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RESEARCH ARTICLE

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Presenting characteristics, comorbidities, and outcomes of patients coinfected with COVID-19 and *Mycoplasma pneumoniae* in the USA

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Abstract

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) is spreading at a rapid pace, and the World Health Organization declared it as pandemic on 11 March 2020. *Mycoplasma pneumoniae* is an "atypical" bacterial pathogen commonly known to cause respiratory illness in humans. The coinfection from SARS-CoV-2 and mycoplasma pneumonia is rarely reported in the literature to the best of our knowledge. We present a study in which 6 of 350 patients confirmed with COVID-19 were also diagnosed with *M. pneumoniae* infection. In this study, we described the clinical characteristics of patients with coinfection. Common symptoms at the onset of illness included fever (six [100%] patients); five (83.3%) patients had a cough, shortness of breath, and fatigue. The other symptoms were myalgia (66.6%), gastrointestinal symptoms (33.3%-50%), and altered mental status (16.7%). The laboratory parameters include lymphopenia, elevated erythrocyte sedimentation rate, C-reactive protein, lactate dehydrogenase, interleukin-6, serum ferritin, and D-dimer in all six (100%) patients. The chest X-ray at presentation showed bilateral infiltrates in all the patients (100%). We also described electrocardiogram findings, complications, and treatment during hospitalization in detail. One patient died during the hospital course.

KEYWORDS

coronavirus, epidemiology, immune responses, interleukin, pandemics, pathogenesis, respiratory tract, SARS coronavirus, virus classification

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) has infected more than 2.4 million people and resulted in more than 170 000 deaths worldwide caused by severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2).[1] COVID-19 was declared as a global pandemic by the World Health Organization.[2] COVID-19 can be associated with other organisms causing pneumonia. The symptoms caused by COVID-19 are like the other common respiratory pathogens, and it is essential to identify them and treat them appropriately. Patients who have COVID-19 can also get rarely coinfected with other respiratory pathogens. Coinfection of both COVID-19 and influenza has been described.[3,4]

Mycoplasma pneumoniae pneumonia is commonly seen in younger adults and is the common reason for atypical pneumonia.[5]

The coinfection from SARS-CoV-2 and mycoplasma pneumonia is rarely reported in the literature.[6,7] The goal of this study is to provide a detailed description of the clinical characteristics, relevant laboratory associations, treatments, and complications in such coinfection that have never been described before.

2 | METHODS

2.1 | Patients

The present study is a retrospective cohort review of all consecutive COVID-19 patients who were admitted to a community teaching hospital between 1 March and 15 April 2020. The institutional review board of Interfaith Medical Center, Brooklyn, New York, approved the study protocol with patient consent exemption. The patients who were coinfected both with COVID-19 and *M. pneumoniae* were a total of 6 among 350 patients.

2.2 | Data collection

Subject data were extracted from electronic medical records, and the data was deidentified for analysis. The following data was collected—patient's demographic information, pertinent clinical data including medical comorbidities, laboratory data, chest X-ray, electrocardiogram (EKG). The mycoplasma diagnosis was made based on the serologies (enzyme-linked immunosorbent assay), and COVID-19 diagnosis was made based on polymerase chain reaction (PCR).

2.3 | Outcome assessment

We are discussing the patient's clinical characteristics, comorbidities, complications, and clinical outcomes of patients presenting with COVID-19 and *M. pneumonia*.

2.4 | Statistical analysis

The statistical package for social sciences (SPSS) software (IBM SPSS, version 25) was used for statistical analysis was performed using. Frequencies and percentages were used to summarize categorical and continuous variables. The descriptive values were expressed as mean ± standard deviation (SD).

