Radiology of COVID-19 in Children

Çocuklarda COVID-19 Radyolojisi

Gulsah BAYRAM ILIKAN[1], Mehmet GUMUS[2]

[1]Deparment of Radiology, Ankara City Hospital, Ankara, Turkey
[2]Deparment of Radiology, University of Ankara Yıldırım Beyazıt, Ankara, Turkey

ABSTRACT

The coronavirus disease 2019 (COVID-19), which has been accepted as a pandemic since March 2020, has caused millions of patients and hundreds of thousands of deaths all over the world. The diagnosis of which is important due to its high contagiousness, there are many publications evaluating the radiological approach of this disease in adults, however there are very few reports of pediatric patients worldwide. The aim of this study is to evaluate the radiological approach in pediatric COVID-19 patients by literature review and to guide diagnosis and treatment follow-up with radiological findings.

Key Words: Computerized tomography, COVID-19, Pediatrics, Radiology, X-ray

ÖZ

Mart 2020'den itibaren pandemi olarak kabul edilmiş olan Koronavirüs Hastalığı-2019 (COVID-19) tüm dünyada milyonlarca hastaya, yüzbinlerce ölüme neden olmuştur. Yüksek bulaştırıcılığı nedeniyle tanısının önem kazandığı bu hastalığın erişkin hastalardaki radyolojik yaklaşımını değerlendiren birçok yayın yapılmıştır. Ancak tüm dünyada çocuk hastalara ait bildirimler oldukça azdır. Çocuk COVID-19 hastalarında radyolojik yaklaşımın literatür taraması ile değerlendirilmesi, radyolojik bulgular eşliğinde tanıya ve tedavi takibine yol gösterici olması amaçlanmıştır.

Anahtar Kelimeler: Bilgisayarlı tomografi, COVID-19, Çocuk, Radyoloji, Direk grafi

INTRODUCTION

The coronavirus disease 2019 (COVID-19) spread rapidly worldwide starting from China in December 2019 and was declared a pandemic by World Health Organization on 11 March 2020 (1). This single-stranded RNA virus is known to primarily attach to the upper respiratory tract, causing pneumonia. Due to its high and easy contagiousness, its differential diagnosis becomes important especially in this season, when all other viral upper respiratory tract infections increase (2,3).

Even though it is seen as pleasing that the rate of infection of pediatric patients at first was quite low, it is observed that as the number of cases infected by the virus increases, the number of pediatric patients increases. Although the clinics of pediatric patients are milder than adults, they are effective in the spread of the disease. They usually snatch the virus from their families, however the duration of virus spread with their gaita is longer than their family members, therefore they remain infectious for a long time (4). In addition, it is known that, with delayed diagnosis and treatment, the disease can progress and develop lung damage (5). For these reasons, the diagnosis of the disease has become more important in this age group.

Currently, the definitive diagnostic method is the molecular representation of the virus in the body. The definite widely accepted diagnostic method is to show the virus with Reverse Transcription-Polymerase Chain Reaction (RT-PCR) in the

BAYRAM ILIKAN G : 0000-0001-5833-022X
GUMUS M : 0000-0003-1240-8284

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Correspondence Address / Yazışma Adresi:

Gulsah BAYRAM ILIKAN
Deparment of Radiology, Ankara City Hospital, Ankara, Turkey
E-posta: gulsahbayram@hotmail.com

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sample taken with nasal – oropharyngeal swab (6). However, the specificity of this viral nucleic acid test is high and its sensitivity is low (7). Radiological imaging methods come to the fore in cases where the PCR test is unavailable or if the test is a false negativity (3). In addition, the need for imaging methods has increased in the follow-up.

Chest X-ray (CXR) is accepted as the first step imaging method in many upper or lower respiratory tract diseases worldwide. However, it has been reported in many publications that its diagnostic value is quite low in COVID-19 pneumonia (8). It becomes important in the clinical follow-up of diagnosed cases, especially in the group of patients with acute respiratory distress syndrome (ARDS), who need intensive care.

In this pandemic process, thorax computerized tomography (CT) examination is accepted as the most popular radiological examination in showing pneumonic infiltration. Although it is not easy to access all over the world, CT guides the definition of COVID-19 suspicious cases, by showing the infiltration even before the PCR test is concluded. Therefore, early isolation of these patients can contribute to reducing the transmission rate (8).

Case or serial reports of pediatric patients are very low compared to adults. The purpose of this literature review is to evaluate the radiological approach in pediatric patients, to contribute to the diagnosis process in the presence of radiological imaging findings, to evaluate the place of radiology in follow-up during treatment.

