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Original Article

Clinical characteristics of immunocompetent children with cytomegalovirus pneumonia: A single-center retrospective cohort study

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ABSTRACT

Objective: Cytomegalovirus (CMV) pneumonia in immunocompetent children remains underrecognized, and standardized diagnostic criteria are lacking. We aimed to describe the clinical characteristics of immunocompetent children with CMV pneumonia and to evaluate the relationship between bronchoalveolar lavage (BAL) fluid and serum CMV DNA loads and laboratory results.

Materials and Methods: In this retrospective cohort study, medical records of 62 immunocompetent children who underwent flexible bronchoscopy for recurrent pneumonia or persistent wheezing between November 2023 and January 2025 were reviewed. CMV pneumonia was defined by detection of CMV DNA in BAL using real-time polymerase chain reaction (PCR). Quantitative CMV DNA load in BAL and serum were expressed as international units per milliliter (IU/mL). Demographic, clinical, laboratory, and radiological findings were recorded. Correlations between CMV DNA load in BAL and serum and blood indices were analyzed.

Results: Twenty patients (32.2%) were diagnosed with CMV pneumonia. The median age was six years (1.5-9.7), and 55% were male. The most common presenting symptom was chronic cough (85%). Patchy consolidation was the most frequent radiographic finding (45%), while chest computed tomography most commonly demonstrated consolidation (55%), often with bilateral (70%) and multilobar involvement (70%). Serum CMV PCR was positive in six patients (30%). No significant correlation was observed between BAL CMV DNA load (median; 2650 IU/mL; IQR; 311-16874) and serum CMV DNA load (median; 700 IU/mL; IQR; 443-2650) ($p > 0.963$). BAL CMV DNA load showed a strong positive correlation with serum monocyte count ($r = 0.861$, $p<0.001$) and mean platelet volume (MPV) ($r = 0.759$, $p < 0.001$). Eleven patients (55%) received intravenous ganciclovir at 5 mg/kg/per dose twice daily for 21 days, and demonstrated clinical and radiological improvement without documented significant adverse effects.

Conclusion: BAL CMV PCR demonstrated a higher detection rate than serum CMV PCR in immunocompetent children with recurrent pneumonia or persistent wheezing. Elevated monocyte count and MPV may reflect CMV-related pulmonary inflammation.

Keywords: Bronchoscopy, bronchoalveolar lavage, children, cytomegalovirus, pneumonia

Introduction

Cytomegalovirus (CMV) is a ubiquitous β-herpesvirus that infects a large proportion of the global population (1,2). In immunocompromised individuals, CMV is well recognized as a cause of severe pulmonary disease (3). However, the clinical significance of CMV pneumonia in immunocompetent children remains poorly understood (4). In children presenting with recurrent pneumonia, persistent wheezing, or unexplained radiological abnormalities, the differential diagnosis is often broad and includes infectious, inflammatory, and structural lung diseases. Increasing evidence suggests that CMV pneumonia may be an underrecognized contributor to such cases, and it is essential for clinicians to remain vigilant and include it in the differential diagnosis (5–7). The current literature underscores the lack of standardized diagnostic and therapeutic protocols for CMV pneumonia in otherwise

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healthy pediatric populations, and randomized controlled trials are lacking to guide clinical practice (2,7,8). The diagnosis relies on a combination of respiratory symptoms, radiological findings consistent with infection, and virological confirmation of CMV infection.

Polymerase chain reaction (PCR) assays detecting CMV DNA in bronchoalveolar lavage (BAL) fluid or serum are frequently employed as diagnostic molecular methods, yet the interpretation of positive results in immunocompetent hosts remains challenging. Previous studies have suggested that CMV DNA detection in BAL fluid is considered the most sensitive and reliable specimen for detecting CMV DNA in the lungs, and may provide diagnostic value in wheezy infants or children with unexplained respiratory symptoms (5,6,9,10). However, the correlation between viral load and clinical severity, radiological manifestations, or treatment outcomes is still uncertain. Additionally, the role of serum CMV PCR remains controversial, as many children with CMV pneumonia may test negative in peripheral blood despite having positive BAL results (5,6).

