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Case Report
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Three Cases of Infectious Mononucleosis in Children: A Case Report and Literature Review

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Abstract

Objective: *To investigate the heterogeneous clinical presentations, essential diagnostic criteria, and treatment strategies for pediatric Infectious Mononucleosis (IM), underscoring the importance of early recognition and management of severe complications.*

Methods: *We present three pediatric cases confirmed as Epstein-Barr virus (EBV)-associated IM. This includes a 9-year-old boy with severe IM complicated by Hemophagocytic Lymphohistiocytosis (HLH), and two mild-to-moderate cases (a 3-year-old boy and a 5-year-old girl). Clinical features, laboratory results, therapeutic interventions, and outcomes were analyzed.*

Results: *All patients presented with fever, cervical lymphadenopathy, elevated atypical lymphocytes, and positive EBV serology. The severe case manifested massive lymphadenopathy, hepatosplenomegaly, systemic edema, and abnormal HLH-related parameters. He achieved full recovery within 15 days following treatment with high-dose intravenous immunoglobulin (IVIG; 2g/kg) combined with methylprednisolone pulse therapy. The moderate cases recovered within 12-13 days after conventional management (low-dose IVIG or oral corticosteroids).*

Conclusion: *Pediatric IM exhibits significant clinical heterogeneity. Severe cases are more frequently observed in school-aged children and may be complicated by HLH. Early identification of high-risk features and prompt initiation of immunomodulatory therapy are critical. Comprehensive laboratory assessment is essential for risk stratification and guiding individualized treatment.*

Keywords: *Infectious Mononucleosis; Children; Epstein-Barr Virus; Hemophagocytic Lymphohistiocytosis; Case Report*

1. Introduction

Infectious Mononucleosis (IM) is a common clinical syndrome in children, predominantly caused by the Epstein-Barr virus (EBV), a gammaherpesvirus [1]. The classic triad of symptoms includes fever, pharyngitis, and cervical lymphadenopathy, often accompanied by atypical lymphocytosis. However, the disease spectrum is broad, ranging from subclinical infection to life-threatening complications such as Hemophagocytic Lymphohistiocytosis (HLH), airway obstruction, and hepatic failure [2].

Epidemiological studies indicate a peak incidence of IM in Chinese children aged 4-6 years, with school-aged children bearing a higher risk for severe disease compared to their preschool counterparts [3]. HLH, a rare but catastrophic hyperinflammatory complication of IM, is characterized by dysregulated immune activation leading to multi-organ dysfunction [4]. Early diagnosis and aggressive immunomodulatory treatment, including intravenous immunoglobulin (IVIG) and corticosteroids, are pivotal in reducing mortality for severe IM cases [5]. This report details three pediatric IM cases of varying severity to enhance the understanding of the disease's clinical diversity and to inform management decisions.

2. Case Presentation

2.1 Case 1: Severe IM with HLH in a 9-year-old boy

A 9-year-old boy was admitted for persistent high-grade fever (39.0–40.5°C) for 7 days and progressive neck swelling for 3 days. The fever was refractory to antipyretics. He presented with significant fatigue and lethargy. Physical examination revealed massive bilateral cervical lymphadenopathy (largest node 7 × 8 cm), firm and fixed, alongside pharyngeal erythema, Grade II tonsillar enlargement, and dysphagia secondary to pharyngeal edema. Generalized edema and mild hypoalbuminemia were noted. Abdominal examination and ultrasonography confirmed hepatosplenomegaly.

Laboratory Investigations: Leukocytosis with a markedly elevated atypical lymphocyte count (20%). Inflammatory markers (ESR, CRP) were significantly elevated. EBV serology (VCA-IgM) and DNA PCR were positive. Critical HLH workup revealed hyperferritinemia (763 μg/L) and elevated soluble interleukin-2 receptor (sCD25). Bone marrow aspiration demonstrated definitive hemophagocytosis.

Final Diagnosis: Severe EBV-associated Infectious Mononucleosis complicated by Hemophagocytic Lymphohistiocytosis [6].

Management and Outcome: The patient received high-dose IVIG (2 g/kg) and methylprednisolone pulse therapy (20 mg/kg/day), alongside supportive care. Defervescence occurred on day 4. Lymphadenopathy, edema, and hepatosplenomegaly showed significant resolution within 10-12 days. Laboratory parameters normalized, and he was discharged in good condition on day 15.

2.2 Case 2: Moderate IM in a 3-year-old boy

A 3-year-old boy presented with a 5-day history of intermittent high fever (39.5–41.0°C), responsive to antipyretics but recurring, and cervical lymphadenopathy for 2 days. Examination showed bilateral cervical lymph nodes (largest 2 × 3 cm), soft, mobile, and mildly tender. Pharyngeal erythema and Grade I tonsillar hypertrophy were present. A transient truncal maculopapular rash appeared and resolved spontaneously. Abdominal ultrasound identified hepatosplenomegaly.

