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Apnea-Predominant Malignant Pertussis with Extreme Hyperleukocytosis in a 38-Day-Old Infant: A Life-Saving Rule of Double-Volume Exchange Transfusion

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Case Report

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Abstract

Bordetella pertussis is a highly contagious bacterial infection that causes whooping cough, also known as pertussis. Clinically, pertussis is often characterized by intense coughing paroxysms and a characteristic inspiratory whoop. Malignant pertussis is the most severe form, defined by rapidly progressive acute respiratory distress and extreme leukocytosis, and poses a significant risk of rapid clinical deterioration and poor outcomes.

We describe in this case report a 38-day-old baby girl admitted to our Neonatal Intensive Care Unit (NICU) with severe Bordetella pertussis infection. On admission, she was in moderate respiratory distress with atypical recurrent prolonged episodes of apnea. Laboratory investigations showed markedly elevated white blood cell count with predominant lymphocytosis, and PCR-confirmed Bordetella pertussis infection complicated by pneumonia. Although receiving maximal supportive care, her clinical condition was worsening due to progressive respiratory failure and severe hyperleukocytosis. However, after exchange transfusion (ET), she showed dramatic improvement and was safely discharged home with a normalized white cell count. This case underscores the need for early recognition of pertussis, particularly in young infants who may present with atypical symptoms and supports considering a timely exchange transfusion as a life-saving intervention when the leukocyte burden is rapidly escalating.

1. Background

Pertussis, commonly known as whooping cough, is an acute, highly contagious respiratory tract infection caused by the gram-negative bacterium Bordetella pertussis [1, 2]. Although pertussis infection can affect people of all ages, infants are most affected since they have the highest age-specific incidence and most hospitalizations and fatalities from the illness [1]. Despite widespread vaccination worldwide, its incidence has resurged significantly in recent years, particularly affecting newborns and young infants who are not yet eligible for complete vaccination [3, 4]. Malignant pertussis, the most severe form of infection, is characterized by extreme hyperleukocytosis (typically white blood cell count > 50,000/μL) and rapidly progressive acute respiratory distress, often complicated by pulmonary hypertension and/or refractory cardiopulmonary failure [5, 6].

Lymphocytosis is one of the most noticeable laboratory signs of infantile pertussis [7]. Moreover, the severity of lymphocytosis can result in blood hyperviscosity, leading to compromised pulmonary perfusion and eventually elevating the risk of cardiorespiratory failure. The degree of leukocytosis has been shown to correlate proportionally with disease severity and most fatalities [8–10]. Therefore, exchange blood transfusion (ET) and leukapheresis have been widely used as effective methods to reduce leukocyte load and improve patients' outcomes [9].

This case describes a 38-day-old female infant with PCR-confirmed pertussis infection who developed severe pneumonia with rapidly progressive respiratory failure, profound lymphocytosis, and frequent apnea attacks. Unlike classic pertussis, this infant presented with apnea as the predominant symptom

rather than typical paroxysmal whooping cough. The patient ultimately underwent double-volume exchange transfusion, which led to clinical stabilization and complete recovery. This example illustrates the severity and fatality of pertussis in early infancy and underscores the growing need for exchange transfusion as a life-saving intervention in infants with severe leukocytosis.

2. Case presentation

A 38-day-old baby girl presented with a 4-day history of worsening apnea, cough, and poor oral intake. The parents reported episodes of cyanosis and occasional post-tussive vomiting. The baby was a product of spontaneous vaginal delivery, born at term, with no significant perinatal or postnatal history. She had only received the hepatitis B vaccine at birth. The mother had not received the Tdap vaccine during pregnancy. Notably, there was a history of recent sick contact in the family.

