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CASE STUDY

SYMPTOMATIC IRON DEFICIENCY TREATMENT BEYOND THE GUIDELINES

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ABSTRACT

Iron deficiency anemia defined as diminished red blood cells due to several causes which lead to low iron stores in the body. In this case report, an adult female who has a symptomatic iron deficiency, while her complete blood count and serum ferritin level were within lower normal levels. Continuous treatment with oral iron over many years never improved her complain. She responded to parenteral iron infusions, which she still require over the last three years. This case is a clear example that patients biochemical elements level is variant, and not all patients respond to one scale of treatment; it also shows the effect of the flexibility in using the guideline protocols in treating the rare cases.

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INTRODUCTION

The guidelines are document plans used in specific diseases for diagnosis and treatment. It is the best of the research and professional work accumulative experience. Sometimes they are not effective because of the disease variations or due to the heterogeneity of patients' response to treatments [1]. Iron deficiency anemia (IDA) defined as a reduction in red blood cells (RBC) and hemoglobin (Hb) production due to diminished stored iron in the body [2]. Serum ferritin reflects iron stores; it is also an acute phase reactant protein, which increases in patients with chronic inflammation or infection, so IDA could exist even when serum ferritin is within normal level [3]. Many patients with IDA are not responding to oral iron treatment, due to acquired defects of inflammatory intestinal mucosa disorders, which lead to refractory oral iron treatment, which usually corrected only by parenteral iron supplementation.

Careful investigations for nonresponders to oral iron therapy revealed an absorptive defect for iron. There is at least one well-documented instance of an acquired defect of the iron delivery problem associated with signs of iron deficient erythropoiesis caused by loss of human transferrin receptor function [4]. Defective iron absorption also may occur in celiac disease, tropical sprue or other malabsorption syndromes [5]. Iron stores could deplete if iron requirements become more than intake as in puberty, pregnancy or chronic blood loss as in heavy menstruation, piles or cancer colon [6]. Signs of IDA are pallor, palpitations, hair loss, faint, glossitis, angular cheilitis, koilonychia, brittle and weak nails, symptoms of fatigue, anxiety sleepiness, tinnitus, poor appetite, restless legs syndrome [7]. The aim of reporting this case because of the complaint of iron deficiency without anemia and because of the effectiveness of the treatment plan which was beyond the guideline protocols. This case also could indicate the variation of the normal level of the biomedical elements, and the need for treating some cases in lower normal levels of serum ferritin.

Case presentation

39 years old female patient presented with symptoms of IDA in the form of fatigue, sleepiness, palpitations, occasional faint. She has no signs or symptoms of celiac disease, no psychological problems, no menorrhagia or any blood loss, no weight loss or any sign of infection, malignancy or any chronic disorder. She has normal RBC count, Hb, normal Mean corpuscular volume (MCV), mean corpuscular hemoglobin(MCH) and serum ferritin. She was treated with oral iron for

three years with no response in increasing serum ferritin level. Due to the severe symptoms of iron deficiency manifestations, she was treated with parenteral iron Saccharate Complex 2oo mg daily for five days, where she showed an excellent response to increasing serum ferritin level and improving clinical status to normal. When her serum ferritin dropped again after three months to lower normal levels, she presented again with same symptoms of iron deficiency. Since about three years this lady still not responding to oral iron, and she requires intravenous iron on regular basis although her hemoglobin is normal and serum ferritin drop to lower normal level. The laboratory results as follow complete blood count and serum ferritin during the course of treatment with parenteral iron [Table 1]. White Blood Cell : 6.8 (4.0-10) 10^9 /L, RBC: 4.81 (3.8-4.8) 10^{12}/L, Haemoglobin: 126 (120-150) g/L, Haematocrit: 0.376 (0.36-0.46) L/L, Platelet Count : 170 (150-410) 10^9/, MCV : 79 (83-101) fl, MCH : 26 (27-32) pg, mean corpuscular haemoglobin concentration (MCHC) : 332 (315-345) g/L . Biochemistry results : Total protein: 67 (61-79) g/L, Albumin: 41 (35-48) g/L, Total Bilirubin: 16 (3-25) Umol/L, Alanine transaminase: 29 (10-60) IU/L, aspartate aminotransferase: 21 (10-42) IU/L, Glucose: 4.8 (3.9-6.1) mmol/L, potassium: 3.77 (3.6-5.1) mmol/L, Sodium: 139 (134-144) mmol/L, Calcium: 2.29 (2.1-2.6) mmol/L, Renal functions: Blood urea nitrogen: 3.2 (2.5-7.1) mmol/L, Creatinine: 48 (53-97) mmo . Thyroid-stimulating hormone: 1.27 (0.43 -4.1) uLu/ml. Ferritin: 12.8 (11-306.8 ng/ml). Vitamin D: 66.10 (50-75) nmol/L, International normalized ratio (INR) :1.02, activated partial thromboplastin time (APTT) : 34.8 (26-37) second, High-performance liquid chromatography (HPLC) : Hb A: 97.39 (96-98) %, Hb F: <1 %; Hb A2: 2.61 (1.5-3.5) %.