3 | RESULTS

3.1 | Clinical characteristics

Our study found that 6 patients were coinfected with COVID-19 and mycoplasma among 350 patients infected with COVID-19, with an incidence rate of 1.7%. Among the 350 patients, 30 patients (8.5%) were Hispanics, 10 (2.8%) were Caucasians, 5 (1.5%) were Asians (1.5%), and 305 (87.1%) were African-Americans. The clinical characteristics of the coinfected patients were listed in Table 1. The age range of these patients was from 39 to 68 years (mean age ± SD = 57 ± 10.6 years). Among the six patients, four were females and two were males. All the patients were African-Americans except for one Hispanic female. Among the comorbidities, hypertension was present in the majority (five patients—83.3%) and congestive heart failure in half (three patients—50%) of the patients. One-third (two patients—33.3%) of the patients had diabetes, hyperlipidemia, and bronchial asthma. Only one patient (16.7%) had a history of malignancy and one patient with end-stage renal disease (ESRD). The body mass index ranged from 22.6 to 40.7 (mean ± SD = 28 ± 6.5). One-third of the patients (two patients—33.3%) are active smokers, and one patient (16.7%) has a history of alcohol intake. Only one patient was taking Angiotensin-converting enzyme inhibitors on admission. The majority of the patients had hypertension, five of them were African-Americans and one of them was morbidly obese.

All the patients had a fever (100%). Cough, shortness of breath, and fatigue were present in the majority (five patients—83.3%). Two-thirds (four patients—66.6%) had myalgias, half of them (three patients—50%) had nausea, and one-third (two patients—33.3%) had diarrhea and vomiting. Only one patient (16.7%) had altered mental status. The length of the stay ranged from 5 to 11 days, and one patient expired on the fifth day of admission.

3.2 | Vital signs, EKG, and chest X-ray at presentation

The vital signs, EKG, and chest X-ray at presentation were summarized in Table 2. The temperature ranged from 99.8°F to 103.1°F. The respiratory rate ranged from 18 to 22 breaths per minute. 83.3% of the patients were hypoxic, with one patient needing mechanical ventilation, one patient needing nonrebreather, and three patients needing oxygen delivery by nasal cannula, and two among them needed high flow.

Bilateral infiltrates were present in all the patients on a chest X-ray at presentation (100%), as shown in Figure 1. Two patients (33.3%) has prolonged QT interval on EKG (QTc males 431-450; females 451-470). There were no new ST-T segment changes in any of these patients.

3.3 | Laboratory parameters for all the patients

The laboratory parameters for all the patients were summarized in Table 3.

White cell count was elevated in two patients (33.3%), while all the patients had lymphopenia, and neutrophils were elevated in the majority of the patients (five patients—83.3%). All the patients had a normal platelet count. Out of six patients, only one patient had anemia of chronic disease due to a history of ESRD at admission (16.6%). As there was no drop in hemoglobin/hematocrit for all the

TABLE 1 Clinical characteristics of patients infected with COVID-19 and *Mycoplasma pneumoniae*

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	N (%)
Age	39	54	68	60	67	54	NA
Sex	Female	Female	Male	Female	Female	Male	NA
Body mass index	26.8	23.5	22.6	28.3	40.7	26	NA
Ethnicity							
African-American	Yes	Yes	Yes	Yes	NA	Yes	83.3
Hispanic	NA	NA	NA	NA	Yes	NA	16.7
Comorbidities							
Hypertension	No	Yes	Yes	Yes	Yes	Yes	83.3
Diabetes	No	Yes	No	No	No	Yes	33.3
Congestive heart failure	No	Yes	Yes	No	Yes	No	50
Bronchial asthma	No	No	Yes	No	No	Yes	33.3
Current smoker	Yes	No	Yes	No	No	No	33.3
Coronary artery disease	No	No	No	No	Yes	No	16.7
Alcohol use	Yes	No	No	No	No	No	16.7
Hyperlipidemia	No	No	Yes	No	Yes	No	33.3
End-stage renal disease	No	No	No	No	No	Yes	16.7
H/o of malignancy	No	No	No	No	Yes	No	16.7
Clinical presentation							
Cough	Yes	Yes	Yes	Yes	No	Yes	83.3
Myalgia	Yes	No	Yes	Yes	No	Yes	66.6
Fever	Yes	Yes	Yes	Yes	Yes	Yes	100
Shortness of breath	Yes	Yes	Yes	Yes	Yes	No	83.3
Nausea	Yes	Yes	No	Yes	No	No	50
Vomiting	Yes	No	No	Yes	No	No	33.3
Diarrhea	No	Yes	No	Yes	No	No	33.3
Fatigue	Yes	Yes	Yes	Yes	No	Yes	83.3
Altered mental status	No	No	No	No	Yes	No	16.7
Length of stay, d	9	8	11	10	5	5	

Abbreviation: NA, not applicable.