The cornerstone of treatment for severe CMV infections is intravenous ganciclovir (8,11). Data on its use in immunocompetent children with CMV pneumonia are limited, and potential benefits must be weighed against the risk of toxicity (12). Understanding whether CMV viral load in BAL or serum predicts response to ganciclovir may help guide treatment decisions in this context.

In this retrospective study, we aimed to examine the clinical characteristics of immunocompetent children with CMV pneumonia and identify the relationship between BAL and serum CMV DNA loads.

Materials and Methods

This retrospective cohort study was conducted at the Departments of Pediatric Pulmonology and Pediatric Infectious Diseases at İzmir City Hospital between November 2023 and January 2025.During the study period, a total of 62 children (aged <18 years) underwent flexible bronchoscopy due to recurrent pneumonia or persistent wheezing. Among them, 25 patients were found to have CMV DNA positivity in bronchoalveolar lavage (BAL) fluid by PCR and were considered eligible for the study. Five patients were excluded due to immunodeficiency (n=2), congenital CMV infection (n=1), and malignancy (n=2). Thus, the final study population consisted of 20 patients. The study flowchart is presented in Figure 1. Patients were eligible if CMV DNA was detected in BAL fluid by PCR. Children with known primary or secondary immunodeficiency, malignancy, congenital CMV infection, and those receiving immunosuppressive therapy were excluded.

Clinical data were extracted from the institutional electronic medical system and compared between patients with positive and negative serum CMV DNA results.

Clinical data collection

Demographic and clinical data included age, sex, age at onset of symptoms, presenting symptoms (cough, wheezing, dyspnea, fever, recurrent pneumonia, and diarrhea), anthropometric measurements, physical examination findings (tachypnea, respiratory distress, rhonchi, rales, and hypoxemia), laboratory

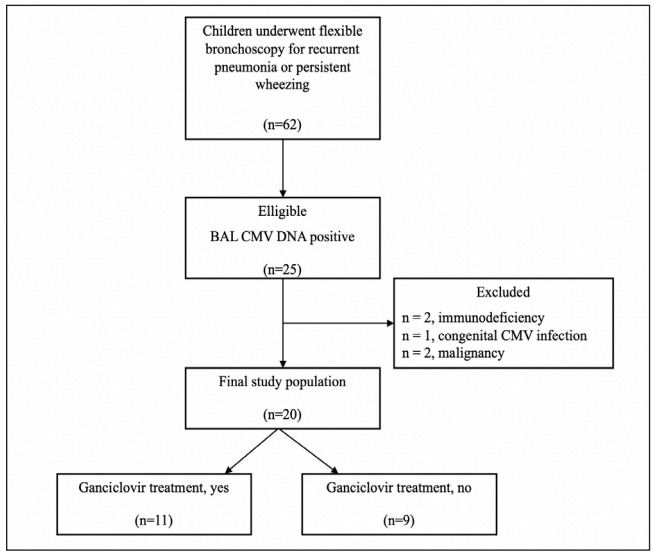


Figure 1: Flowchart of participants included in the study.

results, radiological findings (chest radiographs and computed tomography (CT) scans), and BAL analyses (microbiological and cytological).

Weight and height z-scores were calculated according to the Centers for Disease Control and Prevention (CDC) growth charts. Body mass index (BMI) was calculated using the weight (kg)/height (m^2) formula for children older than 2 years, and BMI z-scores were also determined using the CDC growth charts (13).

Chest radiographs obtained at admission were retrospectively reviewed for the presence of interstitial infiltrates, consolidation, atelectasis, hyperinflation, and pleural effusion.

Chest CT findings, as previously reported by a pediatric radiologist, were retrospectively extracted from the patients' medical files. Lobar involvement was recorded separately for each pulmonary lobe (right upper, right middle, right lower, left upper, and left lower lobes). The number of involved lobes was documented for each patient. Bilateral involvement was defined as the presence of parenchymal abnormalities affecting both lungs. Multilobar involvement was defined as involvement of two or more lobes. In addition to distribution, specific radiological patterns—including consolidation, atelectasis, mosaic perfusion, ground-glass opacities, bronchiectasis, pleural effusion, centrilobular small nodules, interlobular septal thickening, and tree-in-bud pattern, were noted.

