Viral Pneumonias

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KEYWORDS

• Viral pneumonia • Tomography x-ray computed • Community-acquired infections
• Immunocompromised hosts

KEY POINTS

- Radiologic findings of influenza usually appear as bronchiolitis, bronchopneumonia, or manifestations of airway-centric infection. H1N1 influenza may have a similar appearance but can also cause an organizing pneumonia pattern.
- The respiratory syncytial virus, parainfluenza virus, and human metapneumovirus have a predilection for airway-centric infection. They usually cause mild symptoms in immunocompetent adults but more likely to cause bronchopneumonia in immunocompromised patients.
- Adenovirus causes nonsegmental consolidation, particularly in the setting of outbreaks of novel serotypes. In the setting of other viral lower respiratory tract infections, lobar consolidation usually suggests bacterial superinfection.
- Cytomegalic virus (CMV) and herpes simplex virus in the respiratory tract of hospitalized patients represent reactivation of latent infection, which is not always pathogenic. When pathogenic, such as in the setting of lung transplants, CMV often causes ground-glass opacities and micronodules.

INTRODUCTION

Viral pneumonia upended the world in 1918 and again in 2020, but it has also been a major source of respiratory illness in the intervening century. More than 200 species of virus are capable of infecting humans and 3 to 4 new human viruses are discovered each year.[1] A handful of these viruses infect the lower respiratory tract, causing significant morbidity and mortality among humans and resulting in over $6.4 billion in hospital stays.[2] Although many pathogens causing community-acquired pneumonias still go undiagnosed, the development of real-time polymerase chain reactions (PCRs) for numerous respiratory viruses has dramatically increased the documentation of viral pneumonias over the last 2 decades.[3] Recognition of radiologic features that prompt

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testing for viral pathogens could reduce the use of unnecessary antibiotics, and in selected cases prompt institution of antiviral agents.[4,5]

Most viral pneumonias are community-acquired; however, a few are associated with health care settings. Immunocompromised patients are often infected with these community-acquired viruses, but are at greater risk of severe infection, including with those which are typically indolent. This article will review the imaging of community-acquired and health care–associated viral pneumonia, as well as viral pneumonia in the immunocompromised host. COVID-19 is specifically discussed by Sing and colleagues elsewhere in this issue.

COMMUNITY-ACQUIRED VIRAL PNEUMONIA

The overwhelming majority of viral pneumonias are community acquired. Some of these viruses, such as RSV and parainfluenza, are acquired as children and result in mild, self-limited illness. Among adults with pneumonia in whom a pathogen can be detected, viruses are the primary or coinfecting pathogen in 26% of cases requiring hospitalization.[4] Immunocompetent patients requiring hospitalization are generally elderly and often have underlying conditions such as chronic obstructive pulmonary disease (COPD).[5] The main pathogens comprising community-acquired viral pneumonia are influenza, human metapneumovirus (HMPV), respiratory syncytial virus (RSV), adenovirus, and rhinovirus. Hantavirus pulmonary infections are much less common, but are clinically important because they can cause severe, often fatal, respiratory failure in otherwise healthy, young adults.

INFLUENZA

Before the COIVD-19 pandemic, influenza was the principal cause of severe viral pneumonia in the world. Influenza can be broadly categorized into one of the multiple groups (A, B, C, or D), influenza A is most predominant.[6] In the United States, between the years 2010 and 2018, 4 to 23 million medical visits and 12,000 to 79,000 deaths occurred each year due to influenza.[7] Cases decreased dramatically in 2020 likely due to personal public health measures (eg, mask wearing) and reduced medical office visits instituted to minimize the spread of COVID-19.[8]

Most patients with influenza experience a self-limited upper respiratory infection of the airways, which only occasionally progresses to the lower respiratory tract.[6,9,10] Influenza pneumonia is typically mild, but in pregnant patients,[11] elderly patients, and/or those with chronic underlying disease, such as heart failure or COPD, the pneumonia can be severe and sometimes fatal.[10,12,13]

Influenza is predominantly an airway-centric infection and imaging manifestations often reflect this (**Table 1**). In severe infections, however, diffuse disease can obscure the underlying airway findings. Radiographs typically demonstrate ill-defined reticulonodular opacities in a central distribution (in contrast to peripheral/subpleural reticular opacities seen in edema), reflecting the airway-centric process. Less commonly, radiographs can also show multifocal consolidation. On computed tomography (CT), features of bronchitis (bronchial wall thickening) and bronchiolitis (tree-in-bud opacities) may be present[6,9] (**Fig. 1**). When airspace opacities occur, ground-glass opacities and multifocal consolidation are more common than localized consolidation, and often occur in a peribronchial distribution[9] (**Figs. 2** and **3**). Pleural effusions are rarely seen in the pneumonias caused by influenza as the sole pathogen.[6,9] Secondary infections are common in severe cases of influenza, and are suggested by radiological features such as focal lobar consolidation or worsening opacities following initial improvement.[6,9] In a series of patients accrued before 2009, diffuse airspace disease was only rarely

Table 1
Imaging patterns of viral pneumonia by etiology

	Diffuse Ground Glass	Consolidation—Not Bronchocentric	Consolidation—Bronchocentric	Organizing Pneumonia	Tree-In-Bud Micronodules	Micronodules, Not Tree-In-Bud	Linear/Interstitial
Seasonal influenza	+	+	++		++	+	
H1N1	++	+	++	++	+	+	
Adenovirus	+	+++	+		+	+	
HMPV	+		+		+++	+	
RSV	+		+		+++	+	
Parainfluenza	+		++		+++	+	
Hantavirus	+++	++					+++
HSV	++		++			+	+
CMV	+++	++	+		+	++	
VZV	+	+				+++	

Increasing + indicates increasing relative frequency of the associated pattern. The purpose of this table is to indicate general trends; the absence of a + is not to suggest a complete absence of this finding on all imaging.