IMAGING RECOMMENDATIONS

Many factors should be considered before deciding on imaging methods in COVID-19. First, the radiology department faces the risk of transmission due to the high contagiousness of the disease. Secondly, the examination and the environmental cleaning after the examination requires cost. The third is the radiation which the patient will be exposed (9,10). Radiation becomes more important especially in the child age group.

The clinic of the patient is the most important factor to be taken into consideration in the choice of radiological examination. Thorax radiological imaging findings of COVID-19 disease are similar to many other viral pneumonias and inflammatory diseases (2). Therefore, there should be high clinical suspicion and supported with radiological findings.

CT is not recommended as the first diagnostic examination for pediatric patients. Pediatrics whose clinic is mild, for example, whose symptoms are only fever or coug, should be tested first with PCR. If the test is positive, CT can be performed in case of deterioration in the clinic or inadequate clinical recovery or for differential diagnosis in the presence of underlying diseases such as malignancy, immunodeficiency, diabetes mellitus, heart disease. In children with moderate or severe clinic, the first diagnostic test should be PCR, but CXR must be performed. CT can be used in clinical follow-up to show the degree of pulmonary involvement. It can be use to make other differential diagnoses in the case of PCR negativity or if the disease suspicion continues on CT images, leads to test repetition (11). However, considering the harmful effects of radiation, it is more convinient to prefer CXR in follow-up imaging rather than CT (12).

CHEST RADIOGRAPHY

In a few studies comparing CXR with CT in adults, it is stated that the sensitivity of CT, which is around 90%, is around 30-40% in CXR. It was emphasized that CXR was more effective in the follow-up of the progression than the diagnosis of the disease (13,14). In a series of few patients in pediatrics, CXR has been reported to detect findings in 40% of patients, which is similar to adults (11,15,16).

Whether PCR test result is negative or positive, the normal CXR does not prove that there is no lung involvement. The finding that may indicate COVID-19 in CXR is bilateral, peripheral radiopacity, especially located in the lower lobes (Figure 1). Unilateral, multifocal, lobar, centrally located or diffuse opacities, peribronchial thickening, plevral effusion can be observed as atypical findings (11) (Figure 2). Since these findings can be observed in many other viral or atypical pneumonia, detailed evaluation with CT is required.

COMPUTERIZED TOMOGRAPHY

The most common CT finding in adult patients is bilaterally, peripheral and subpleural, multifocal ground glass opacity (GGO), especially located in the lower lobes. This may or may not accompany consolidation. While centrilobular distribution, pleural effusion and lymphadenopathy are more common in other pneumonias; air bronchogram, reversed halo sign and excessive lobe involvement should suggest COVID-19 (2). As the disease progresses, it has been shown that GGO intensifies, multiple consolidations, fibrotic bands can develop, pleural thickening or bronchiectasis may occur. In the most advanced state, infiltration covers the entire parenchyma and “white lung” may occur. When ARDS develops, it has been shown that patients need for intensive care unit (ICU) and this is the highest cause of mortality (17). Regression of parenchymal involvement observed as signs of healing begins to appear approximately 2 weeks after the onset of the disease.

CT Findings in Pediatrics

Table I: CT differences between adults and pediatrics.

	Adults	Pediatrics
CT findings	more severe	milder
Positive CT	more	less
Numbers of involved lobes	more	less
Ground-glass opacity	wider	focal
Bronchial wall thickening	less	more
Peribronchial distribution	less	more

CT: *Computerized tomography.*

Table II: CT imaging findings of PCR (+) pediatric patients.