Laboratory Data

Complete blood count (CBC) parameters, including leukocyte count (×10³/μL), neutrophil count (×10³/μL), lymphocyte count (×10³/μL), monocyte count (×10³/μL), eosinophil count (×10³/μL), platelet count (×10³/μL), mean platelet volume (MPV, fL), plateletcrit (PCT, %), and platelet distribution width (PDW, %), were retrospectively extracted from the electronic medical record system. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated by dividing the absolute neutrophil and platelet counts, respectively, by the absolute lymphocyte count.

Inflammatory markers, including C-reactive protein (CRP, mg/L) and serum immunoglobulin G (IgG, g/L), were also retrieved from the same database.

Quantitative CMV DNA levels from both serum and BAL samples (hereafter referred to as CMV DNA load) were recorded from the hospital's microbiology laboratory database, which had been analyzed by real-time PCR assay. Results were expressed as international units per milliliter (IU/mL). The lower limit of detection was 150 IU/mL, with a quantification range of 150–1×10^7 IU/mL. No predefined viral-load cut-off was used for the diagnosis of CMV pneumonia (5,7,8). CMV DNA results were interpreted in conjunction with clinical presentation and radiological findings.

All laboratory analyses were performed in the hospital's central laboratory according to standardized operating procedures and internal quality control protocols.

Bronchoscopy and BAL procedure

Flexible bronchoscopy was performed under general anesthesia using an appropriately sized flexible bronchoscope (EB-530P, Fujifilm Corporation, Tokyo, Japan). The procedure was conducted in a dedicated operating room by the same pediatric pulmonologist (14). After airway inspection, BAL was performed by instilling sterile 0.9% saline solution (1 mL/kg, with a maximum of 20 mL per aliquot) into the most affected segment, as determined radiologically, or the right middle lobe/lingula in cases of diffuse disease. The instilled fluid was immediately aspirated with gentle suction and collected into sterile mucus traps.

The first aliquot was sent for bacterial, fungal, and mycobacterial cultures. The remaining pooled aliquots were divided as follows: one portion for cytological examination (differential cell count and cytopathology) and one for viral PCR analysis (including CMV and other respiratory viruses). Samples were transported to the laboratory within 30 minutes of collection and processed immediately under sterile conditions, following standardized operating protocols. BAL differential cell counts were interpreted according to established pediatric reference values. Neutrophilia was defined as neutrophils >5% of total cells, and eosinophilia as eosinophils >1%, based on previously published reference ranges (15).

Treatment protocol

Intravenous ganciclovir was initiated in patients with high BAL CMV DNA load and/or positive serum CMV PCR results, particularly in the presence of severe or persistent respiratory symptoms and significant radiological abnormalities. It was administered at a dose of 5 mg/kg/per dose twice daily. The planned treatment duration was 21 days. Treatment decisions were made by a multidisciplinary team including pediatric pulmonology and infectious diseases specialists.

After the initial 14 days of therapy, patients were reassessed for clinical response and potential adverse effects. Clinical response was defined as improvement in baseline respiratory symptoms (wheezing, cough, or dyspnea) and/or radiological stabilization or improvement on chest imaging. In the absence of drug-related toxicity, treatment was continued and completed for a total duration of 21 days.

Statistical analysis

Descriptive data are presented as numbers for categorical variables and as mean and standard deviation (SD) or median and interquartile range (IQR) for continuous variables, depending on the data distribution, as assessed by the Shapiro–Wilk test. Group comparisons were conducted using the Pearson χ^2 test or Fisher's exact test for categorical variables, and the Student's t-test or Mann–Whitney U test for continuous variables, as appropriate. Correlations between viral load and clinical characteristics were assessed with Spearman's correlation coefficient. A p-value <0.050 was considered statistically significant. Statistical analyses were performed using SPSS version 26.0 (IBM, Armonk, NY).