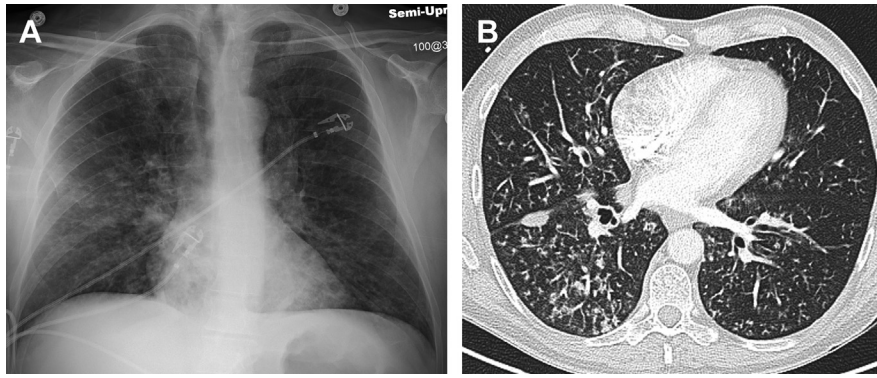

Fig. 1. Influenza B in a 60-year-old man. (*A*) Frontal chest radiograph demonstrates perihilar-predominant bilateral reticulonodular opacities with bronchial wall thickening. (*B*) Axial chest CT shows extensive bilateral centrilobular nodules, including tree-in-bud distribution, and bronchial wall thickening indicating bronchiolitis and bronchitis, airway-centric disease. Incidental focal fluid within the right major fissure.

caused by influenza and was more typical of bacterial pneumonia.[9] Acute respiratory distress syndrome (ARDS), however, is seen in other variants of influenza (see below, H1N1).

New strains arise as influenza viruses circulate in swine, birds, and humans, and genetic reassortment occurs between viruses from different animals.[14] One such reassortment resulted in the swine-origin H1N1 pandemic in 2009. This influenza A subtype was classified as H1N1 based on the surface glycoproteins hemagglutinin (H) and neuraminidase (N), which promote propagation of the virus into lower respiratory tract cells.[14] Similar to seasonal influenza infections, most patients experienced an uncomplicated clinical course, but a small percentage of patients developed severe respiratory distress.[15] Although the overall mortality from H1N1 influenza was not increased markedly compared with circulating strains, there was a dramatic shift in mortality toward younger patients, such that 87% of fatalities occurred in patients younger than 65 years.[16]

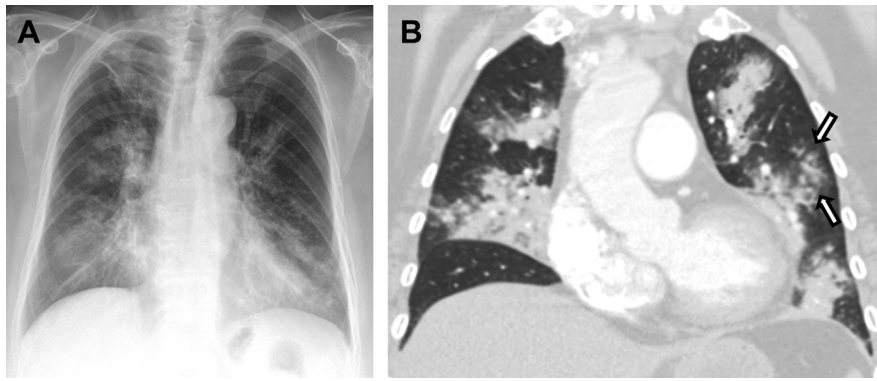

Fig. 2. Influenza A in a 73-year-old woman. (*A*) Frontal chest radiograph shows bilateral centrally distributed hazy opacities. (*B*) Coronal chest CT demonstrates bilateral peribronchovascular consolidation consistent with bronchopneumonia. There are also small acinar nodules in the left upper lobe (*arrows*).

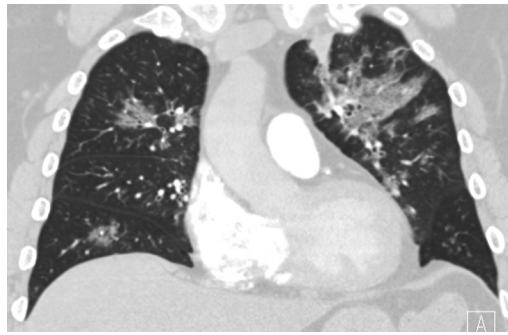

Fig. 3. Bronchopneumonia caused by H3N1 influenza A in a 66-year-old man. Coronal chest CT demonstrates bilateral peribronchovascular ground-glass opacities with interlobular septal thickening.

Although radiographs in swine-origin H1N1 infections are usually normal. Chest radiographs and CTs in swine-origin H1N1 that progresses to pneumonia often include features of consolidation within multiple lobes, with lower lobe predominance.[17] H1N1 can also result in an organizing pneumonia pattern, with peribronchovascular and peripheral/subpleural ground-glass opacities and consolidation[18,19] (**Fig. 4**). Finally, H1N1 can progress to ARDS (**Fig. 5**). Compared with ARDS by other types of severe community-acquired pneumonia, H1N1-related ARDS may lead to worse oxygen exchange and increased use of extracorporeal membrane oxygenation.[20]

Some animal-origin influenza viruses can replicate in human cells but have not yet acquired genetic constituents that enable efficient human-to-human transmission. Two such viruses include H5N1 and H7N9 influenza. Together, over 2,000 human infections have been reported with these organisms, accompanied by a high mortality rate.[21] Reports of imaging are limited to very small series. In general consolidation and ground-glass opacities were multifocal at the time at initial imaging and commonly progressed to bilateral disease within several days.[22,23] Pleural effusions were reported to be more frequent in H5N1 than usually seen in human influenza, but remained rare in H7N9 influenza. Occasional pneumatoceles and cavities were also reported with H5N1 pneumonia.[22]

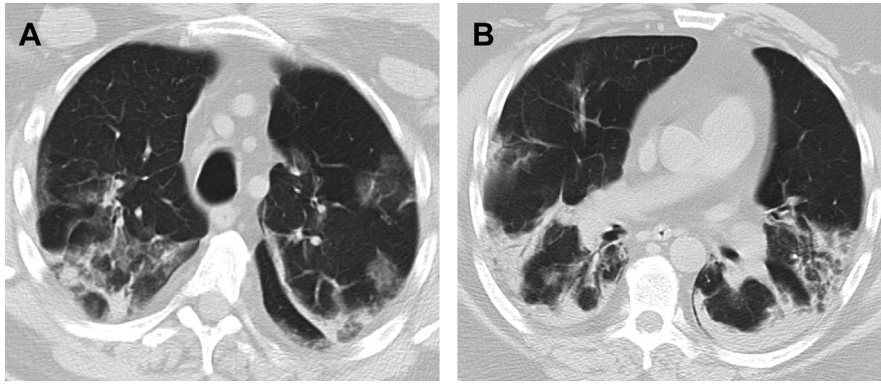

Fig. 4. H1N1 in a 44-year-old man. (*A*, *B*) Axial chest CT images show bilateral peribronchovascular and peripheral ground-glass opacities and consolidation in an organizing pneumonia pattern.

