Turkish Journal of Pediatric Disease
Türkiye Çocuk Hastalıkları Dergisi

Polycythemia in a Pediatric Patient with Chronic Kidney Disease: Overuse of Erythropoetin During COVID-19 Isolation

Kronik Böbrek Yetmezliği Tanılı Çocuk Hastada, COVİD-19 İzolasyonu Sırasında Eritropoetin'in Aşırı Kullanımından Dolayı Ortaya Çıkan Polisitemi Olgusu

Yaşar KANDUR[1], Ayşegül ALPCAN[2], Mehmet YOZGAT[2], Serkan TURSUN[2]

[1] Department of Pediatric Nephrology, School of Medicine, Kirikkale University, Kirikkale, Turkey
[2] Department of Pediatrics, School of Medicine, Kirikkale University, Kirikkale, Turkey

ABSTRACT

We describe a case of a patient with Chronic Kidney Disease who developed polycythemia due to Erythropoiesis Stimulating Agents overuse during COVID-19 isolation. A 12-year-old male had not been able to attend routine controls since had been in isolation for 4 months after the COVID-19 outbreak. He had continued to take Erythropoiesis-Stimulating Agents during that period at the starting dose of 150 U/kg/week. He had been on peritoneal dialysis in the last year because of end-stage renal failure. Laboratory investigation revealed a hemoglobin (Hb) level of 20.8 g/dl, hematocrit level of 66%, creatinine level of 6.5 mgr/dl. He underwent daily phlebotomy sessions (10cc/kg/session). During this period aspirin was also started (5mg/kg). After 5 sessions his Hb level decreased to 14 gr/dl and hematocrit to 40%. Pediatric nephrologist should be aware that there is a potential risk of polycythemia with Erythropoiesis Stimulating Agents when Hb level is not appropriately followed on a routine basis.

Key Words: Chronic Kidney Disease, Erythrocyte Stimulating Agent, Polycythemia

ÖZ

COVİD-19 izolasyonu sırasında Eritrosit Stimule Ajanın (ESA) aşırı kullanımına bağlı gelişen polisitemi vakası sunmayı amaçladık. On iki yaşında ki kronik böbrek yetmezliği tanılı erkek hastamız, COVİD-19 pandemisinden dolayı 4 ay boyunca tecritte kaldığı için rutin kontrollerine gelememişti. Bu süre zarfında haftada 100 U/kg idame dozunda ESA almaya devam etti. Hasta periton diyaliz tedavisi altındaydı. Laboratuvar incelemelerinde hemoglobin (Hb) seviyesi 20.8 g/dl, hematokrit % 66, kreatinin 6.5 mgr/dl bulundu. Hastaya günlük flebotomi seansları (10cc/kg/seans) uygulandı. Bu dönemde aspirin tedavisi de başlandı (5 mg/kg). Beş seans sonunda Hb seviyesi 14 gr/dl'ye, hematokriti % 40'a düştü. Kronik Böbrek yetmezliği hastalarında hemoglobin düzeyi rutin şekilde takip edilmediği takdirde ESA' ya bağlı polisitemi gelişebileceği başta aile hekimi olmak üzere tüm hekimler tarafından bilinmeli ve izolasyonda olsa dahi hastalar gerekirse ev ziyarteleri ile takip edilmeli.

Anahtar Kelimeler: Kronik Böbrek Yetmezliği, Eritrosit Uyarıcı Ajan, Polisitemi

INTRODUCTION

Anemia in chronic kidney disease (CKD) is correlated to a decrease in erythropoietin (EPO) production due to kidney dysfunction (1). National Kidney Foundation Dialysis Outcome Quality Initiative (NKF-DOQI) advised that hemoglobin (Hb) levels should be maintained between 11 and 12 g/dL in CKD patients (2). Erythropoiesis-Stimulating Agents (ESAs) are very capable drugs, targeting a significant hemoglobin (Hb) level. Polycythemia refers to an increased hemoglobin concentration in peripheral blood. Drug-induced polycythemia can occur with excess use of ESAs (3). The following values are used to diagnose polycythemia (4): hemoglobin>16.5 g/dL (10.3 mmol/L) in men or >16.0 g/dL (10.0 mmol/L) in women. On 12 January

