REVIEW

Practical guide for pediatric pulmonologists on imaging management of pediatric patients with COVID-19

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Abstract

Understanding of coronavirus disease 2019 is rapidly evolving with new articles on the subject daily. This flood of articles can be overwhelming for busy practicing clinicians looking for key pieces of information that can be applied in daily practice. This review article synthesizes the reported imaging findings in pediatric Coronavirus disease 2019 (COVID-19) across the literature, offers imaging differential diagnostic considerations and useful radiographic features to help differentiate these entities from COVID-19, and provides recommendations for requesting imaging studies to evaluate suspected cases of pediatric COVID-19.

KEYWORDS

coronavirus disease, COVID-19, imaging, pediatric

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), first presented as an outbreak of unexplained pneumonia cases in Wuhan, Hubei province, China in December of 2019.[1,2] Over the next 4 months, COVID-19 has rapidly spread worldwide with infections reported in over 200 countries.[3] As of 26 April 2020, there have been 2 804 796 cases and 193 722 deaths related to COVID-19 across the globe with 899 281 cases and 46 204 deaths reported in the United States.[3] Although morbidity and mortality are predominantly observed in the adult population, there have been an increasing number of reports of severe clinical courses, most frequently in patients with underlying comorbid medical conditions,

including multiorgan failure and death in infants and children due to COVID-19 infection.[4-11]

Unfortunately, the current fundamental understanding of COVID-19 is limited due to the novel nature of the virus. However, numerous articles related to imaging findings are published daily on the subject. This flood of articles can be overwhelming for practicing clinicians, including pediatric pulmonologists, looking for key pieces of useful and practical information for imaging management of their pediatric patients that can be directly applied to their current daily clinical practice. Therefore, the purpose of this article is to provide: (a) an up-to-date and practical source of information regarding the imaging manifestations of COVID-19 pneumonia in pediatric patients; (b) provide guidance for utilizing imaging studies for pediatric patients with suspected COVID-19

infection; and (c) discuss differential diagnostic considerations for pediatric patients.

2 | WHAT IS COVID-19?

COVID-19 is a respiratory viral disease caused by the SARS-Cov-2 virus, an enveloped single-stranded RNA virus, which is readily transmitted human-to-human primarily through respiratory droplets; although transmission through contact with conjunctival membranes has also been described.[12] The SARS-CoV-2 virus gains entry into human cells via binding of the ACE2 receptor, facilitated by the presence of the TMPRSS2 membrane protease, replicates within the cell and is then discharged by the cell into the body often disabling or destroying the host cell in the process.[13] The ACE2 receptor and TMPRSS2 are co-expressed in the lungs, heart, intestinal smooth muscle, liver, kidneys, neurons, and immune cells which may explain the potential for multiorgan injury recently observed in pediatric patients.[11,13,14] In the lungs, viral ACE2 receptor binding in alveolar epithelial cells and alveolar macrophages leads to alveolar damage.[2] The virus is also believed to alter the functioning of the immune system and has been shown to increase expression of the pro-inflammatory cytokine IL-6 and chemokines MCP1, CXCL1, CXCL5, and CXLC10 in ex vivo lung tissue.[2,15]

3 | CLINICAL PRESENTATION OF COVID-19 IN CHILDREN

The most common clinical symptoms in pediatric patients with COVID-19 are fever and cough with a sore throat, rhinorrhea and/or nasal congestion, diarrhea, fatigue, or dyspnea reported in a small number of cases.[12,16-19] Children infected with COVID-19 generally demonstrate milder clinical symptoms compared with adults, possibly related to lower maturity and function of the angiotensin-converting enzyme-2 (ACE2), the levels of which are increased by COVID-19 binding of ACE2 receptor, and/or the immaturity of the developing immune system.[2,6] In fact, one study with over 2000 pediatric cases of COVID-19 found that less than 6% of cases were classified clinically as severe and only one death occurred.[6] However, it is important to keep in mind that even children who are asymptomatic or demonstrate mild symptoms still play an important role in disease transmission.[20]

As with most viral pneumonias, the laboratory findings in COVID-19 pneumonia are often nonspecific in pediatric patients. Complete blood count (CBC) is frequently normal, although neutropenia, lymphopenia, and thrombocytopenia have been observed.[16,18,20] Elevation of inflammatory markers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), has also been reported with variable frequency.[16-18] In severe cases, alterations in coagulation factors and elevated levels of liver enzymes, lactate dehydrogenase (LDH), and D-dimer may be seen.[20] For the initial diagnosis of SARS-CoV-2, the Center for Disease Control and Prevention recommends collecting an upper respiratory specimen,

preferably a nasopharyngeal swab if possible, to be tested by RT-PCR.[21] If a lower respiratory specimen is also available, it should be tested, but inducing sputum is not recommended.[21] Alternative specimen types include nasal, mid-turbinate, and throat swabs, but the utility of these samples is not well understood.