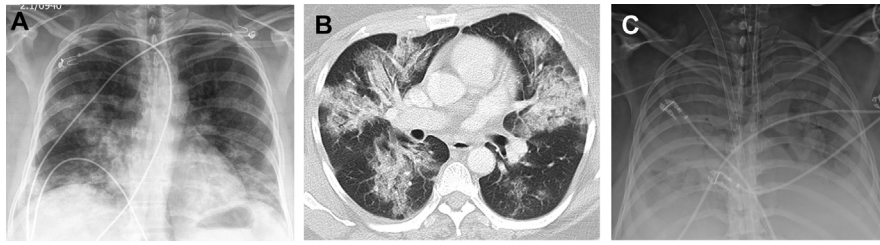

Fig. 5. Forty-three-year-old otherwise healthy woman with H1N1 infection demonstrating progression from bronchopneumonia to ARDS. (*A*) Initial frontal chest radiograph demonstrates bilateral hazy perihilar and basilar airspace opacities. (*B*) Axial chest CT on the same day shows bilateral peribronchovascular ground-glass opacities, with areas of interlobular septal thickening. (*C*) Frontal chest radiograph 11 days later shows near-complete opacification of both lungs and an extracorporeal membrane oxygenation (ECMO) catheter.

Testing for influenza can be performed by a variety of means including nasal swab, respiratory aspirate, or respiratory lavage. The rapid influenza detection method can return results in less than 15 minutes, has a high specificity for the detection of influenza (>98%), but the sensitivity ranges between 50% and 70%.[7] Reverse transcription–polymerase chain reaction (RT-PCR) has a higher sensitivity for detection of influenza and it should be performed in cases where there is clinical suspicion for influenza infection but a negative rapid test.[7] Viral cultures may be performed when there is clinical concern for possible drug resistance or a variant influenza that may be related to an emerging pandemic.[7]

Treatment of seasonal influenza with one of four antiviral medications: oseltamivir, peramivir, baloxavir, or zanamivir is recommended within 24 to 48 hours of the onset of symptoms.[23,24] Oseltamivir or zanamivir are used in the treatment of swine-origin H1N1 influenza.[23]

ADENOVIRUS

Adenovirus is spread through fecal-oral route in children and aerosolized droplets among adults. Its overall incidence peaks in summer months; however, epidemics are typically seen in winter or early spring.[25–27] Most adenovirus infections (80%) that occur in children are mild; however, pneumonia can occur in up to 20% of infants.[27] Among immunocompetent adults, lower respiratory tract infections occur in small epidemic outbreaks within closely confined groups of adults such as within the military. There are numerous serotypes of adenovirus, with serotypes −1 through 7, −21, and −14 responsible for most febrile respiratory illnesses in adults. Serotype 14, one of the newer serotypes to affect North America manifested as a military base outbreak of pneumonia in 2006. Likely abetted by limited humoral immunity in the populace, the serotype rapidly spread to over 15 states by 2007.[27]

Chest radiographs of adenovirus pneumonia are similar to nonviral community-acquired pneumonia, and are less likely to produce a dominant airway centric pattern compared with the virus described in the next section. Radiographs may show unilateral or bilateral consolidation, and patchy hazy opacities.[28,29] On chest CT, most patients demonstrate unilateral or bilateral consolidation[9,29,30] (**Fig. 6**). Patchy ground-glass opacities are less common and nodules are infrequent. Although pleural effusions are uncommon on chest radiographs, they have been seen on CT in up to three-fourths of patients.[30] Lymphadenopathy is seen in approximately one-third of patients who undergo CT scanning.

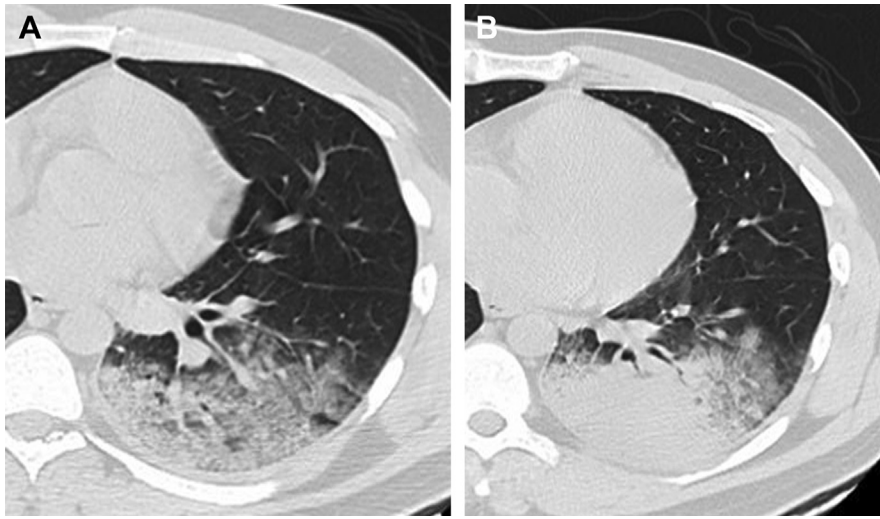

Fig. 6. Adenovirus in an otherwise healthy man in his early 20s. (*A*, *B*) Axial chest CT images demonstrate focal left lower lobe mixed consolidation and ground-glass opacities.

