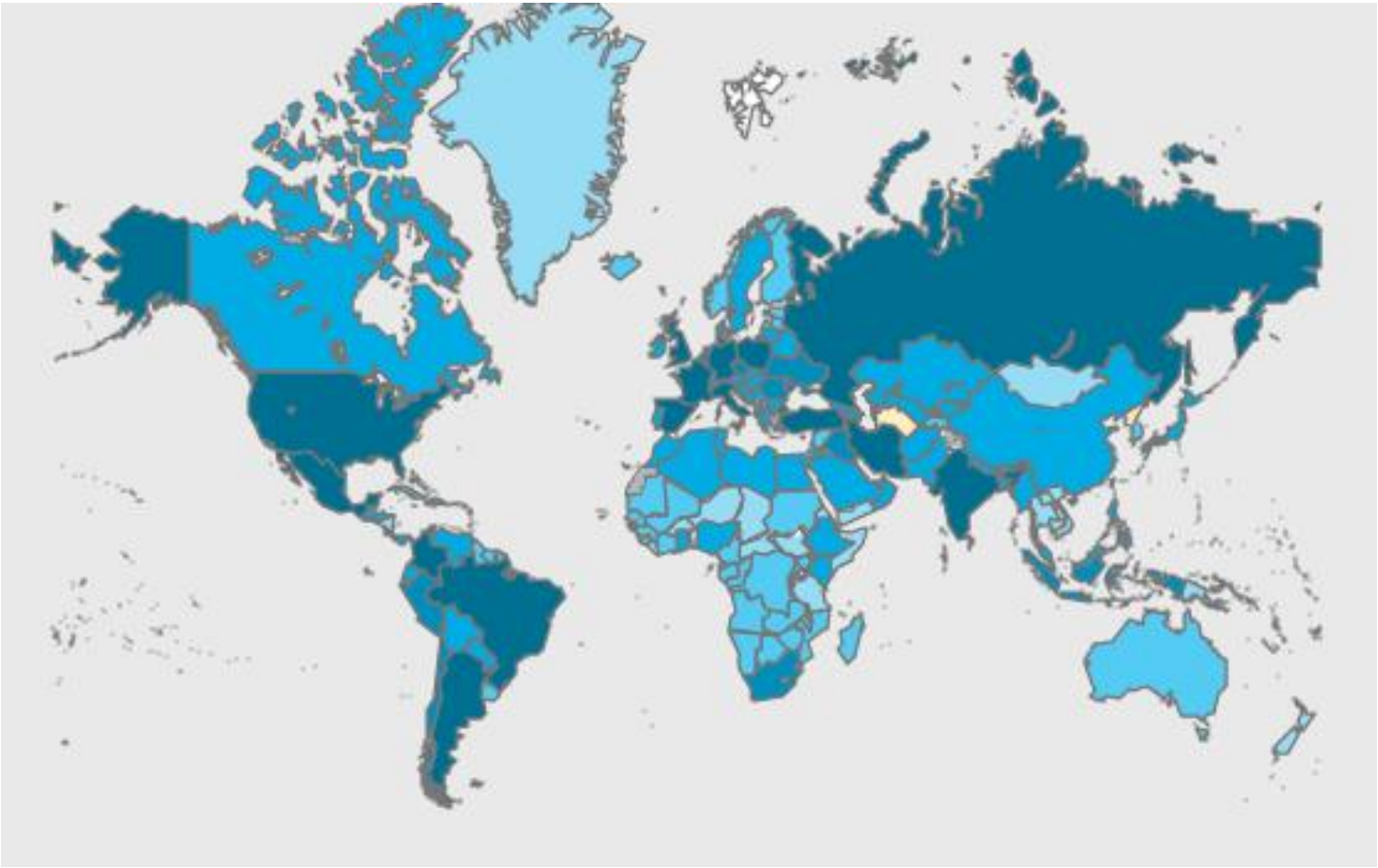
Recurrence or Relapse of COVID-۱۹ in Older Patients

Shima Raeesi, MD

Geriatrician

٧٥،١١٠،٦٥١ confirmed cases of COVID-١٩,
١،٦٨٠،٣٩٥ deaths



- Isolation and containment are the main measures to break chain contamination in primary prevention.