Results

Patient characteristics

The medical records of 62 pediatric patients who underwent flexible bronchoscopy for recurrent pneumonia or persistent wheezing were retrospectively assessed. The median age was six years (1.5-9.7), and 11 patients (55%) were male. The median age at onset of symptoms was 2.5 years (0.8-4.3). The most frequent presenting symptom and physical examination finding were chronic cough (85%), respectively. The demographic and clinical characteristics of the study population are presented in Table I.

Hematologic parameters, chest CT findings, and flexible bronchoscopy results

The median serum leukocyte count was 8.74x10^3/µL (7.02-12.04), the monocyte count was 0.74x10^3/µL (0.54-1.11), and MPV was 9.9 fL (9.4-10.5). The hematologic parameters of the study population are presented in Table II.

On chest radiography, patchy consolidations were observed in 9 patients (45%), hyperinflation in 7 (35%), atelectasis in 6 (30%), interstitial infiltrates in 2 (10%), and pleural effusion in 1 (5%).

All patients exhibited pathological abnormalities on chest CT. The most frequent CT findings were consolidation (55%)

Table I: Demographic characteristics of immunocompetent children diagnosed with CMV pneumonia

Symptom*	
Cough	17 (85)
Wheezing	13 (65)
Recurrent pneumonia	13 (65)
Dyspnea	8 (40)
Fever	2 (10)
Diarhea	1 (5)
Physical examination	
Weight (kg)†	18.5 (10.5-30)
Height (cm)†	110.5 (79-134)
BMI†	16.9 (15.2-19.5)
zWeight (kg)†	-0.56 (-1.37-0.03)
zHeight (cm)†	-0.38 (-1.6-0.22)
zBMI†	-0.3 (-1-0.43)
Rhonchi*	10 (50)
Rales*	8 (40)
Tachypnea*	7 (35)
Respiratory distress*	6 (30)
Hypoxemia*	2 (10)

:** *n(%),* **†:** *median (IQR),* ***BMI: *body mass index,* ***IQR:*** *interquartile range*

Table II: Hematologic parameters, chest CT findings, and flexible bronchoscopy results of immunocompetent children diagnosed with CMV pneumonia

Hematologic parameters*	
Leukocytes (10^3/μL)	8.74 (7.02-12.04)
Neutrophil (10^3/μL)	4.16 (2.87-6.84)
Lymphocyte (10^3/μL)	2.95 (2.56-5.72)
Monocytes (10^3/μL)	0.74 (0.54-1.11)
Eosinophil (10^3/μL)	0.26 (0.07-0.53)
Platelet (10^3/μL)	351.5 (272.5-419)
MPV (fL)	9.9 (9.4-10.5)
PCT (%)	0.3 (0.2-0.4)
PDW (%)	11.1 (9.7-12)
CRP (mg/L)	1 (0.6-4.5)
IgG (g/L)	10.8 (8-13.3)
NLR	1.4 (0.8-2)
PLR	112.5 (66.4-144.2)
Chest CT findings†	
Consolidation	11 (55)
Atelectasis	9 (45)
Mosaic perfusion	7 (35)
Ground-glass opacity	6 (30)
Bronchiectasis	4 (20)
Pleural effusion	2 (10)
Centrilobular small nodules	7 (35)
Interlobular septal thickening	5 (25)
Tree-in-bud pattern	3 (15)
Bronchoscopy results†	
Mucosal Appearance	
Normal	17 (85)
Pale	1 (5)
Pale with nodular changes	2 (10)
Secretions, yes	13 (65)
BAL analysis	
BAL co-infection†	13 (65)
Haemophilus influenzae	8 (40)
Influenza A	3 (15)
RSV	1 (5)
AGBHS	1 (5)
BAL leukocytes (mm^3)*	375 (112.5-800)
BAL PMNL (%)*	45 (10-78.7)
BAL CMV DNA (IU/mL)*	1416 (311-16874)

***: median (IQR), †: n(%), AGBHS:** group A β-hemolytic streptococcus, **BAL:** bronchoalveolar lavage, **CRP:** C-reactive protein, **CT:** computed tomography, **MPV:** mean platelet volüme, **NLR:** neutrophil-to-lymphocyte ratio, **PCT:** plateletcrit, **PDW:** platelet distribution width, **PLR:** platelet-to-lymphocyte ratio, **PMNL:** polymorphonuclear leukocytes, **RSV:** Respiratory syncytial virus*

and atelectasis (45%) (Table II). Bilateral lung involvement was present in 14 patients (70%), whereas 6 patients (30%) had unilateral involvement. Multilobar involvement was observed in 14 patients (70%), with a median of 2 lobes involved (1–5). Regarding lobar distribution, involvement was detected in the right upper lobe in 9 patients (45%), right middle lobe in 8 (40%), right lower lobe in 12 (60%), left upper lobe in 11 (55%), and left lower lobe in 12 patients (60%).