Diagnosis of adenovirus pneumonia can be achieved through PCR, immunohistochemical staining, or culture of bronchoalveolar lavage (BAL) fluid. Outbreaks of adenovirus pneumonia have led to oral immunization against adenovirus by the military; however, immunization is not currently available for civilians. There is no specific antiviral drug approved to target adenovirus. As adenovirus is a DNA virus, some patients with severe pneumonia are treated with cidofovir, an antiviral agent that inhibits DNA polymerase.[27]

HMPV, RSV, AND PARAINFLUENZA

RSV and parainfluenza virus have long been recognized as causing lower respiratory tract infections. HMPV is a relatively newly discovered pathogen, first classified as a paramyxovirus in 2001. More recently, HMPV and RSV have been moved to the family Pneumoviridae. Nevertheless, both share many characteristics with parainfluenza virus, particularly the propensity for airway infection.[6,31,32] These viruses are typically acquired as children; however, reactivation or reinfection can occur in adulthood secondary to waning immunity.[5] HMPV, RSV, and parainfluenza viruses have been detected in 4%, 3%, and 2% of hospitalized adults with community-acquired pneumonia, respectively.[4]

Among immunocompromised hosts, these viruses are important pathogens. Infections occur in 5% to 10% of hematopoietic stem cell transplant (HSCT) and transplant patients in the first 100 days posttransplant, and affect the lower tract in approximately 5% to 50% of these cases.[33,34] RSV, HMPV, and parainfluenza can all result in rapidly fatal pneumonia in immunocompromised patients.[5,6,25,32,35]

HMPV, RSV, and parainfluenza pulmonary infections have a propensity for airway-centric involvement secondary to preferential infection of ciliated respiratory epithelial cells.[31] Airway centric infection manifests as centrilobular nodules with and without tree-in-bud configuration, bronchial wall thickening, and as peribronchiolar ground-glass opacities or consolidation[6,9,31,34,36] (**Figs. 7–9**). In a retrospective evaluation of 100 (both immunocompetent and immunocompromised) patients diagnosed with

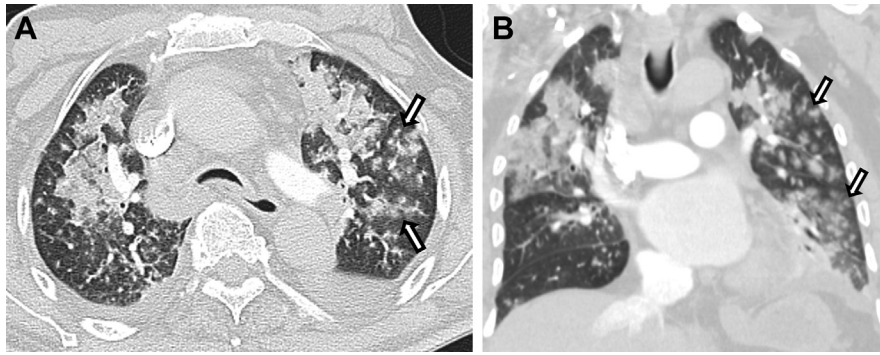

Fig. 7. Human metapneumovirus in a 63-year-old man. (*A*) Axial and (*B*) coronal chest CT images demonstrate bilateral peribronchovascular consolidation and ground-glass opacities indicative of bronchopneumonia. Centrilobular nodules (*arrows*) are also consistent with airway-centric disease. Incidental note of probable tracheomalacia on (*A*).

HMPV, the most commonly observed radiographic abnormality was bilateral, peribronchovascular airspace opacities.[32] CTs were performed only a minority of the cohort, most commonly demonstrating bilateral, ground-glass opacities. Centrilobular nodules were present in slightly less than half of these patients.[32] Although findings of small airway disease can be obscured in cases of extensive pneumonia in immunocompromised hosts, in a small series of patients with either HSCT or lung transplant, small nodules or tree in bud opacities were still observed on CTs in more than a third of patients.[37]

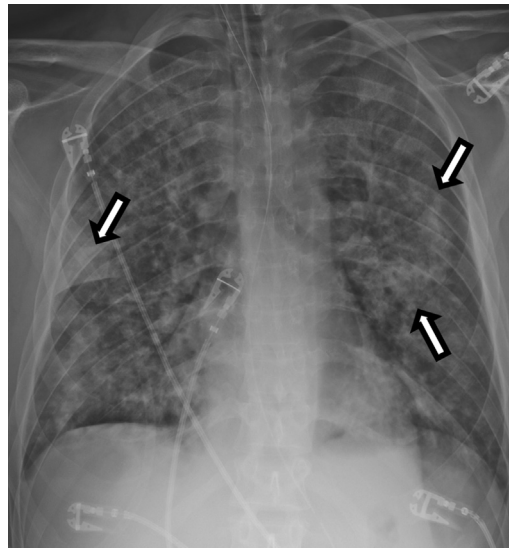

Fig. 8. Respiratory syncytial virus in a 29-year-old man with acute myelogenous leukemia status poststem cell transplant. Frontal chest radiograph demonstrates bilateral reticulonodular opacities and bronchial wall thickening compatible suggesting bronchiolitis and bronchitis. There are more focal airspace opacities in the right mid and lower lung, and left perihilar lung (*arrows*) likely representing associated pneumonia.

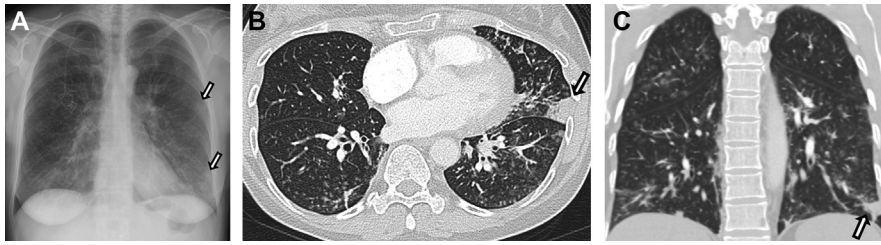

Fig. 9. Parainfluenza in a 61-year-old woman with multiple myeloma on chemotherapy. (*A*) Frontal chest radiograph shows bronchial wall thickening central reticulonodular opacities. There are also patchy airspace opacities in the left mid and lower lung (*arrows*). (*B*) Axial and (*C*) coronal CT images demonstrate bilateral solid and ground-glass centrilobular nodules, as well as localized consolidation in the lingula and left lower lobe (*arrow*).