TABLE 2 Vital signs, electrocardiogram (EKG), and chest X-ray at presentation

Vital Signs	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Temperature, °F	102	101.5	99.8	100.9	102	103.1
Respiratory rate	18	20	22	20	22	18
Systolic blood pressure, mm Hg	108	135	133	138	105	91
Diastolic blood pressure, mm Hg	75	73	82	70	59	53
Oxygen saturation	95	95	96	95	100	95
Oxygen delivery method	Room air	Nasal cannula	High-flow nasal cannula	High-flow nasal cannula	Mechanical ventilation	Nonrebreather
Chest X-ray						
Unilateral infiltrate	No	No	No	No	No	No
Bilateral infiltrate	Yes	Yes	Yes	Yes	Yes	Yes
EKG						
PR interval, ms (120-200)	146	150	154	158	174	162
QT_c interval, ms (males, 431-450; females, 451-470)	401	510	430	474	500	455
New ST-T wave changes	No	No	No	No	No	No

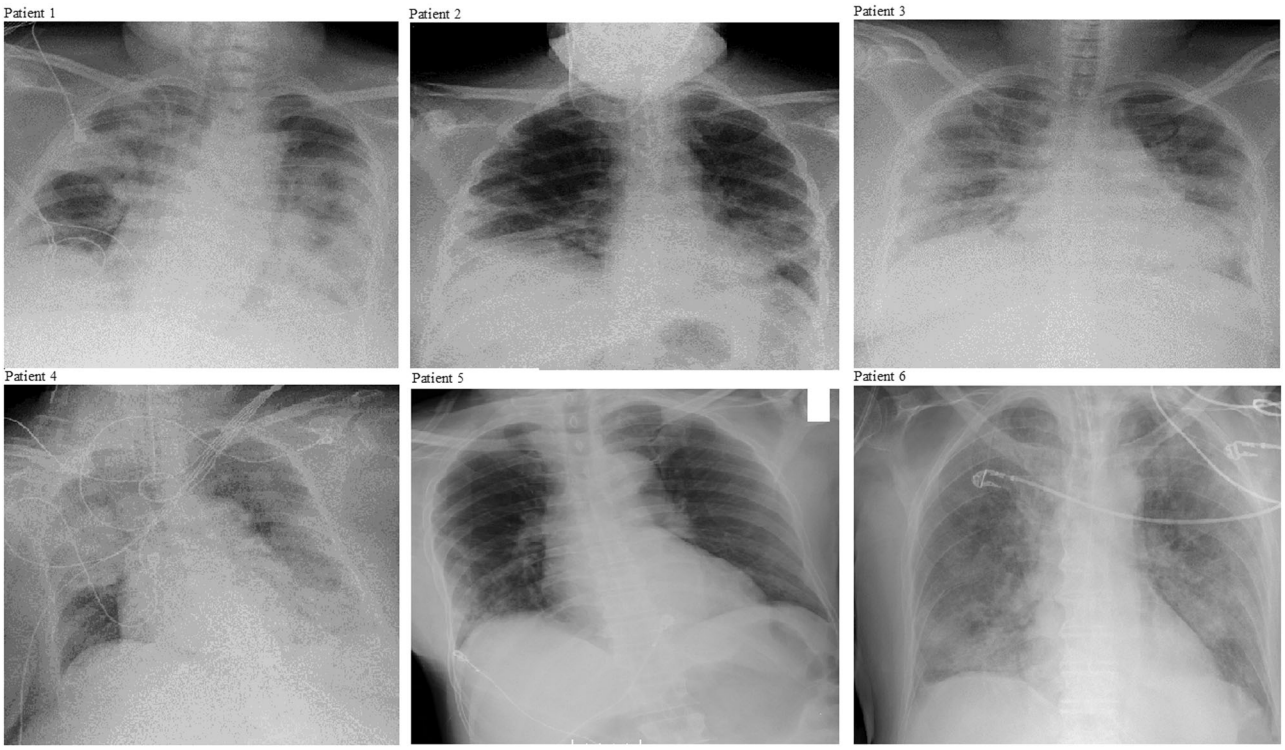

FIGURE 1 Chest X-rays of all the patients showing bilateral lung infiltrates

patients during the entire hospital course, cold agglutinin test was not performed. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), lactate dehydrogenase (LDH), interleukin-6 (IL-6) serum ferritin, and D-dimer was elevated in all the patients.

Troponin levels were elevated in the majority (five patients—83.3%), ranged from 0.01 to peak level of 2.21 ng/mL. Brain natriuretic peptide was elevated in half (three patients—50%) of the patients, ranged from 10 to 1335 pg/mL. The fibrinogen level was elevated in the majority (five patients—83.3%) and ranged from 368 to 660 mg/dL. The procalcitonin levels ranged from 0.12 to 2.37 mmol/L, which were elevated in a third of patients (two patients—33.3%). The lactic acid was elevated in one-third of patients (two patients 33.3%) and ranged from 0.9 to 3.5 mmol/L. The aspartate aminotransferase was elevated in four patients (66.6%), while alanine aminotransferase was elevated in only one patient (16.6%). The blood urea nitrogen (BUN) and creatinine were elevated in two-thirds of the patients (four patients—66.6%). The peak BUN level was 74.8 mg/dL, and peak creatinine level was 2.02 mg/dL. Potassium and magnesium levels were normal in all the patients. Prothrombin time/activated partial thromboplastin time were within normal limits.