On flexible bronchoscopy, 17 patients (85%) had normal mucosal appearance, and 13 (65%) had abundant secretions. BAL cytology demonstrated neutrophilia in 16 patients (80%), with eosinophilia in one patient. Co-infections were identified in BAL samples in 13 patients (65%), including *Haemophilus influenzae* (40%), Influenza A (15%), group A β-hemolytic *streptococcus*, and Respiratory syncytial virus in each patient.

Table III: Comparative analysis of demographic, clinical, and laboratory findings according to ganciclovir treatment status

	yes	no	p
Number of patients	11	9	-
Age (months)*	6 (1-9)	6 (3.3-11.5)	0.503
Gender (male)†	8 (72.7)	3 (33.3)	0.078
Onset age (months)*	1 (0.8-4.5)	3.8 (0.9-6.8)	0.552
Symptom†			
Cough	8 (72.7)	9 (100)	0.089
Wheezing	7 (63.6)	6 (66.7)	0.888
Recurrent pneumonia	8 (72.7)	5 (55.6)	0.423
Dyspnea	5 (45.5)	3 (33.3)	0.582
Fever	2 (18.2)	0	0.178
Diarhea	1 (9.1)	0	0.353
Physical examination			
zWeight*	-0.9 (-1.5-(-0.2))	-0.4 (-0.8-0.5)	0.175
zHeight*	-0.5 (-2.8-0.2)	-0.3 (-1.3-0.7)	0.370
zBMI*	-1 (-1.7-1.1)	-0.1 (-0.8-0.4)	0.336
Rhonchi†	5 (45.5)	5 (55.6)	0.653
Rales†	5 (45.5)	3 (33.3)	0.582
Tachypnea†	5 (45.5)	2 (22.2)	0.279
Respiratory distress†	4 (36.4)	2 (22.2)	0.492
Hypoxemia†	1 (9.1)	1 (11.1)	0.881
Monocytes (10^3/μL)*	1050 (740-1600)	600 (300-730)	0.010
MPV (fL)*	10.3 (10.1-10.8)	9.4 (8.4-9.7)	0.001
Chest CT findings†			
Bilateral involvement	8 (72.7)	6 (66.7)	0.769
Multilobar involvement	8 (72.7)	6 (66.7)	0.769
Consolidation	6 (54.5)	5 (55.6)	0.964
Atelectasis	5 (45.5)	4 (44.4)	0.964
Mosaic perfusion	3 (27.3)	4 (44.4)	0.423
Ground-glass opacity	3 (27.3)	3 (33.3)	0.769
Bronchiectasis	1 (9.1)	3 (33.3)	0.178
Pleural effusion	2 (18.2)	0	0.178
Centrilobular small nodules	3 (27.3)	4 (44.4)	0.423
Interlobular septa thickening	1 (9.1)	4 (44.4)	0.069
Tree-in-bud pattern	1 (9.1)	2 (22.2)	0.413
Serum CMV positivity†	6 (54.5)	0	0.008
Serum CMV DNA (IU/mL)*	212 (0-873)	0	0.038
BAL CMV DNA (IU/mL)*	9110 (3137-24744)	330 (247-539)	0.001
BAL PMNL (%)*	45 (10-50)	70 (7.5-80)	0.710
BAL leukocytes (mm^3)*	800 (80-800)	340 (115-915)	0.656

***: median (IQR), †: n(%), BAL:** bronchoalveolar lavage, **BMI:** body mass index, **IQR:** interquartile range, **CT:** computed tomography, **MPV:** mean platelet volüme, **PMNL:** polymorphonuclear leukocytes*

The median BAL CMV load was 1416 IU/mL (311-16874). In contrast, only six patients (30%) had detectable serum CMV DNA, with a median viral load of 700 (443-2650).

