Ground glass opacities are not always COVID-19: a case of acute eosinophilic pneumonitis caused by daptomycin

Rajalakshmi Valaiyapathi, Meng-San Wu, Alastair McGregor

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Department of Infectious Diseases, Northwick Park Hospital, London North West University Healthcare NHS Trust, Harrow, UK
(R Valaiyapathi MRCP, M-S Wu MRCP, A McGregor FRCPath)

Correspondence to:
Dr Rajalakshmi Valaiyapathi, Department of Infectious Diseases, Northwick Park Hospital, London North West University Healthcare NHS Trust, Harrow HA1 3UJ, UK
r.valaiyapathi@nhs.net

An 83-year-old man was admitted to our hospital reporting a 3-week history of cough and exertional dyspnoea. At the time of admission, the patient was 4 weeks into a 6-week course of daptomycin and rifampicin because he had an infected prosthetic knee joint; he also had a history of pituitary hypoplasia and had not been vaccinated against SARS-CoV-2.

On examination, he was afebrile, his vital signs were normal, and there was no sign of active infection in the prosthetic knee joint.

Laboratory investigations showed a long-standing lymphopenia of $0{\cdot}7\times10^9$ cells per L (normal 1·5–4·0) and a raised C-reactive protein (CRP) concentration of 186·5mg/L (normal 0–5). The patient's eosinophil cell count was $0{\cdot}3\times10^9$ per L (normal 0–0·4), haemoglobin concentration 97 g/L (normal 130–170), and platelet cell count was 322×10^9 per L (normal 150–400). RT-PCR of four consecutive nasopharyngeal swabs for SARS-CoV-2 were negative; routine sputum culture and sensitivity, tuberculosis work-up, respiratory viral screen, and HIV serology were all negative.

Chest imaging—both x-ray and CT—showed bilateral, predominantly peripheral pulmonary infiltrates (figure).

The patient was initially treated as presumed PCR-negative COVID-19 and the antibiotics were replaced with ceftriaxone; dexamethasone was not indicated because he was not hypoxic.

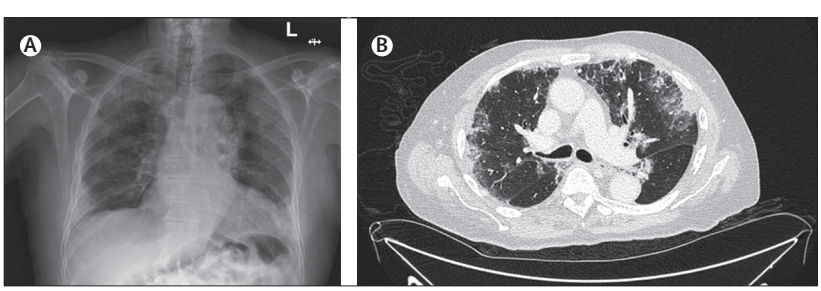

Figure: **Acute eosinophilic pneumonitis**
(A) Chest x-ray at admission shows bilateral—predominantly peripheral—pulmonary infiltrates involving the upper zones. (B) Chest CT at admission shows extensive peripherally distributed ground glass changes.

On day 7, due to persisting cough, a bronchoscopy was done; examination of the washings showed an eosinophilic infiltrate. A diagnosis of acute eosinophilic pneumonitis (AEP) was established through the modified Philit criteria: a respiratory illness of less than 1 month duration, pulmonary infiltrates on chest imaging, an eosinophilia of at least 25% in bronchoscopic washings, and the exclusion of other pulmonary eosinophilic diseases such as allergic bronchopulmonary aspergillosis and vasculitis. We thought parasitic infections were unlikely to be the cause—given the absence of a peripheral blood eosinophilia or any history of travel to a country where such infections are endemic. Additionally, the patient had no occupational or lifestyle exposure risk factors. And finally, x-ray and CT findings were not suggestive of fungal infections or allergic bronchopulmonary aspergillosis. Antineutrophil cytoplasmic antibody test was negative. The patient responded rapidly to high dose prednisolone and was allowed home 14 days after he was admitted. At follow-up 3 months later, the patient's chest x-ray was normal.

Common causes of AEP include inhaled toxins—such as smoking, inhalational drugs, and dust—medications, and parasitic and fungal infections. Daptomycin therapy is a well recognised cause of eosinophilic pneumonitis, and we believe this was the most likely cause in our case.

Notably, the patient's symptoms, biochemical, and radiological findings—including lymphopenia, raised CRP, and bilateral peripheral pulmonary infiltrates—pointed towards a diagnosis of PCR-negative COVID-19. Clinicians need to be on the look out for those subtle nuances that might indicate alternative diagnoses.

Contributors
We all provided care for the patient and managed the case. RV wrote the first draft. MSW and AM reviewed and edited the manuscript. AM supervised the write-up. Written consent for publication was obtained from the patient.

Declaration of interests
We declare no competing interests.