	Numberof patients	Normal	Unilateral involvement	Bilateral involvement	CT findings
Lu X et al. (24)*	138	27			• GGO (56/138) • Local patchy shadowing (32 /138) • Bilateral patchy shadowing (21/138) • Interstitial abnormalities (2/138)
Ma YL et al. (25)	115	27			• GGO + consolidation (47/115) • white lung (2/115) • Increased bronchovascular shadows (39/115)
Qiu H et al. (23)	36	17			• GGO (19/36)
Wang XF et al. (26)	34		-	34	• multiple patchy or nodular GGO and/or infiltrating shadows (34/34)
Wang D et al. (27)	31	17			• patchy GGO and nodules, (9/31) • GGO +consolidation (1/31) • Increased bronchovascular shadows (2/31)
Zheng F et al. (28)	24	8	5	11	• bilateral patchy shadows or lung consolidations (24/24)
Xia W et al. (21)	20	4	6	10	• Consolidation with surrounding halo sign (10/20) • GGO (12/20) • fine mesh shadow (4/20) • tiny nodules (3/20) • Subpleural lesions with localized inflammatory infiltration (20/20)
Feng K et al.(29)	15	6			• small nodular GGO (7/15) • speckled GGO (2/15)
Chen A et al. (20)	14	7	3	4	• GGO (3/7) • GGO with consolidation (1/7) • Nodules (1/7) • Bronchial wall thickening (2/7)
Zhong Z. (30)	9	4			• GGO or spot-like mixed consolidation (5/9)
Zhou Y. (31)	9	1			• GGO (1/9) • GGO + consolidation (6/9) • Consolidation (1/9)
Sun D et al. (5)	8		2	6	• multiple patch-like shadows (7/8) • GGO (6/8) • pleural effusion (1/8) • 'white lung-like' change (1/8)
Hu Z et al. (32)	7	7			
Li W et al. (19)	5	2	3	-	• Patchy GGO (3/5)
Liu W. (8)	5	1	-	4	• Patchy GGO (1/5) • Patchy shadows (3/5)
Liu M et al .(33)	5	1	3	1	• Unilat GGO and/ or consolidation (3/5) • bilat GGO (1/5)
Liu H et al. (22)	4	1	2	1	• GGO (1/4) • consolidation (2/4) • air broncogram (1/4) • pleural effusion (1/4)
Lou XX et al. (34)	3				• GGO (1/3) • GGO+consolidation (1/3) • Consolidation (1/3)
Zhang T et al. (35)	3	1			• GGO (2/3)
Rahimzadeh G et al. .(36)†	3	1	-	2	• GGO with consolidation 2/3

Li Y et al (7)	2		-	2	• tiny nodules (1/2) • ncreased and slightly disordered bronchovascular bundles (1/2)
Park JY et al. (37)	1		1	-	• GGO + consolidation (1/1)
Tang A et al. (38)	1	1			
Lin J et al. (39)	1	1			
Pan X et al. (40)	1	1			
Yin X et al. (41)	1		1	-	• Cord shadow (1/1)
Other Case reports (6) ‡	17	4			• GGO (4/17) • GGO + consolidation (6/17) • consolidation (1/17) • Increased bronchovascular shadows, scattered small strip-like opacities (2/17)
Total	512	139	26	75	

CT: *Computerized tomography,* ***GGO:*** *Ground-glass opacity,* ******* *Since 33 of 171 patients in the series had no CT findings, 138 CTs were evaluated*
† Since 3 of 9 patients in the series had positive PCR result, 3 CTs were evaluated, ‡ taken from Duan et al. (12, 42-52)

While CT findings are found in 86% of adult patients, this rate has been reported to be 63% in a limited number of pediatric patients (18). COVID-19 has a wide range of non-specific findings in children. The findings are milder than adults, and typical CT findings are less common in children compared to adults (Table I) (16). The most common finding is focal GGO, which is observed in the peripheral and posterior lobes (6, 19) (Figure 3). Compared to adults, GGO is more focal and tends to hold few lobes. It was stated that peribronchial spreading and bronchial wall thickness were observed more in children. Consolidation or interlobular septal thickening can be visualized, although not common (Figure 4.). However, it should not be forgotten that this appearance is also observed in many other atypical pneumonia (20). It can be said that differential diagnosis is difficult in children, it is even more difficult, especially in children with the underlying disease. For example, many other factors such as mycoplasma, RSV, H1N1 can be detected in the immunsupressed malignant patients. It should also be noted that CT findings can also be quite complicated in the presence of coinfection. Clinic and presence of contact history will be the main guide in differential diagnosis (21, 22). For example, while children are more symptomatic in H1N1 and SARS infections, they are more likely to be asymptomatic in COVID-19 (23). The presence of pleural-based distribution, pleural effusion, and lymphadenopathy should suggest other causative viral or atypical pneumonias (11) (Figure 5).

In Table II, we summarized the CT findings of PCR positive COVID-19 cases under the age of 18, which have been reported so far in the literature (5-8,12,19-52). Accordingly, 139 (27%) of 512 CTs were normal, while 373 (73%) had findings. No information was given about unilateral or bilateral findings in 411. In the remaining 101 CT, 26 (26%) of the findings were unilateral, while 75 (74%) were bilateral. While GGO was the most common CT finding (34%), consolidation alone (27%) or consolidation with GGO (18%) were other frequently observed findings. It was observed that pleural effusion, fibrous bands, and reticular pattern were not frequent, but also “white lung” was observed in several patients with severe condition. However, the terminologies used to describe CT findings are not standard. For example, “patchy shadows” was probably used to describe consolidation. The definition of GGO and / or consolidation is not clear enough, so it is not known how many patients have consolidation. Therefore, the rates we give for CT findings should be approximated.

