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RESEARCH ARTICLE

Clinical Characteristics of Adult COVID-19 Pneumonia and Other Viral Pneumonias: Comparisons of Imaging Findings

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ABSTRACT
Different viral infections show characteristic imaging findings based on their particular pathophysiology. SARS-COV-2 shows characteristically high transmissibility and virulence, and it can evade the human immune system. COVID-19 patients frequently develop severe illness involving cytokine storm leading to acute respiratory distress syndrome (ARDS), as well as alveolar flood and severe vascular damage resulting in sepsis and organ damage. These basically develop from bilateral ground-glass infiltrations that are also found in the adult viral pneumonias, such as measles, respiratory syncytial virus, human metapneumovirus, and cytomegalovirus pneumonias. Secondary bacterial pneumonia due to co-infection with bacteria is a major issue in viral pneumonia, especially in influenza pneumonia, but patients with adult viral pneumonias are very different from bacterial pneumonia patients, and they are usually young, produce less sputum, and sometimes show characteristic skin lesions, including rash and vesicular lesions. Accurate diagnosis of the specific pathogen of viral pneumonia is important to perform the appropriate treatment and prevent infection, and it can recently be performed by multiplex PCR.

Key words: Cytomegalovirus, human etapneumovirus, Influenza virus, Measles virus, Respiratory syncytial virus, SARS-CoV-2

INTRODUCTION

In the current management of infectious disease, it is important to bear in mind measures to deal with viral infections, particularly COVID-19 (infection with the novel coronavirus SARS-CoV-2), which is causing a historic pandemic.[1,2]

SARS-CoV-2 has been shown to exhibit characteristically high infectiousness (transmissibility) and virulence (fatality rate). The basic mechanism whereby COVID-19 becomes severe has been shown to resemble that of influenza and other viral infections; it involves cytokine storm leading to the development of acute respiratory distress syndrome (ARDS), as well as alveolar flood and severe vascular damage, resulting in sepsis and organ damage.[3-5] The management of viral infections has taken a new step forward with the proactive use of antivirals such as remdesivir or steroids as therapeutic drugs.

In viral pneumonias other than COVID-19 pneumonia, such as measles, respiratory syncytial virus (RSV), human metapneumovirus (hMPV), and cytomegalovirus (CMV), adult patients are much more likely to develop severe illness than children, and the highest incidences arise in children younger than 5 years and in adults older than 75 years.[6] Distinguishing viral pneumonia from bacterial pneumonia is important, and recommendations from the American Thoracic Society are that diagnosis of pneumonia should be made on the basis of chest radiography, because interstitial infiltrates on chest radiographs are generally believed to suggest a viral cause of pneumonia, whereas alveolar infiltrates indicate a bacterial cause.[6,7]

It is now clear that different viral infections exhibit characteristic imaging findings on the basis of their particular pathophysiology and clinical manifestations, and they are summarized in this review.

REVIEW

1. Pathophysiology and chest imaging findings of COVID-19 and other viral infections

Since the 2020 season, COVID-19 has run rampant worldwide. Although we have dealt with many previous acute epidemic viral infections, chiefly influenza, a pandemic of this magnitude has not occurred since the "Spanish flu" a century ago.[1] However, it does have many features in common with the infectious diseases with which we do have experience, such as human immunodeficiency virus (HIV) and influenza, and measures for dealing with it may be essentially the same as those for previous viral infections.