Correlation analysis of laboratory findings with CMV PCR

BAL CMV DNA load showed a strong positive correlation with serum monocyte count ($r=0.861$, $p<0.001$) and MPV ($r=0.759$, $p<0.001$). Scatter plots illustrating these correlations are presented in Figure 2.

Serum CMV DNA load were not significantly correlated with serum monocyte count or MPV ($p>0.486$). Notably, no significant correlation was observed between BAL and serum CMV loads ($p>0.963$).

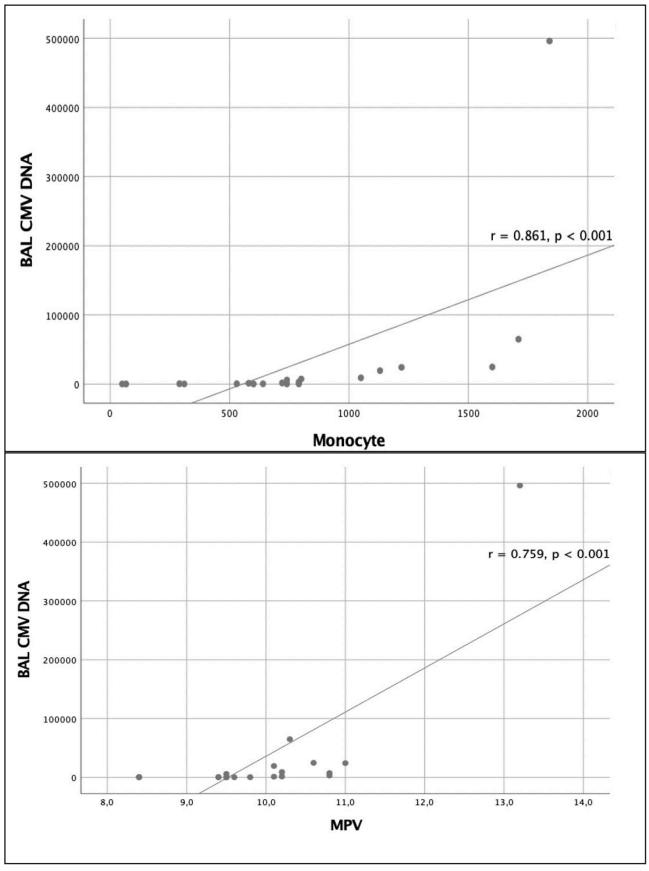


Figure 2: Scatter plot graphics and correlation between BAL CMV DNA (y-axis) and hematologic parameters (x-axis)

Comparison of patients based on treatment

All patients with positive serum CMV PCR results (n=6) received intravenous ganciclovir treatment. In addition, five patients with negative serum CMV PCR but high BAL CMV DNA load and severe clinical or radiological findings were also treated. Eleven patients (55%) received intravenous ganciclovir (5 mg/kg/per dose, twice daily) for 21 days. No clinically significant adverse effects were observed.

During a median follow-up of 1.3 years (1.2-1.5), all treated patients demonstrated both clinical and radiological resolution without complications.

Compared with the non-treatment group (n=9), the treatment group (n=11) had significantly higher serum monocyte count (1.05 vs 0.6x10^3/µL, p=0.010), MPV value (10.3 vs 9.4 fL, p =0.001), and BAL CMV DNA load (9.110 vs 330 IU/mL, p=0.001). No significant differences were observed between the groups regarding demographic characteristics, clinical presentation, anthropometric measurements, physical examination findings, other laboratory results, chest CT findings, or BAL analyses (Table III).

Follow-up chest radiographs demonstrated radiological improvement in all 11 patients who received antiviral treatment. Among the nine patients who did not receive antiviral therapy, persistent atelectasis was observed in one patient and residual hyperinflation in one patient, while the remaining patients showed radiological resolution.

