

Recurrent Severe Pneumonia with Hypogammaglobulinemia, Severe Undernutrition and Sepsis in an Incompletely Immunized Infant: A Suspected case of Primary Immunodeficiency

Dr. Pradhyumn Pamecha¹, Dr. Harish Papani², Dr. Priyadarshna Pamecha³

¹[Department of Paediatrics, SBKS MI & RC, Vadodara, India, 391760]

²[Department of Paediatrics, SBKS MI & RC, Vadodara, India, 391760]

³[Department of Conservative Dentistry and Endodontics, Geetanjali Dental & Research Institute, Udaipur, Rajasthan, 313001, India]

Abstract:

Background: Pneumonia is the leading infectious cause of death in children under five years of age. Recurrent or non resolving pneumonia in early infancy, especially with a family history of early childhood death, should prompt evaluation for an underlying primary immunodeficiency/inborn error of immunity (IEI). Severe undernutrition and incomplete immunization further increase susceptibility and severity.

Case presentation: A 7 month old, full term, incompletely immunized male infant (BCG and birth dose OPV only) was admitted to the pediatric intensive care unit with respiratory distress and hypoxemia (SpO₂ 87% on room air). Respiratory illness had begun at 5 months of age and had required repeated outpatient visits and hospital admissions. An elder sister had died at about 11 months of age. The infant was severely underweight and wasted, he had pallor and hepatomegaly. High resolution computed tomography (HRCT) showed consolidation with an air bronchogram and internal cavitation in the right upper and middle lobes, diffuse bilateral ground glass opacities, interlobular septal thickening, mosaic attenuation and cystic change with traction bronchiectasis. Serum IgG (<3.20 g/L) and IgA (<0.25 g/L) were low. CFTR gene analysis was negative and echocardiography was normal. On day 7 the infant deteriorated, requiring invasive ventilation and adrenaline infusion with escalation of antimicrobial therapy and addition of antifungal cover. He later died of cardiorespiratory failure.

Conclusion: Infantile onset of recurrent severe pneumonia, low immunoglobulins, a sibling death in infancy and complex lung changes on HRCT together point to an IEI. Recognizing these warning signs early allows targeted immunological evaluation, timely immunoglobulin replacement, avoidance of live vaccines and genetic counselling for the family.

Key Word: Immunodeficiency; Inborn errors of immunity; Hypogammaglobulinemia; Recurrent pneumonia; Severe acute malnutrition; Sepsis; Infant

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I. Introduction

Pneumonia remains the single largest infectious cause of death among children younger than five years, accounting for more than 600,000 deaths worldwide in 2019¹. The burden is highest in low and middle income countries, where undernutrition and gaps in immunization coverage are common. Conjugate vaccines against *Streptococcus pneumoniae* and *Haemophilus influenzae* type b have substantially reduced pneumonia morbidity and mortality². Malnutrition independently and markedly increases the risk of death from pneumonia^{3,4}.

Most children with pneumonia have a single episode. Recurrent pneumonia, defined as two or more episodes in a year or three or more episodes at any time, is usually associated with an identifiable underlying cause⁵. Immune deficiency is one such cause and must be considered actively in infants^{5,6}. Inborn errors of immunity (IEI) are a group of more than 480 genetic disorders that impair host defence^{7,8}. Antibody and combined immunodeficiencies typically present in the second half of infancy, when transplacentally acquired maternal IgG wanes. Recurrent respiratory tract infection is the most frequent presenting feature^{6,9}.

We report a 7 month old infant with recurrent severe pneumonia, low serum immunoglobulins, severe undernutrition and incomplete immunization, who developed sepsis with progressive respiratory failure. The case illustrates how clinical, family and laboratory clues converge to suggest an underlying IEI. It also shows how coexisting malnutrition and lack of vaccine protection amplify disease severity.

II. Case Report

A 7 month old male infant, born at term and fed breast milk supplemented with formula, was referred to our pediatric intensive care unit (PICU) with increasing respiratory distress. His respiratory illness had begun at 5 months of age, two months before admission. Since then he had needed several outpatient consultations and hospital admissions. At those facilities he had received several courses of antibiotics, antiviral therapy, systemic corticosteroids and anti tubercular therapy before referral to our centre for further evaluation and management.