Most CT findings of RSV and parainfluenza are similar to those seen with HMPV. Both demonstrate tree-in-bud opacities and bronchial wall thickening on CT in most patients.[38] Ground-glass opacities or consolidation are seen in one-fourth to one-third of patients.[9] Parainfluenza may be more likely than RSV to cause patchy basilar multifocal consolidation.[39] Pleural effusions occasionally occur in RSV pneumonia, which differs from parainfluenza and HMPV pneumonia in which associated effusions are rare.[6,9]

Imaging cannot confidently differentiate HMPV, RSV, and parainfluenza pneumonias from other common community-acquired pathogens causing airway centric infections, such as mycoplasma or Hemophilus influenza (**Fig. 10**). In addition, HMPV can cause nodular consolidation in approximately a third of cases, a feature more often considered to be associated with bacterial pneumonia.[32] Accordingly, specific diagnosis of these airway-centric infections is usually based on RT-PCR or serology. Therapy in symptomatic adults is supportive as there are no current targeted therapies.[5]

RHINOVIRUS

Rhinovirus, a primary respiratory-tract pathogen, which peaks in incidence in summer and fall, is best known for causing, "the common cold," a syndrome of upper

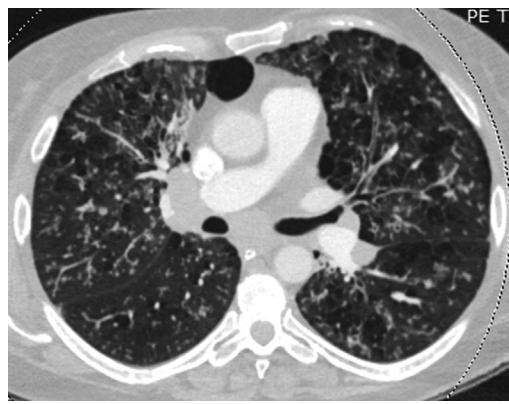

Fig. 10. Haemophilus influenzae pneumonia in a 50-year-old woman with emphysema. Axial chest CT demonstrates numerous centrilobular nodules throughout both lungs, some of which have tree-in-bud morphology, consistent with infectious bronchiolitis imaging appearance is very similar to the previous cases of parainfluenza pneumonia.

respiratory symptoms including rhinorrhea and cough.[40,41] In addition, rhinovirus is increasingly recognized as a cause of community-acquired pneumonia, albeit more frequently among immunocompromised than immunocompetent patients. In the former, it may be more common than the airway-centric viruses (eg, RSV, HMPV) infections described earlier. Coinfections with other viruses or with bacterial pathogens are common in both patient groups.[40,42]

There are relatively few studies depicting the radiologic appearance of rhinovirus pneumonia. A selected series of patients in which BAL was performed, focused predominantly on immunocompromised patients. Imaging demonstrated bilateral opacities in most cases, approximately half of which were predominantly peribronchial.[42] Nodules were also present, but were less common (**Fig. 11**). Mortality from rhinovirus-associated pneumonia and influenza pneumonia were similar in this cohort. In general, however, in the absence of bacterial coinfection, rhinovirus may be less likely to cause severe symptoms than the viruses discussed earlier. This observation and the current lack of an effective antiviral agent targeting rhinovirus render its detection of uncertain clinical importance. Treatment is currently supportive or should be directed at the copathogen.

HANTAVIRUS

Hantavirus is a potential cause for fulminant pneumonia in an otherwise healthy adult with a relevant environmental exposure. It is a zoonotic infection acquired through inhaling aerosolized rodent excreta. “New World” hantaviruses have resulted in several small outbreaks in the western United States, the first in the Four Corners area in 1993.[43,44] (In contrast to New World hantaviruses, “Old World” viruses in Asia and Europe and most commonly result in hemorrhagic fever with renal syndrome.). In North and South America, New World hantavirus can manifest as cardiovascular and respiratory failure referred to as Hantavirus Pulmonary Syndrome (HPS). In these patients, hantavirus directly infects lung endothelial cells and macrophages, which leads to extensive pulmonary edema and shock.[43]

Radiologically, HPS may mimic cardiogenic pulmonary edema; albeit, with a normal cardiac silhouette. Early findings include Kerley B lines and peribronchial cuffing, all suggesting interstitial edema[45,46] (**Fig. 12**). Most patients rapidly progress to extensive

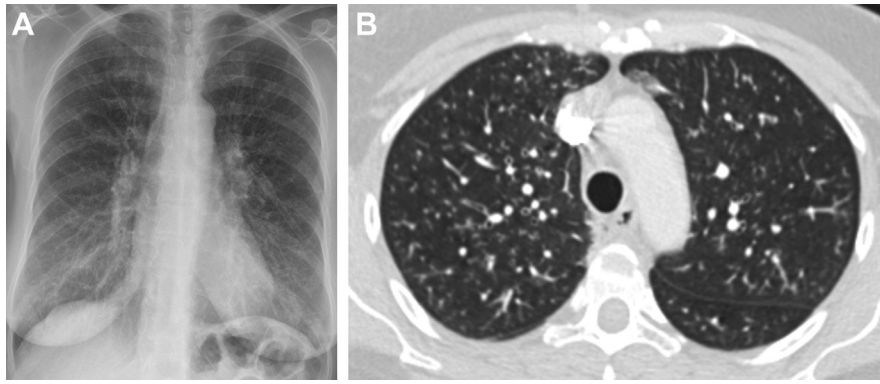

Fig. 11. Fifty-nine-year-old woman with productive cough and positive rhinovirus PCR. (*A*) Frontal chest radiograph shows subtle bilateral micronodules throughout both lungs. (*B*) Axial chest CT confirms bilateral 2-3 mm centrilobular tree-in-bud nodules in the upper lobes.

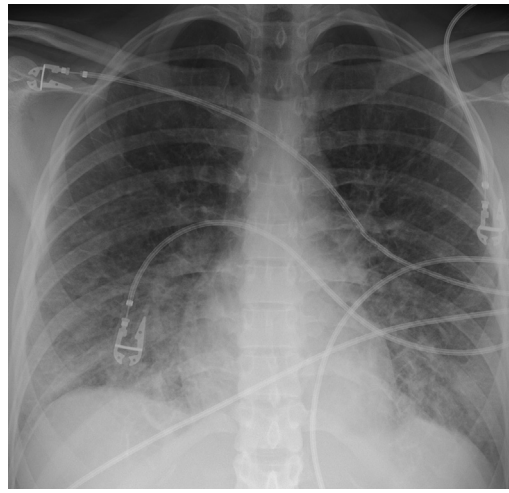

Fig. 12. Linear reticular pattern of early hantavirus in a 26-year-old woman. Frontal chest radiograph demonstrates fine reticular and hazy opacities with lower lung predominance.

bilateral predominantly perihilar or bibasilar hazy airspace opacities on chest radiographs (Fig. 13). Reports of CT findings in hantavirus are limited to small case series or case reports, and may be skewed toward less severely affected patients who are hemodynamically stable. Available reports have shown bilateral central or basilar-predominant ground-glass opacities with smooth interlobular septal thickening, occasionally with concurrent small ill-defined nodules or focal consolidation.[47,48] The majority of patients have small pleural effusions.