4 | ROLE OF IMAGING IN DIAGNOSIS OF PEDIATRIC COVID-19

The role of imaging evaluation of pediatric patients with known or suspected COVID-19 pneumonia is currently an area of active discussion within the radiology community at national and international levels. Due to the potential overlap in imaging features of COVID-19 with other infections, which can lead to decreased specificity, the American College of Radiology (ACR) currently states that neither chest radiography (CXR) nor chest computed tomography (CT) should be used to screen for or as a first-line test to diagnose COVID-19.[22] However, imaging studies play an important role, especially in pediatric patients with a moderate-to-severe clinical course, in establishing a baseline, assessing for associated complications related to comorbid medical conditions, and evaluating disease progression/treatment response.[23] Ultimately, the decision to pursue radiologic evaluation should be made after weighing the potential benefits (ie, establishing baseline so that disease progression can be assessed and identifying complications of comorbid conditions, such as sudden respiratory compromise related to underlying chronic lung disease) with the potential risks (ie, pediatric radiation exposure, exposure to increased number of radiology staff, decreased availability of imaging machine/facility due to required cleaning time and air turnover time).

5 | IMAGING FINDINGS OF COVID-19 IN CHILDREN

5.1 | Chest radiography

The literature describing CXR findings in COVID-19 pneumonia is currently scarce in adult patients and almost non-existent for pediatric patients. The most frequently observed CXR abnormality in adult COVID-19 patients is bilateral patchy consolidation and ground-glass opacities with a peripheral and lower lung zone distribution[24,25] (Figure 1). CXR sensitivity for the detection of COVID-19 pneumonia has been reported ranging from 69% to 89% in adult patients.[26,27] A single pediatric COVID-19 study, which included 10 patients, reported observing patchy unilateral opacities in 4/10 (40%) of patients[28] (Figure 2A).

5.2 | Chest CT

CT imaging findings in pediatric COVID-19 patients have been reported with greater frequency compared to CXR, although an even
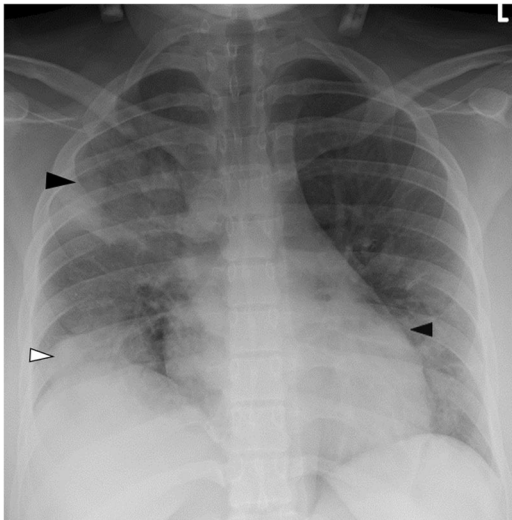
FIGURE 1 Seventeen-year-old female with no significant comorbid medical conditions who presented with shortness of breath and hypoxemia. RT-PCR testing confirmed the diagnosis of COVID-19 pneumonia. Frontal chest radiograph obtained at hospital admission shows patchy peripheral predominant consolidation (white arrowhead) and ground-glass opacities (black arrowheads) in the right upper lobe and bilateral lower lung zones. RT-PCR, reverse transcription-polymerase chain reaction

greater amount of chest CT data is available across the literature for adult patients. This likely relates to reporting/publication bias as CT's are performed in sicker patients and thus more likely to show abnormality. CXR is the first imaging study recommended for the evaluation of pediatric COVID-19 disease. The most commonly observed CT abnormalities in pediatric COVID-19 pneumonia are mixed bilateral ground-glass opacities and consolidation in a peripheral and/or subpleural distributions[17,29-32] (Figures 2B and 3). The "halo" sign, a focal consolidation with a surrounding ground-glass opacity border, has been visualized in up to 50% of pediatric COVID-19 patients with abnormal CT examination[17,33] (Figure 2B). Bronchial wall thickening and peribronchovascular opacities occur more frequently in pediatric patients than adults, however they are less frequently reported than the aforementioned "typical" pattern.[30] "Crazy paving" has been reported in 2/22 (9%) pediatric COVID-19 patients by one group.[29] Lymphadenopathy and pleural effusions are extremely rare and should suggest consideration of alternative diagnoses.[17,30]

5.3 | Evolution of chest CT

As more cases of pediatric COVID-19 pneumonia have come to attention, a pattern of evolution of imaging findings has begun to surface.[23] In the early stage of the infection, a focal area of inflammation with a surrounding rim of ground-glass may be observed ("halo" sign) which likely relates to localized inflammation and surrounding vascular congestion. As the initially localized inflammation

begins to spread to adjacent alveoli, a pattern of more diffuse ground-glass is observed on CT related to evolving alveolitis. Once the infection becomes more established the involved alveoli become filled with fluid and inflammatory cells, which on CT appears as progression to more consolidative opacities.

6 | RECOMMENDATIONS FOR REQUESTING IMAGING STUDIES IN PEDIATRIC COVID-19

Given the limited data available in regard to the use imaging studies for evaluation of suspected or known COVID-19 pneumonia in pediatric patients, imaging recommendations are based on the ACR Appropriateness Criteria for pneumonia in immunocompetent children ≥3 months of age and for fever without source or unknown source for neonates.[34,35] In addition, the algorithm for requesting imaging studies in pediatric patients with suspected COVID-19 pneumonia is based on the recently published international expert consensus statement on chest imaging in pediatric COVID-19 patient management[23] (Table 1).