Discussion

This study characterises the clinical features of immunocompetent children with CMV pneumonia and underscores the potential diagnostic value of BAL CMV PCR. Among children who underwent flexible bronchoscopy, the proportion with CMV pneumonia was 32.2%, suggesting that CMV pneumonia may not be uncommon in this selected population. Serum CMV PCR was positive in fewer than one-third of these cases, supporting BAL as a more sensitive diagnostic modality than serum testing. Higher monocyte counts and MPV were significantly associated with BAL CMV load.

The exact frequency of CMV pneumonia among children has not been clearly established. Most studies have focused on CMV pneumonia developing in patients with immunodeficiency or those who have undergone hematopoietic stem cell transplantation (5,11,16-18). In a study evaluating children with primary immunodeficiency, CMV pneumonia was detected in 6.8% (16). The incidence of CMV infection among pediatric hematopoietic stem cell transplantation patients has been reported to range from 8% to 14.5% (17,18). Population-based prevalence data for CMV pneumonia in immunocompetent children are lacking. Current knowledge derives largely from studies of flexible bronchoscopy cohorts—typically children with persistent symptoms or lower respiratory tract infections. In a study including 102 infants who underwent flexible bronchoscopy for persistent wheezing and diffuse interstitial infiltrates on radiological evaluation, CMV PCR in BAL fluid was positive in 51 patients (5). In a cohort of 49 immunocompetent children hospitalized for CMV infection, 41% were found to have CMV pneumonia (11). In our bronchoscopy-based cohort, CMV pneumonia was identified in 32.2% (20/62) of cases. This proportion is higher than previously reported, likely attributable to routine BAL CMV PCR testing in our center. These findings suggest that CMV should be considered in the differential diagnosis of recurrent or persistent lower respiratory disease, and BAL CMV PCR should be obtained when appropriate.

Previous studies suggest that direct detection of CMV in the respiratory tract is more indicative of CMV pneumonitis than detection in serum samples (19,20). Serum CMV DNA was positive in only one-third of the patients in our study, and we found no correlation between serum CMV DNA and BAL CMV DNA. A previous study reported that 33% of BAL CMV PCR-positive infants had serum CMV PCR positivity (5). They concluded that BAL CMV PCR was more effective than serum CMV PCR in diagnosing lower respiratory tract infections due to CMV in immunocompetent infants. In another study investigating infants with pertussis, BAL CMV PCR was found to be positive in 15% of those who were serum CMV-negative (9). On the other hand, the correlation between CMV viral loads in serum and BAL samples remains controversial (5,9,21). While no correlation was found in immunocompetent infants, another study evaluating serum and BAL CMV load among adult immunocompromised patients showed a strong positive correlation (5,21). Our findings suggest that the presence of CMV DNA in the lower airways may represent a localized infection independent of

systemic dissemination observed in immunocompromised individuals.

The clinical interpretation of CMV DNA detected in BAL fluid is challenging, as CMV may be present in the lower respiratory tract due to asymptomatic viral shedding, and no universally accepted viral-load threshold has been defined. In hematopoietic stem cell transplant recipients, a pragmatic BAL CMV DNA threshold of approximately 500 IU/mL has been proposed to help distinguish CMV pneumonia from asymptomatic shedding, whereas in lung transplant recipients, higher thresholds around 4500 IU/mL have been suggested for the diagnosis of CMV pneumonia (22,23). Berengua et al. (24) reported that BAL CMV load of ≥1258 IU/mL (6290 copies/mL) in immunosuppressed adults would be indicative of clinically relevant viral replication in the lung. Despite these proposed values, all major studies and consensus discussions consistently underscore that CMV DNA levels should be interpreted within the clinical and radiological context rather than relying on a fixed numeric threshold applicable to all settings. In immunocompetent children, BAL CMV PCR positivity has been mainly used as microbiological support within a compatible clinical syndrome rather than relying on a validated numeric cut-off, and BAL testing may outperform blood PCR for lower respiratory tract involvement (5). Therefore, in the present study, BAL CMV DNA positivity was interpreted as microbiological support in a compatible clinical and radiological setting rather than based on a fixed quantitative threshold.