This is because the severity of any viral infection is determined mainly by its infectiousness (transmissibility) and virulence (fatality rate). Compared with the previous two severe coronavirus infections [severe acute respiratory syndrome-1 (SARS-1) and Middle Eastern Respiratory Syndrome (MERS)], COVID-19 (SARS-CoV-2) is comparatively more infectious, but not particularly virulent. At first, it was therefore regarded as similar to seasonal influenza, which occurs on a yearly basis, but experience has shown that, in fact, it is not such a simple infection.[4,8]

On average, its infectiousness is similar to that of influenza, but it has been found that under conditions of close contact, crowded spaces, and closed spaces with poor ventilation, known as the "three Cs," its transmission rate is comparable to that of measles, and it infects almost all persons who are present in the same place, causing "clusters."[1,9,10] This may be because it is asymptomatic for around a week after infection occurs, during which time it proliferates while evading the human immune system via a devious mechanism similar to that of HIV.[4,11-13]

Its overall virulence (fatality rate) in Japan is believed to be on the order of a few percent, but since this still makes it far more lethal than regular influenza, and high numbers of serious cases in older people have been reported, it cannot be ignored.[2,8] In younger people, it is usually a comparatively mild infection, but even when it is almost asymptomatic, it has been reported to cause pneumonia, with distinctive bilateral ground-glass shadows evident on chest computed tomography (CT) and other modalities.[8] However, because these shadows and consolidation can progress to diffuse acute respiratory distress syndrome (ARDS)-type shadows suggestive of severe pulmonary edema, they require extremely careful management (Figure 1).[4,12] In terms of both infectiousness and virulence, it is a formidable infection with a dualistic character, exhibiting completely different characteristics under different conditions and in different age groups.