All the patients were tested positive for SARS-CoV-2 by PCR. *M. pneumoniae* immunoglobulin M (IgM) and immunoglobulin G (IgG) were elevated in all the patients ranged from 909 to 1737 U/mL and 657 to 955 U/mL, respectively. All the patients were tested negative for both influenza A and B by PCR and urine Legionella Pneumophila antigen. Sputum, urine, and blood cultures were negative for all patients.

3.4 | In-hospital complications

The complications that occurred during the hospital course were summarized in Table 4. Only one patient (16.7%) required intensive care unit (ICU) stay and developed acute respiratory distress syndrome needing mechanical ventilation, developed shock needing vasopressor support, eventually leading to multiorgan failure and death. The acute cardiac injury was present in the majority (five patients—83.3%), and two-thirds (four patients—66.6%) developed acute kidney injury.

The medications used for the treatment of patients were listed in Table 5. All the patients received ceftriaxone for pneumonia, zinc, and vitamin C. About half of them (three patients—50%) received azithromycin or doxycycline with no overlap. Hydroxychloroquine was given to two patients (33.3%), and steroids were given to two patients (33.3%). The patient who died was treated with ceftriaxone, azithromycin, and steroids, but did not receive hydroxychloroquine.

4 | DISCUSSION

The novel coronavirus SARS-Cov-2 causes fever, cough, and shortness of breath and is spreading at an unrelenting pace daily. The United States has the highest number of patients infected, and mortality than any other country in the world.[1] SARS-CoV-2 has spike (S) protein that utilizes membrane-bound angiotensin-converting enzyme 2 aided by serine proteases to gain entry into the human cell and cause infection.[8]