CXR and chest CT are currently the primary imaging studies used for evaluating pediatric COVID-19 pneumonia, which are discussed in the following paragraphs. Of note, utilization of chest ultrasound (US) as an imaging modality of choice for initial or follow-up evaluation in pediatric COVID-19 has not been evaluated in the current literature, and thus no specific recommendations are currently provided. However, in other forms of pediatric pneumonia, the main role of chest US is to evaluate the size and complexity of pleural effusions, which are a rare finding in pediatric COVID-19 pneumonia.[17,30,34]

6.1 | Chest radiography

Similar to other types of pediatric pneumonia, CXR is not indicated for most pediatric patients with known or suspected COVID-19 with mild clinical symptoms that do not require hospitalization; although CXR is usually indicated in neonates with fever and respiratory symptoms.[34,35] Importantly, CXR is the most appropriate first imaging test for children with mild clinical symptoms who have underlying risk factors for deterioration (ie, underlying chronic lung disease, congenital heart disease, malignancy, or immunocompromised state) or who develop acute worsening in symptoms. For pediatric patients with suspected or known COVID-19 infection with moderate-to-severe clinical symptoms requiring hospitalization (ie, hypoxia, moderate, or severe dyspnea, signs of sepsis, shock, cardiovascular compromise, altered mentation), CXR is usually indicated to establish an imaging baseline and to assess for an alternative diagnosis.[34]

Sequential CXRs may be helpful to assess pediatric patients with COVID-19 who demonstrate worsening clinical symptoms or to assess response to supportive therapy. However, routine daily chest radiographs for stable pediatric COVID-19 patients in the intensive care unit (ICU) are not recommended as they have not been shown to
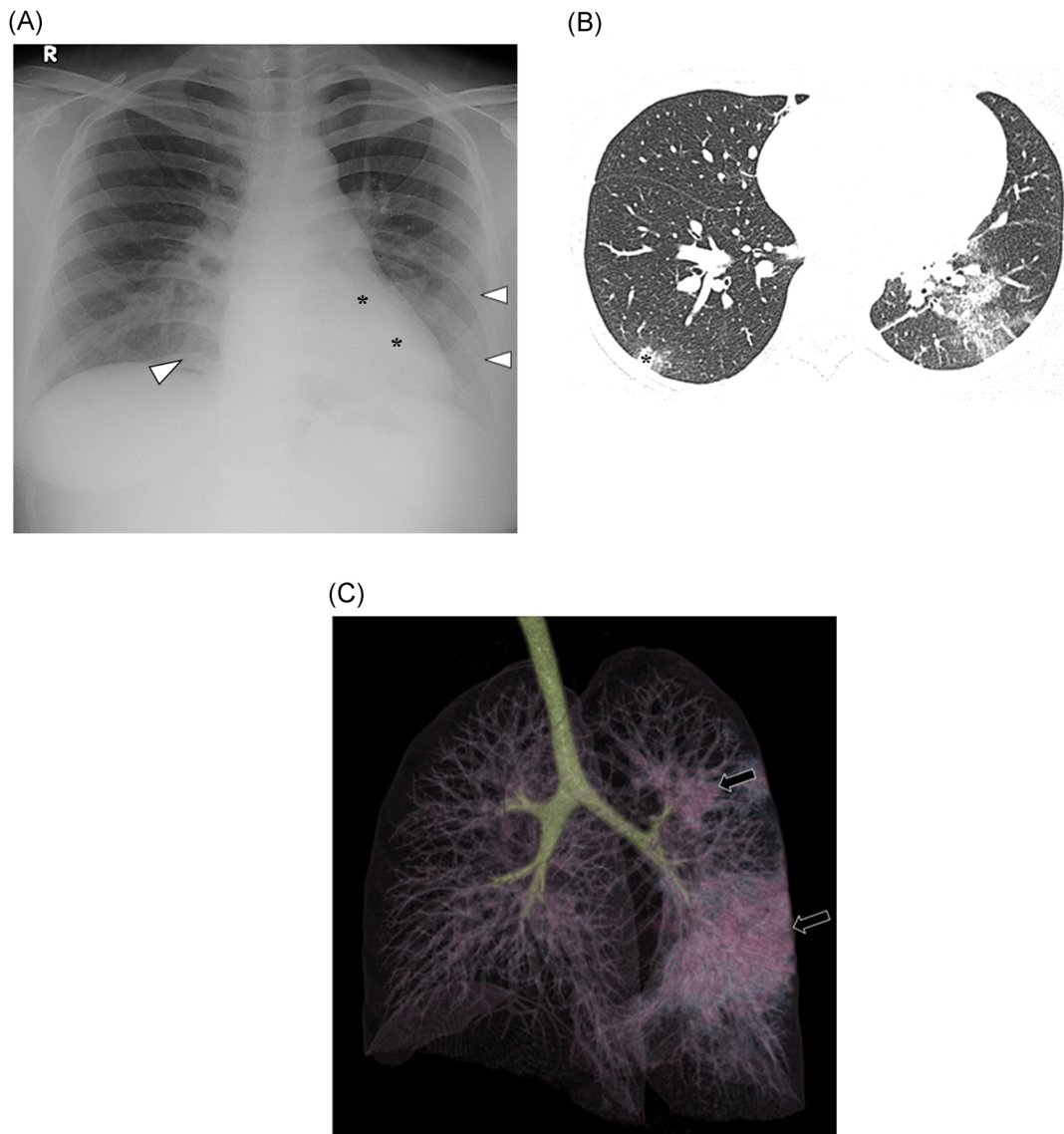
FIGURE 2 Fifteen-year-old female with traveling history in an endemic area in Europe and positive RT-PCR test for COVID-19 who presented with increasing cough and shortness of breath. A, Frontal chest radiograph shows ground-glass opacities (white arrowheads) in bilateral lower lung zones in addition to more confluent consolidation (black asterisks) in the left lower lobe, retrocardiac region. B, Axial lung window CT image shows bilateral peripheral predominant consolidation and ground-glass opacity in the lower lobes. Rounded subpleural consolidation with surrounding rim of ground-glass (black asterick) in keeping with the "halo" sign is visualized in the right lower lobe. C, 3D volume-rendered CT image shows air-space disease (black arrows) in the left upper and lower lung zones. The location and extent of the air-space disease are better visualized on this 3D volume-rendered CT image in comparison to chest radiograph (A). CT, computed tomography; RT-PCR, reverse transcription-polymerase chain reaction [Color figure can be viewed at wileyonlinelibrary.com]