KANDUR Y : 0000-0002-8361-5558
ALPCAN A : 0000-0001-9447-4263
YOZGAT M : 0000-0002-3001-7589
TURSUN S : 0000-0003-3354-6360

Conflict of Interest /*Çıkar Çatışması:* *On behalf of all authors, the corresponding author states that there is no conflict of interest.*

Financial Disclosure / *Finansal Destek*: The authors declared that this case has received no financial support.

***Confirmation / Onay*:** All human studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Informed consent was obtained from the parents.

How to cite / *Atıf Yazım Şekli* : Kandur Y, Alpcan A, Yozgat M, Tursun S. Polycythemia in a Pediatric Patient with Chronic Kidney Disease: Overuse of Erythropoerin During COVID-19 Isolation. Turkish J Pediatr Dis 2021;15:434-436.

Correspondence Address / Yazışma Adresi :
Yaşar KANDUR
Department of Pediatric Nephrology, School of Medicine, Kirikkale University, Kirikkale, Turkey
E-posta: yaskan30@yahoo.com

Received / Geliş tarihi : 30.11.2020
Accepted / Kabul Tarihi : 27.01.2021
Online published : 14.04.2021
Elektronik yayın tarihi
DOI: 10.12956/tchd.833625

2020, the World Health Organization (WHO) confirmed that a novel coronavirus was the cause of a pandemic respiratory illness. This pandemic has affected many countries including our country. Patients under risk were suggested to be isolated. In the present report, we describe a case of a CKD patient who developed polycythemia due to ESA overuse during COVID-19 isolation.

CASE REPORT

A 12-year-old male was admitted to the hospital with a high hemoglobin level that was detected at routine outpatient evaluation. He had not been able to attend routine controls since he had been in isolation for 4 months after the COVID-19 outbreak. He had continued to take ESA at the maintanance dose of 100 U/kg/week that had been started upon the the diagnosis of anemia at a level of Hb 8.7 gr/dl, 6 months ago. He had a history of nephrotic syndrome (FSGS) for 10 years and had been on peritoneal dialysis in the last year because of end-stage renal failure. On physical examination, his blood pressure was 140/80 mm Hg (he had been on an ACE inhibitor and a calcium channel blocker). Additionally, he had slight facial edema. Laboratory investigation revealed a Hb level of 20.8 g/dl, hematocrit level of 66 %, white blood cell count 11.800/mm^3,

Table I: Patients hemoglobin levels dependent on ESA usage, during follow-up period.

Date	Hb(gr/dl)	ESA dose (U/kg/week)
December 2019	8.7	150
February 2020	11.2	100
16.6.2020	20.8	stopped
20.6.2020	14.0	(after 5 session of phlebotomy)
August 2020	13.9	---
October.2020	7.2	150 (started)

platelet count of 240.000/mm^3, creatinine level of 6.5 mgr/dl, urea level of 135 mg/dl, potassium level of 5.3 meq/L, a sodium level of 143 meq/L, and a parathormone level of 132 pg/ml. Venous blood gas analysis revealed ph:7.39 , bicarbonate 25.2 mEq/L. His urinalysis was normal except the density which was 1005. His previous Hb results were as follows: December 2019: 8.7 gr/dl, February 2020: 11.2 gr/dl (Table I). He was admitted to the hospital and underwent daily phlebotomy sessions (10cc/kg/session). During this period aspirin was also started (5 mg/kg). After 5 sessions, his Hb level decreased to 14 gr/dl and hematocrit to 40 %. He was discharged to return to the outpatient clinic for a check later. ESA was stopped until the time when anemia will re-appear.