Upon admission, the infant appeared irritable, tachypneic, with episodes of typical whooping cough followed by occasional apneic attacks. Despite this, her oxygen saturation remained well maintained on high-flow nasal cannula. On examination, she was in moderate respiratory distress, including tachypnea, nasal flaring, and mild subcostal and suprasternal retraction. Lung auscultation revealed decreased air entry bilaterally with scattered expiratory rhonchi. Central nervous system examination findings were within normal limits, and both cardiovascular and abdominal examination showed no abnormality. No limb edema was observed, with normal skeletal examination.

Blood samples were obtained and cultures sent for analysis. Lumbar puncture was performed as part of the septic workup. Empirical antibiotic therapy was initiated with azithromycin (10 mg/kg once daily intravenously for 5 days). Due to worsening lung function and suspicion of secondary bacterial pneumonia, cefepime (50 mg/kg/dose intravenously every 8 hours) and vancomycin (15 mg/kg/dose intravenously every 6 hours) were added. C-reactive protein (CRP) was 6.3 mg/L. Complete blood count revealed leukocytosis with a white blood cell (WBC) count of 20.1 × 10^9/L and a lymphocyte percentage of 54.47% (absolute lymphocyte count 10.93 × 10^9/L). Liver and kidney function tests were within normal limits.

Definitive diagnosis was confirmed via nasopharyngeal swab polymerase chain reaction (PCR) targeting IS481 and BP283, which was positive for Bordetella pertussis. All other septic workups were negative. The clinical presentation was consistent with pertussis complicated by prolonged apnea and pneumonia; a clinically significant complication in neonates and young infants.

Chest radiography on day 1 demonstrated accentuated bronchovascular markings with diffuse bilateral ground-glass and reticular opacities, along with right upper and mid-zone opacities [Figure 1A]. Repeat imaging on day 2 revealed progression of these findings with increasing bilateral consolidation [Figure 1B]. The rapid radiological progression correlated with clinical deterioration and rising white blood cell count.

On day 4 of admission, the infant experienced a prolonged episode of apnea, which was eventually complicated by cyanosis, severe oxygen desaturation, and significant bradycardia. She wasn't responding to bag-valve-mask ventilation, accordingly, she was intubated and connected to mechanical ventilation [See Fig. 2].

Thereafter, the infant's condition deteriorated further, with apneic episodes persisting despite mechanical ventilation. Despite adequate hydration, serial laboratory investigations demonstrated a worsening white blood cell (WBC) count, reaching 70.2 × 10^9/L [See Table 1]. Table 1 summarizes the serial complete blood count trends throughout the admission.

Table 1
Serial complete blood count trends

Day	WBC (×10^9/L)	Lymphocytes (%)	Neutrophils (%)
Day 1	20.1	54.47	30.9
Day 2	37.1	61.19	24.1
Day 3	42.9	42.9	40.8
Day 4	70.2	39.82	38.8
Day 5	68.4	36.2	43.8
Day 9 (pre-ET #1)	82.9	35.2	48.7
Day 9 (pre-ET #2)	95.7	35.2	45.8
Day 9 (post-ET)	25.4	28.0	51
Day 10	43.0	23.38	60.7
Day 11	42.2	27.8	58.9
Day 12	36.5	11.64	20.12
Day 13	28.5	33.16	51
Day 14	25.7	36.94	51.1
Day 25	11.9	45.96	37.1

On day 9, the WBC count rose to 95.7 × 10^9/L, prompting urgent double-volume exchange transfusion. The procedure was performed through an umbilical venous catheter using irradiated, leukocyte-reduced packed red blood cells reconstituted with fresh frozen plasma (2:1) at approximately 160 mL/kg (720 mL total) over 2 hours. Exchange transfusion was completed uneventfully, with immediate WBC reduction to 25.4 × 10^9/L, followed by a transient rebound to 43.0 × 10^9/L and gradual subsequent decline.