impact adverse outcomes, pediatric ICU or hospital length of stay, or duration of ventilator requirements in pediatric ICU patients in general.[36]

6.2 | Chest CT

Due to the increased radiation sensitivity of pediatric patients, chest CT is not recommended as an initial diagnostic test for pediatric patients with known or suspected COVID-19 pneumonia.[37] However, there are clinical situations where chest CT may be appropriate. For example, a chest CT may be considered to address a specific clinical question in the pediatric patients presenting with acute symptoms (ie, hypoxia, dyspnea, tachycardia), worrisome abnormal laboratory findings (such as an elevated D-dimer), or to evaluate a patient demonstrating clinical deterioration or not responding as expected to supportive treatment.
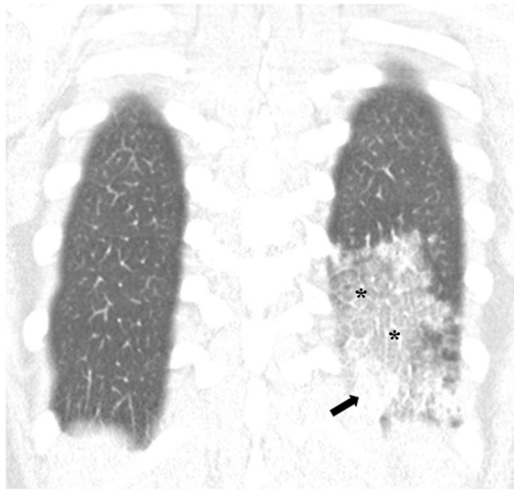
FIGURE 3 Sixteen-year-old female with COVID-19 who presented with shortness of breath. RT-PCR test confirmed the diagnosis of COVID-19. Coronal lung window CT image shows subpleural ground-glass opacity with intralobular septal thickening ("crazy paving"; black asterisks) and areas of consolidation (black arrow) in the posterior left lower lobe. RT-PCR, reverse transcription-polymerase chain reaction

7 | DIFFERENTIAL DIAGNOSTIC CONSIDERATIONS: DECIPHERING THE CONFUSION FOR PEDIATRIC PULMONOLOGISTS

Several pediatric lung disorders can have overlapping imaging findings with COVID-19 pneumonia and they can be primarily organized into four main categories including infectious etiologies, immune-related conditions, hematological dyscrasias, and inhalation-related lung injury. These are summarized in Table 2 and discussed in the following section. Of note, imaging findings from other coronavirus related pneumonias, such as severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS), can also overlap with those found in pediatric patients with COVID-19. Potentially helpful imaging features that may offer differentiation among different coronavirus-related pneumonias in the pediatric population, namely that both SARS and MERS tend to initially present as unilateral/unifocal consolidative or ground-glass opacities and MERS patients may present with pleural effusion and/or pneumothorax, were recently published and, therefore are not discussed in detail in this article.[38]

TABLE 1 Algorithm for ordering imaging studies in pediatric patients with suspected COVID-19 infection
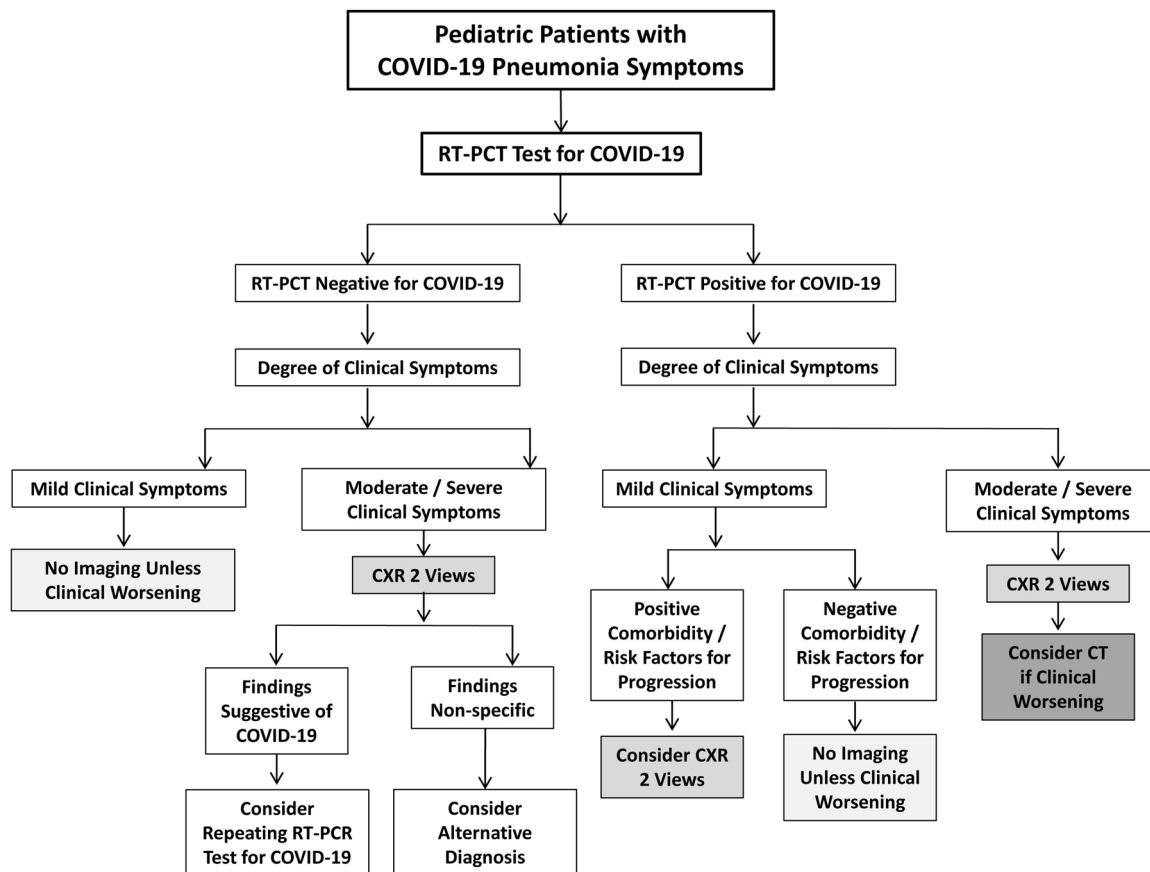
TABLE 2 Differential diagnostic considerations of imaging findings for pediatric COVID-19 infection