- The tertiary prevention is based on the assumption of **effective immunization of infected individuals** to prevent recurrence of the infection.

- The first cases of possible **reinfection** by SARSCoV-٢ were reported in April ٢٠٢٠ among adults.

Recurrence or relapse of the SARS-CoV-۲ infection in a series of older patients

Saint-Etienne, France

Patient ١

An ٨٤-year-old woman

Medical history:

- High blood pressure
- Heart failure
- Atrial fibrillation treated by rivaroxaban
- Diabetes mellitus, type II, treated with insulin
- Chronic renal failure
- Chronic respiratory failure under long-term oxygen (١٥ h a day)

Patient ١

- **Cough** and **fever**
- Oxygen desaturation at ٧٩%

- Biological markers:
  - CRP: ٨٨ mg/L
  - Lymphocyte count: ٧٧٠ cells/L
  - Neutrophil count: ٢٧٧٠ cells/L

Patient ١

- Computed tomographic (CT) scan: **Bilateral ground glass lesions** predominating on the right lung. (March ٢٤)

- **Positive SARS-CoV-٢ RT-PCR** (Nasopharyngeal sample) (March ٢٦)
  Cycle threshold (Ct): ٣١.٤

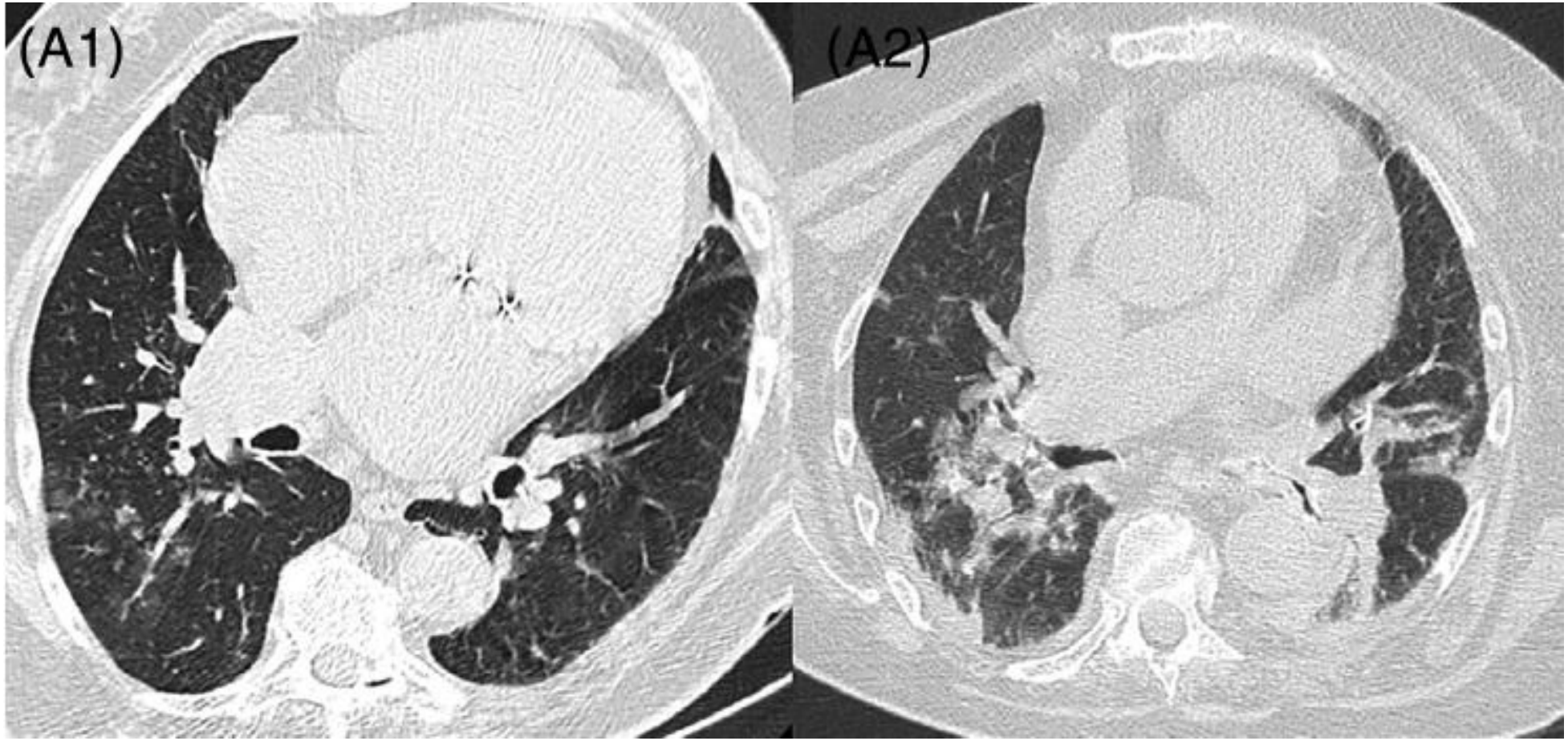

Hospitalized in an acute-care unit
Levofloxacin (۷ days)
Short course of corticosteroids