Transthoracic echocardiography was performed and revealed normal biventricular function, no evidence of pulmonary hypertension, and no structural abnormalities. The patient was successfully extubated

from mechanical ventilation after gradual weaning on day 16. The general condition of the patient improved significantly afterwards, with resolution of the apneic spells. Although the cough persisted for a while, the whooping episodes disappeared. A brain MRI was done during admission to rule out any ischemic or hemorrhagic changes which showed no abnormalities. Lastly, on day 25, the infant was safely discharged from the hospital in stable general condition with a white cell count of 11.9 × 10^9/L, and only a mild residual cough. Upon discharge, the infant received routine vaccinations commencing at two months of age. Household contacts were prescribed azithromycin chemoprophylaxis. This clinical picture points to a successful recovery from the respiratory insult with no aftereffects.

3. Discussion

Our case highlights an atypical presentation of infantile pertussis, where the primary symptom was recurrent apnea rather than the classical paroxysmal whooping cough commonly associated with pertussis. Such rare presentations can be observed in infants under 3 months of age, which may delay diagnosis. This emphasizes the significance of keeping a high index of suspicion for pertussis in this age group presenting with respiratory distress and unexplained apnea.

Malignant pertussis or severe pertussis infection is considered one of the leading causes of morbidity and mortality in young infants. Malignant pertussis is defined as pertussis infection complicated by extreme hyperleukocytosis (typically white blood cell count > 50,000/μL), rapidly progressive acute respiratory distress, pulmonary hypertension, and/or refractory cardiopulmonary failure. Early clinical and laboratory predictors that may help identify infants at risk of malignant pertussis include age under 3 months, unexplained apnea, rapidly rising white blood cell count (e.g., > 30,000/μL within 24–48 hours), profound lymphocytosis (> 50% of total WBC), and history of sick contact with incomplete maternal vaccination [11–13]. When comparing typical cases to current literature, it is found that practically all patients have paroxysmal whooping cough [7]. Severe symptoms such as respiratory distress, apnea, and post-tussive vomiting were uncommon among patients, occurring in less than 20% of instances [7, 14, 15]. Besides this, malignant pertussis is often complicated by secondary pneumonia, hyperleukocytosis, pulmonary hypertension, seizures, and, eventually, it might lead to multi-organ failure. Aspiration of stomach contents during coughing fits or impairment of mucociliary clearance caused by tracheal cytotoxin (TCT) has been identified as two probable causes of superimposed pneumonia, which is considered a leading cause of death in newborns and young children [16].

In the acute phase of the infection, lymphocytosis is a notable screening marker for pertussis [11]. The underlying mechanism behind lymphocytosis is thought to involve pertussis toxin disrupting G-protein-mediated signaling pathways, thereby preventing the normal migration of lymphocytes from the bloodstream, and eventually causing marked leukocytosis, primarily lymphocytosis [17]. Severe leukocytosis, a critical marker for disease severity, is defined as a leukocyte count exceeding 50,000/μL and is associated with high mortality rate [12, 13]. This elevated risk is primarily driven by leukocytosis-induced microvascular obstruction, which eventually accumulates in the pulmonary vasculature, leading to pulmonary hypertension and eventually heart failure [13]. This phenomenon has led to the

incorporation of leukoreduction therapies into the management of malignant pertussis. Without urgent interventions, the mortality risk exceeds 80% for those with hyperleukocytosis [13, 18].