Underlying etiologies	Differential diagnostic considerations	Typical imaging findings	Key differentiating imaging findings from COVID-19 pneumonia
Infectious	Typical segmental or lobar bacterial pneumonia	* Focal airspace opacity restricted to single segment or lobe * Sometimes with air bronchogram(s) * Possible pleural effusion and/or LAD	* Involvement of single pulmonary segment or lobe * Pleural effusion and/or LAD
	Round pneumonia	* Solitary round opacity with well-defined borders * Sometimes with air bronchogram(s) * Often posterior in one of the lower lobes	* Solitary lesion with well-defined borders
	H1N1	* Hyperinflation with central peribronchial thickening (mild) * Bilateral symmetric consolidative and ground-glass opacities with central distribution * Possible centrilobular nodules * Possible pneumomediastinum	* Central distribution of lung parenchymal opacities * Centrilobular nodules (CT) * Pneumomediastinum
	Mycoplasma pneumonia	* Segmental or lobar consolidation * Parahilar peribronchial opacities * Focal reticulonodular opacities * Possible pleural effusion	* Segmental or lobar consolidation * Focal reticulonodular opacities * Pleural effusion
	Fungal infection	* Pulmonary nodules, consolidation, ground-glass opacity ± cavitation * "Halo" sign (early) * "Air crescent" sign (treatment response)	* Multiple pulmonary nodules without "halo" sign * "Air crescent" sign or cavitation
Immune-related	Hypersensitivity pneumonitis	*GGO and/or poorly defined centrilobular nodules (early) with possible air trapping in upper/mid lung distribution (CT) *Peribronchial septal thickening, honeycombing, bronchiectasis in upper/mid lungs (late) (CT)	* Peribronchovascular distribution in upper and/or mid lung zones * Centrilobular nodules (CT)
Hematological dyscrasias	Eosinophilic pneumonia	* Upper and/or mid lung zone predominant peripheral GGO and/or consolidation * Patchy or diffuse interstitial opacities * Possible "halo" sign * Possible pleural effusion	* Upper and/or mid lung zone distribution * Pleural effusion
Inhalation-related lung injury	EVALI	* Bilateral symmetric GGO and/or consolidation in lower lobes * Subpleural sparing * Possible "atoll" sign * Possible centrilobular nodules	* Subpleural sparing * Centrilobular nodules * "Atoll" sign

Abbreviations: CT, computed tomography; EVALI, E-cigarette vaping-associated lung injury; GGO, ground-glass opacity; H1N1, Swine-origin influenza A; LAD, lymphadenopathy.

7.1 | Infectious etiologies

7.1.1 | Typical segmental or lobar pneumonia

Pediatric patients presenting with typical segmental or lobar pneumonia, which is usually a community-acquired bacterial infection, have a somewhat nonspecific clinical presentation of high fever, malaise, and cough; although possible inspiratory chest pain or abdominal pain related to pleural irritation may be observed. The typical imaging appearance observed is a focal air space opacity restricted to a single segment or lobe of the lung with air bronchogram(s)[39] (Figure 4). The radiologic signs of volume loss (ie, elevation of the adjacent hemi-diaphragm, displacement of the pulmonary fissures, mediastinal shift) classically seen with atelectasis are generally absent. The most useful feature for distinguishing this entity from COVID-19 pneumonia is the involvement of a single pulmonary segment or lobe; however, the presence of pleural effusion or mediastinal/hilar lymphadenopathy (which may be seen with bacterial pneumonia but are rare in COVID-19 pneumonia) would also be helpful.

