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**Case Report**

# Neonatal Leukemoid Reaction Caused by *Enterococcus Fecalis* Septicemia

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## Abstract

**Background:** Leukemoid reaction is not uncommon in neonatal period. It is usualy caused by Down syndrome, antenatal corticosteroids, or perinatal infections. The *Enterococcus fecalis* is a kind of nosocomial opportunistic pathogen and can cause neonatal septicemia with high mortality. However, neonatal leukemoid reaction induced by *Enterococcus fecalis* septicemiais is relativity rare. Here, we reported a three-day-old newborn suffered from leukemoid reaction caused by *Enterococcus fecalis* septicemia.

**Case Description:** A three-day old boy was hospitalized in our NICU of the Second Hospital of Dalian Medical University for jaundice and leukocytosis with comphalitis. Blood routine test displayed leukocytosis with immature cells, bone marrow smear examination showed leukemoid reactions, and the secretion of umbilicus culture showed infection of *Enterococcus fecalis*. Cefathiamidine was administrated for anti-infection. The baby symptoms eased rapidly, and leukocytosis was return to normal gradually.

**Conclusion:** *Enterococcus fecalis* can cause neonatal septicemia, which can lead to neonatal leukemoid reaction. Early diagnosis and reasonable antibiotics administration are very important to improve the prognosis of neonatal leukemoid reaction.

**Keywords:** Leukemoid reaction; Newborn; *Enterococcus fecalis*

## 1. Introduction

Neonatal leukemoid reaction (NLR) is defined as the white blood cell (WBC) count >50 × 109/L or absolute neutrophil count (ANC) >30 × 109/L (within 1 week after birth) or ANC greater than 2 standard deviations of the

corresponding mean gestational age, with immature cells [1]. Many causes contribute to NLR. The common diseases are Down syndrome, antenatal corticosteroids, chorioamnionitis, funisitis, perinatal infections and so on [2]. The *Enterococcus fecalis (E. fecalis*) is a kind of nosocomial opportunistic pathogen, which is known to cause neonatal septicemia with high mortality. However, the incidence of NLR in *E. fecalis* septicemia is rare, and few papers have been reported [3]. Here, we reported a neonatal LR caused by *E. fecalis* septicemia and provided clinical experience for its early diagnosis and treatment.

## 2. Clinical Information

A three-day-old boy was admitted to our NICU of the Second Hospital of Dalian Medical University for jaundice and leukocytosis. He was G1P1, 41+3wk, with the birth weight of 3490g and no asphyxia. On the second day after birth, the boy was poor feeding with less activity, skin jaundice and abdominal distention. WBC count of 56.43 × 109/L, with an ANC of 44.58 × 109/L. Total bilirubin was 275.3umol/L. Physical examination: T: 36.7°C P: 138/min, R: 34/min, BP 66/40 mmHg, yellow staining of sclera, face and trunk skin. The liver and spleen were not touched under the rib. The umbilical ring was red and swollen, and purulent and bloody secretions were also seen in the umbilical fossa. Laboratory testing: WBC count of 54.23 × 109/L, with an ANC of 42.11 × 109/L, 6% myelocyte, and 7% metamylocyte. C-reactive protein (CRP) was 14.88 mg/dl, and Procalcitonin (PCT) was 0.27 ng/ml. The cefoperazone was administrated empirically, and other symptomatic and supportive treatments were also given. But the baby condition has not improved. Three days later, WBC count was 50.07 × 109/L, with an ANC of 39.05 × 109/L; the secretion of umbilicus culture showed growth of *E. fecalis*. Then the antibiotics were changed to cefathiamidine which was reasonable according to drug sensitivity later. Bone marrow smear examination showed distinctly active proliferation of nucleated cell without any blast cells. Erythrocyte and megakaryocyte series were normal. Examination of blood culture, urine culture, stool culture, cerebrospinal fluid were all normal. After 3 days of cefathiamidine therapy, the baby's condition has been in remission and the blood counts started to decrease. WBC became 38.41 × 109/L, with an ANC of 26.11 × 109/L, and one week of the treatment, WBC was 25.26 × 109/L. CRP and PCT remained negative all throughout. The swelling of umbilicus and secretion of umbilicus were disappeared. After 10 days of cefathiamidine therapy, the repeated secretion of umbilicus culture was sterile. Cefathiamidine were continued for 14 days and WBC returned to normal (Table 1). The neonate was discharged.