“Halo sign”, followed by Xia et al. (21) in 50 % of patients, is a focal consolidation area with a lower density, accompanied by peripheral GGO. Although it was emphasized that it can be evaluated as a typical finding in pediatric patients, it is not a defined finding in many other CTs in the literature.

In a study in which the CT findings were evaluated by different age groups, bilateral lung involvement was most frequently observed in children under 3 years of age, and unilateral involvement and normal CT findings were higher in children over 6 years of age. Since the immune systems may not be fully mature yet, it has been emphasized that special attention should be paid to children under 3 years old (28).

Although it is not recommended to perform patient follow-up with CT in clinically mild patients, many pediatric patients with nonspecific clinical findings require CT examinations and repetitive PCR tests (29). It was observed that as the disease progressed, GGOs intensified, consolidations were developed at a higher rate, parenchymal involvement became widespread, followed in more lobes, fibrosis, bronchiectasis, air bronchogram, interlobular septal thickening could develop. It was observed that plavral effusion or pleural thickening may be accompanied by “white lung”, which is defined as the most advanced ARDS finding (5) (Figure 6). As expected during the recovery period, the density and number of lesions and the rate of involvement decrease or disappear. Fibrotic bands can remain. (21).

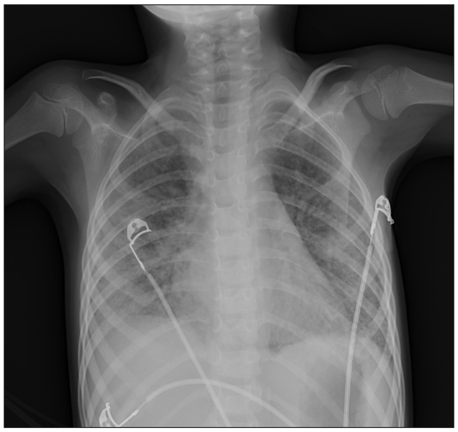

Figure 1: 8 years old, PCR (+) male patient, diffuse radioopacity in both lungs, especially in the lower lobes.

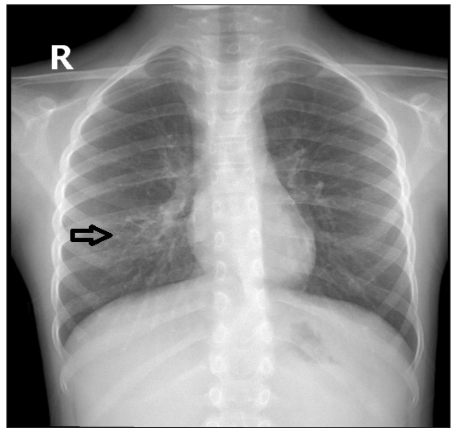

Figure 2: 7 years old, PCR (+) female patient, scattered radioopacity, peribronchial thickening in the right lung lower lobe (open arrow).

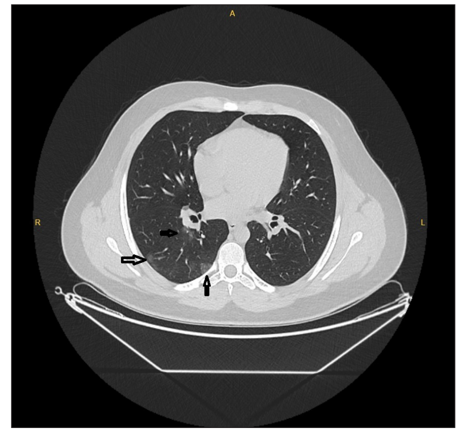

Figure 3: 17 years old, PCR (+) male patient, scattered, focal, peripheral ground glass densities in the right lung lower lobe(arrows).

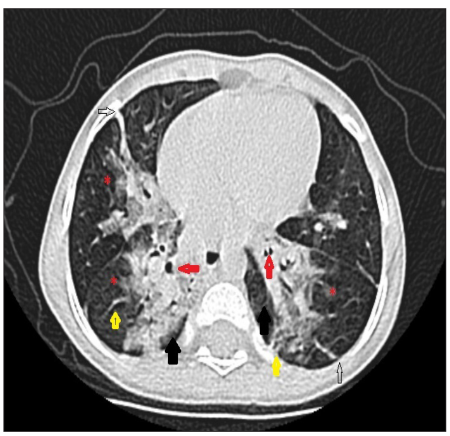

Figure 4: 2 years old, PCR (+) female patient, widespread consolidation (black arrows), air bronchogram (red arrows), ground glass opacity (red stars), interseptal thickening (yellow arrows), fibrotic bands (arrows), mainly observed in the lower lobes in both lungs.

