European Journal of Case Reports in Internal Medicine

Surviving Extreme Anaemia

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Doi: 10.12890/2021_002357 - European Journal of Case Reports in Internal Medicine - © EFIM 2021

Received: 03/02/2021
Accepted: 08/02/2021
Published: 05/03/2021

How to cite this article: Esteves ME, Fernandes J, Oliveira Monteiro P, Almeida M, Nogueira-Silva L, Almeida J. Surviving extreme anaemia. *EJCRIM* 2021;**8**: doi:10.12890/2020_002357.

Conflicts of Interests: The Authors declare that there are no competing interests.

ABSTRACT

Before the development of transfusion medicine, severe anaemia was an important cause of morbidity and mortality. The discovery of haematopoietic mechanisms and essential nutrients made it possible to easily treat and prevent this condition. Nevertheless, it is often fatal in patients presenting with extreme anaemia (haemoglobin levels <2 g/dl). We report the rare case of a 54-year-old woman who presented with profound megaloblastic anaemia (haemoglobin of 1.7 g/dl) due to vitamin B12 deficiency, and was successfully treated.

LEARNING POINTS

- The discovery of vitamin B12 in the 20th century led to the successful and easy treatment of thousands of patients with anaemia.
- Focus on patient adherence to treatment and medical advice is essential in order to manage chronic conditions such as post-gastrectomy nutritional deficiencies.
- Extreme anaemia is very rare and associated with high mortality; treatment should be tailored to acute or chronic anaemia and in cases where haemodynamic stability is guaranteed, a restrictive blood transfusion strategy should be considered to reduce the risk of complications.

KEYWORDS

Severe anaemia, vitamin B12, nutritional deficiency

INTRODUCTION

Active blood loss is usually the main concern when extreme anaemia is found: significant acute-onset bleeding without proper management can develop into haemorrhagic shock and death. Other more insidious disorders, such as cancers, infections, malnutrition, and haemopoietic or drug-induced conditions, can also cause severe anaemia. Increased cardiac output, decreased peripheral vascular resistance, and decreased oxygen affinity of red blood cells (RBC) are some of the physiological changes that occur in response to anaemia, and patients will develop dyspnoea, easy fatigue, or tachycardia on exertion, and usually resort to healthcare before haemoglobin levels start to plummet.

When a restrictive blood transfusion strategy is implemented, moderate anaemia (haemoglobin (Hb) of 7–10 g/dl) is not associated with increased mortality [1]. In patients without major haemorrhage, chronic anaemia or acute coronary syndrome, the Hb level threshold for RBC transfusion is currently 7 g/dl [2, 3], as morbidity and mortality increases when Hb levels are below 7 g/dl. Carson et al. [4] retrospectively

studied the relationship between the nadir of postoperative Hb levels and mortality, in 300 patients who refused blood transfusions, and showed that the 30-day mortality for Hb of 7–8 g/dl was 0%. However, it increased significantly when values were lower than 5 g/dl: 34% for 4–5 g/dl, 25% for 3–4 g/dl, 54% for 2–3 g/dl, and 100% for 1–2 g/dl (n=7). These outcomes have not been studied for patients with very severe chronic anaemia.

CASE DESCRIPTION

We report the case of a 54-year-old woman admitted at the emergency department with severe fatigue and functional limitation, having been bedridden for the past few months following a 5-year progressive deterioration of general status. In addition to the asthenia, she complained of paraesthesia in all four limbs (without any discernible pattern), episodes of self-limiting lower limb palsy (affecting both legs in an alternating fashion), and frequent falls in the last year which she said were caused by dizziness and lack of balance. She denied any relevant trauma or evident blood loss. Throughout this lengthy period, she had always refused to seek medical attention.

At 49 years of age, she had been diagnosed with gastric cancer (an antral ulcerated lesion with histological features of adenocarcinoma with a solid tubular pattern with isolated signet ring cells, pT3N0R0) and underwent total gastrectomy and chemotherapy (8 cycles, capecitabine plus oxaliplatin), without any complications, but was lost to follow-up at the end of the treatment.

