Case Report

An Exceptional Case of Cobalamin Deficiency that Presented with Extremely High Indirect Bilirubin Levels

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Abstract: Cobalamin deficiency anemia is a type of anemia that present with weakness, fatigue, icteric sclera and neuropathy. Main causes of cobalamin deficiency are low intake or decreased absorption (gastric and intestinal causes). In present case, we report a 65-year-old male who presented to the emergency department with signs and symptoms of cobalamin deficiency including bilateral peripheral neuropathy, icteric skin and sclera, and abdominal pain in right upper quadrant. He had low cobalamin and extremely high bilirubin levels (8mg/dL) in serum. After the diagnosis of cobalamin deficiency established, 1mg daily cobalamin treatment initiated for five days which would follow weekly and monthly intramuscular injections consequently. Hemolysis and other causes of elevated indirect bilirubin levels were excluded in differential diagnosis. Clinical and laboratory improvements were achieved after the treatment. In conclusion, physicians should kept in mind cobalamin deficiency even in subjects with unusual high levels of indirect bilirubin.

Keywords: Anemia, Cobalamin deficiency, Indirect hyperbilirubinemia, Treatment, Neuropathy, Symptoms.

INTRODUCTION

Cobalamin is an essential vitamin for many bodily functions. Although its stores last for years, dietary deficiency or malabsorption may eventually cause cobalamin deficiency. Patients with cobalamin deficiency may present with a wide range of signs and symptoms including hematological, gastrointestinal and neurological findings [1]. Laboratory findings of cobalamin deficiency include low reticulocyte count, anemia alone or along with leukopenia and thrombocytopenia, decreased cobalamin levels, mildly increased indirect bilirubin levels due to ineffective erythropoiesis, and elevated serum lactate dehydrogenase levels [2].

In present case, we report a 65 year old man with cobalamin deficiency whom presented with extremely high indirect bilirubin levels.

CASE REPORT

A 65 year old man presented to emergency department of our institution for nausea, vomiting, abdominal pain for 2 days. He also complained for numbness in his both hands. He had a history of hypertension (for 15 years) and coronary heart disease (for 3 years). His daily medications include ramipril 5mg for 10 years, acetyl salicylic acid 100mg, metoprolol 50 mg and pantoprazole 40 mg for three years.

His vital signs were normal on physical examination. Right upper quadrant of the abdomen was tender on palpation without rebound tenderness. His skin and sclera were icteric. Rest of the physical examination was unremarkable.

Laboratory studies revealed total bilirubin: 8.1 mg/dL, indirect bilirubin: 8 mg/dL, serum cobalamin: 118 pg/mL, lactate dehydrogenase: 590 U/L, C-reactive protein: 206 mg/L, Hb: 7.6 g/dL, and MCV: 114 fL. Other hemogram and biochemical tests were normal. Corrected reticulocyte was 0.5% suggestive of hypo proliferative anemia. Peripheral blood smear examination showed macrovalocytosis in erythrocytes and hyper segmentation in neutrophils with no signs of hemolysis, spherocytosis or schistocytes. Abdominal ultrasound revealed multiple milimetric stones in gallbladder and thickened gallbladder wall. He transported to internal medicine ward with diagnoses of acute cholecystitis and cobalamin deficiency. Haptoglobulin levels (208 mg/dL) of the subject was high which was in suggestive of hemolytic anemia. Direct and indirect coombs tests were negative. Piperacillin tazobactam 4.5gram three times a day initiated for cholecystitis. Intramuscular injections of cyanocobalamin at a dose of 1mg initiated daily for 5 days which would followed by weekly and monthly injections. İcteric appearance and peripheral neuropathy signs and symptoms were diminished gradually. Similarly, indirect bilirubin levels were also gradually decreased. However, an elevation in direct bilirubin was developed. According to the gastroenterology and surgery department consultations, cholecystostomy catheter was implemented by an interventional radiologist. 400 cc of bile were drained with the catheter and his abdominal pain was relieved. On fifth day of hospitalization, all of his signs and symptoms were diminished and laboratory parameters were improved. He discharged with full recovery on 5th day of the hospitalization.