The infant had received BCG and oral polio vaccine (OPV) at birth. He had not received the hepatitis B birth dose or any subsequent vaccines under the national immunization schedule. The parents reported a similar immunization pattern in his siblings. An elder sister had died at about 11 months of age, seven years earlier; the parents attributed her death mainly to severe anemia. An elder brother is alive, asymptomatic and is thriving well.

On admission, the infant had tachycardia, tachypnoea and pallor. His oxygen saturation was 87% on room air, with subcostal and suprasternal retractions. Air entry was reduced on the right side and bilateral crepitations were heard. The liver was palpable 5–6 cm below the right costal margin. Examination of the other systems was unremarkable. Anthropometry showed acute malnutrition with severe underweight and wasting.

Investigations

The chest radiograph showed homogeneous opacification of the right upper zone. HRCT of the chest showed extensive consolidation with an air bronchogram and internal cavitation in the right upper and middle lobes, with mosaic attenuation. Both lungs showed diffuse ground glass opacities with interlobular septal thickening. Multiple cystic and fibrocystic changes with traction bronchiectasis were seen, predominantly in the right middle lobe and extending into the right upper lobe.

Serum immunoglobulin estimation showed low IgG (<3.20 g/L) and low IgA (<0.25 g/L), with IgE of 17.9 IU/mL. Because of the recurrent respiratory infections, cystic fibrosis was considered; CFTR gene analysis was negative. Two dimensional echocardiography was normal, which excluded structural heart disease and cardiac failure as causes of the respiratory distress and hepatomegaly. Blood culture and cannula tip culture were sterile. Key investigations are summarised in Table 1.

Table no 1: Key investigations

Investigation	Result
Chest radiograph	Homogeneous opacification, right upper zone
HRCT chest	Consolidation with air bronchogram and internal cavitation (right upper and middle lobes); mosaic attenuation; diffuse bilateral ground glass opacities with interlobular septal thickening; cystic/fibrocystic change with traction bronchiectasis (right middle > upper lobe)
Serum IgG	<3.20 g/L (low)
Serum IgA	<0.25 g/L (low)
Serum IgE	17.9 IU/mL
CFTR gene analysis	Negative
2D echocardiography	Normal
Blood culture	Sterile
Cannula tip culture	Sterile

Treatment

The infant was started on high flow nasal cannula (HFNC) oxygen at 8 L/min with FiO₂ – 40% and intravenous antibiotics were continued. On day 7 of admission his respiratory distress worsened abruptly and he was intubated and mechanically ventilated. Adrenaline infusion was started for circulatory support with fentanyl for analgesia and sedation. Antibiotics were escalated and antifungal therapy was added. Suspected infection with respiratory and cardiovascular dysfunction requiring invasive ventilation and vasoactive support was consistent with sepsis with septic shock as defined by the Phoenix criteria¹⁰.

Outcome and follow-up

Despite ventilatory, inotropic and broad spectrum antimicrobial support, recurrent fever spikes persisted and laboratory parameters did not improve. The infant's condition progressively deteriorated and subsequently, he died of cardiorespiratory failure. The clinical course is summarised in Table 2.

Table no 2: Timeline

Age / hospital day	Event
Birth	Term delivery; BCG and OPV0 given; no further immunizations
5 months	Onset of recurrent respiratory illness; multiple outpatient visits and admissions; antibiotics, antivirals, corticosteroids and anti-tubercular therapy at outside facilities
7 months, day 1	Admitted to PICU; SpO ₂ 87% on room air; HFNC 8 L/min, FiO ₂ – 40%; antibiotics

	continued
Days 1–7	Echocardiography normal; cultures sterile; CFTR analysis negative; IgG and IgA low; HRCT showing consolidation, cavitation, ground-glass opacities and bronchiectasis
Day 7	Acute respiratory deterioration; intubation and mechanical ventilation; adrenaline and fentanyl infusions; antibiotics escalated; antifungal added
Subsequent course	Persistent fever spikes; progressive cardiorespiratory failure; death

III. Discussion

This infant showed several recognized warning signs of an IEI. His respiratory illness began at 5 months of age and recurred and progressed over the next two months despite repeated hospital treatment. His serum IgG and IgA were low and an elder sibling had died in infancy^{6,9}. The ESID working definitions and international practice parameters emphasize exactly this pattern for prompt immunological evaluation: infection that is unusually severe, recurrent or persistent despite treatment, together with a family history of early death or suspected immunodeficiency^{6,9}. Onset in the second half of infancy coincides with the decline of maternal IgG. This is the characteristic window in which agammaglobulinemia and combined immunodeficiencies become clinically apparent^{7,9}.