Further information concerning the patient's history obtained from her family and her electronic medical records revealed she had experienced severe asthenia after the chemotherapy had ended and had since declined any external support or healthcare assistance. They also confirmed the absence of any evident blood loss. The patient only agreed to go to the emergency department due to the persistence of her son, who contacted the national pre-hospital emergency system. The family did not provide any further explanations besides the refusal of the patient to seek any medical attention.

On physical examination, we found a prostrated, emaciated and severely malnourished individual, showing severe cutaneous and mucosal pallor and severe peripheral oedema. She was somnolent, but easily awaken by verbal stimuli (Glasgow Coma Scale score of 14 due to confusion). Besides a global decrease in muscle strength due to the evident sarcopenia, she showed no other focal neurological deficits, including sensory or proprioceptive dysfunction. Peripheral oxygen saturation was 83%, although she was eupnoeic: arterial blood gas analysis showed a PaO_2 of 93 mmHg but an unmeasurable Hb (pH 7.48, $PaCO_2$ 29 mmHg, HCO_3- 22 mmol/l, lactate 6.74 mmol/l, glucose 107 mg/dl). She presented with sinus tachycardia ranging from 90 to 120 bpm, an arterial blood pressure of 80/44 mmHg, and a prolonged capillary refill time. There were no other positive findings on examination.

Laboratory studies on admission (*Table 1*) showed extreme macrocytic anaemia (Hb of 1.7 g/dl, mean corpuscular volume (MCV) of 121.4 fl and haematocrit of 5.1%), signs of haemolysis (high indirect bilirubin of 1.15 mg/dl, remarkably high LDH of 5063 U/l, haptoglobin consumption, and negative Coombs test), thrombocytopenia of 59×10^9 platelets/l, and a normal leucocyte count. Even though blood samples were scarce, upon suspicion of megaloblastic anaemia, the laboratory managed to broaden the blood analysis: vitamin B12 was not measurable (<84 pg/ml), and folic acid deficiency and HIV infection were excluded (*Table 1*).

The patient was admitted to the ICU and a slow correction of the anaemia was started with 2 units of packed RBC, parenteral correction of vitamin B12 deficiency (1 mg once daily) and oral supplementation with folic acid (5 mg once daily). Ultrasonography and thoraco-abdominal computed tomography (CT) showed generalized subcutaneous oedema, and mild pleural and pericardial effusions, but no other findings or signs of cancer relapse. A cerebral CT scan excluded intracranial lesions.

Haemodynamic stability was achieved without the need for more blood products, and there was sustained haematological improvement with the described strategy. Platelet levels reached a minimum of 28×10^9/l on day 3 but started to improve on day 4 and were within the normal range on day 5. On the 5th day of hospitalization, haemoglobin (Hb) was 8.5 g/dl, haemolysis markers were steadily decreasing, and the patient's symptoms were improving, so she was transferred to the medical ward.

She received nutritional and psychiatric evaluation, and the treatment plan was adjusted. Six days later, she was discharged home for outpatient management.

On patient follow-up at 3 and 5 months, she showed normal haematological values, total functional autonomy, and resolution of the peripheral neuropathic symptoms.

DISCUSSION

The vast majority of vitamin B12 uptake in the gastrointestinal tract depends on its binding with the intrinsic factor produced by gastric parietal cells and its absorption in the distal ileum. Conditions compromising nutritional intake and diseases causing dysfunction of gastric parietal cells and the associated absence of intrinsic factor, or dysfunction of the distal ileum, will result in B12 deficiency as the body's stores start to become depleted [5]. Patients may present with a macrocytic anaemia (macrocytic red cells, anisocytosis, macroovalocytes, which were first described in 1855 by Addison [6]), leukopenia, thrombocytopenia, signs of intravascular haemolysis, elevated levels of