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DISCUSSION

We reported an interesting cobalamin deficiency case with extremely high indirect bilirubin levels whom consequently developed acute cholecystitis. He responded well to standard cobalamin treatment and cholecystostomy.

Cobalamin is an essential vitamin for bodily functions. Meat and dairy products are rich in cobalamin. Dietary cobalamin is processed by gastric acid pepsin and bind to haptocorrin. Cobalamin-haptocorrin complex is degraded by pancreatic proteases in duodenum. Cobalamin binds to intrinsic factor (IF) in ileum, which was secreted from gastric cells. The cobalamin-IF complex enter into intestinal cells via cubilin-aminonless (CUBAM) receptors on the surface of intestinal mucosal cells. Cobalamin binds to transcobalamin in portal circulation. Finally, it is converted into adenosylcobalamin and methylcobalamin in the tissues [3].

Causes of cobalamin deficiency include decreased intake (vegetarian nutrition), impaired absorption (bariatric surgery, gastrectomy, and resection of terminal ileum, celiac disease, bacterial overgrowth, and gastric atrophy), pernicious anemia, long term treatment with metformin or proton pump inhibitors, and inherited transcobalamin II deficiency. The subject reported in present case was given proton pump inhibitor for 3 years and that could be the cause of cobalamin deficiency.

Signs and symptoms of the cobalamin deficiency are as follows: dyspnea, fatigue, ankle edema, icteric skin and sclera neuropathy, dementia, subacute combined degeneration, and nausea and vomiting [1]. Present case had neuropathy, nausea and vomiting (which could also triggered by acute cholecystitis), anemia, and macrovalocytosis and hyper segmentation in peripheral blood smear.

Laboratory findings of cobalamin deficiency include incidental increase of mean corpuscular volume (MCV), neutrophil hyper segmentation, mild to severe anemia, leukopenia, thrombocytopenia, low reticulocyte count, elevated indirect bilirubin and lactate dehydrogenase levels [4]. The patient in present case report suffered from all of the above except leukopenia and thrombocytopenia. Unexpectedly higher levels of indirect bilirubin levels warranted other causes of indirect hyperbilirubinemia, however, hemolysis and other causes were excluded with laboratory studies.

Treatment of cobalamin deficiency is depend to cyanocobalamin or methylcobalamin replacement by oral or intramuscular route [5]. Initially, 1mg of cyanocobalamin may be injected daily by IM rote for 5 days which would followed by 1mg weekly and 1mg monthly injections until the body stores restored. Alternatively, 0,5-1mg cyanocobalamin or methylcobalamin may be given by oral route. Both routes are similarly effective in relieving signs and symptoms abut IM treatment may have a quicker response. We treated the patient with IM cobalamin injections and he responded very well to the treatment.

CONCLUSION

Cobalamin deficiency may present with unexpectedly high indirect bilirubin levels. Physicians should kept cobalamin deficiency in patients with extremely high indirect bilirubin levels.

CONFLICT OF INTEREST

Declared none.

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REFERENCES

[1] Briani C, Dalla Torre C, Citton V, *et al*. Cobalamin deficiency: Clinical picture and radiological findings. Nutrients 2013; 5(11): 4521-39. DOI: 10.3390/nu5114521.

[2] Oberley MJ, Yang DT. Laboratory testing for cobalamin deficiency in megaloblastic anemia. Am J Hematol 2013; 88(6): 522-6. DOI: 10.1002/ajh.23421.

[3] Chen X, Remacha AF, Sardà MP, Carmel R. Influence of cobalamin deficiency compared with that of cobalamin absorption on serum holo-transcobalamin II. Am J Clin Nutr 2005; 81(1): 110-4. DOI: 10.1093/ajcn/81.1.110.P

[4] Aktas G, Alcelik A, Tekce BK, *et al*. Could mean platelet volume and red cell distribution width predict vitamin B12 deficiency? J Adv Med Med Res 2014; 4: 4965-71.

[5] Andrès E, Kaltenbach G, Noel E, *et al*. Efficacy of short-term oral cobalamin therapy for the treatment of cobalamin deficiencies related to food-cobalamin malabsorption: A study of 30 patients. Clin Lab Haematol 2003; 25(3): 161-6. DOI: 10.1046/j.1365-2257.2003.00515.x.

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