Diagnosis can be confirmed serologically through positive IgM and IgG analysis, or through reverse transcriptase PCR for the viral genome. Hantavirus is associated with a high morbidity rate, 40% worldwide; however, treatment is primarily supportive and no FDA-approved methods are currently available.[43]

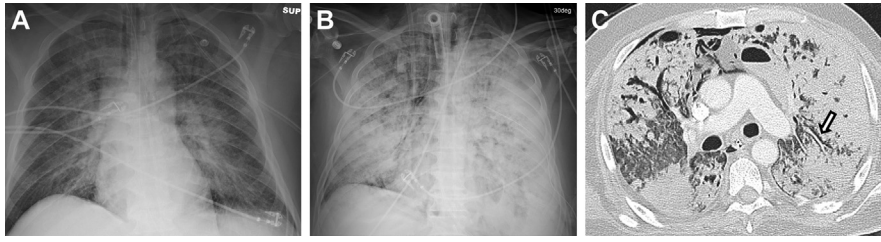

Fig. 13. Progression of hantavirus to ARDS in a 54-year-old man. (*A*) AP chest radiograph demonstrates bilateral perihilar hazy opacities in a "bat wing," pattern as well as Kerley B lines, with normal size of the cardiac silhouette and no pleural effusions. (*B*) AP frontal chest radiograph 3 days later demonstrates extensive bilateral consolidation and hazy opacities which obscure the cardiac silhouette. There is a small right pneumothorax, and lucencies along the right mediastinum and right heart border representing pneumomediastinum. ECMO cannula is in place. (*C*) Chest CT shows extensive bilateral consolidation. Pneumomediastinum and Macklin effect in the left lower lobe suggest barotrauma (*arrow*).

HOSPITAL-ASSOCIATED VIRAL PNEUMONIA

Although most viral infections are community-acquired, a few viruses such as Herpes simplex virus (HSV) contribute to morbidity and mortality in immunocompetent adults in the hospital setting. HSV infection can produce bronchopneumonia secondary to reactivation of existing virus within immunocompromised patients (eg, with hematologic malignancies) and in some immunocompetent patients with underlying conditions (eg, burns, major surgeries, diabetes, and prolonged mechanical ventilation.).[49,50]

Because the incidence of HSV infection is low, studies of radiologic findings combine immunocompetent and immunocompromised patients. In one study of 23 patients, all demonstrated multifocal patchy or segmental airspace opacities on radiographs, which were both central and peripheral in the majority.[50] Approximately half of patients had pleural effusions. Chest CT findings of multifocal ground-glass opacities combined with areas of peribronchiolar consolidation and interlobular septal and bronchial wall thickening have been reported in most patients.[50,51] Nodules are less common in HSV infection than in varicella, but may be present on CT in 30% of patients (see Brixey and colleagues' article, "Non-Imaging Diagnostic Tests For Pneumonia,"in this issue). These may be centrilobular ground-glass nodules or discrete nodules larger than 5 mm, some of which can manifest a halo sign. Pleural effusions may be seen but lymphadenopathy is uncommon. In critically ill patients, oral and BAL positivity for HSV is nonspecific and by itself is not proof of HSV pneumonia (**Fig. 14**). For example, HSV has been detected in up to 71% of respiratory samples from ARDS patients.[52]

Several other viruses have been implicated in nosocomial infections, but their role remains uncertain. Like HSV, CMV can reactivate after latent infection and has been implicated as another source of ventilator-acquired pneumonia (see below). Controversy exists regarding whether CMV positivity actually worsens clinical outcomes or contributes to lung injury.[53,54] Acanthamoeba polyphaga mimivirus (mimivirus) is an ameba-associated virus, which has recently been isolated within the lower respiratory

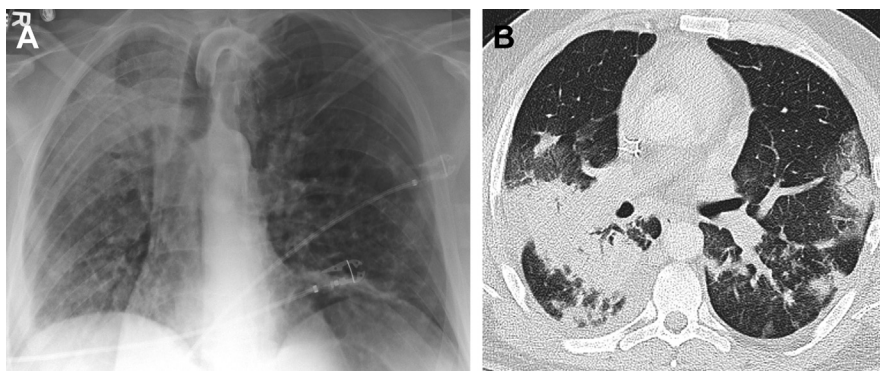

Fig. 14. Forty-four-year-old man with pseudomonas pneumonia. Herpes virus demonstrated on bronchoscopy performed on during after 2 weeks of hospitalization. (*A*) Frontal chest radiograph shows a right upper lung consolidation, more suggestive of bacterial pneumonia. (*B*) Axial chest CT demonstrates extensive consolidation in the superior segment of the right lower lobe, and additional smaller foci of consolidation in the left lower lobe. The multifocal consolidation is most consistent with a bacterial pneumonia. Presence of HSV virus on bronchoscopy may be incidental and not contribute significantly to the patient's pneumonia.

tract of hospitalized adults and adults in long-term care facilities.[55] However, its status as a true pathogen is controversial, and suspected cases of mimivirus pneumonia are limited to case reports.[56,57]

VIRAL PNEUMONIA IN THE IMMUNOCOMPROMISED PATIENT

Community-acquired viral respiratory infections also commonly affect immunocompromised individuals. Viruses that usually result in limited symptoms in immunocompetent hosts can cause severe pneumonia in those patients. Immunocompromised hosts most at risk for severe viral pneumonia include those following HSCT, or solid organ transplantation.[6] Radiologic studies of community-acquired pneumonia frequently combine both immunocompetent and immunocompromised patients to increase sample size, and therefore in the case of several pathogens, the imaging appearance in both patient groups has been reviewed above. Cytomegalovirus (CMV) is a ubiquitous pathogen whose association with pneumonia is largely confined to immunocompromised adults. Varicella pneumonia is most common in immunocompromised patients but remains a cause of severe pneumonia in immunocompetent adults in countries without universal varicella vaccination.