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	Admission	Day 1	Day 2	Days 3-4	Day 5	Day 6	3 Months	5 Months
Haemoglobin (g/dl)	↓1.7	↓4.7	↓7.6	↓8.5–8.6	↓8.2	↓8.7	14.7	14.5
Haematocrit	↓5.1%	↓13.4%	21%			27.7%	44.4%	44.4%
MCV (fl)	↑121.4	92	91.1			92.5	83.5	85.2
MCH (pg)	↑40.5	32	32			29.5	27.6	27.8
RDW-SD (fl)	↑105	48.5	49.3			54.7	44.3	41.4
Reticulocytes ($\times 10^{12}$/l)		↓1.45			2.84			
Leucocytes ($\times 10^{9}$/l)	4.25	4.49	5.24	2.25–2.33	3.12	3.84	6.39	8.99
Neutrophils	2.76					1.55		4.79
Lymphocytes	1.4					1.69		3.46
Monocytes	0.06					0.33		0.41
Eosinophils	0.01					0.26		0.29
Immature granulocytes	0.02					0.01		
Platelets ($\times 10^{9}$/l)	↓59	↓38	↓28	↓50–121	154	218	175	233
Peripheral blood smear	Anisocytosis, poikilocytosis,							
Hypochromia	0–2 Schizocytes			Platelet rouleaux				
Lactate dehydrogenase (U/l)	↑5063	↑3515	↑3320			↑1878	216	236
Haptoglobin (mg/dl)	<8							
Total bilirubin (mg/dl)	↑3.7	↑2.54	↑3.54		0.87	0.59	0.54	0.35
Indirect bilirubin (mg/dl)	↑1.15		0.83		0.27			0.06
Coombs tests	Negative							
HIV 1+2 antigen and antibody	Negative							
Folic acid (ng/dl)	↓7.8							>20
Vitamin B12 (pg/ml)	↓<83				>2000		1412	1361
Iron (µg/dl)	190						112	70
Transferrin (ng/dl)	150						297	295
Transferrin saturation	↑90%						27%	17%
Ferritin (ng/ml)	207						61.3	

DOI: 10.12890/2021_002357

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	Admission	Day 1	Day 2	Days 3-4	Day 5	Day 6	3 Months	5 Months
Aspartate transaminase (U/l)	↑175	↑189	↑173		27	34	27	24
Alanine transaminase (U/l)	↑187	↑258	↑290		81	71	24	26
Gamma-glutamyl transferase (U/l)	22	24	21		19	20	20	19
Alkaline phosphatase (U/l)	59	55			46		163	191
C-reactive protein (mg/l)	6					0.8		
Sedimentation rate (mm/1st h)						6		
Total protein (g/l)	↓51.8						75.2	
Albumin (g/l)	↓33.4	↓26.3			↓29		44.9	
Serum protein electrophoresis							Normal	
Uric acid (mg/dl)	9.3						4.3	
Urea (mg/dl)	67						30	
Creatinine (mg/dl)	1.03						0.59	
Troponin I – hs (ng/l)	8.6							
Brain natriuretic peptide (pg/ml)	627						27	
Thyroid-stimulating hormone (IU/ml)	2.34						1.66	
Classic gastric tumour markers								
CEA (ng/ml)								1.7
CA 19.9 (U/ml)								7
CA 72.4 (U/ml)								0.5

hs, high sensitivity; MCH, mean corpuscular haemoglobin; MCV, mean corpuscular volume; RDW-SD, red cell distribution width-standard deviation.

Table 1 Laboratory results throughout patient follow-up

homocysteine and methylmalonic acid, and a wide spectrum of neurological symptoms ranging from altered mental status and cognitive defects, to myelopathy and peripheral neuropathy [5].

The discovery of vitamin B12 and its biochemical role in humans has spanned two centuries of breakthroughs, clinical reports and pivotal studies [6], leading to two different Nobel Prizes (Medicine in 1934 [7, 8] and Chemistry in 1964). Consequently, vitamin B12 deficiency can now be easily diagnosed and treated [6]. Even though dietary deficiency and pernicious anaemia are frequently found in the general population, and the number of patients surviving gastrointestinal disorders and surgery has increased, extreme insufficiency presenting as life-threatening anaemia, pancytopenia or myelopathy, is far less common than in the past.