Several inherited disorders are plausible here. In the IUIS classification, predominantly antibody deficiencies and combined immunodeficiencies, including severe combined immunodeficiency (SCID), both present with hypogammaglobulinemia and severe sinopulmonary infection in infancy^{7,8}. The death of an elder sister in infancy suggests a heritable disorder that affects both sexes, which is consistent with autosomal recessive inheritance. In a large Indian series, SCID presented in early infancy with pneumonia as the predominant infection and carried high mortality without definitive treatment¹¹. That series also documented a substantial burden of BCG related complications among infants who had received BCG at birth¹¹. An international multi-centre study similarly showed that BCG given to infants with undiagnosed SCID frequently causes local and disseminated disease¹². This underlines the value of identifying at risk families before live vaccines are given.

The HRCT findings in this infant were consolidation with cavitation, bilateral ground glass opacities, mosaic attenuation and early cystic change with traction bronchiectasis. These represent a pattern of severe, destructive and persisting lung infection. Bronchiectasis, consolidation and interstitial changes are well described pulmonary manifestations of primary antibody deficiency. Structural lung damage can develop early when repeated infection goes unchecked¹³. Negative CFTR analysis and a normal echocardiogram supported an immunological, rather than cystic fibrosis related or cardiac, basis for the recurrent pneumonia⁵.

Severe undernutrition was an important contributor in this case. Malnutrition impairs barrier function, cell mediated immunity and antibody responses¹⁴. Children with severe acute malnutrition and pneumonia have a several fold higher risk of death than well nourished children^{3,4,15}. In this infant, a likely intrinsic immune defect combined with secondary nutritional immunosuppression would have reduced his capacity to contain infection. Equally, the absence of pneumococcal, Hib and other scheduled vaccines removed protection against the leading bacterial causes of childhood pneumonia².

The infant's course culminated in sepsis with septic shock as defined by the 2024 Phoenix criteria with respiratory failure requiring invasive ventilation and cardiovascular dysfunction requiring adrenaline¹⁰. Management followed the principles of the Surviving Sepsis Campaign pediatric guidelines: early respiratory support, vasoactive therapy with adrenaline and escalation of broad spectrum antimicrobial and antifungal cover¹⁶. Infants with an underlying IEI are vulnerable to bacterial, fungal and opportunistic pathogens. Their sepsis may progress despite appropriate supportive care, which reflects the profound defect in host defence.

For children with suspected antibody or combined immunodeficiency, the essentials of care are:

1. Early recognition
2. Immunological evaluation, including lymphocyte subset analysis
3. Immunoglobulin replacement and antimicrobial prophylaxis
4. Avoidance of live vaccines
5. For SCID, hematopoietic stem cell transplantation^{6,9}

Outcomes of transplantation are best when it is performed early in infancy, before serious infection is established. Newborn screening for SCID using T-cell receptor excision circles allows diagnosis before symptoms develop and has transformed outcomes where it has been implemented¹⁷. In settings without such screening, clinical vigilance remains essential. This is particularly true for families with a history of unexplained infant deaths, which provides an opportunity for genetic counselling and for early evaluation of future siblings.

IV. Conclusion

Infantile onset of recurrent severe pneumonia, low serum immunoglobulins, a sibling death in infancy and destructive lung changes on HRCT together point strongly to an underlying inborn error of immunity.

Coexisting severe undernutrition and incomplete immunization amplify disease severity and mortality in such infants. The key learning points from this case are:

1. Recurrent or non resolving pneumonia beginning in the second half of infancy, particularly with low serum immunoglobulins, should prompt evaluation for an inborn error of immunity.
2. A family history of unexplained death in infancy is a major warning sign and should be specifically asked about in every infant with recurrent severe infection.
3. Severe undernutrition and incomplete immunization act synergistically with an underlying immune defect to increase the severity and mortality of pneumonia.
4. Early identification of at risk infants allows immunoglobulin replacement, antimicrobial prophylaxis, avoidance of live vaccines, definitive therapy and genetic counselling for the family.

Patient consent

Written informed consent for publication of this case report and accompanying images was obtained from the patient's parents.

Conflict of interest

None

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