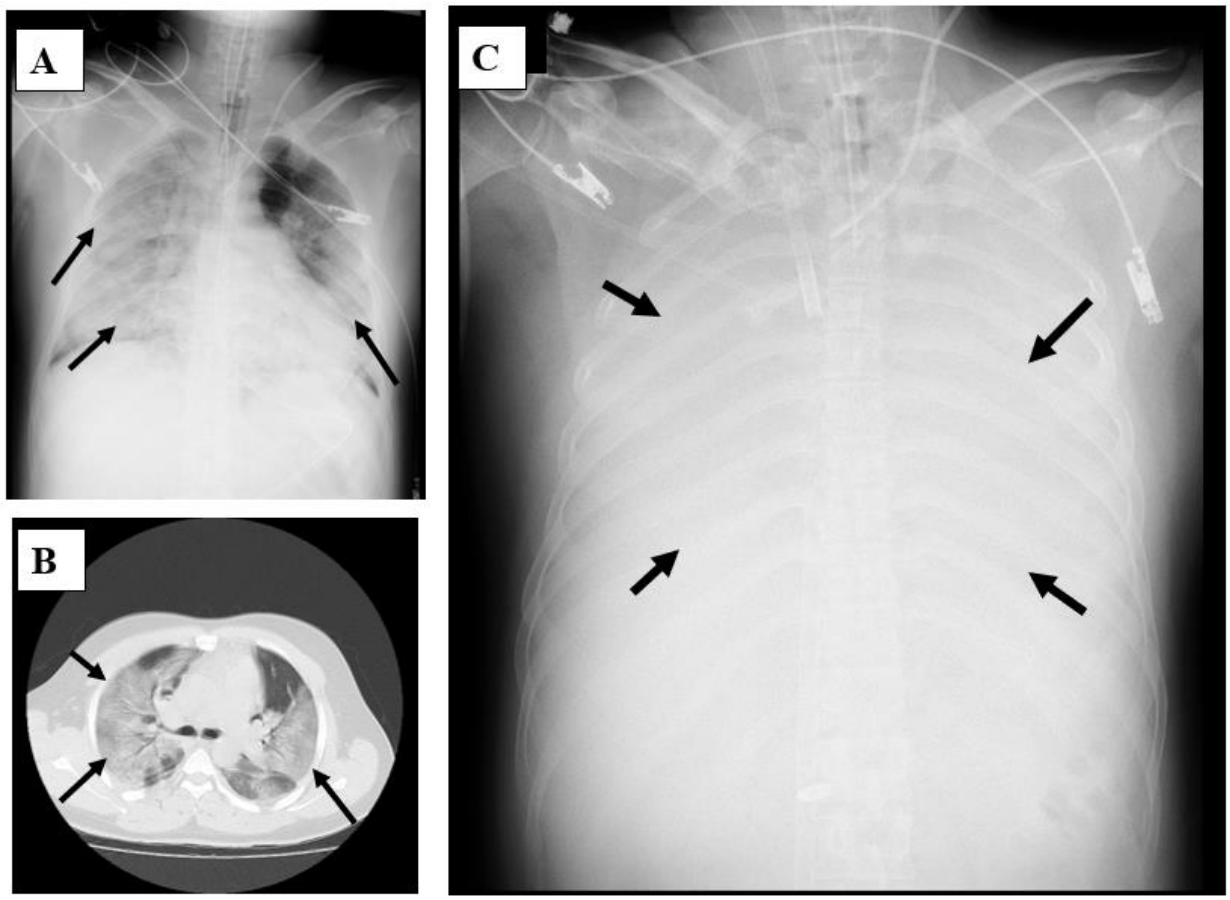

Figure 1: Chest X-ray (A and C) and computed tomography (B) findings of a 26-year-old male COVID-19 patient. Bilateral massive ground-glass shadows are seen on admission (A and B, arrows), but two days later, the shadows are worse, and both lung fields and the heart cannot be seen (C, arrows); the patient survived following remdesivir treatment and extracorporeal membrane oxygenation (ECMO).

In addition to SARS-CoV-2, other respiratory viruses capable of causing sepsis and pneumonia that have recently come under scrutiny include the influenza virus, RSV, and hMPV.[14,15] For these and others, including parainfluenza viruses, enteroviruses, adenoviruses, and rhinoviruses, the main route of infection is droplet transmission, and the viruses known to cause the common cold (including summer colds) also warrant some degree of attention.[16]

Other viruses, such as measles, which usually cause rashes and other generalized symptoms as a result of hematogenous spread, are also known to cause severe pneumonia and pulmonary lesions (Figure 2).[17] They occur mostly in young people, and the older the patient, the more likely the patient is to develop pneumonia as a complication and suffer severe disease. Measles is a highly contagious, potentially fatal, but vaccine-preventable disease caused by measles virus, and its symptoms include fever, maculopapular rash, and at least one of cough, coryza, or conjunctivitis.[17] Complications can affect many organs and often include otitis media, laryngotracheobronchitis, stomatitis, and diarrhea. Massive pneumonia and neurological complications are uncommon, but serious. There is no specific antiviral therapy for the treatment of measles, and disease control largely depends on prevention. However, despite the availability of a safe and effective vaccine, measles is still endemic in many countries and causes considerable morbidity and mortality; therefore, caution is needed, especially in adult-onset measles.

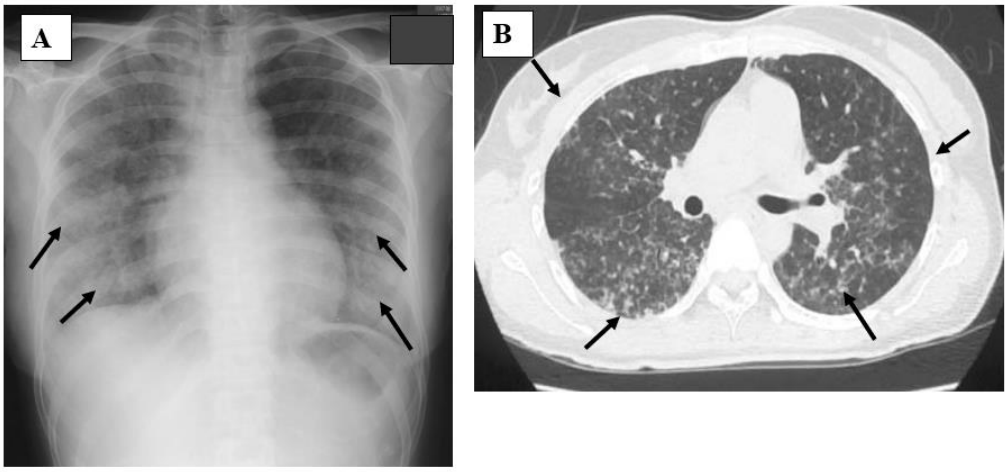

Figure 2: Chest X-ray (A) and computed tomography (B) findings of a 33-year-old man with measles pneumonia. Slight bilateral ground-glass shadows are seen (arrows), but he showed severe hypoxia. He was ultimately rescued after respiratory management by ventilator in the intensive care unit.