In 1947, MacDonald et al. had already recognized the development of a macrocytic anaemia in gastrectomized patients, "if they live long enough", and its morphological similarity to the "Addisonian anaemia" [9]. In 1966, Williams et al. demonstrated the benefit of permanent vitamin B12 supplementation after gastrectomy, regardless of the presence of haematological signs [10]. Currently, it is standard practice to guarantee lifelong adequate iron, B12 and folate monitoring in this set of patients.

In our patient's case, the loss to follow-up after her gastrectomy hindered the appropriate follow-up and supplementation. Such an extremely low haemoglobin level only seems possible if there has been a slow and progressive depletion of B12 stores along with physiological and functional adaptation to the progressive anaemia. Active bleeding was excluded as the patient reported no gastrointestinal or genitourinary blood loss, a CT scan showed no signs of internal bleeding or recurrence of oncological disease, and all haematological parameters steadily improved under treatment.

While we are aware of several anecdotal unpublished reports, we only found 23 published reports of patients with similar anaemia (haemoglobin levels <2 g/dl). The lowest value recorded in a patient who survived was 0.4 g/dl. Our case seems to be the third reported of a patient surviving what seems to be extreme chronic anaemia (*Appendix Table 1*) [11, 12].

In the absence of haemorrhagic shock, the standard therapy in these patients was treatment with a restrictive transfusion strategy, supporting haemodynamic and symptom stability, as transfusion complications such as ischaemic stroke, reversible cerebral vasoconstriction syndrome and hyperhaemolysis can occur. This is similar to the treatment provided to our patient, who recovered without any sequelae or complications.

CONCLUSION

Reports of patients with extreme anaemia (Hb <2 g/dl) are now very rare after the advent of blood transfusion medicine in the second half of the 20th century, along with wider access to better healthcare, improved management of critical situations and bleeding control, the implementation of enteral and parenteral supplementation with iron, folate and vitamin B12, and active anaemia screening in the general population.

As reported anecdotally in the literature, this type of severe anaemia only seems to be possible if there is slow progressive depletion of vitamin B12 stores in the absence of adequate nutrition. Adherence to treatment and medical advice is essential in patients who will also require life-long follow-up.

REFERENCES

1. Roubinian NH, Murphy EL, Mark DG, Triulzi DJ, Carson JL, Lee C, et al. Long-term outcomes among patients discharged from the hospital with moderate anemia: a retrospective cohort study. *Ann Intern Med* 2019;**170**(2):81–89.
2. NICE. Blood transfusion, NICE guideline [NG24] Published date: 18 November 2015. Available from https://www.nice.org.uk/guidance/ng24
3. Mueller MM, Van Remoortel H, Meybohm P, Aranko K, Aubron C, Burger R, et al. Patient blood management: recommendations from the 2018 Frankfurt Consensus Conference. *JAMA* 2019;**321**(10):983–997.
4. Carson JL, Noveck H, Berlin JA, Gould SA. Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion. *Transfusion* 2002;**42**(7):812–818.
5. Stabler SP. Vitamin B12 deficiency. *N Engl J Med* 2013;**368**(2):149–160.
6. Scott JM, Molloy AM. The discovery of vitamin B12. *Ann Nutr Metab* 2012;**61**:239–245.
7. Minot GR, Murphy WP. Treatment of pernicious anemia by a special diet. *J Am Med Assoc* 1926;**87**(7):470–476.
8. Castle WB, Ham TH. Landmark article Oct 31, 1936: Observations on the etiologic relationship of achylia gastrica to pernicious anemia. V. Further evidence for the essential participation of extrinsic factor in hematopoietic responses to mixtures of beef muscle and gastric juice and to hog stomach mucosa. By W.B. Castle and T.H. Ham. *JAMA* 1984;**251**(4):514–521.
9. MacDonald RM, Ingelfinger FJ, Belding HW. Late effects of total gastrectomy in man. *N Engl J Med* 1947;**237**(24):887–896.
10. Williams JA, Baume PE, Meynell MJ. Partial gastrectomy: the value of permanent vitamin-B-12 therapy. *Lancet* 1966;**1**(7433):342–344.
11. Lindgren A, Lasson A. [Hb 17g/1! The patient survived without obvious sequelae. A case report of extreme pernicious anemia]. *Lakartidningen* 2008;**105**(43):3015–3017.
12. Shiraishi W, Une H, Iwanaga Y, Yamamoto A. A case of post-transfusion posterior reversible encephalopathy syndrome with cerebral hemorrhage that may be associated with fat-soluble vitamin deficiency. *Clin Neurol* 2014;**54**(6):518–521.