TABLE 3 Laboratory parameters for all the patients

Parameters	Reference range	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	N (%) abnormal
White cell count	4.5-11 (10^3/μL)	4.2	3.7	5.6	6.2	13.4	12.9	33.3
Hemoglobin	Female: 11-15 g/dL; male: 13-17 g/dL	13.6	12.1	13.6	12.5	12	9.8	16.6
Platelet count	130-400 (10^3/μL)	161	271	141	249	140	228	0
Lymphocytes	22-48 (%)	6.4	16	8.5	6.5	3.5	4.5	100
Neutrophils	40-70 (%)	75.6	57.9	75	88	90	91.3	83.3
ESR	0-20 mm/h	53	103	65	102	39	120	100
CRP	0-10 mg/L	108	46	56	144	146	114	100
LDH	125-220 U/L	500	778	345	390	1408	474	100
Troponin I	0.00-0.03 ng/mL	0.06	0.09	0.4	0.01	2.21	0.1	83.3
BNP	10-100 pg/mL	41	265	1335	10	567	35	50
IL-6	0.0-15.5 pg/mL	300	54.6	245	346	74.5	200	100
Serum ferritin	30-400 ng/mL	1200	810	1535	469	2920	3052	100
D-dimer	0-500 ng/mL	1095	2032	4625	1445	3862	1592	100
Fibrinogen	193-507 mg/dL	542	660	546	650	567	368	83.3
PCT	0.5-1.9 mmol/L	0.57	0.37	0.65	0.12	2.37	2.2	33.3
AST	5-34 U/L	37	29	44	35	229	20	66.6
ALT	10-55 U/L	26	12	16	27	106	20	16.7
Lactic acid	0.5-1.9 mmol/L	2.1	1.5	1.8	1.2	3.5	0.9	33.3
BUN	9.8-20.1 mg/dL	6.7	39.7	38.5	10.9	40.7	74.8	66.6
Creatinine	0.57-1.11 mg/dL	0.79	2.02	1.51	0.75	1.85	1.24	66.6
SARS-COV-2	PCR	Positive	Positive	Positive	Positive	Positive	Positive	NA
Influenza	Type A Ag/Ab; type b Ag/Ab PCR	Negative	Negative	Negative	Negative	Negative	Negative	NA
Urine legionella Ag	Negative	Negative	Negative	Negative	Negative	Negative	Negative	NA
Mycoplasma pneumonia IgM	<770 U/mL	1261	1075	1389	1167	1737	909	NA
Mycoplasma pneumonia IgG	<100 U/mL	816	955	725	707	806	657	NA

Abbreviations: Ab, antibody; Ag, antigen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IgG, immunoglobulin G; IgM, immunoglobulin M; IL-6, interleukin-6, LDH, lactate dehydrogenase; NA, not applicable; PCR, polymerase chain reaction; PCT, procalcitonin; SARS-COV-2, severe acute respiratory syndrome-coronavirus 2.

TABLE 4 Complications of the patients

Complications	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	N (%) Y
ARDS	No	No	No	No	Yes	No	16.7
Shock	No	No	No	No	Yes	No	16.7
Acute cardiac injury	Yes	Yes	Yes	No	Yes	Yes	83.3
Acute liver failure	No	No	No	No	Yes	No	16.7
Acute kidney injury	No	Yes	Yes	No	Yes	Yes	66.6
Mechanical ventilation	No	No	No	No	Yes	No	16.7
Death	No	No	No	No	Yes	No	16.7
ICU stay	No	No	No	No	Yes	No	16.7

Abbreviations: ARDS, acute respiratory distress syndrome; ICU, intensive care unit.

TABLE 5 List of medications

Medications	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	N (%) Y
Ceftriaxone	Yes	Yes	Yes	Yes	Yes	Yes	100
Azithromycin	Yes	No	Yes	No	No	Yes	50
Doxycycline	No	Yes	No	Yes	Yes	No	50
Hydroxychloroquine	No	No	Yes	Yes	No	No	33.3
Steroids	No	No	No	No	Yes	Yes	33.3
Vitamin C	Yes	Yes	Yes	Yes	Yes	Yes	100
Zinc	Yes	Yes	Yes	Yes	Yes	Yes	100