Laboratory Investigations: Leukocytosis with 12% atypical lymphocytes. Elevated ESR (50 mm/h) and CRP (93 mg/L). Positive EBV-IgM and EBV DNA. Mild transaminitis was noted.

Final Diagnosis: Moderate EBV-associated Infectious Mononucleosis [6].

Management and Outcome: Treatment consisted of IVIG (1 g/kg) and oral prednisone (1 mg/kg/day), with supportive measures. Fever resolved by day 3. Lymphadenopathy and hepatosplenomegaly improved markedly within one week. All laboratory results normalized by day 10, and he was discharged on day 12.

2.3 Case 3: Moderate IM in a 5-year-old girl

A 5-year-old girl was admitted for persistent fever (39.0–40.0°C) for 6 days and cervical lymphadenopathy for 3 days, with poor response to oral antipyretics. Bilateral cervical lymph nodes (largest 3 × 4 cm), firm and non-tender, were palpated. Pharyngeal erythema and Grade II tonsillar enlargement were evident. No hepatosplenomegaly was detected.

Laboratory Investigations: Leukocytosis with 10% atypical lymphocytes. Elevated inflammatory markers. Positive EBV serology. Direct Coombs' test was positive. Liver function tests were within normal limits.

Final Diagnosis: Moderate EBV-associated Infectious Mononucleosis with a positive Direct Coombs' test [6].

Management and Outcome: She was managed with IVIG (1 g/kg) and supportive care. Defervescence occurred on day 4. Lymphadenopathy resolved by day 9. All laboratory parameters, including the Coombs' test, normalized by day 11. She was discharged on day 13 without sequelae.

3. Discussion

This case series highlights the spectrum of clinical severity in pediatric EBV-IM, from self-limiting moderate disease to life-threatening HLH.

3.1 Clinical Heterogeneity and Age Correlation

The marked contrast between Case 1 and the two moderate cases (2 & 3) underscores the significant heterogeneity of IM. The severe presentation in the school-aged child (Case 1), featuring massive lymphadenopathy, systemic involvement, and HLH, aligns with observations of increased severity risk in older children [3]. This may be attributed to a more robust, and potentially dysregulated, cell-mediated immune response in this age group compared to preschoolers, whose immune response to primary EBV infection might be less vigorous [2].

3.2 Diagnostic and Prognostic Markers

Consistent with diagnostic criteria, all cases showed EBV-VCA-IgM positivity and atypical lymphocytosis (>10%). The markedly elevated atypical lymphocyte count (20%) in Case 1 reflected significant immune dysregulation [7]. The HLH-associated markers (ferritin, sCD25) were crucial for identifying the hyperinflammatory state; early diagnosis of HLH is vital as it can reduce mortality from over 80% to below 20% with appropriate treatment [8]. The positive Direct Coombs' test in Case 3, even in the absence of clinical hemolysis, indicates subclinical immune-mediated red cell sensitization, warranting monitoring and highlighting the value of comprehensive serological testing.

3.3 Tailored Treatment Approaches

The treatment responses observed validate current stratified management principles. For severe IM with HLH (Case 1), combined immunomodulation with high-dose IVIG and corticosteroids is the cornerstone, effectively dampening the cytokine storm [5, 9]. The rapid recovery demonstrates this regimen's efficacy. For moderate cases (Cases 2 & 3), less aggressive intervention with low-dose IVIG or oral steroids sufficed, leading to complete recovery without exposing the children to unnecessary intensive therapy.

3.4 Limitations

This study has limitations inherent to small case series: limited statistical power, absence of long-term follow-up for potential sequelae (e.g., chronic fatigue), and lack of genetic studies in the severe case to investigate potential predispositions to HLH (e.g., mutations in UNC13D) [10].

4. Conclusion

Pediatric IM demonstrates a wide clinical spectrum. A high index of suspicion for severe complications like HLH is necessary, particularly in school-aged children presenting with warning signs such as massive lymphadenopathy, hepatosplenomegaly, and hyperferritinemia. Early, aggressive immunomodulatory therapy is paramount in such cases. Thorough laboratory evaluation, including EBV serology, atypical lymphocyte count, and HLH-specific biomarkers, is essential for accurate diagnosis, risk stratification, and guiding individualized treatment. Future prospective studies with larger cohorts and genetic analyses are warranted to further elucidate pathogenesis and refine therapeutic protocols.

Conflict of Interest Statement

All authors declare that they have no conflicts of interest.

Author Contributions

LI Huirong: Responsible for data collection, data analysis, and manuscript drafting.

WANG Xin, LIU Xiaoxiao, WANG Qi: Participated in data collection and data analysis.

MA Xizhao: Engaged in manuscript revision.

JIAO Fuyong: Provided research guidance and participated in manuscript revision.

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