Clinical and biological improvements
COVID-۱۹ rehabilitation care unit (April ۷)
CRP and lymphocyte rate were normalized

Patient ١

On May ٤ (more than ١ month after the first episode):

- **Hyperthermia** and **respiratory signs**
- Readmitted into an acute-care unit dedicated to COVID-١٩
- SARS-CoV-٢ RT-PCR tests (May ٨) in nasopharyngeal swab and sputum, and were **positive**
  (Ct of ١٧.٥ and ١٨.١)

Patient ١



Patient ١

- Biological **inflammatory syndrome**
  - CRP: ٣٠٤,٥ mg/L
  - Deep lymphopenia (٤٧٠ cells/L)
  - Interleukin (IL)-٦: ٢٣٥ ng/L

- Neutralizing antibodies to SARS-CoV-٢ were **negative** on May ٨ and faintly positive (rate of ١:١٠) on May ١٥

Patient ١

- Oxygen therapy
- Noninvasive ventilation (May ١٢)

- Levofloxacin (May ٥)
- Aztreonam (May ٨)

- Methylprednisolone, ٦٠ mg/d (May ١٠)

- Tocilizumab (٨ mg/kg) (May ١٢)

Patient ١

- Finally died on May ١٧
- Respiratory and heart failure despite high-dose furosemide

Patient ٢

- A ٩٠-year-old dependent woman
- Living in a nursing home

- Medical history:
  - Diabetes mellitus, type II
  - Hypertension
  - Hypothyroidism
  - Alzheimer’s disease

Patient ٢

In early April ٢٠٢٠:

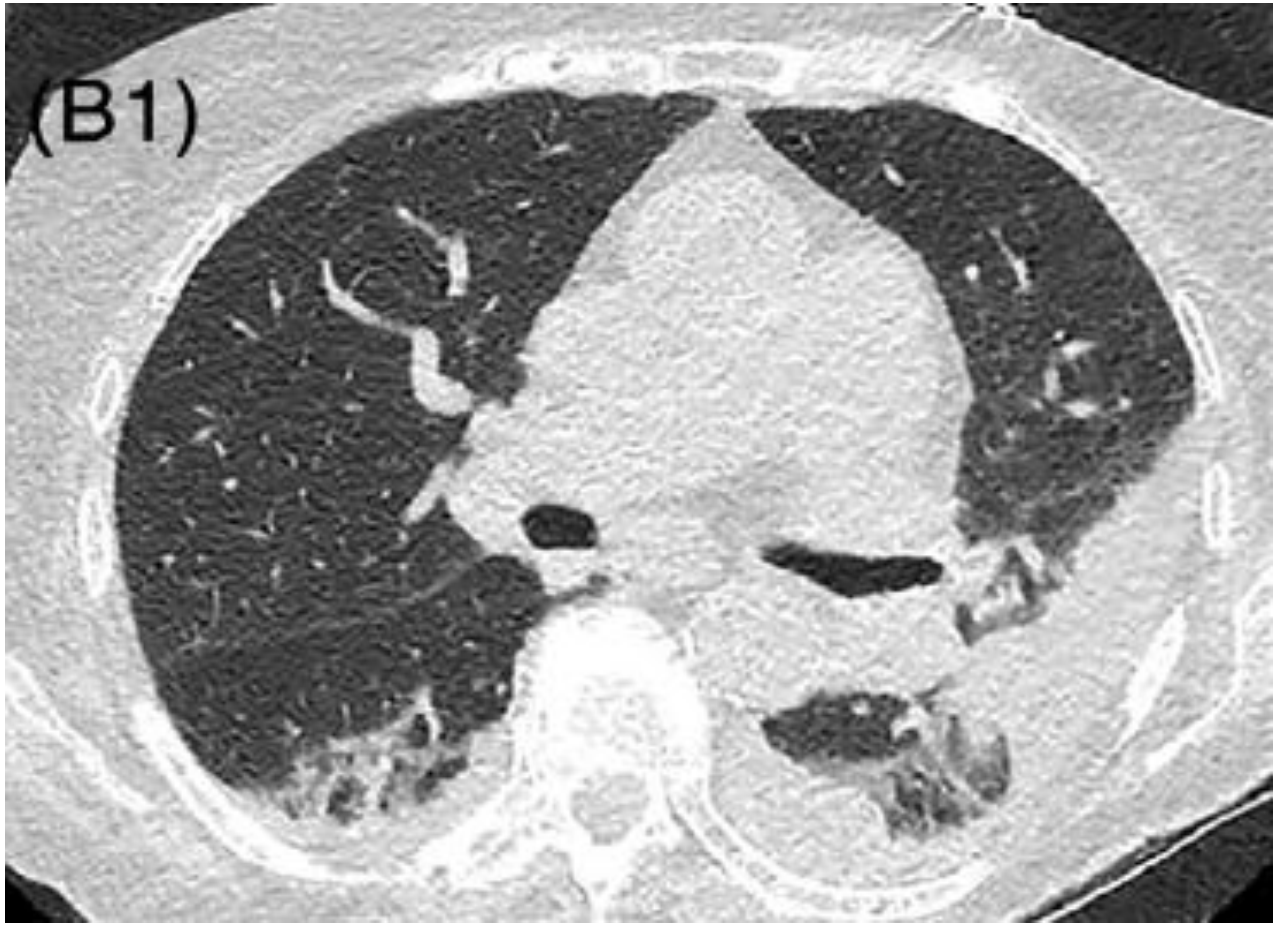
- Cardiorespiratory decompensation
- Atrial fibrillation
- Fever

Patient ۲

- Biological markers:
  - CRP: ۵۵ mg/L
  - Lymphocyte count: ۱۶۷۰ cells/L
  - Neutrophil count: ۷۲۹۰ cells/L

- SARS-CoV-۲ RT-PCR positive test on a nasopharyngeal specimen (April ۵)
  (Ct of ۲۱)