DISCUSSION

The introduction of ESAs enabled a dose-dependent treatment of anemia of CKD (5). Erythropoiesis-Stimulating Agents promotes the survival of erythroid progenitors by binding to its receptor. However, clinicians should weigh the risk-benefit ratio of ESAs treatment, based on a reduced transfusion need against the increased risk for serious adverse events. A higher Hb target for anemia improves physiological and clinical parameters as well as the quality of life (6). The 2007 guideline update recommended a target of the range of 11 to 12 g/dL of Hb in all CKD patients, and Hb level should never exceed 13 g/dL (6). The Turkish social security system recommends and also obligates erythropoetin dosage as follows; a starting dose 50-150 Unite/kg/week for Hg<11 gr/dl and a maintance dose 25-75 U/kg/week for Hg 11-12 gr/dl. Our patient received ESA in the light of these guides.

Also known as bloodletting, phlebotomy is a major therapeutic procedure that has been performed by physicians (7). Currently, therapeutic phlebotomy is approved for polycythemia. However, patients can be asymptomatic as was our patient. However, patients may also develop thrombotic events (8). The major goal of treatment is to reduce the rate of thrombotic events. To address thrombotic risk, aspirin should be added to phlebotomy (9). Moreover, a hematocrit level greater than 65% may give rise to symptoms of hyperviscosity. So, we also started aspirin for our patient. By lowering blood viscosity, phlebotomy results in an improvement of cerebral perfusion as well as sensory and mental function (10).

We are of the opinion that pediatric nephrologist should give an increased focus on anemia treatment in CKD, being aware that there is a potential risk of polycythemia with ESAs when Hb level is not appropriately followed on a routine basis. We believe that similar cases of drug under usage or over usage have occurred in patients with CKD during the COVID-19 pandemic. Therefore, these patients should be closely monitored by their family physicians at home by telephone, or by visiting them in person. In addition, as pediatric nephrologists, we should inform other pediatricians and family physicians for risks such as the one experienced by our patient.

REFERENCES

1. Stauffer ME, Fan T. Prevalence of anemia in chronic kidney disease in the United States. PLoS One 2014; 9:e84943.
2. National Kidney Foundation: NKF-DOQI. Clinical practice guidelines for the treatment ofAnemia of chronic renal failure. New York, National Kidney Foundation. AmJ Kidney Dis 2006;47:S11–S145.
3. Robinson N, Giraud S, Saudan C, Baume N, Avois L, Mangin P, Saugy M. Erythropoietin and blood doping. Br J Sports Med 2006;40 Suppl:i30–4.

4. Ibrahim HN, Ishani A, Foley RN, Guo H, Liu J, Collins AJ. Temporal trends in red blood transfusion among US dialysis patients, 1992-2005. Am J Kidney Dis 2008;52:1115-21.
5. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, revised 4th edition, Swerdlow SH, Campo E, Harris NL, et al. (Eds), International Agency for Research on Cancer (IARC), Lyon 2017.
6. Lawler EV, Bradbury BD, Fonda JR, Gaziano JM, Gagnon Dr. Transfusion burden among patients with chronic kidney disease and anemia. Clin J Am Soc Nephrol 2010;5:667-72.
7. KDOQI. KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for anemia in chronic kidney disease: 2007 update of hemoglobin target. Am J Kidney Dis 2007 50: 471-530.
8. Parapia LA. History of bloodletting by phlebotomy. Br J Haematol 2008;143: 490-5.
9. Fallah M, Kharazmi E, Sundquist J, Hemminki K. Higher risk of primary cancers after polycythaemia vera and vice versa. Br J Haematol 2011;153: 283-5.
10. Research C for DE and Drug Safety and Availability - FDA Drug Safety Communication: Modified dosing recommendations to improve the safe use of Erythropoiesis-Stimulating Agents (ESAs) in chronic kidney disease.2017.
11. Berk PD, Wasserman LR, Fruchtman SM, Goldberg JD. Treatment of polycythemia vera: a summary of clinical trials conducted by the Polycythemia Vera Study Group. In: Polycythemia Vera and the Myeloproliferative Disorders, Wasserman LR, Berk PD, Berlin NI (eds), WB Saunders, Philadelphia;1995;166.