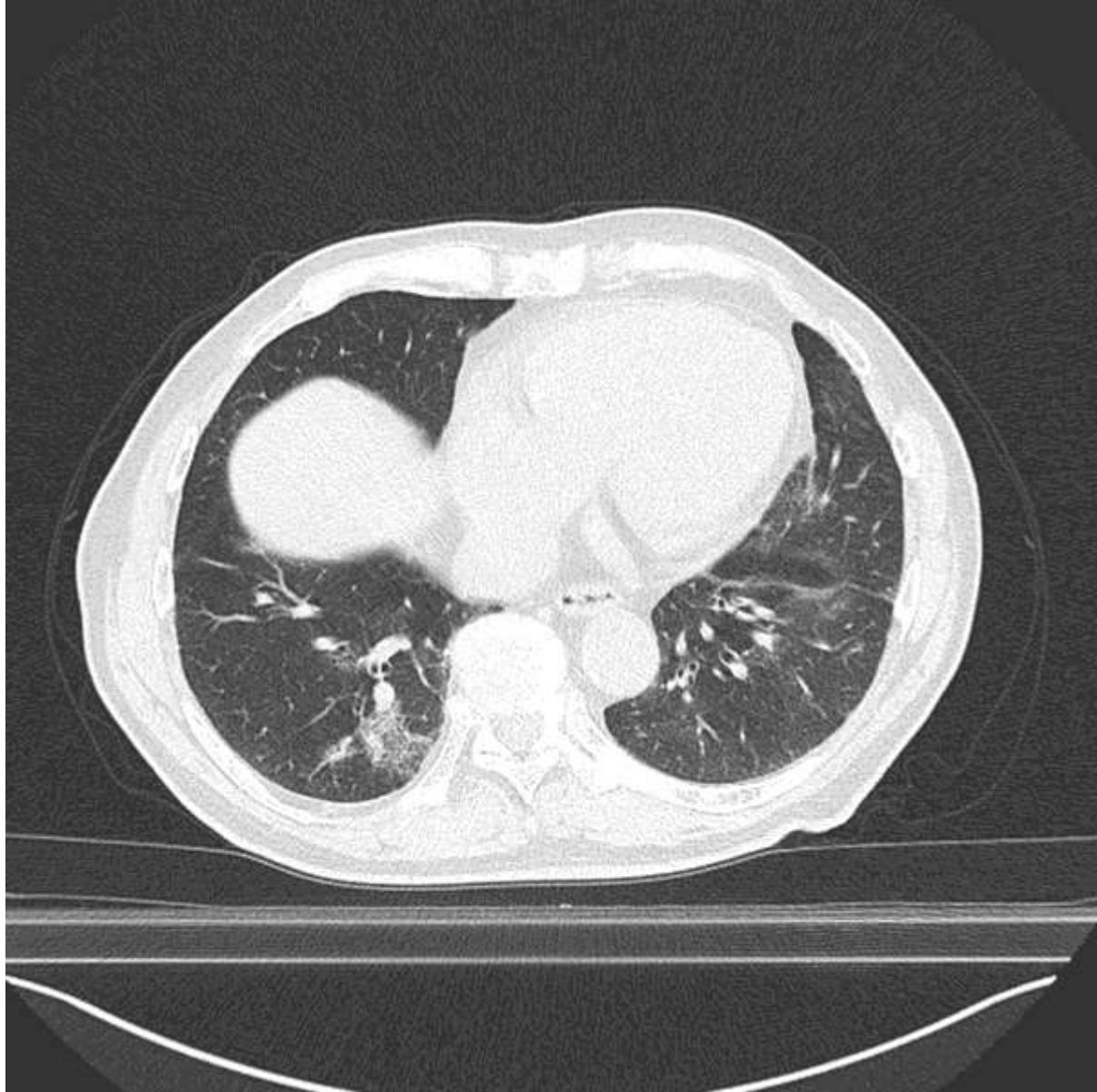








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