Table 1 Complete blood count and serum ferritin levels during the course of treatment

Time	WBC	RBCs	Hb	HCT	MCV	MCH	PLCT	Ferritin
After 18 months	6.2	4.78	128	0.397	83	27	204	69.4
After 15 months	5.0	4.50	124	0.377	84	28	177	150.6
After 12 months	5.1	4.63	125	0.386	83	27	165	70.5
After 9 months	6.2	4.59	125	0.384	84	27	198	35.2
After 6 months	6.5	4.79	130	0.396	83	27	201	51.3
After 3 months	5.2	4.52	124	0.375	83	28	178	34.0
On presentation	6.8	4.81	126	0.376	79	26	170	12.8

DISCUSSION

The biochemical markers have several limitations because influenced by many factors, and the normal range is not statistically applicable to all people in the same standard, but there is always standard of deviation, that is why there are some methods of treatment beyond the guidelines [8, 9, 10]. In this case modulating the treatment was the only solution to treat this lady with long-standing agony, after all, other conventional methods of treatment were failed. **Iron store** of this patient is consistent with normal reference range. Her hemoglobin and all other investigations are within the normal values; in the meanwhile, she showed unexpected manifestations of severe iron deficiency. The iron element has a vital cofactor functions in many biochemical processes, such as oxygen transport, cellular respiration, lipid metabolism, tricarboxylic acid cycle, gene regulation and DNA synthesis. That explains the generalized effect of iron deficiency on all over the body activity and functions [11]. According to IDA, this case should not be treated because of the normal values of RBC, Hb, serum ferritin and other CBC parameters, without having any infection, chronic inflammation or malignancy. When this patient commenced on oral iron, there was no response, while the parenteral iron raised serum ferritin level significantly, and the symptoms of iron deficiency disappeared. That means not all people have the same reference range values. As in this patient, iron deficiency manifestations started when serum ferritin was within lower normal range. The conflict between the guidelines and the patient's need could be faced in the clinical practice [12, 13 and 14]. The physicians should be aware of this conflict which could happen in some occasion between the guidelines and the patient's requirement [15]. In the unusual cases, the senior clinicians may evaluate the benefit of a drug versus its side effect with the patient's need and that should be reported to update the guidelines protocols. Patients' complaints must be taken into consideration, especially when the treatment is not toxic to the patient. This case shows the effect of the flexibility in using the guidelines protocols in facing the unusual situations. This study adds to the literature a beyond guideline case report in iron deficiency treatment beside other beyond guideline treatment in oncology, vascular and bronchial asthma and some other disorders [16, 17, 18 and 19]. The manifestations of general weakness in females are common which could indicate the need to increase up to the lower level of the reference value of serum ferritin [20].

CONCLUSION

Despite the great importance of the guidelines, the beyond guideline treatments were used in several diseases. We used it in this case with good response. That indicates the need to update the treatment methods it also indicates the variation in the lower reference value of serum ferritin level, especially in females.