7.1.2 | Round pneumonia

Round pneumonia describes a specific type of childhood pneumonia, most frequently observed in children ≤8 years old due to immaturity of the pores of Kohn and channels of Lambert used for collateral gas exchange, that typically appears as a spherical or rounded opacity on CXR.[40] The clinical presentation of pediatric round pneumonia is nonspecific, with fever and cough as the most common symptoms. On imaging, round pneumonia appears as a solitary round opacity with well-defined borders most frequently observed posteriorly in one of the lower lobes of the lung, although can occur elsewhere in the lungs[40] (Figure 5). The most useful features for distinguishing this entity from pediatric COVID-19 pneumonia are a solitary lesion (COVID-19 tends to be bilateral and multifocal) and well-defined margins. Opacities seen in pediatric COVID-19 pneumonia often have less well-defined borders.

7.1.3 | Swine origin influenza A

Swine origin influenza A (H1N1) was responsible for a pandemic of viral respiratory illness in 2009 and subsequently joined other influenza viruses that continue to circulate with occasional sporadic outbreaks.[41] The most common clinical symptoms include fever and cough, although additional symptoms including rhinorrhea, sore throat, headache, chest pain, vomiting, abdominal, pain, diarrhea, and dyspnea have been reported with less frequency.[42] The majority of pediatric patients have a mild clinical course and demonstrate no abnormality on CXR.[42,43] In mild cases with radiographic abnormality, the most common findings are bilateral symmetric prominent peribronchial markings and hyperinflation.[42] Pediatric patients with more severe disease requiring hospitalization most frequently demonstrate one or more consolidative and/or ground-glass opacities in a bilateral symmetric pattern[42] (Figure 6). On chest CT, a bilateral central distribution of consolidation and ground-glass opacities with associated bronchovascular thickening is typical and centrilobular nodules may be present.[43,44] Interestingly, pneumomediastinum has been observed in a few cases, possibly related to alveolar rupture

FIGURE 4 Seven-year-old male who presented with fever, cough, and elevated white blood cell count. Frontal chest radiograph shows a focal air space opacity (black arrow) in the left lower lobe. Sputum culture confirmed the diagnosis of a community-acquired bacterial infection
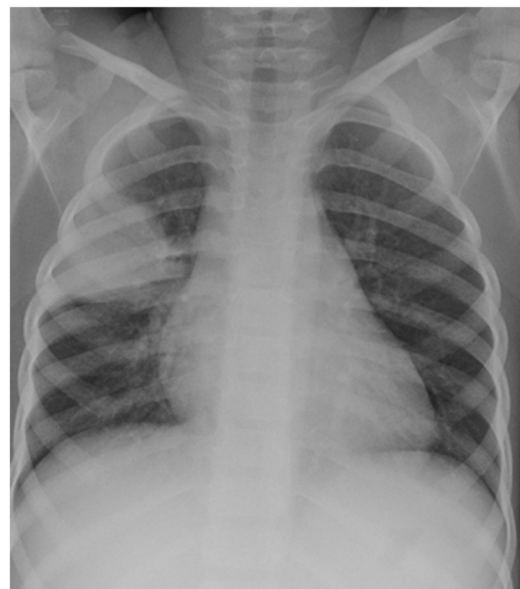

FIGURE 5 Three-year-old male who presented with fever, cough, and right-sided chest pain. Frontal chest radiograph shows a solitary round opacity with well-defined borders in the right upper lung zone, compatible with a round pneumonia. Sputum culture later confirmed the diagnosis of *Streptococcus pneumoniae* infection

FIGURE 6 Five-year-old male with H1N1 infection who presented with fever, cough, and rhinorrhea. Frontal chest radiograph shows bilateral, multifocal, central distribution of foci of consolidation and associated areas of ground-glass opacity
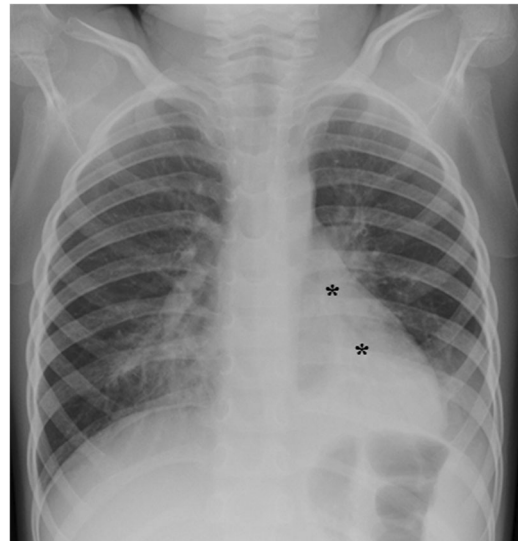

FIGURE 7 Five-year-old male with mycoplasma pneumonia who presented with fever, cough, myalgia, and headache. Frontal chest radiograph shows consolidation in the left lower lobe (black asterisks) with parahilar peribronchial opacity

from hyperinflation or bronchial injury from forceful coughing.[43-45] The most useful imaging features to differentiate H1N1 related pneumonia from COVID-19 are a central distribution of lung parenchymal opacities, the presence of centrilobular nodules on CT, or pneumomediastinum.[38] However, in the absence of these characteristic imaging findings, differentiating these two entities may be difficult.