Patient ٢



- **CRP stable at ٥٥**
- **Chronic pressures sores**

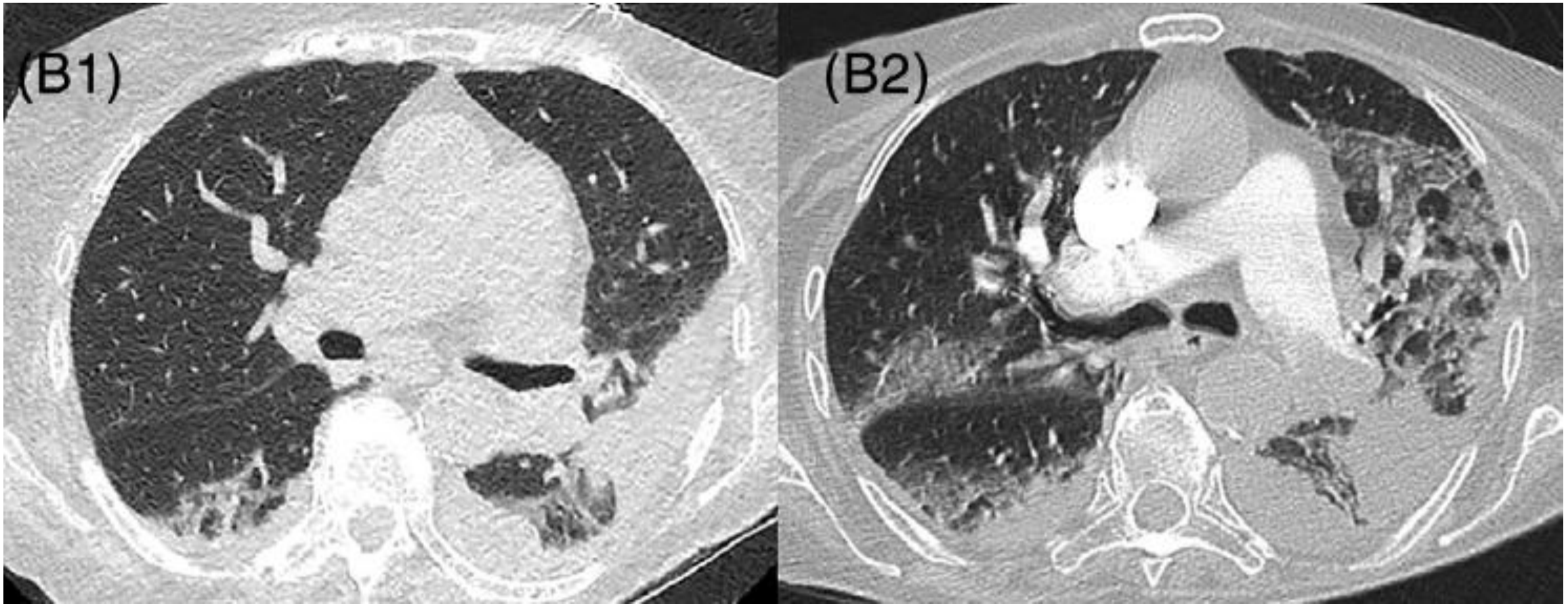
Patient ٢

On May ١١:

- Major dehydration
- Hypernatremia (١۶۶ mmol/L)
- Oxygen saturation at ٩٣% under ۴ L of oxygen
- Melena
- Marked deterioration of her general condition
- Marked lymphopenia (١٨٠ cells/L)
- CRP:١٨١ mg/L
- The SARS-CoV-٢ RT-PCR test was positive on a nasopharyngeal swab. Ct at ١٨,٨