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References

1. Siemieniuk RA, Agoritsas T, Macdonald H, Guyatt GH, Brandt L, Vandvik PO (2016). "introduction to BMJ Rapid Recommendations." BMJ. 354: i5191
2. Mathew W Short and Jason E Domagalski. Iron Deficiency Anemia: Evaluation and Management. Volume 87, Number 2, January 15, 2013. American Academy of Family Physicians .same

3. Goddard AF, James MW, McIntyre AS, Scott BB; British Society of Gastroenterology. Guidelines for the management of iron deficiency anemia. *Gut*. 2011; 60(10):1309-1316. same
4. Shuangying Hao, Huihui Li, Xiaoyan Sun, Juan Li, Kuanyu Li. An unusual case of iron deficiency anemia is associated with the extremely low level of transferrin receptor. *Int J Clin Exp Pathol* 2015;8(7):8613-8618
5. Luigia De Falco, Mayka Sanchez, Laura Silvestri *et al*. Iron refractory iron deficiency anemia. ©2013 Ferrata Storti Foundation. doi:10.3324/haematol.2012.075515
6. Nazanin Abbaspour, Richard Hurrell, and Roya Kelishadi. Review on iron and its importance for human health. *J Res Med Sci*. 2014 Feb; 19(2): 164-174
7. Tanmay Padhi & Swetalina Pradhan. Prevalence of restless legs syndrome in leprosy patients. *Lepr Rev* (2014) 85, 218-223
8. Colombo M, Sangiovanni A. Treatment of hepatocellular carcinoma: beyond international guidelines. *Liver Int.* 2015 Jan; 35 Suppl 1:129-38. doi: 10.1111/liv.12713.
9. Anais Vallet-Pichard and Stanislas Pol. Hepatitis B virus treatment beyond the guidelines: special populations and consideration of treatment withdrawal. *Ther Adv Gastroenterol* 2014, Vol. 7(4) 148-155
10. Asai Y, Baibergenova A, Dutil M, *et al*. Management of acne: Canadian clinical practice guideline. CMAJ : *Canadian Medical Association Journal*. 2016; 188(2):118-126. doi:10.1503/cmaj.140665.
11. G. Cairo, F Bernuzzi, and S. Recalcati.A Precious Metal: Iron, An Essential Nutrient for all Cells. *Genes & Nutrition* Vol. 1, No. 1, pp. 25-40, 2006
12. Chen AI1, Advani RH. Beyond the guidelines in the treatment of peripheral T-cell lymphoma: new drug development. *J Natl Compr Canc Netw*. 2008 Apr; 6(4):428-35.
13. Vallet-Pichard A, Pol S. Hepatitis B virus treatment beyond the guidelines: special populations and consideration of treatment withdrawal. *Therapeutic Advances in Gastroenterology*. 2014;7(4):148-155. doi:10.1177/1756283X14524614.
14. A. Srivastava. Haemophilia care - beyond the treatment guidelines. Haemophilia (2014), 20 (Suppl. 4), 4-10
15. Erickson J, Sadeghirad B, Lytvyn L, Slavin J, Johnston BC. The Scientific Basis of Guideline Recommendations on Sugar Intake: A Systematic Review. *Ann Intern Med*. [Epub ahead of print 20 December 2016] doi: 10.7326/M16-2020
16. Sophonneary Prak, Miriam Iuell Dahl, Joel Conkle, Sam Oeurn Un and Arnaud Laillou. Beyond the guidelines for the treatment of severely malnourished children with complications-assessment from Cambodia. BMC Nutrition20151:10.https://doi.org/10.1186/s40795-015-0004-z
17. Benneth A. Bauer. Duration of Anticoagulation: Applying the Guidelines and Beyond. ASH Education Book December 4, 2010 vol. 2010 no. 1 210-215.
18. Jonathan Davidson. Pharmacotherapy of post-traumatic stress disorder: going beyond the guidelines. *BJPsych Open* (2016) 2, e16-e18. doi: 10.1192/bjpo.bp.116.003707
19. Paul E Marik. Surviving sepsis: going beyond the guidelines. *Annals of Intensive Care* 20111:17
20. Vaucher P, *et al*. Effect of iron supplementation on fatigue in nonanemic menstruating women with low ferritin: a randomized controlled trial. *CMAJ*. 2012 Jul 9.

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