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	Year	Age, gender	Diagnosis	Hb nadir	Treatment	Outcome	Notes
Biesma et al. [1]	1997	21 y, M	Haemolytic anaemia secondary to B19 parvovirus infection in a sickle-cell β-thalassemia patient	1.13 g/dl	RBC transfusion	Improved	
Zollinger et al. [2]	1997	58 y, F	Haemorrhagic complications during spinal tumour excision	1.1 g/dl	RBC transfusion	Improved	
Yamashita et al. [3]	1999	42 y, F	Uterine myoma	1.2 g/dl	RBC transfusion Hysterectomy	Improved	
Imaizumi et al. [4]	1999	61 y, M	Haematuria due to bladder tumour	1.8 g/dl	RPC transfusion	Improved	
Heo et al. [5]	2003	47 y, F	Aplastic anaemia	1.5 g/dl	RBC transfusion	Improved	Complicated after RBC transfusion with RCVS and PRES
Lindgren et al. [6]	**2008**	**?**	**Pernicious anaemia**	**1.7 g/dl**	**Unknown**	**Improved**	**Article in Swedish, not available**
Schuettpelz et al. [7]	2009	6 y, F	Ceftriaxone-induced haemolytic anaemia in a sickle cell disease patient	0.4 g/dl	RBC transfusion Corticosteroids and IVIG Plasmapheresis	Improved	Complicated afterwards with ischaemic stroke. On discharge was under neurorehabilitation and improving
Kunzmann et al. [8]	2010	23 y, F	Piperacillin-induced haemolytic anaemia	1.6 g/dl	RBC transfusion Corticosteroids	Improved	
Dai et al. [9]	2010	53 y, M	Haemorrhagic shock due to multiple stab wounds	0.7 g/dl	RBC transfusion Balanced salt solution and plasma substitutes	Improved	Extreme haemodilution in which appropriately crossmatched blood was not available
De Prost et al. [10]	2012	27 y, M	Acute splenic sequestration in a sickle cell disease patient	1.7 g/dl	RBC transfusion Splenectomy	Improved	
Rovira et al. [11]	2013	26 y, F	Immune haemolytic anaemia following allogeneic stem cell transplantation	<2 g/dl	RBC transfusion Corticosteroids and IVIG Splenectomy	Death	No access to lowest Hb level – values derived from graphic interpretation
Graffeo et al. [12]	2013	39 y, F	Placental abruption complicated with haemorrhagic shock and disseminated intravascular coagulation	1.9 g/dl	Caesarean delivery EPO Hyperbaric oxygenation	Improved	Refused blood components
Odronic et al. [13]	2014	53 y, F	Cocaine-induced microangiopathic haemolytic anaemia	1.8 g/dl	RBC transfusion Plasmapheresis	Improved	