SARS-CoV-2 can circulate in the environment with other microorganisms and can change with disease patterns.[9] The influenza epidemic in Wuhan, China, was interfered with by COVID-19 emergence.[9] In a study analyzing two centers in China, the coinfection pattern differed significantly, and a large proportion of patients in Quindao had other seasonal respiratory pathogens in patients with COVID-19 compared to Wuhan. The coinfection rate was 23.3% with mycoplasma pneumonia and COVID-19 in Quindao, China.[10] SARS-CoV is another zoonotic beta coronavirus that has close genetic homology with SARS-CoV-2. Mycoplasma coinfection with SARS-CoV has been detected on the serological assay but was not detected on the respiratory specimen PCR, thus limiting the incidence of coinfection.[11]

Mycoplasma pneumonia is one of the important causes of respiratory tract infections in adults and children and confers 4% to 8% of community-acquired bacterial pneumonia.[5] The number of cases can increase in epidemics and close clusters.[12] The infection can range in severity from mild to life-threatening. An annual estimation of 2 million cases results from this infection leading to 100 000 hospitalizations of adults in the United States.[5] The infections tend to be more common in summers but can occur in any climate.[5] The symptoms of COVID-19 and *M. pneumoniae* pneumonia are similar with fever, cough, and shortness of breath.

All the patients in this study had both COVID-19 PCR and mycoplasma serologies positive. All the inflammatory markers were elevated, including IL-6, CRP, ESR, and serum ferritin, LDH, D-dimer that have been consistent with prior reported COVID-19.[13,14] All the patients had lymphopenia, which is typical of viral infections.[13] Most of the patients had elevated troponin I levels, which signifies acute cardiac injury. Bilateral infiltrates were present in all the patients on a chest X-ray at presentation.

Fan et al reported a case of a 36-year-old male in Singapore who had coinfection with mycoplasma and COVID-19. The patient had severe lymphopenia, and moderate thrombocytopenia needed ICU admission and ventilator support. The patient also had cold agglutinin titer of 1:8 and mycoplasma pneumonia antibody titer of 1:160, no hemolysis, or significant anemia was noted, and the direct agglutinin test was negative.[6] Xu et al[7] discussed a 49-year-old female patient who had coinfection SARS-COV-2 and mycoplasma. The patient presented with productive cough and chest congestion but no fever. Computed tomography of the chest showed bilateral ground-glass opacities in lower lobes and patchy shadows in the right upper lobe. The patient test positive for COVID-19 and mycoplasma and was treated with lopinavir/ritonavir, peramivir, interferon-α2b (anti-virals) as well as cefonicid sodium, azithromycin, and moxifloxacin (antibiotics). The patient fully recovered and was discharged from the hospital.

The diagnostic method of choice for mycoplasma pneumonia is nucleic acid amplification tests like PCR and multiplex assays because they have high sensitivity and specificity compared to serologies and culture.[15-17] Serological tests can be used when molecular tests are not available or as an adjunct to the molecular tests.[18] A single high IgM titer or a fourfold rise in IgG titers are used for serological diagnosis as in our patients.[19]

There is no effective proven therapy for COVID-19 as of now, and supportive care is a vital aspect of care. Many treatment strategies have been utilized like hydroxychloroquine, remdesivir, azithromycin, lopinavir/ritonavir, and tocilizumab.[13,20] The first-line therapies for *M. pneumoniae* are macrolides, tetracyclines, and fluoroquinolones.[21-23] Fortunately, the majority of the patients responded well to the treatment and were discharged from the hospital.

5 | CONCLUSION

The COVID-19 pneumonia is a serious condition and can be associated with the common respiratory pathogens. This can be dangerous and can result in protracted respiratory symptoms, prolonged ICU stay, morbidity, and mortality if not detected and treated appropriately. The physicians should screen for the common respiratory pathogens with appropriate diagnostic tests.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

VG, PRG, MAM, and NR were involved in data collection, review, and preparation of the manuscript. VMK, MB, SN, and SA were involved in the analysis of data and final review of the manuscript, the

preparation of tables. All the authors reviewed the manuscript and agreed with the findings and interpretation.

ETHICS STATEMENT

The institutional review board of Interfaith Medical Center, Brooklyn, New York, approved the study protocol with patient consent exemption.

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