Patient ٢

On May ١٤



Patient ٢

- Palliative care
- The patient finally died on May ١٩

Patient ۳

An ۸۴-year-old woman

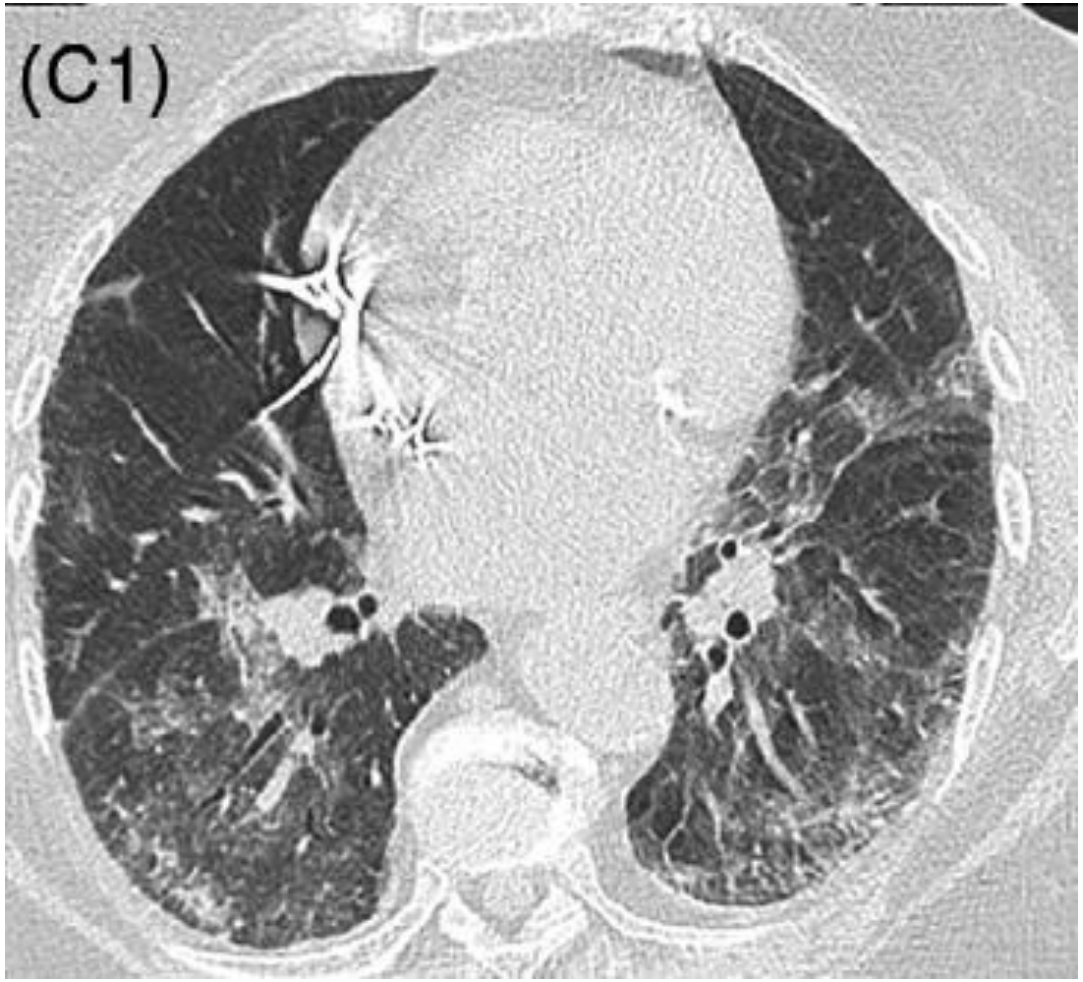
Medical history:

- **Rhythmic heart disease** treated with a pacemaker
- **Pulmonary embolism** treated with rivaroxaban
- **Hypertension**
- **Rheumatoid arthritis** treated with methotrexate, ۱۵ mg/wk and corticosteroids (prednisone, ۱۳ mg/d)

Patient ٣

- Fever
- Asthenia
- Ageusia
- Dry cough
- Polypnea (٣٢/min)
- Oxygen desaturation with ٩٣% under ٣ L of oxygen

Patient ۳



Patient ۳

- CRP:۳۱.۵ mg/L
- Lymphocytes: ۷۳۰ cells/L

- The SARS-CoV-۲ RT-PCR test performed on nasopharyngeal sample was **negative twice**