After being discharged, the patient was followed up on 42 days after birth, and the growth and development of the infant were normal. WBC count was 10.1 × 109/L, with an ANC of 5.2 × 109/L. Hemoglobin was 13.3 g/dL and platelet count was 199 × 109/L, showing that all values were normal.

| | **Before Therapy** | **After Cefathiamidine Therapy** | | | | |
|---|---|---|---|---|---|---|
| | | **Day 3** | **Day 5** | **Day 7** | **Day 10** | **Day 14** |
| WBC ($\times 10^9$/L) | 54.23 | 38.41 | 33.67 | 25.26 | 20.23 | 17.22 |
| ANC ($\times 10^9$/L) | 42.11 | 26.11 | 22.22 | 15.91 | 11.12 | 8.95 |
| Hemoglobin (g/dL) | 20.3 | 18.6 | 17.0 | 15.5 | 15.2 | 14.6 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Platelet count ( × $10^9$/L) | 138 | 142 | 158 | 195 | 188 | 208 |
| Immature cells (%) | 6% Myelocyte, 7% Metamylocyte | 2% Promyelocyt, 2% Myelocyte | Negative | 2% Myelocyte, 3% Atypical Lymphocytes | Negative | Negative |
| CRP (mg/dl) | 14.88 | 6.64 | 2.58 | Negative | Negative | Negative |
| Procalcitonin (PCT) (ng/ml) | 0.27 | 0.06 | Negative | Negative | Negative | Negative |
| Total Bilirubin (umol/L) | 302.23 | 268.99 | 148.78 | 132.02 | 101.23 | 86.78 |

**Table 1:** The change in laboratory finding before and after Cefathiamidine therapy.

## 3. Discussion

Neonatal sepsis is classified as early-onset (EOS) and late-onset (LOS), according to the age of onset and timing of the sepsis episode. Traditionally, laboratory-confirmed neonatal sepsis is diagnosed by isolating the causative agent from a normally sterile body site (blood, CSF, urine, pleural, joint, and peritoneal fluids) [4]. When blood and other sterile site cultures are negative, but the infant manifests symptoms (such as temperature instability, poor feeding, less cry, less movement, abdominal distention, hepatomegaly, apnoea, Jaundice, et al.) consistent with infection, which may be considered as "clinical"sepsis [5]. The commonly used non-culture based diagnostic tests include: leukocytosis (WBC >30 × 109/L between 6 h to 3 day after birth or WBC >20 × 109/L 3 day after birth) or leukocytopenia (WBC <5 × 109/L); The ratio of immature to total neutrophils (I/T) increased (I/T >0.16 within 3 day after birth or I/T >0.12 3 day after birth); CRP increased (>3 mg/dl within 6 h after birth, >5 mg/dl between 6 to 24 h after birth or >5 mg/dl 24 h after birth); PCT>0.5 ng/ml [6-7]. Enterococcus is a normal colonizing bacteria in human intestine [8], but it can also cause early neonatal septicemia (EOS). Stoll et al. reported that 3% of 389 children with EOS were caused by Enterococcus faecalis infection [9].

The neonatal leukemoid reaction is common in clinic, especially in premature and low birth weight infants, and the incidence varies from 1.3% to 15% [10-11]. It is due to some non-leukemic factors that induce the release of some cytokines from bone marrow and cause the hyperproliferation reaction of normal bone marrow. The most common clinical reaction is neutropenia, most of which is an acute inflammatory reaction caused by infection factors. Moreover, the peripheral blood smear shows nuclear shifting to the left, immature granulocytes, toxic particles, alkaline phosphatase activity and integral of neutrophils. NLR can be mainly divided into infection factors and non-infection factors. Infection factors are the most common factors in neonatal leukemoid reactions, including bacterial, fungal, viral, spirochete, Rickettsia and so on [12]. It does not require special treatment. When the primary cause is removed, the hemogram can gradually recover.

This case is characterized by Enterococcus faecalis omphalitis, EOS and NLR. The diagnosis of this case is clinical septicemia. Although there was no evidence of positive blood bacterial culture, the clinical manifestation with increasing WBC and CRP supported for clinical septicemia diagnosis, and it was considered that Enterococcus faecalis from the umbilicus enters the blood to bring about leukocyte like reaction caused by septicemia. As we know that Enterococcus faecalis is a common colonizing bacterium. But for newborns, due to the low immune function, bacteria and their toxins can enter the blood circulation through the fracture before the umbilical cord falls off, which is easy to develop into septicemia. This makes us pay more attention to neonatal comphalitis. Early diagnosis and sensitive antibiotics administration are very important to improve the prognosis of neonatal leukemoid reaction.

## Conflict of Interest

Authors declare to have no conflict of interest.

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