Cytomegalovirus (CMV) and other viruses in the herpes family are also known to cause pneumonia, and these, including varicella, constitute very important opportunistic infections at times of immunodeficiency.[18,19] CMV pneumonia is a common complication in organ transplant patients and others who are immunosuppressed, and since this goes on to cause sepsis and severe respiratory failure necessitating management in the intensive care unit in most cases, it requires attention. CMV infection of the respiratory tract leads to severe interstitial pneumonitis in both lung fields of the immunocompromised host, which is often associated with a poor clinical course (Figure 3). Many of the complications of CMV infection are caused by indirect effects of the virus,[20] including acute and chronic graft rejection, graft-versus-host disease, and superinfection by other viruses, bacteria, and fungi, although the incidence of CMV pneumonia has been decreased by routine antiviral prophylaxis, including ganciclovir and valganciclovir, in susceptible populations.[21]

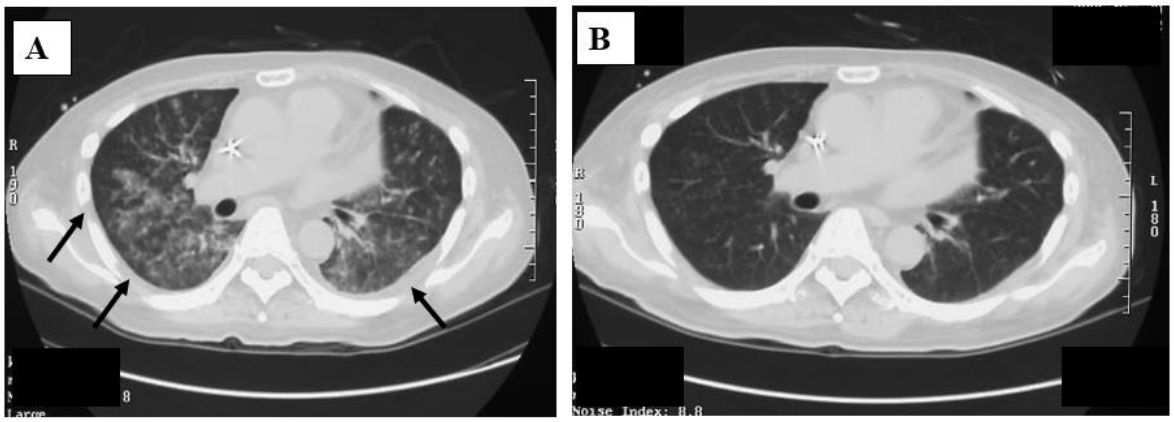

Figure 3: Chest computed tomography findings of a 47-year-old man with cytomegalovirus pneumonia. He was also co-infected with HIV and had been receiving treatment, but bilateral ground-glass shadows are found on admission (A, arrows). Ganciclovir 300 mg/day plus methylprednisolone (mPSL) **[Please spell out all abbreviations on first use. Please confirm.]** 1 g (x3 days) were started, and he shows improvement 2 weeks later (B).

2. Characteristic symptoms, physical examination, laboratory tests, and chest imaging findings of viral pneumonia

As just described, unlike patients with pneumonia due to bacterial infection, those with viral pneumonia produce little sputum and are generally comparatively young (mostly aged <65 years), making it comparatively easy to differentiate from bacterial pneumonia.[22,23] The increase in the inflammatory reaction, including elevated white blood cell count and C-reactive protein, is also less pronounced. On chest X-rays and CT scans, they are distinguished by the absence of the unilateral infiltrative shadows and consolidation seen in bacterial pneumonia, with

bilateral ground-glass shadows being the main finding.

