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*Corresponding author: jovanovska.a@gmail.com

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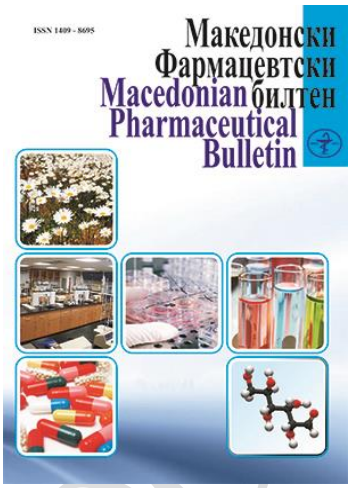

Title: Transient erythroblastopenia of childhood: a benign cause of severe anemia in a 3-year-old boy

Authors: Aleksandra Jovanovska[1*], Valentina Cvejoska-Cholakovska[2], Svetlana Kocheva[1]

[1] *Department of Hematology and Oncology, University Clinic for Children's Diseases, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Mother Teresa 17, 1000 Skopje, N. Macedonia*

[2] *Department of Pulmonology and Allergology, University Clinic for Children's Diseases, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Mother Teresa 17, 1000 Skopje, N. Macedonia*

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Transient erythroblastopenia of childhood: a benign cause of severe anemia in a 3-year-old boy

Aleksandra Jovanovska[1*], Valentina Cvejoska-Cholakovska[2], Svetlana Kocheva[1]

[1] *Department of Hematology and Oncology, University Clinic for Children's Diseases, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Mother Teresa 17, 1000 Skopje, N. Macedonia*

[2] *Department of Pulmonology and Allergology, University Clinic for Children's Diseases, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Mother Teresa 17, 1000 Skopje, N. Macedonia*

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Abstract

Transient erythroblastopenia of childhood (TEC) is an acquired, self-limiting disorder characterized by temporary red cell aplasia in previously healthy children. Laboratory findings typically reveal normocytic, normochromic anemia with reticulocytopenia. Although the precise etiology of TEC is not fully understood, viral infections have been suggested as a potential contributing factor. Clinically, it often presents with pallor and fatigue. Management is generally supportive, with transfusion indicated only in cases of symptomatic anemia. We report the case of a previously healthy three-year-old boy who developed severe anemia following a mild viral infection and required a single red blood cell transfusion. The child experienced a complete recovery, with normalization of hemoglobin and reticulocyte counts over the subsequent weeks. Early recognition of this condition ensures appropriate management, helps avoid unnecessary investigations, and reinforces the excellent prognosis associated with TEC.

Key words: transient erythroblastopenia, childhood, anemia, reticulocytopenia, red blood cell transfusion, viral infection

*Corresponding author: jovanovska.a@gmail.com

Introduction

Transient erythroblastopenia of childhood (TEC) is an acquired, benign form of pure red cell aplasia that typically affects children under 4 years of age (Mejía Sang et al., 2024). TEC is characterized by moderate to severe normochromic, normocytic anemia and reticulocytopenia secondary to the absence of erythroid precursors in an otherwise normocellular bone marrow (Mejía Sang et al., 2024; van den Akker et al., 2014).

The exact etiology of this disease remains unclear; however, multiple studies and case reports suggest that it may be triggered by a viral infection followed by a post-viral immune response that temporarily suppresses erythropoiesis in the bone marrow (Mejía Sang et al., 2024; van den Akker et al., 2014). Clinical manifestations include skin and mucosal pallor, cardiac flow murmurs and tachycardia. In severe cases, hemodynamic instability may be present (Schinasi et al., 2011). Initial diagnostic studies should focus on identifying other potential causes of anemia. The diagnosis of TEC is often confirmed retrospectively due to its self-limiting clinical course, becoming evident when hemoglobin and reticulocyte count return to normal spontaneously. Recovery typically occurs within 1 to 2 months. Symptomatic cases may require red blood cell transfusion. In this article, we present the case of a 3-year-old boy diagnosed with TEC.

Case presentation

A three-year-old previously healthy boy was referred to our department for evaluation and management of severe anemia. Two weeks prior to admission, routine immunization had been scheduled. At that time, the child was examined by his primary care physician, who noted marked pallor. A complete blood count (CBC) was ordered, revealing a hemoglobin level of 85 g/L. His previous hemoglobin measurement, obtained two months earlier, had been within the normal range (123 g/L).

Upon admission, the patient showed no signs of acute infection. Approximately one month prior to hospitalization, the parents reported mild respiratory symptoms, including cough and nasal congestion. The child had a generally balanced diet, and the family history was unremarkable for anemia or bleeding disorders.

*Corresponding author: jovanovska.a@gmail.com

Physical examination revealed pallor and tachycardia. There was no evidence of peripheral lymphadenopathy, organomegaly, bruising, or petechiae. No dysmorphic features were noted. His height and weight were in the 25th and 10th percentiles, respectively.