7.1.4 | Mycoplasma pneumonia

Mycoplasma pneumonia is an atypical bacterial pneumonia that is a frequent cause of community-acquired pneumonia (CAP) in pediatric patients. The causative organism, Mycoplasma pneumonia, lacks a cell wall and thus does not respond to typical antibiotic coverage. As a result, this diagnosis may be suspected clinically in pediatric patients with persistent symptoms despite antibiotic therapy.[46] The remaining common clinical symptoms, including low-grade fever, dry cough, and myalgia, overlap significantly with many forms of viral pneumonias. The imaging appearance of pediatric mycobacterial pneumonia can have a somewhat variable appearance. The most commonly observed patterns include lobar or segmental consolidation (may overlap with appearance of typical bacterial pneumonia), parahilar peribronchial opacity (similar to other pediatric viral pneumonias), and focal reticulonodular opacities[46,47] (Figure 7). Age may impact the imaging appearance observed as a large study with 393 pediatric patients hospitalized with mycoplasma pneumonia found the parahilar peribronchial opacity pattern was most frequent in children younger than 2 years of age and the lobar consolidation pattern was most frequent in kids aged 5 years or older.[47] In the same study, a segmental or lobar consolidation pattern also

corresponded to a longer duration of symptoms, higher rate of extra-pulmonary manifestations, longer length of hospitalization, and duration of antibiotics.[47] Pleural effusion may be observed in up to 20% to 35% of cases.[46,47] The most useful features for differentiating mycoplasma pneumonia from COVID-19 pneumonia are the presence of a segmental or lobar consolidation, focal reticulonodular opacities, or presence of pleural effusion. However, due to the variable imaging appearance of mycoplasma pneumonia, imaging overlap with COVID-19 may occur.

7.1.5 | Fungal infection (angioinvasive aspergillosis)

In the immunocompromised pediatric patient (eg, pediatric patients with primary immunodeficiency syndromes, receiving chemotherapy, or post-allogenic bone marrow transplant), invasive fungal disease, such as angioinvasive aspergillosis, is an important differential diagnostic consideration for pediatric patients with suspected COVID-19 infection. The clinical presentation, which may include fever, cough, chest pain, hemoptysis, and/or pneumothorax, is nonspecific and may have considerable overlap with that of COVID-19 pneumonia.[48] Chest radiographs of angioinvasive aspergillosis are somewhat insensitive, but may demonstrate single or multiple pulmonary nodules, consolidation, ground-glass opacities and cavitation. Chest CT during the early phase of infection may show the "halo" sign, caused by a central area of pulmonary necrosis surrounded by a rim of blood products (Figure 8). Such "halo" sign is now known to be also present during early phase of pediatric COVID-19 pneumonia.[17,23,38] Following initiation of antifungal therapy, the imaging appearance may evolve to an "air crescent" sign or central region of cavitation, as the necrotic lung tissue retracts from viable parenchyma, which

FIGURE 8 Six-year-old female with leukemia who presented with fever and cough. The patient was later found to have angioinvasive aspergillosis. Axial lung window CT image shows ground-glass opacity surrounding a round consolidation (black arrow), known as "halo" sign. CT, computed tomography

FIGURE 9 Eleven-year-old female who presented with fever, dry cough, and malaise. The patient was later diagnosed with acute hypersensitive pneumonitis due to the exposure to damp, moldy farmhouse. Axial lung window CT image shows bilateral diffuse upper lung zone ground-glass opacities. CT, computed tomography

is indicative of a treatment response in the setting of fungal infection in immunocompromised pediatric patients.[48,49] The most useful imaging features for distinguishing angioinvasive aspergillosis from COVID-19 pneumonia are the presence of multiple pulmonary nodules without the "halo" sign, the "air crescent" sign, or observation of cavitation. However, when the "halo" sign is present or more ground-glass or consolidative opacities are observed, differentiating these entities on imaging is difficult.

7.2 | Immune-related etiology

7.2.1 | Hypersensitivity pneumonitis

Hypersensitivity pneumonitis (HP) is a form of interstitial lung disease which occurs in a small subset of patients who develop an immune-mediated reaction following inhalational exposure to various organic antigens. Affected pediatric patients may present acutely with non-specific viral-like symptoms (fever, dry cough, malaise) or with a more gradual progressive onset of exercise intolerance, cough, weight loss, and fever.[50] The imaging findings observed in hypersensitivity pneumonitis depend on when in the disease course the patient is evaluated. CXR is less sensitive than CT for the detection of HP. On chest CT, acute HP presents with bilateral upper lung predominant ground-glass opacities and/or poorly defined centrilobular nodules[50,51] (Figure 9). Such ground-glass opacities are one of the most frequently observed imaging findings in pediatric patients with COVID-19 pneumonia and can be an overlapping imaging finding with acute HP.[16-18,30,31] Areas of lobular air-trapping may also be observed in the sub-acute form.[51] In chronic HP, chest CT may show changes of developing fibrosis including septal thickening, honeycombing, and traction bronchiectasis, typically with a peribronchovascular distribution in the upper and mid lungs.[50,51] The most useful features for differentiating acute-to-subacute HP from COVID-19 are the distribution of ground-glass opacities that are upper lung zone predominant with relative sparing of the lung bases and, if present, centrilobular nodules.