The cornerstone of treatment to eradicate Bordetella pertussis remains with early and appropriate antibiotic administration, particularly macrolides [10]. Management of pertussis with hyperleukocytosis remains challenging, with no clear guidelines. However, it mainly involves supportive care alongside targeted interventions to reduce leukocyte burden. Infants with respiratory failure or apnea require supportive respiratory care, ranging from supplemental oxygen and noninvasive ventilation to invasive mechanical ventilation, with early consideration of ECMO in refractory cases. To address the burden of hyperleukocytosis, several effective leukoreductive methods have been described. Several studies have proven that exchange transfusion can be an effective emergency intervention for rapidly lowering WBC counts [10, 19, 20]. Leukapheresis has also been reported as an effective intervention for rapidly reducing severe leukocytosis, potentially improving outcomes [19, 21]. Although no standardized guidelines exist for exchange transfusion in malignant pertussis [22], several published studies have suggested WBC thresholds between 70,000 and 100,000/μL, especially when clinical deterioration is present [10, 12, 13, 20]. In this patient, double-volume exchange transfusion was undertaken because of a WBC count of 95.7×10^9/L, rapidly progressive leukocytosis despite maximal supportive care, and worsening respiratory failure with persistent apneic episodes despite mechanical ventilation. Our patient's response to double volume exchange transfusion was comparable to previous reports in similar age groups. However, the rarity of apnea as the presenting symptom emphasizes the need for heightened clinical recognition.

Exchange transfusion carries potential risks, including electrolyte disturbances (particularly hypocalcemia), coagulopathy, transfusion reactions, infection transmission, and hemodynamic instability [23, 24]. In our patient, these risks were mitigated through the use of irradiated, leukocyte-reduced blood products; monitoring of ionized calcium with replacement as needed; slow controlled infusion over two hours; continuous hemodynamic monitoring; and performance by experienced NICU personnel under aseptic conditions. This approach requires blood bank support and skilled NICU staff, resources that may be limited in resource-constrained settings.

Unlike previously reported cases of exchange transfusion for severe pertussis in which classic paroxysmal cough predominated and pulmonary hypertension was frequently documented, our patient presented with apnea as the primary symptom, an atypical finding in young infants. Despite extreme hyperleukocytosis, echocardiography revealed normal pulmonary pressures, and the infant achieved complete recovery without neurologic or respiratory sequelae. These observations yield three clinically actionable insights. First, apnea-predominant presentations in young infants can signify pertussis in the absence of classic cough. Second, timely exchange transfusion may facilitate favorable outcomes even with extreme hyperleukocytosis. Third, the absence of pulmonary hypertension should not delay leukoreductive intervention when extreme leukocytosis is present. Given the rarity of apnea as an initial manifestation, clinicians should maintain a low threshold for pertussis testing in young infants presenting with unexplained respiratory distress and marked leukocytosis.

In conclusion, in this single case, exchange transfusion was associated with rapid reduction of WBC and clinical improvement. Our experience, consistent with published case series, suggests that exchange transfusion should be considered early in the management of malignant pertussis with extreme hyperleukocytosis, before other complications develop. Ultimately, the awareness of atypical presentations in this vulnerable age group and timely treatment can significantly improve outcomes. This case report advances our knowledge of the illness and reinforces the need for further research and guidelines to develop early detection and intervention strategies.

Abbreviations

NICU: Neonatal Intensive Care Unit

PCR: Polymerase Chain Reaction

ET: Exchange transfusion

CRP: C-reactive protein

MRI: Magnetic Resonance Imaging

ECMO: Extracorporeal Membrane Oxygenation

WBC: White blood cell

RBC: Red blood cell

HGB: Hemoglobin

HCT: Hematocrit

MCV: Mean corpuscular volume

MCH: Mean corpuscular hemoglobin

MCHC: Mean corpuscular hemoglobin concentration

RDW-CV: Red cell distribution width – coefficient of variation

PLT: Platelet count

MPV: Mean platelet volume

Declarations

Ethics approval and consent to participate:

This case report complies with the Declaration of Helsinki, and according to hospital policy, formal ethical approval was not required for a single non-interventional case report. Written informed consent for participation in this case was obtained from the patient's parents.

Consent for publication

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

Availability of data and materials:

No new data were generated in this report. All relevant clinical data are included within this article. Additional anonymized information is available upon reasonable request, subject to institutional approval.

Competing Interests:

The authors declare no conflicts of interest, financial or otherwise.