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	Year	Age, gender	Diagnosis	Hb nadir	Treatment	Outcome	Notes
Yeykal et al. [14]	2014	43 y, M	GI bleeding secondary to C. difficile colitis	1.8 g/dl	EPO, iron and folate supplements Aminocaproic acid, FFP and VIIIa coagulation factor IVIG Surgery	Improved	Refused blood components
De Araújo et al. [15]	2014	27 y, F	Haemorrhagic complications during surgical correction of scoliosis	1.4 g/dl	Normovolaemic haemodilution Hyperoxic ventilation EPO, iron, vitamin B12 and folate supplements	Improved	Refused blood components
Dou et al. [16]	2014	50 y, F	Menorrhagia (uterine leiomyoma and adenomyosis)	1.5 g/dl	RBC transfusion	Improved	Complicated after RBC transfusion with PRES
	2014	46 y, F	Menometrorrhagia (uterine leiomyoma)	1.4 g/dl			
Shiraishi et al. [17]	**2014**	**36 y, F**	**Severe malnutrition due to peculiar eating habits**	**1.4 g/dl**	**RBC transfusion Iron, vitamin B complex and folate supplements**	**Improved**	**Complicated after RBC transfusion with PRES and multiple intracranial haemorrhages and visual disturbances (also due to vitamin K and A deficiency)**
Singh et al. [18]	2015	36 y, F	Menorrhagia (uterine fibroid)	1.7 g/dl	RBC transfusion	Improved	Complicated after RBC transfusion with development of PRES
Lim et al. [19]	2015	68 y, F	Chinese traditional medicine consisting of frequent bloodletting ('Sahyeol') in a patient with schizoid personality disorder	1.4 g/dl	RBC transfusion Iron supplement	Improved	1 Year after, she returned to bloodletting habits and was admitted again with values of Hb of 1.5 g/dl – after she was transferred to a neuropsychiatry ward
Chojnowski et al. [20]	2016	22 y, M	Acute pre-T-lymphoblastic leukaemia patient undergoing induction and consolidation therapy	1.3 g/dl	EPO, iron and folate supplements Total parenteral nutrition	Improved	Refused blood components
Schmitt et al. [21]	2016	34 y, M	Colon adenocarcinoma	1.8 g/dl	RBC transfusion Iron supplement	Improved	
Bienz et al. [22]	2020	NB, M	Fetomaternal haemorrhage	1.2 g/dl	RBC transfusion	Improved	

The only two cases of extreme chronic anaemia are highlighted (in bold). EPO, erythropoietin; F, female; FFP, fresh frozen plasma; Hb, haemoglobin; IVIG, intravenous immunoglobulin; M, male; NB, new-born; PRES, posterior reversible encephalopathy syndrome; RBC, red blood cells; RCVS, reversible cerebral vasoconstriction syndrome; y, years.