- **No other infectious cause** was found

- Sputum could not be collected

- **Oxygen withdrawal**
- **Normalization of the inflammatory syndrome**

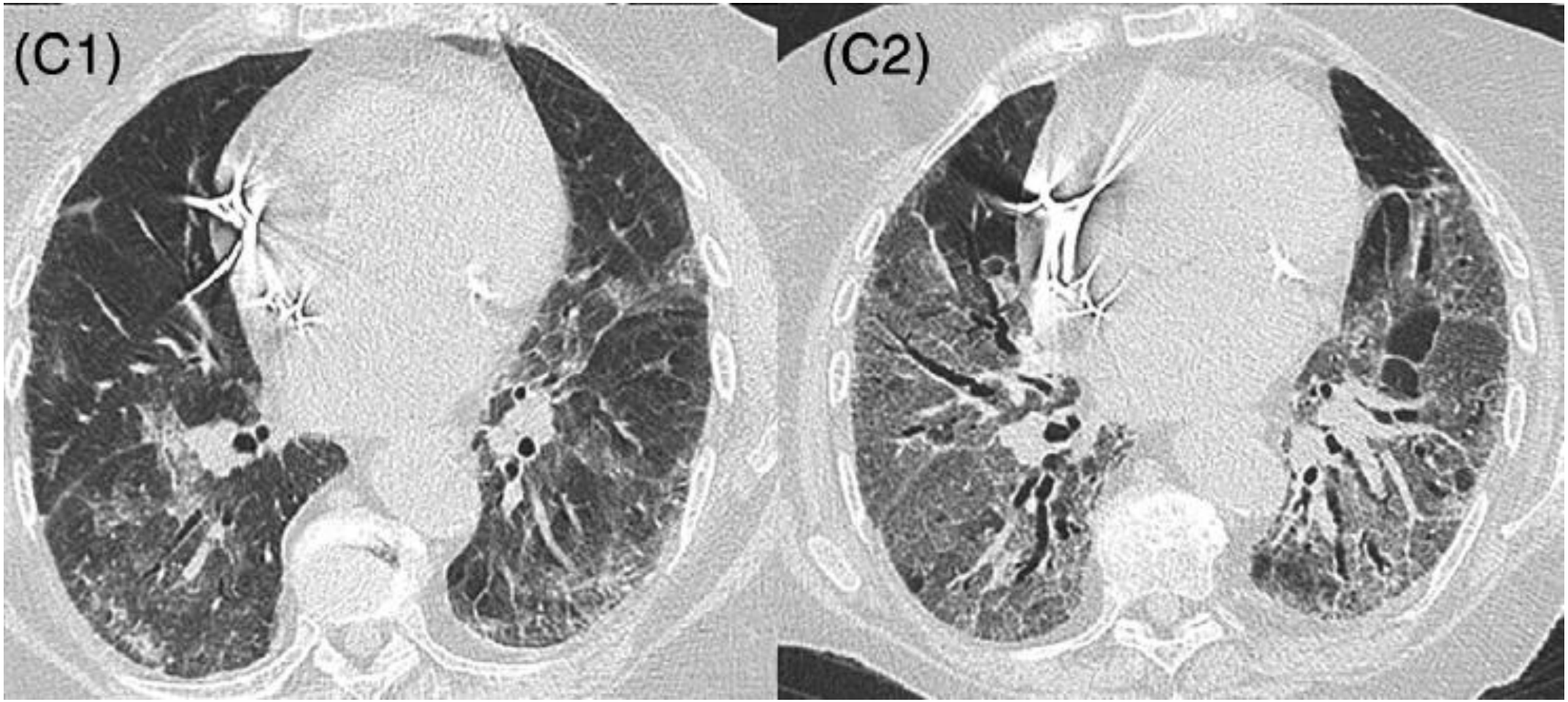
- **Discontinuation of methotrexate treatment**
- **Replaced by an increase in corticosteroids (prednisone = ٦٠ mg/d)**

Patient ٣

On May ٦: **Sudden respiratory deterioration**

- ٨٠% desaturation requiring oxygen therapy
- Dry cough
- Fever
- Nasopharyngeal samples for SARS-Cov-٢ RT-PCR test were found positive.
  (Ct at ١٦.٩ and ١٤.٧ on May ٨ and ١١, respectively)

Patient ٣



Patient ٣

At readmission:

- Marked lymphopenia: ٢٣٠ cells/L
- CRP: ١۴۶ mg/L
- IL-۶: ٢٠١ ng/L
- A rise of neutralizing antibodies against SARS-CoV-٢ was observed from May ٨ to May ١٥ (titers from <١٠ to ۴٠)

Patient ۳

- Ceftriaxone
- Methylprednisolone, ۶۰ mg/d
- High-flow oxygen

- ۱۱ days later: **Cotrimoxazole** (Pneumocystosis superinfection)

- After validation in a multidisciplinary meeting: **Convalescent COVID-۱۹ plasma transfusion**

Patient ٣

- The respiratory status deteriorated
- Major desaturation despite ٢٠ L of oxygen