Laboratory evaluation on admission revealed normocytic, normochromic anemia (hemoglobin 65 g/L; red blood cells 2.37 × 10^{12}/L; hematocrit 19.3%; mean corpuscular volume 81.6 fL) with a markedly reduced reticulocyte count (0.09%). White blood cell and platelet counts were within normal limits (Table 1). There were no clinical or laboratory findings suggestive of bleeding or hemolysis. Iron studies, including serum iron, ferritin, and transferrin, as well as lactate dehydrogenase and unconjugated bilirubin, were normal. Direct antiglobulin test (DAT) was negative. Serum vitamin B12 and folate levels were within normal limits (Table 2). Bone marrow aspiration demonstrated markedly decreased erythroid precursors, while myeloid and megakaryocyte maturation was normal. Serological tests for parvovirus B19, Epstein-Barr virus, and cytomegalovirus were negative.

The patient received a red blood cell transfusion, resulting in an increase of hemoglobin to 104 g/L. He was subsequently discharged in stable condition. During follow-up over the next three months, he remained asymptomatic, with complete resolution of anemia indicated by normalization of reticulocyte counts and hemoglobin levels.

Considering the clinical course and laboratory findings — severe anemia in a previously healthy child, reticulocytopenia, suppressed erythropoiesis, and subsequent full recovery — the final diagnosis was transient erythroblastopenia of childhood (TEC).

Table 1 and 2

Discussion

TEC is an acquired, self-limited, benign form of pure red cell aplasia that occurs in previously hematological healthy children (Mejía Sang et al., 2024). Most cases occur in children ages 1 to 4 years, with a median age at diagnosis of 19 months (van den Akker et al., 2014). However, the disorder may occur in infants younger than 6 months of age (Moritake et al., 2012; Schinasi et al., 2011; Ware and Kinney, 1991). The patient reported here, who was 3-year-old was within the typical age range for TEC. The annual incidence of TEC has been reported to be between

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*Corresponding author: jovanovska.a@gmail.com

4.3 and 20 per 100,000 children (Mejía Sang et al., 2024). The true incidence may be higher because many cases remain undiagnosed and resolve spontaneously. Boys are affected slightly more common than girls (van den Akker et al., 2014).

The etiology of TEC is not well understood but seems to involve some virus infection as a potential trigger for suppression of erythropoiesis. Our patient had a history of a preceding viral illness several weeks before the onset of anemia, a finding consistent with previously reported cases in the literature (Burns and Woodward, 2019). Viruses that have been found in patients with TEC include parvovirus B19, human herpes virus type 6, and echovirus 11 (Elian et al., 1993; Ogawa and Yanagisawa, 2016; Penchansky and Jordan, 1997; Prassouli et al., 2005), however the association of TEC with these pathogens as well as Epstein-Barr virus and cytomegalovirus remains inconsistent (Skeppner et al., 2002). More recently has been reported TEC in a 2-year-old male patient linked to a SARS-CoV-2 infection (Rivetti et al., 2024). The underlying mechanism of erythroblastopenia is immune mediated suppression of erythropoiesis including IgG and IgM mediated pathways and cell-mediated immunity (Burns and Woodward, 2019; Mejía Sang et al., 2024). One study showed that a preceding viral infection may have caused activation of suppressor T-cells and interferon secretion leading to cell-mediated suppression of erythropoiesis (Tamary et al., 1993). Although TEC is typically considered an acquired condition, cases reported in siblings have raised the possibility of a genetic predisposition in some individuals (Shaw and Meeder, 2007).

Children with TEC usually have normocytic, normochromic anemia and a low reticulocyte count. One retrospective study involving a cohort of 36 children found that the median hemoglobin at presentation was 44g/L with absolute reticulocyte count 0 x 10^9/L. In addition, mild neutropenia and slightly elevated platelet count were reported in 47% and 64% of patients, respectively (van den Akker et al., 2014). The patient described in our case-report experienced a severe acute anemia and reticulocytopenia without any other hematological abnormalities consistent with pure red cell aplasia (PRCA). Other two major cause of PRCA in children are Diamond-Blackfan anemia (DBA) and transient red cell aplasia associated with parvovirus B19 infection in context of chronic hemolysis.

The differential diagnosis of TEC from DBA in early infancy may be difficult. DBA is a rare congenital form of PRCA that is usually diagnosed in infants less than 6 months of age. Inheritance is autosomal dominant in 45% of cases, whereas the remainder 55% of cases, typically

*Corresponding author: jovanovska.a@gmail.com

present sporadically. Twenty-five percent of DBA-affected patients are linked to a genetic mutation involving ribosomal protein 19 (RPS 19) (Da Costa et al., 2020). In addition to anemia, various congenital malformations, such as thumb malformations, urogenital abnormalities and craniofacial anomalies, are reported in nearly 40% to 50% of affected patients. Laboratory evaluation reveals moderate to severe anemia that is normochromic and usually macrocytic (MCV >100FL). Fetal hemoglobin and erythrocyte adenosine deaminase levels are elevated (Da Costa et al., 2020). These laboratory studies are typically normal in TEC. Most patients with TEC undergo a full spontaneous recovery within 1 to 2 months, while patients with DBA require corticosteroids and/or continued red cell transfusions in case of steroid resistance and are candidates for hematopoietic stem cell transplantation (Da Costa et al., 2020).