7.3 | Hematological dyscrasia

7.3.1 | Eosinophilic pneumonias

The term eosinophilic pneumonia is used to describe a group of diffuse pulmonary parenchymal lung diseases, which may be primary (idiopathic) or secondary (related to parasitic or fungal infections or medications), characterized by eosinophil induced damage to both alveolar air spaces and pulmonary interstitium.[52,53] Depending on the underlying etiology, affected pediatric patients may present acutely with cough, hypoxia, and fever, or have a more chronic presentation with insidious onset of pulmonary symtpoms.[52] There is some imaging overlap in the CXR manifestations of some forms of eosinophilic pneumonia which may present as single or multifocal peripheral non-segmental consolidative opacities or increased reticular markings, often in the upper and mid lung zones.[52] Pleural effusions may also be present. The CT findings observed depend on the underlying cause of eosinophilic pneumonia, but in many forms upper and mid lung predominant peripheral ground-glass or consolidative opacities, possibly with a "halo" sign, maybe observed[47] (Figure 10). Pediatric patients may have less pronounced imaging findings compared to adults as one small study found the aforementioned typical findings in 2/5 (40%) of patients, while 3/5 (60%) only demonstrated patchy or diffuse interstitial opacities.[53] The most useful features to differentiate eosinophilic pneumonia from COVID-19 related infection are an upper and mid lung distribution of parenchymal abnormality and/or the presence of a pleural effusion.

7.4 | Inhalational-related lung injury

7.4.1 | E-cigarette or vaping-associated lung injury

E-cigarette or vaping-associated lung injury (EVALI) is a relatively new clinical entity that describes a pattern of lung injury associated
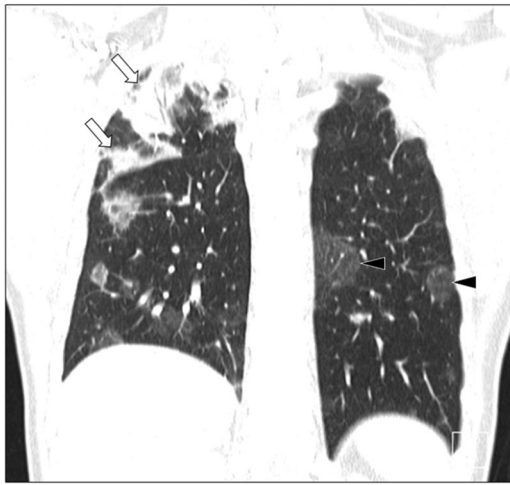
FIGURE 10 Eighteen-year-old female who presented with dry cough and hypoxia from acute eosinophilic pneumonia. Coronal lung window CT image shows multifocal non-segmental ground-glass (arrowheads) and consolidative (arrows) opacities predominately located in the peripheral upper and mid lung zones. CT, computed tomography

with the use of electronic cigarettes or vaping products in adolescents and young adults. Clinically, affected pediatric patients typically present with respiratory symptoms (cough, chest pain, dyspnea on exertion), gastrointestinal complaints (nausea, vomiting, diarrhea, and/or abdominal pain), and constitutional symptoms (fatigue, fever, weight loss).[54] The most frequent pattern of imaging abnormality is bilateral symmetric ground-glass opacities and/or consolidation in a lower-lobe distribution with relative subpleural sparing.[54,55] Centrilobular nodules and the "atoll" sign (central ground-glass opacity with a rim of consolidation) have been observed on CT in some pediatric patients.[54,55] (Figure 11) The most helpful imaging features to help differentiate EVALI from COVID-19 are subpleural sparing of lung opacities, centrilobular nodules, and/or the "atoll" sign, although some imaging overlap does occur between these entities.[38]

8 | FUTURE DIRECTIONS

A clear understanding of the clinical implications of imaging abnormalities is important for pediatric patients with known or suspected COVID-19 pneumonia. In the future, studies evaluating the correlation between specific imaging findings, clinical severity, and disease outcomes (ie, improvement, progression, mortality) will help improve management of these pediatric patients. Furthermore, as no long-term data is yet available, future studies investigating post-recovery sequelae of disease including alterations of pulmonary function tests and risk for development of permanent lung injury such as pulmonary fibrosis will be important.
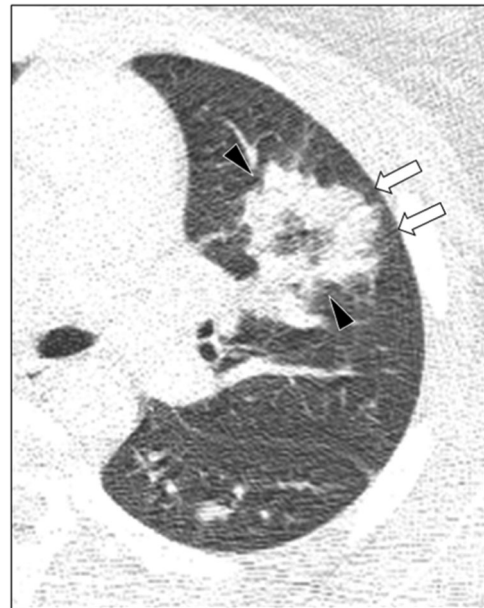

FIGURE 11 Seventeen-year-old male with a history of electronic cigarette product use with nicotine and tetrahydrocannabinol who presented with respiratory distress. Axial lung window CT image shows a central ground-glass opacity surrounded by a denser complete ring of consolidation, also known as the "atoll" sign (arrowheads). Subpleural sparing (arrows) is also seen. CT, computed tomography

9 | CONCLUSION

As our understanding of COVID-19 continues to evolve, the amount of new information appearing in the literature can be daunting to practicing clinicians. This paper provides a summary of presently known clinical and imaging characteristics observed in pediatric COVID-19 patients, offers practical guidance for requesting imaging studies to evaluate these pediatric patients, and discusses useful differential diagnostic considerations.

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