Circulating monocytes have a short half-life (~1.6 days) and exhibit broad responsiveness to pathogens, facilitating their activation and the initiation of innate and subsequent adaptive immune responses (25). Monocytes play a pivotal role in CMV dissemination to organ tissues during primary infection and following reactivation from latency (26). Zdziarski et al. (27) demonstrated that elevated monocyte counts and percentages are positively correlated with CMV replication and may even serve as indicators of active CMV replication. Consistently, in the present study, BAL CMV DNA load was positively correlated with monocyte counts. An increase in monocyte count may occur due to prolonged survival, mobilization from the peripheral pool, or decreased uptake by tissue macrophages (27,28). We suggest that children with recurrent wheezing or pneumonia accompanied by elevated monocyte counts should be evaluated for possible CMV pneumonia.

Mean platelet volume reflects platelet size and is generally associated with platelet activation, as larger platelets are metabolically and enzymatically more active (29). MPV has been shown to correlate with disease severity, mediated by pro-inflammatory cytokines (29,30). In a recent study, Gümüş et al. (31) demonstrated that MPV levels were significantly higher in asymptomatic children infected with SARS-CoV-2. In our cohort, BAL CMV DNA load showed a strong positive correlation with MPV. This finding may reflect platelet activation in the context of CMV-related inflammation within the lower respiratory tract. Future studies are warranted to clarify the specific link between CMV pneumonia and MPV.

Ganciclovir, a guanosine analogue that selectively inhibits CMV DNA polymerase, is licensed for antiviral treatment only in severe or life-threatening CMV disease in immunocompromised patients (32,33). Indications for use in immunocompetent patients remain less clearly defined. In our study, patients with higher BAL CMV load, monocyte count, or MPV value were more likely to receive ganciclovir therapy. In prior reports of CMV pneumonia in immunocompetent children, those who received ganciclovir at 10 mg/kg/day for 14–21 days demonstrated clinical improvement with normalization of chest radiographs, and no severe ganciclovir-related toxicities were observed (5,12,32). Consistent with prior reports, in our cohort, 11 patients (55%) who received intravenous ganciclovir at 5 mg/kg/per dose twice daily for 21 days achieved clinical and radiological recovery, with no complications observed over a median follow-up of 1.3 years. These findings suggest that ganciclovir can be considered a safe therapeutic option for patients with CMV pneumonia.

Limitations

This study has several limitations that should be acknowledged. First, its retrospective design inherently limits the ability to establish causal relationships between CMV viral load and clinical or laboratory findings. Second, the relatively small sample size and single-center setting may restrict the generalizability of the results. Third, no standardized viral-load cut-off was applied, and quantitative CMV PCR results may vary across assay platforms. The presence of co-infections in a considerable proportion of patients further complicates interpretation, as detection of CMV DNA alone does not establish causality. Finally, treatment decisions were not randomized and were more frequently made in patients with higher viral loads introducing potential selection bias.

Conclusion

In conclusion, our study offers valuable insights into the diagnostic and clinical significance of BAL CMV PCR in the diagnosis of CMV pneumonia in immunocompetent children with recurrent wheezing or pneumonia. Elevated monocyte counts and MPV values were associated with higher BAL CMV DNA load, suggesting a potential link between CMV activity and hematologic inflammatory markers. Intravenous ganciclovir therapy led to favorable outcomes without complications in immunocompetent children with CMV pneumonia. We propose that BAL CMV PCR should be considered in the diagnostic workup of children with recurrent pneumonia or persistent wheezing. Larger prospective and randomized studies are required to establish standardized diagnostic and therapeutic protocols.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by İzmir City Hospital (22.01.2025, reference number: 2025/30).

Contribution of the authors

Study conception and design: EO, DY; data collection: ÜAS, GMD; analysis and interpretation of results: EO, İAH; draft manuscript preparation: EO. All authors reviewed the results and approved the final version of the article.

Presented or Pre-print or Published as an abstract or as a thesis
This study was previously presented as an oral presentation at the "Türk Toraks Derneği 28. Yıllık Kongresi, 2025" held on May 2025 in Antalya, Türkiye.

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Conflict of interest
The authors declare that there is no conflict of interest.

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