Given the self-limiting nature of TEC, management should primarily consist of careful observation and supportive care. Children presenting with symptomatic anemia may require red blood cell transfusion to alleviate clinical symptoms. In one retrospective study, approximately 72% of patients received transfusion during the course of their illness (van den Akker et al., 2014). Reticulocytosis, reflecting the recovery of erythropoiesis, typically appears around 12 days after diagnosis (Zeller, 1997). In our patient, reticulocytosis was observed two weeks after the onset of symptoms, consistent with the expected recovery timeline for TEC.

Conclusion

TEC should be considered an important differential diagnosis in young children who present with normocytic, normochromic anemia and a low reticulocyte count, particularly in the absence of hemolysis, nutritional deficiencies, or other underlying hematologic disease. This case highlights the importance of recognizing TEC as a distinct clinical entity to avoid unnecessary investigations and to provide appropriate supportive care. The overall prognosis is excellent, with complete recovery expected and no long-term hematologic sequelae.

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*Corresponding author: jovanovska.a@gmail.com

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*Corresponding author: jovanovska.a@gmail.com

Резиме

Транзиторна еритробластопенија во детството: бенигна причина за тешка анемија кај тригодишно дете

Александра Јовановска[1]*, Валентина Цвејоска-Чолаковска[2], Светлана Кочева[1]

[1] Оддел за хематологија и онкологија, Универзитетска клиника за детски болести, Медицински факултет, Универзитет „Св. Кирил и Методиј“, Мајка Тереза 17, 1000 Скопје, Р. Македонија

[2] Оддел за пулмологија и алергологија, Универзитетска клиника за детски болести, Медицински факултет, Универзитет „Св. Кирил и Методиј“, Мајка Тереза 17, 1000 Скопје, Р. Македонија

Клучни зборови: транзиторна еритробластопенија, детство, анемија, ретикулоцитопенија, трансфузија на еритроцити, вирусна инфекција

Транзиторната еритробластопенија во детството (ТЕС) претставува стекнато, самоограничувачко нарушување кое се карактеризира со привремена аплазија на еритроидната клеточна линија кај претходно здрави деца. Лабораториските наоди типично покажуваат нормоцитна, нормохромна анемија со изразена ретикулоцитопенија. Иако етиологијата на ТЕС сè уште не е целосно разјаснета, вирусните инфекции често се сметаат за можен тригер-фактор. Клинички, состојбата најчесто се манифестира со бледило и замор. Третманот е претежно супортивен, а трансфузија на еритроцити се препорачува само кај деца со симптоматска или тешка анемија. Во овој труд е прикажан случај на претходно здраво тригодишно дете кај кое беше дијагностицирана тешка анемија по блага вирусна инфекција и кое имаше потреба од третман со трансфузија на еритроцити. Детето целосно закрепна, со нормализација на хемоглобинот и ретикулоцитите во наредните недели. Раното препознавање на оваа состојба овозможува соодветно менаџирање и одбегнување на непотребни испитувања, а истовремено ја нагласува одличната прогноза поврзана со ТЕС

*Corresponding author: jovanovska.a@gmail.com

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Table 1. Hematologic parameters over time

Time from onset	Hemoglobin (g/L)	Hematocrit (%)	Red blood cell count x 10^{12}/L	Reticulocytes (%)	White blood cell count x 10^{9}/L	Platelet count x 10^{9}/L
week 0	65	19.3	2.37	0.09	6.96	286
week 1	104	31.3	3.88	0.15	8.15	383
week 2	105	32.6	3.93	3.47	8.26	380
week 4	112	34.8	4.00	2.97	14.11	265
week 8	132	39.1	4.84	1.06	8.78	350
week 12	130	38.4	4.56	0.95	8.68	312

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*Corresponding author: jovanovska.a@gmail.com

Table 2. Biochemical and Iron/Vitamin Parameters at Presentation

Parameter	Result	Reference range
ALT (U/L)	11	9-72
AST (U/L)	27	15-59
LDH (U/L)	172	0-500
Total Bilirubin (µmol/L)	5.0	3.0-22.0
Direct Bilirubin (µmol/L)	2.1	0.0-5.0
Creatinine (µmol/L)	36.6	0.0-104.0
BUN (mmol/L)	4.3	2.6-6.4
Iron (µmol/L)	19.5	6.6-26.0
Ferritin (µg/L)	102.0	30.0-400.0
Transferrin (mg/dL)	176.39	130.0-360.0
Vitamin B12 (pg/mL)	323	187-883
Folate (ng/mL)	19.8	3.1-20.5

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*Corresponding author: jovanovska.a@gmail.com