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Authors' contributions:

RA conceived the case report, collected the clinical data, performed the literature review, and drafted the initial manuscript. SG and NS were involved in the clinical management of the patient, contributed to data acquisition, and critically revised the manuscript for important intellectual content. MN contributed to the literature search, data interpretation, and manuscript editing. OG contributed to the literature search, data interpretation, and manuscript editing. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

Clinical trial number:

Clinical trial number is not applicable.

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Figures

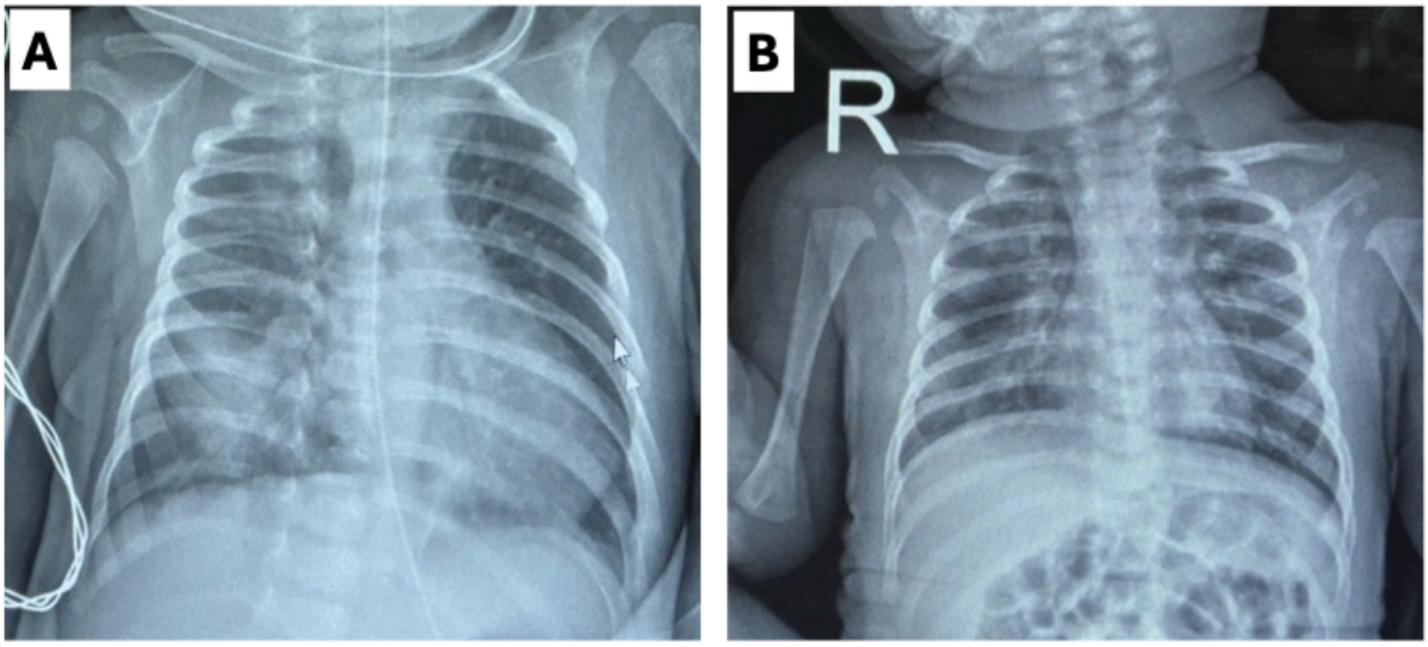


Figure 1

Initial and follow-up chest X-rays in a 38-day-old infant with malignant pertussis. (A) Day 1 chest X-ray demonstrates accentuated bronchovascular markings, bilateral ground-glass opacities, and right lung consolidation. (B) Day 2 chest X-ray shows progression of opacities with increasing bilateral consolidation.



Figure 2

Chest X-Ray done right after intubation. Gastric inflation is observed secondary to bag-valve-mask ventilation.