DOI: 10.1002/jmv.26278

LETTER TO THE EDITOR

JOURNAL OF MEDICAL VIROLOGY WILEY

Pneumococcal coinfection in COVID-19 patients

To the Editor,

We would like to report our experience of two patients coinfected with *Streptococcus pneumoniae* (*S. pneumoniae*) and coronavirus disease 2019 (COVID-19) in the United Kingdom. Our institution serves a population of 500 000 and at the time of writing, 20 June 2020, only two (0.4%) patients of a total of 450 who tested positive for COVID-19 on nasopharyngeal swab specimen using real-time reverse transcriptase-polymerase chain reaction (PCR) have also been diagnosed with *S. pneumoniae* infection as determined by blood culture positivity upon hospitalization. Whether the surge in COVID-19 cases has led to the overlooking of other respiratory illnesses or whether increased hygiene, social distancing, and face mask use has reduced the rate of transmission is open to debate.

We treated two older polymorbid men who presented with a short history of typical symptoms of COVID-19 infection and tested positive for the virus on nasopharyngeal swab. In both cases, *S. pneumoniae* was subsequently isolated in blood culture. Urinary antigen tests were not performed. Both patients had been vaccinated against *S. pneumoniae* with a 23-valent vaccine (PPSV23) (case 1 in 2005 and case 2 in 2003). Both were treated with antibiotics from admission. Case 1, a very frail, white British male aged 86 years, was admitted from a nursing home. He was treated with intravenous amoxicillin and clarithromycin and received a single dose of vancomycin on day 2, pending sensitivities. Blood culture grew Gram-positive cocci in pairs and chains. Antibiotic treatment was subsequently rationalized to intravenous amoxicillin alone on day 3. Cited markers of cytokine release became prominent and the patient died in hospital after 15 days. Case 2 was a Pakistani male aged 82 years who had a better premorbid level of function and was living independently. He was treated with intravenous amoxicillin on admission which was switched to intravenous co-amoxiclav on day 3 on clinical grounds. The patient deteriorated on day 8 and required continuous positive airway pressure support. He was discharged in a good condition after a protracted inpatient spell of 21 days. Patient demographics, clinical characteristics, and outcomes are demonstrated in Table 1.

It is well established that seasonal viral respiratory tract infections have been linked to increased risk of bacterial coinfection[1] and current evidence suggests that the innate immune response against severe acute respiratory syndrome coronavirus 2 can similarly compromise host defense of the respiratory tract against bacteria. Variable incidence of concurrent bacterial infection in COVID-19 has been reported.[2-6]

The fear of misdiagnosis or missed diagnoses of coinfections, when faced with COVID-19 infection, remains high; however, the detrimental effects of widespread empirical antibiotic therapy and propagation of antimicrobial resistance should be considered. The traditional markers used to guide antibiotic treatment such as white cell count, C-reactive protein, and chest radiograph abnormalities may be unhelpful in COVID-19 infection and decision-making surrounding antimicrobial therapy can be challenging. The role of procalcitonin is still unclear.

The National Institute for Healthcare and Excellence (UK) acknowledges that at first presentation, it may be difficult to differentiate between COVID-19 pneumonitis and bacterial pneumonia and recommend that empirical antibiotics should be administered if there is clinical suspicion of added bacterial infection.[7]

We present two (0.4%) COVID-19 patients with confirmed *S. pneumoniae* coinfection, one of whom died. Older adults can respond and present differently (often subclinically) compared to young adults. These are due to differences in physiological and immune responses, which are beyond the scope of our article. Notably, however, it has been argued, although not validated in large sample sizes, that older adults are more prone to bacterial superinfection and that empirical treatment with antibiotics may be justified.[8] In keeping with good medical practice, these should only be continued when there is strong clinical or microbiological evidence of bacterial infection, regardless of COVID-19 test results, and should be de-escalated once the specific organisms are identified.

Although these cases might suggest bacterial coinfection is rare and difficult to clinically distinguish from COVID-19, larger studies are required to clarify this. The necessity of microbiological diagnostic testing, perhaps with a panel consisting of multiplex PCR for seasonal respiratory viruses on swab and urinary antigens for *S. pneumoniae* and *Legionella pneumophila* alongside blood cultures for characterization of bacterial coinfections, is highlighted. Emphasis is also laid on the importance of influenza and pneumococcal vaccination.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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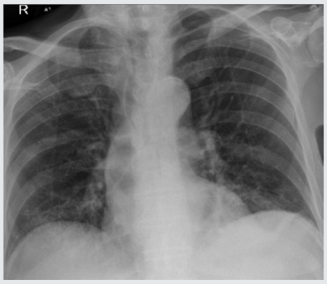
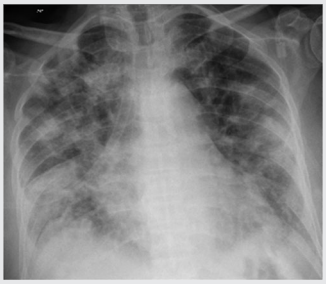
TABLE 1 Demographics, clinical characteristics, treatment, and outcomes

	Patient 1	Patient 2
Demographics		
Age, y	86	82
Sex	Male	Male
Ethnicity	White British	Pakistani
Comorbidities	Alzheimer's disease, hypertension (HTN), and disseminated malignancy of unknown origin	Type 2 diabetes mellitus, ischemic cardiomyopathy, HTN, and chronic kidney disease
Pneumococcal vaccination (PPSV23)	2005	2003
Clinical findings on admission		
Duration of symptom, d	2	2
Chest X-ray		
Symptoms and initial observations		
Symptoms	Dyspnea, fever, and fatigue	Chest pain, fever, and cough
Respiratory rate, breaths/min	24	22
O_2 saturation in room air (%)	92	95
Temperature, °C	38	39
Supine blood pressure, mm Hg	160/98	127/59
Heart rate, beats/min	120	107
Initial laboratory results		
WCC (cells per 10^6/L)	2.01	14.5
Lymphocyte (cells per 10^6/L)	0.19	0.8
Platelets (cells per 10^6/L)	131	192
Lactate dehydrogenase, U/L	396	149
CRP, mg/dL	59	41
D dimer, ng/mL		716
Troponin, ng/mL	114	62
Ferritin ng/mL	1237	788
Blood culture organism	*S. pneumoniae* (serotype 38—not in any current pneumococcal vaccines)	*S. pneumoniae* (serotype 8—present in the 23-valent plain polysaccharide vaccine but not in the 13-valent conjugate vaccine)
Sensitivities	Erythromycin Penicillin	Erythromycin Co-trimoxazole Cefotaxime
Treatment and outcomes		
Other antibiotics	Amoxicillin Clarithromycin vancomycin	Amoxicillin Co-amoxiclav
Admitted to intensive care unit	No	No
Invasive or noninvasive ventilation	No	CPAP
Length of admission (nights)	15	21
Outcome	Death	Discharged

Abbreviations: CPAP, continuous positive airway pressure; CRP, C-reactive protein; WCC, white cell count.

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