However, their oxygen saturation often deteriorates, and they develop serious respiratory failure, and should the distinctive cutaneous signs of an individual virus be present or should a particular virus be prevalent at the time, the possibility of viral pneumonia must be borne in mind in pneumonia management.[24] It is generally known that viral and bacterial infections may occur together, and that secondary bacterial pneumonia may occur after a viral infection; in influenza-related infections in particular, the possibility of increased severity due to double infection with *Streptococcus pneumoniae* or *Staphylococcus aureus* should always be borne in mind.[15,25,26] In these co-infected cases, unilateral infiltration shadows, as well as common bacterial pneumonia, are usually found (Figure 4).[26,27] These chest imaging findings of severe viral pneumonia due to co-infection with bacteria have been known to be the representative patterns in influenza virus infection, and they are different from the other severe pneumonitis found in the other virus infections, such as measles, RSV, hMPV, and CMV.[25,28]

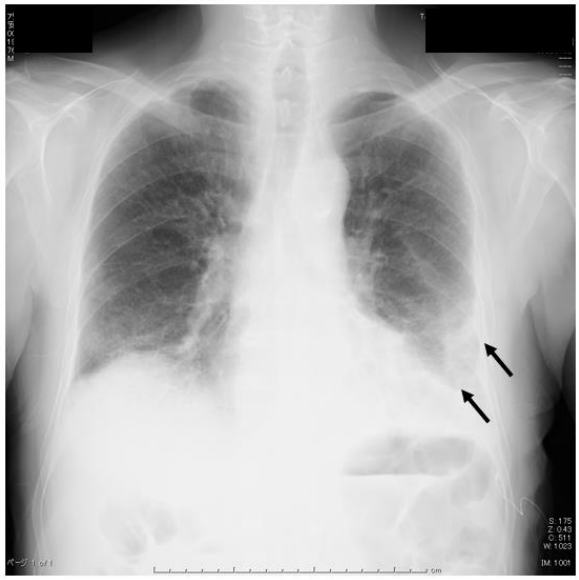

Figure 4: Chest X-ray findings of a 68-year-old man with influenza pneumonia (A). *Haemophilus influenzae* was also isolated from his sputum, suggesting influenza-related bacterial pneumonia. Unilateral infiltration shadows are seen in the left lower lung (arrows), and he improved with peramivir and sulbactam/ampicillin treatment.

For patients in whom viral pneumonia is suspected on the basis of the distinctive physical findings, chiefly of the skin, and laboratory data described above, or in light of the prevalence of the virus or familial transmission status (for example, if viral infection from a child or grandchild is plausible), ideally a definitive diagnosis should, if possible, be made. This is because it enables the more appropriate selection of drugs for treatment, as well as prevention.[22,29] In recent years, genetic diagnosis, such as the polymerase chain reaction (PCR) method, has started to come into general use.[16] For COVID-19 in particular, the greater sensitivity and specificity of PCR tests compared with those of antigen tests have drawn close attention, and they have become essential to making definitive diagnoses. Multiplex PCR method tests, which enable comprehensive screening for multiple viral genes simultaneously, may have already become routine in the clinical setting.[30]

CONCLUSION

The clinical manifestations, pathophysiology, and chest imaging findings of viral pneumonia patients were reviewed, and their viral pathogeneses, symptoms, physical findings, and laboratory data were considered. Viral pneumonia usually presents with bilateral ground-glass opacities on chest imaging, although bacterial pneumonia typically shows unilateral infiltration shadows. SARS-CoV-2 infection shows a characteristic pathogenesis and variation in chest imaging findings dependent on its severity, including massive pulmonary edematous shadows. The basic pathophysiology and clinical manifestations should be carefully considered when characteristic chest imaging findings are seen, and viral infections, such as measles, RSV, hMPV, CMV, and influenza, are suggested.

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