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Clinical Features, Laboratory and Radiological Findings, and Outcomes of *Pneumocystis jirovecii* Pneumonia in Immunocompetent Children

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Pneumocystis jirovecii pneumonia (PJP) is a well-recognized opportunistic respiratory infection that primarily affects human immunodeficiency virus (HIV)-infected individuals and immunocompromised children.[1] *Pneumocystis jirovecii* (PJ) is ubiquitous in the environment and often persists as a dormant colonizer in the lungs of otherwise healthy children, where it remains clinically silent. However, in immunodeficient hosts, the organism can proliferate and cause symptomatic infection. Emerging evidence also suggests that PJP may occasionally occur in immunocompetent individuals.[2]

This study aimed to characterize the clinical presentation, laboratory and radiological findings, co-infection patterns, and treatment outcomes among immunocompetent pediatric patients with PJP. By delineating the clinical profile of this uncommon entity, our findings may facilitate earlier recognition and support timely and appropriate management. This case series provides practical insights into the diagnosis and clinical care of PJP in immunocompetent children.

This single-center retrospective case series was conducted at Zigong First People's Hospital in Sichuan, China. We screened all hospitalized children who underwent bronchoscopy with bronchoalveolar lavage between January 2020 and December 2024 for unexplained pneumonia. Patients were eligible for inclusion if they met the following criteria: (1) age between 1 month and 14 years, irrespective of sex; (2) presence of respiratory symptoms with radiological evidence of pulmonary infiltrates; (3) detection of PJ in bronchoalveolar lavage fluid (BALF) by metagenomic next-generation sequencing (mNGS); and (4) no documented immunodeficiency.

Immunocompetence was determined through clinical history and laboratory assessment, including normal serum immunoglobulin levels (IgG, IgA, IgM), normal lymphocyte subset counts (CD3+, CD4+, CD8+, and NK cells), and absence of underlying conditions such as malignancy, organ transplantation, long-term corticosteroid use, congenital immunodeficiency, or HIV infection. Patients with chronic lung disease, congenital heart disease, or hereditary metabolic disorders were also excluded.

The study was approved by the Zigong First People's Hospital Ethic Committee (approval number: M-2024-015, date: 01.02.2024), and informed consent was waived due to its retrospective design.

We analyzed seven immunocompetent children with PJP, the majority of whom were male (71.4%). The median age at onset was 0.7 years [interquartile range (IQR): 0.3–4.0 years], and 57.1% of patients were younger than one year. All patients presented with cough, three (42.9%) had fever, and one (14.3%) exhibited wheezing. Oxygen therapy was required in five patients (71.4%).

Laboratory findings showed elevated lactate dehydrogenase (LDH) in 71.4% of patients, increased interleukin-6 and eosinophil counts in 57.1%, and abnormal erythrocyte sedimentation rate and serum amyloid A in 42.9%. Elevated neutrophil counts were observed in 28.6%, whereas β-D-glucan (BDG) and C-reactive protein (CRP) were elevated in 14.3%. White blood cell (WBC) counts, procalcitonin (PCT), and IgE levels remained within normal ranges.

mNGS revealed concurrent infections in six patients (85.7%). Rhinovirus was the most frequent co-pathogen (57.1%), followed by *Streptococcus pneumoniae*, *Escherichia coli*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. BALF cultures were negative in 71.4% of cases, while *H. influenzae* and *M. catarrhalis* were isolated in the remaining patients. Those requiring oxygen harbored a higher average number of pathogens (4.0) compared with patients not requiring oxygen (1.5). Bronchoscopic examination showed pallor and mucosal edema in 85.7% of patients. Chest computed tomography

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(CT) revealed bilateral ground-glass opacities in all patients, with partial consolidation observed in two cases.

All patients received trimethoprim–sulfamethoxazole (TMP–SMX) for 21 days without additional antimicrobial therapy. Clinical symptoms improved within a median of 3.0 days (IQR: 2.5–4.0 days), and radiological improvement was observed after an average of 13.4 ± 1.1 days. All patients recovered without complications. Table 1 summarizes the main patient characteristics.

Overall, immunocompetent children with PJP in our series exhibited a relatively uniform clinical phenotype, characterized by mild inflammatory responses, frequent detection of multiple microbial sequences on mNGS, and consistent radiological findings dominated by bilateral ground-glass opacities. LDH levels were elevated in the majority of patients, whereas BDG assays were positive in only a minority. All patients responded favorably to TMP–SMX monotherapy without the need for adjunctive corticosteroids or additional antimicrobial therapy.

Because PJ cannot be cultured on conventional media, the current gold standard for diagnosing PJP is microscopic examination of stained lower respiratory tract samples to detect characteristic cysts or trophic forms. However, traditional staining methods are time-consuming, have low sensitivity, and are highly dependent on examiner expertise. In non-HIV-infected patients, pathogen load is typically low, which increases the risk of false-negative results using conventional microbiological methods.[3]

Given the limitations of traditional microbiological methods, several non-culture-based biomarkers have been investigated to aid in the diagnosis of PJP. BDG, a major component of the PJ cell wall, reflects fungal burden in the blood but lacks specificity, as BDG levels may also rise in other fungal infections. Consequently, serum BDG testing has limited diagnostic specificity for PJP.[4] In our study, the positive rate of BDG in immunocompetent children with PJP was only 14.3%, suggesting low sensitivity in this population.

LDH, a biochemical marker of cellular damage, is often elevated in PJP. Esteves et al.[5] reported that LDH demonstrated high sensitivity (91.3%) but low specificity (35.5%) in HIV-positive patients, highlighting its limitations as a standalone diagnostic marker. In our cohort, 71.4% of immunocompetent children with PJP exhibited elevated LDH, underscoring its potential utility as an adjunctive diagnostic indicator.