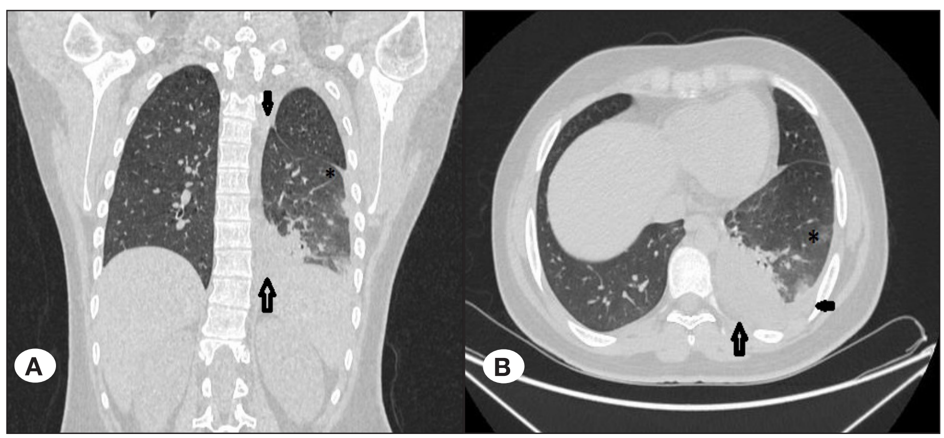

Figure 5: In the coronal **(A)** and axial **(B)** image, pleural-based consolidation in the left lower lobe(arrows), accompanying ground glass opacity (stars) and pleural effusion (little arrows) (3 times COVID-19 PCR test were (-), RSV pneumonia detected).

Figure 6: 7 years old, PCR (+) male patient, 'white lung', perimediastinal pneumotorax and pleural fibrotic bands (arrows).

Figure 7: 13 years old, 3 times PCR (-) female patient, consolidation (arrow), ground glass opacities (star), tree-in bud (little arrow) in the upper left lobe.

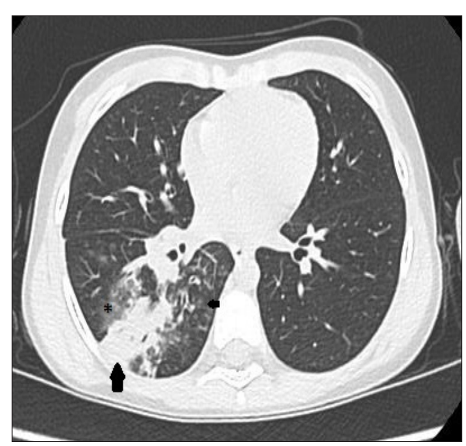

Figure 8: 7 years old, PCR (+) female patient, consolidation (arrow), ground glass opacities (star), tree-in bud (little arrow) in the lower right lobe.

Correlation Between CT and PCR Test

There is no study comparing CT findings with PCR test in pediatric patients yet. In studies comparing the PCR test and CT findings in adult patients, the results of both were generally shown to be compatible with each other (17). However, typical CT findings can be observed in asymptomatic patients with positive PCR test. It is also known that there are patients with typical CT findings, while the PCR test was initially negative,next PCR test may become positive or remain negative (44,53). There were PCR positive patients with normal baseline CT findings, and those with improved infiltration in control CT examinations were also reported. CT findings are mostly observed approximately 10 days after the onset of the disease (54,55). So it is important when CT is applied. Considering the study that reported the sensitivity of the PCR test was 71 % and the sensitivity of CT was 98 %, the value of CT increases especially in the presence of clinical suspicion and contact history (56). Even if the PCR test is negative, it is recommended to repeat the test in the presence of high clinical suspicion and typical CT findings, and the final diagnosis should be made by PCR test result (17) (Figure 7,8).

CONCLUSION

It is very pleasing that the number of children COVID-19 patients are lower than the adults and the clinic is better. Since they are more likely to have the disease asymptomatically, they play an important role especially in the spread of the disease (57,58). Therefore, their diagnosis should be made as soon as possible. Molecular diagnostic methods should be the first step in diagnosis. CXR should be the first choice in patients with mild clinical status. CT should be preferred in the severe clinic. However, CT findings are similar to many other pneumonias. The clinical findings and contact history of the pediatric patient are the two most important factors to be considered before deciding on a radiological examination.

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