Appendix Table 1. Case reports of extreme anaemia (Hb <2 g/dl) in the literature

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APPENDIX REFERENCES

1. Biesma DH, Nieuwenhuis HK. Life-threatening anaemia caused by B19 parvovirus infection in a non-immunocompromised patient. *Neth J Med* 1997;**50**(2):81–84.
2. Zollinger A, Hager P, Singer T, Friedl HP, Pasch T, Spahn DR. Extreme hemodilution due to massive blood loss in tumor surgery. *Anesthesiology* 1997;**87**(4):985–987.
3. Yamashita S, Matsumiya N, Fujii T, Yamaguchi H. A case of progressive congestive heart failure secondary to severe anemia in a patient presenting with uterine hemorrhage. *Resuscitation* 1999;**42**(1):69–72.
4. Imaizumi T, Yagi E, Ushijima K, Suzuki K, Terasaki H, Imaizumi T. A patient with a preoperative hemoglobin concentration of 1.8 g/dL: how was the life-threatening anemia tolerated without any intensive care? *J Anesth* 1999;**13**(2):125–126.
5. Heo K, Park SA, Lee JY, Lee BI, Lee SK. Post-transfusion posterior leukoencephalopathy with cytotoxic and vasogenic edema precipitated by vasospasm. *Cerebrovasc Dis* 2003;**15**(3):230–233.
6. Lindgren A, Lasson A. [Hb 17g/1! The patient survived without obvious sequelae. A case report of extreme pernicious anemia]. *Lakartidningen* 2008;105(43):3015–3017.
7. Schuettpelz LG, Behrens D, Goldsmith MI, Druley TE. Severe ceftriaxone-induced hemolysis complicated by diffuse cerebral ischemia in a child with sickle cell disease. J Pediatr *Hematol Oncol* 2009;**31**(11):870–872.
8. Kunzmann S, Thomas W, Mayer B, Kuhn S, Hebestreit H. Immune-mediated severe hemolytic crisis with a hemoglobin level of 1.6 g/dl caused by anti-piperacillin antibodies in a patient with cystic fibrosis. *Infection* 2010;**38**(2):131–134.
9. Dai J, Tu W, Yang Z, Lin R. Intraoperative management of extreme hemodilution in a patient with a severed axillary artery. *Anesth Analg* 2010;**111**(5):1204–1206.
10. de Prost N, Bartolucci P, Boroli F, Moroch J, Galacteros F, Brun-Buisson C, et al. Extreme acute anemia in an adult sickle cell disease patient: look at the spleen. *Intensive Care Med* 2012;**38**:337–338.
11. Rovira J, Cid J, Gutierrez-Garcia G, Pereira A, Fernandez-Aviles F, Rosinol L, et al. Fatal immune hemolytic anemia following allogeneic stem cell transplantation: report of 2 cases and review of literature. *Transfus Med Rev* 2013;**27**(3):166–170.
12. Graffeo C, Dishong W. Severe blood loss anemia in a Jehovah's Witness treated with adjunctive hyperbaric oxygen therapy. *Am J Emerg Med* 2013;31(4):**756**.e3-4.
13. Odronic S, Quraishy NJ, Manroa P, Kier Y, Koo A, Figueroa P, et al. Cocaine-induced microangiopathic hemolytic anemia mimicking idiopathic thrombotic thrombocytopenic purpura: a case report and review of the literature. *J Clin Apher* 2014;**29**(5):284–289.
14. Yeykal JM, Stausmire JM, Ahmed MY, Pai A. Right hemicolectomy in a severely anemic Jehovah's witness patient with an extremely low preoperative hemoglobin level and the decision to operate. *J Am Osteopath Assoc* 2014;**114**(12):930–935.
15. De Araújo Azi LMT, Lopes FM, Garcia LV. Postoperative management of severe acute anemia in a Jehovah's Witness. *Transfusion* 2014;**54**(4):1153–1157.
16. Dou YH, Fuh JL, Chen SP, Wang SJ. Reversible cerebral vasoconstriction syndrome after blood transfusion. *Headache* 2014;**54**(4):736–744.
17. Shiraishi W, Une H, Iwanaga Y, Yamamoto A. A case of post-transfusion posterior reversible encephalopathy syndrome with cerebral hemorrhage that may be associated with fat-soluble vitamin deficiency. Clin Neurol 2014;54(6):518–521.
18. Singh K, Gupta R, Kamal H, Silvestri NJ, Wolfe GI. Posterior reversible encephalopathy syndrome secondary to blood transfusion. *J Clin Neurosci* 2015;**22**(3):592–594.
19. Lim W-H, Kim S-H, Kim H-L, Kim K-H, Na SH, Lee H-J, et al. Recurrent acute decompensated heart failure owing to severe iron deficiency anemia caused by inappropriate habitual bloodletting. *J Cardiovasc Ultrasound* 2015;**23**(4):253–256.
20. Chojnowski K, Janus A, Bliźniewska K, Robak M, Treliński J. Long-lasting extreme anemia during the therapy of acute lymphoblastic leukemia in a Jehovah's Witness patient. *Transfusion* 2016;**56**(10):2438–2442.
21. Schmitt RE, Buckley CJ. Extreme anemia (hemoglobin 1.8 g/dL) secondary to colon cancer. *Proc (Bayl Univ Med Cent)* 2016;**29**(4):393–394.
22. Bienz MN, Hsia C, Waye JS, Bode M, Solh Z. A novel human β-globin gene variant [Hb London-Ontario, HBB: c.332T>G] is associated with transfusion-dependent anemia in a patient with a hemoglobin electrophoresis pattern consistent with β-thalassemia trait. *Hemoglobin* 2019;**43**(2):129–131.