In addition to laboratory markers, radiological imaging provides crucial information regarding disease extent and progression. Although early imaging findings may be non-specific, classic CT features of PJP include diffuse interstitial infiltrates, bilateral ground-glass opacities—predominantly in a perihilar distribution—and, in some cases, progression to consolidation within 3–5 days.[6] All seven patients in our study demonstrated these characteristic imaging patterns. However, radiographic findings alone cannot definitively distinguish PJP from viral pneumonia, idiopathic pulmonary fibrosis, or pulmonary edema, emphasizing the importance of an integrated diagnostic approach.

Recent advances in diagnostic technology have enabled the use of mNGS, which allows unbiased detection of PJ nucleic acid sequences in blood or BALF samples. mNGS provides rapid and accurate results, substantially improving diagnostic yield. In critically ill pediatric patients, one study reported mNGS sensitivity and specificity of 100% and 96.7%, respectively—considerably higher than those of BDG (86.7% and 56.7%) and LDH (55.6% and 71.4%).[7] However, due to its high sensitivity, mNGS may detect organisms associated with colonization rather than active infection, particularly in immunocompetent hosts. In our cohort, although multiple microbial sequences were identified in several patients, clinical assessments, chest CT findings (predominantly bilateral ground-glass opacities with limited consolidation), and laboratory markers (normal or only mildly elevated CRP, PCT, and WBC) did not support active bacterial co-infection. All patients demonstrated prompt and sustained clinical improvement with TMP–SMX monotherapy, and no additional antimicrobial agents were administered either

TABLE 1. Clinical Characteristics of Immunocompetent Children with *Pneumocystis jirovecii* Pneumonia.

Patient	Age/sex	Oxygen therapy	Clinical features	LDH (U/L)	BDG (ng/L)	mNGS pathogens	BALF culture	Symptom relief (days)
1	0.6/M	No	Cough	323	5.93	PJ, RV-B	Negative	1
2	0.7/M	Yes	Fever, cough	479	57.823	PJ, Hi, HPIV, CVA10	Hi	2
3	0.3/M	Yes	Fever, cough	189	12.34	PJ, *E. coli*, CMV, RV-A, MTB	Negative	3
4	0.3/M	Yes	Cough	312	18.27	PJ, RV-A, CMV	Negative	4
5	6.5/F	Yes	Cough	294	22.43	PJ, SPn, MCat, CA, RV-A	MCat	4
6	4.0/M	Yes	Coughing, wheezing	324	345.921	PJ, NTM, CMV	Negative	5
7	4.0/F	No	Fever, cough	289	6.77	PJ	Negative	3

PJ, *Pneumocystis jirovecii*; RV-A / RV-B, Rhinovirus A/Rhinovirus B; Hi, haemophilus influenzae; HPIV, human parainfluenza virus; CVA10, coxsackievirus A10; *E. coli*, *Escherichia col*i; CMV, cytomegalovirus; MTB, mycobacterium tuberculosis; SPn, streptococcus pneumoniae; MCat, moraxella catarrhalis; CA, candida albicans; NTM, nontuberculous mycobacteria; LDH, lactate dehydrogenase; BDG, (1,3)-β-D-glucan; mNGS, metagenomic next-generation sequencing; BALF, bronchoalveolar lavage fluid; M, male; F, Female.

empirically or in response to mNGS findings. These observations support PJ as the primary causative pathogen rather than a colonizer. While patients requiring oxygen therapy exhibited a higher number of co-detected microbial sequences (mean 4.0 vs. 1.5), similar patterns have been attributed to alterations in pulmonary microbial ecology in more severe disease rather than true polymicrobial infection.[8,9]

The role of adjunctive corticosteroids in non-HIV or immunocompetent pediatric PJP remains uncertain. Corticosteroids have been shown to improve outcomes in HIV-infected patients with PJP, particularly in cases of severe hypoxemia (arterial oxygen tension < 70 mmHg).[10] In our cohort, all patients achieved favorable clinical outcomes with TMP–SMX monotherapy without corticosteroid use. However, because arterial oxygen tension was not measured and none of the patients exhibited signs of severe respiratory compromise, these findings should not be extrapolated to immunocompetent children with marked hypoxemia. Further studies are needed to clarify indications for corticosteroid therapy in this population.

Compared with classical PJP in immunocompromised pediatric patients, the cases in our series exhibited milder clinical manifestations and more favorable outcomes. None required mechanical ventilation or adjunctive corticosteroids, and all recovered with TMP–SMX monotherapy. This contrasts with reports in immunocompromised children, who frequently present with severe hypoxemia, higher mortality, and often require intensive care support and glucocorticoid therapy.[11] In adults without identifiable immunocompromising conditions, PJP shows variable clinical severity.[2,12] A retrospective study further demonstrated that immunocompetent adult patients with PJP were generally older, had higher mortality than immunocompromised counterparts, and that delayed initiation of anti-PJP therapy was independently associated with increased 90-day mortality.[12]

In conclusion, clinicians should remain vigilant for PJP in immunocompetent children. In our series, all patients achieved favorable outcomes with TMP–SMX monotherapy without adjunctive corticosteroids. Patients requiring oxygen therapy exhibited a greater diversity of co-detected pathogens, suggesting a potential association between pathogen heterogeneity and disease severity. Among laboratory markers, elevated LDH was common and may serve as a useful supportive diagnostic indicator, whereas BDG demonstrated poor sensitivity, limiting its diagnostic utility in this population.

Ethics Committee Approval: The study was approved by the Zigong First People's Hospital Ethic Committee (approval number: M-2024-015, date: 01.02.2024).

Informed Consent: Retrospective study.

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