CYTOMEGALOVIRUS

CMV causes a systemic infection that can present acutely with mononucleosis, pharyngitis, fever, and lymphadenopathy.[58] The virus commonly establishes chronic, latent infection that can reactivate in immunocompromised hosts such as after HSCT, solid organ transplant (particularly lung transplant), and among those with acquired immunodeficiency syndrome (AIDS). Although it is not specifically a respiratory pathogen, it can cause severe pneumonia in these patients. CMV prophylaxis is very effective in the setting of HSCT, reducing infection from 20% to 70% to 1% to 3%, but is less so in lung transplant recipients (see Michelle Hershman and Scott Simpson's article "Thoracic Infections in Solid Organ Transplants; Radiological Features and Approach to Diagnosis," in this issue).[59]

Because CMV within the lungs usually represents reactivation of a systemic infection rather than inhaled pathogen its manifestations in the lung are pleomorphic and not confined to airway disease. The most common abnormality on chest radiographs is bilateral hazy opacities, which manifest as bilateral ground-glass opacities on chest CT.[60–62] Multiple centrilobular micronodules are also a common finding. In severe cases, multifocal consolidation can predominate or be intermixed with ground-glass opacities (**Figs. 15** and **16**). Interlobular septal thickening and pleural effusions are less common findings. Nodules with halo sign are uncommon and cavitary nodules have been reported but are rare.[60,62,63]

CMV is the most common viral infection among patients living with HIV, but has become much less prevalent following the advent of HAART. In the setting of HIV findings, CMV infection findings are similar to those described earlier. Radiographs commonly demonstrate bilateral hazy opacities seen as ground-glass opacities on CT. Consolidation, discrete masses, and nodules can also occur, and airway abnormalities (bronchiectasis and bronchial wall thickening) can be seen on CT.[64] Pneumocystis jiroveci pneumonia (PJP) can be difficult to distinguish from CMV as both infections are seen in patients with very low CD4 counts and can manifest as diffuse ground-glass opacities. However, CMV infection is associated with micronodules and macronodules more frequently than pneumocystis.[62] Consolidation and the halo sign have also been seen in CMV to a significantly higher degree. The relative likelihood of

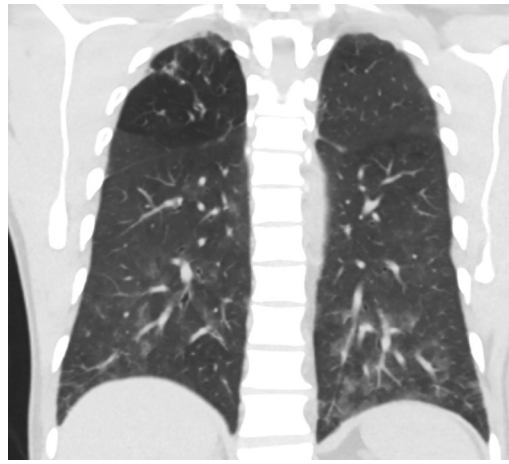

Fig. 15. Cytomegalovirus in a 52-year-old man status postrenal transplant. Coronal chest CT with dominant findings of bilateral lower lobe peribronchovascular ground-glass opacities. There are a few nodules in the right lung apex. (*Courtesy of* Brent P. Little, MD, Jacksonville, Florida.).

CMV versus PJP is also highly dependent on viral/and or pneumocystis prophylaxis, respectively.

Diagnosis of CMV pneumonitis is difficult, similar to HSV pulmonary infection (see above, "hospital-associated viral pneumonias"). As with other latent infections, the presence of CMV virus on viral cultures of BAL fluid is not proof of pathogenic CMV infection.[54,64] More definitive diagnosis can be made by BAL cytology or other

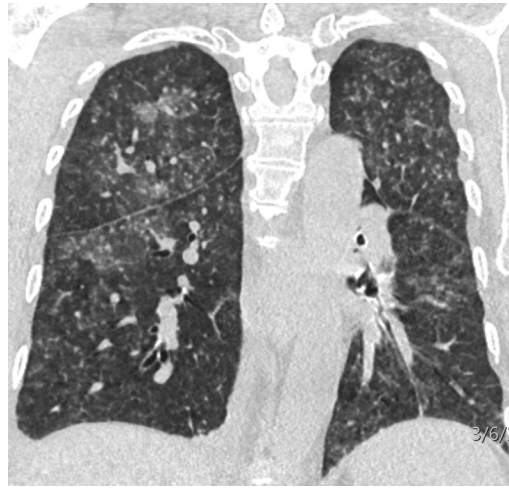

Fig. 16. CMV in a 62-year-old female with a history of orthotopic heart transplant for non-ischemic cardiomyopathy. Her CMV prophylaxis was stopped early on posttransplant due to thrombocytopenia/anemia. Coronal chest CT demonstrates diffuse bilateral nodules with mild peribronchovascular ground-glass opacities. (*Courtesy of* Farouk Dako, MD, MPH, Philadelphia, Pennsylvania.).