- She finally died on May ٢٣

Clinical and Laboratory Characteristics

Characteristics	Patient 1	Patient 2	Patient 3
General characteristics			
Age, y	84	90	84
Sex	F	F	F
Comorbidities	Yes	Yes	Yes
Diabetes mellitus, type II		☑	
Arterial hypertension	☑	☑	☑
Heart disease	☑	☑	☑
Cancer	☑		
Chronic obstructive pulmonary disease	☑		
Immunosuppression			☑
COVID-19 (first time)			
Diagnosis of COVID-19	Yes	Yes	Yes
SARS-CoV-2 PCR test	Yes/Mar 26	Yes/Apr 5	No/Apr 15
Chest CT scan	Yes/Mar 24	No/Apr 5	Yes/Apr 16
Biological markers			
Neutrophil count, $\times 10^9$ cells/L	2.77	8.23	6.17
Lymphocyte count, $\times 10^9$ cells/L	0.77	2.16	0.13
C-reactive protein, mg/L	88	47	160
Treatments received	Yes	Yes	Yes
Antiviral therapy			
Antibiotics	☑	☑	☑
Corticosteroids	☑	☑	☑
Death	No	No	No

Clinical and Laboratory Characteristics

Biological markers before the second COVID-19			
Neutrophil count, $\times 10^9$ cells/L	5.98	7.29	10.41
Lymphocyte count, $\times 10^9$ cells/L	1.27	1.67	0.73
C-reactive protein, mg/L	8.7	55	31.5
COVID-19 (second time)			
Diagnosis of COVID-19	Yes	Yes	Yes
SARS-CoV-2 PCR test	Yes/May 6	Yes/May 6	Yes/May 7
Chest CT scan	Yes/May 4	Yes/May 14	Yes/May 7
Biological markers			
Neutrophil count, $\times 10^9$ cells/L	11.96	11.64	10.93
Lymphocyte count, $\times 10^9$ cells/L	0.47	0.89	0.23
C-reactive protein, mg/L	304.5	181	146.9
IL-6, ng/L	235		201
Treatments received	Yes	Yes	Yes
Antiviral therapy			
Antibiotics	☑	☑	☑
Corticosteroids	☑	☑	☑
Immunotherapy	☑	-	☑
Death	Yes/May 17	Yes/May 19	Yes/May 23

Discussion

- Two episodes of COVID-١٩
- Separated by a symptom-free interval of weeks

- SARS-CoV-٢ reinfection or COVID-١٩ relapse?

Discussion

- **Viral replication** was found during the second episode in all three cases

- All virological and bacteriological infectious samples were **negative**, except for COVID-١٩
- The three women were placed in **isolation rooms** in hospital units dedicated to COVID-١٩, with caregivers trained and equipped to comply with the isolation measures

- The **symptom-free interval was relatively short**

- The hypothesis of **reinfection with a new strain is also unlikely**

Discussion

- A **relapse of COVID-١٩** seems to be the preferred hypothesis that would yet need **comparisons of strains** with sequencing to be affirmed.

- The absence of antibodies presented at readmission for two of the three patients is in favor of a **possible reactivation**.

Discussion

- The **immune reaction** may be the cause of clinical deterioration
- One hypothesis would be that these episodes are linked to the **persistence of the virus in a reservoir** (sanctuary site).
- **Immunosenescence** would have a role in the observed clinical pictures, with a possible nonresponse at the time of the first COVID-١٩ episode.

Discussion

- The three cases we present here **did not received diagnostic tests**, supposedly negative, during the transient improvement in clinical signs.

- **Prolonged infections** and **reactivations**

- If the risk of recurrence is confirmed, it will be crucial to analyze the **risk factors** (comorbidities, undernutrition, lymphopenia, and weak immune reaction with a low or even negative serology) but also their **severity**.

Discussion

- It can be assumed that the **cytokine storm** could be **greater** than during the first contamination, leading to more serious and more frequently lethal forms.

- In the case of the second wave, special attention should be paid to older patients who were affected by COVID-١٩ during the first wave.