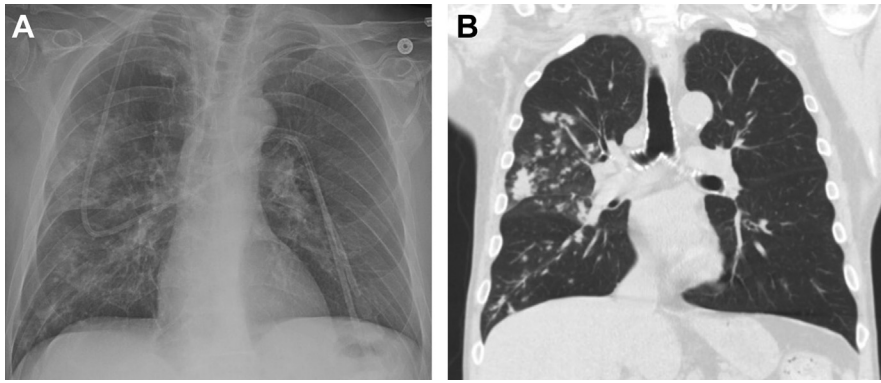

Fig. 17. Varicella pneumonia in a 72-year-old man with multiple myeloma status postautologous transplant complicated. (*A*) Frontal radiograph demonstrates multiple nodules in the right lung. (*B*) Coronal chest CT demonstrates a focal area of nodular consolidation with clustered adjacent centrilobular micronodules. Fewer micronodules are present in the lower lobe. (*Courtesy of* Shamus Moran, MD, Seattle, Washington.).

methods (see Brixey et al.).[64] First-line treatment is with the systemic antiviral intravenous ganciclovir. Foscarnet and cidofovir are antivirals which may be used for resistant infections.[5]

VARICELLA

Varicella, member of the herpes family, can cause severe pneumonia in immunocompromised patients and unvaccinated immunocompetent adults. Most children in the United States are vaccinated against the varicella virus after 12 months of age;[65] however, vaccination is only widespread in predominantly high socioeconomic countries.[66] Individuals who did not receive the vaccination and were not infected as children are at risk of contracting varicella as an adult, and between 5% to 15% of infected adults develop pneumonia.[65] Compared with children, varicella pneumonia

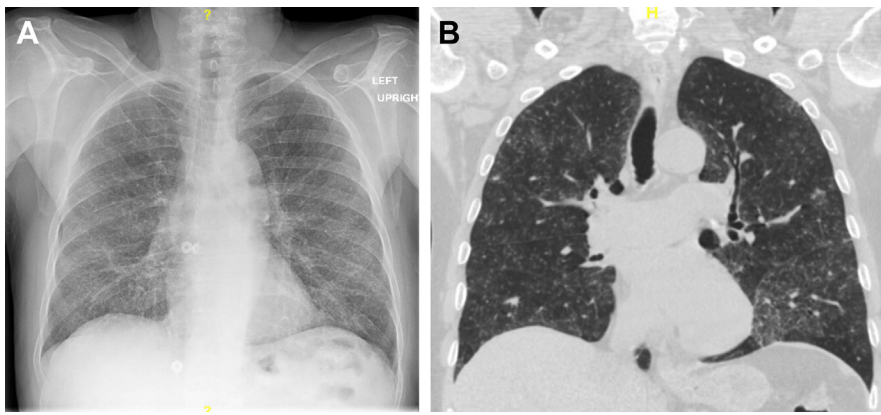

Fig. 18. Varicella pneumonia in a 54-year-old man with multiple myeloma, relapsed following HSCT. (*A*) Frontal chest radiograph shows diffuse bilateral reticular and micronodular opacities. (*B*) Coronal chest CT confirms the diffuse solid and ground-glass micronodules in a random distribution. The distribution suggests a hematogenous component of spread of infection. (*Courtesy of* Shamus Moran, MD, Seattle, Washington.).

in adults is associated with a 4 to 50 fold greater risk of hospitalization and a 174 fold greater risk of death.[66] Severe pneumonia typically develops an average of 3 days after the characteristic varicella rash and can rapidly progress to acute respiratory distress syndrome.[67] Mortality of intubated patients reaches 50%.[65]

Chest radiographs demonstrate ill-defined nodules measuring less than 1 cm, which may coalesce. Occasional findings include consolidation, hilar lymphadenopathy, or pleural effusions.[6,67] Chest CT in immunocompetent hosts often display 1 to 10 mm centrilobular nodules with and without ground glass halos, as well as randomly-distributed nodules.[68,69] CTs of immunocompetent and immunosuppressed patients with severe pneumonia contain centrilobular nodules in 50%, consolidation and ground-glass opacities in less than half, and effusions in approximately one-third of cases (**Figs. 17** and **18**).[68] Randomly distributed 2 to 3 mm calcified nodules are typical of healed infection.[6]

First-line therapy of varicella is the antiviral acyclovir, administered intravenously. In the setting of typical skin rash and exposure history, therapy is often initiated before the diagnosis is confirmed with PCR.[5]

SUMMARY

Viral pneumonia is prevalent among both immunocompetent and immunocompromised hosts, typically causing more severe disease in the latter. Several viral pneumonias, such as influenza, HMPV, RSV, and parainfluenza demonstrate similar airway-centric distribution, the likelihood of a specific organism often dependent on seasonal epidemics. Other viral pneumonias, such as adenovirus, frequently cause pneumonias with imaging findings indistinguishable from community-acquired bacterial pneumonias. For a few organisms, additional factors are central to the likelihood of infection, for example, environmental exposure for Hantaviruses and vaccination status for Varicella. In organisms that typically cause chronic infections in humans, such as HSV and CMV, the relationship between infection and clinical pneumonia is complex and incompletely understood.

CLINICS CARE POINTS

- HMPV, RSV, and parainfluenza pulmonary infections have a propensity for airway centric involvement with associated imaging findings of bronchiolitis and bronchopneumonia. Since this imaging appearance can be mimicked by bacterial pathogens, diagnosis is usually based on PCR.
- Influenza is also an airway centric infection causing bronchiolitis and bronchopneumonia. Diffuse airspace disease is rare in most seasonal outbreaks but occurs more commonly with infection with novel influenza viruses, such as H1N1 and avian influenza.
- Adenovirus can cause lobar type consolidation, which in the setting of infection with other virus pathogens (including influenza) suggests bacterial co-infection.
- Both HSV and CMV infections represent systemic reactivation of a latent infection rather than an acute primary pulmonary infection and positive respiratory cultures are not proof of pneumonia. Among immunocompromised hosts (patients living with advanced AIDS), CMV most commonly presents with ground glass opacities and centrilobular micronodules.
- Varicella and Hantavirus can cause severe pneumonia in otherwise healthy adults, one in the absence of prior vaccination or childhood infection, the other following specific environmental exposure. Imaging is dominated by micronodules in the setting of varicella, and linear interstitial opacities in the setting of Hantavirus Pulmonary Syndrome (HPS).

DISCLOSURE

The authors have nothing to disclose.

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