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Case Report

Non transfusional haemochromatosis in patient of thalassemia minor

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Abstract

Haemochromatosis as an acquired form is seen in hematological conditions which necessitates chronic blood transfusions. Beta thalassemia minor patients are generally transfusion independent but still can have secondary iron overload like condition which affects heart, liver, pancreas. Our patient was diagnosed to have thalassemia minor while getting investigated for iron overload state with chronic liver disease and diabetes which turned out to be secondary haemochromatosis on liver biopsy.

Keywords: Secondary haemochromatosis, Thalassemia minor, Iron.

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1. Introduction

Haemochromatosis is a disorder where the body absorbs and stores excess iron. And sometimes this extra iron can be harmful to vital organs like liver, heart, pancreas, gonads and joints. Haemochromatosis can be primary, secondary and neonatal. Most common form is the primary haemochromatosis due to the mutation in HFE gene. A mutation in the HFE gene causes increased absorption of iron despite normal dietary iron intake. The HFE mutation that most commonly causes hemochromatosis is homozygosity for C282Y variant.[1] This mutation is seen very uncommon among Asian population. Secondary haemochromatosis occurs due to excess iron in diet or blood transfusions for erythropoietic disorders. Neonatal haemochromatosis is a rare presentation which occurs due to injury to liver in the womb.

Secondary hemochromatosis is mainly caused by haemoglobinopathies like thalassemia, sickle cell anemia, hereditary spherocytosis. These conditions lead to erythropoietic hemochromatosis, a condition that results from the absorption of excess iron because the patient is producing excessive amounts of red blood cells due to underlying disease that causes red blood cells to be more fragile, and therefore have a shortened lifespan.[2] When the cells are destroyed, the iron from them is deposited in the body tissues. The same mechanism is seen in patients who receive multiple transfusions of red blood cells. Thalassemia is a congenital hemoglobinopathy which is characterized by peripheral hemolysis and ineffective erythropoiesis leading to anemia. Classical clinical presentation of beta thalassemia can be minor, intermedia or major. Thalassemia major necessitates regular blood transfusions resulting in iron accumulation in the body while thalassemia minor is associated with mild anemia not requiring transfusions. We report a case of 62 year female patient with thalassemia minor presenting with late onset secondary haemochromatosis, diabetes and cirrhosis.

2. Case Presentation

62 year female presented to outpatient department with complaints of generalized weakness, increased fatiguability since 2 years, darkening of skin and weight loss since 1 year. Patient was diagnosed to have diabetes 6 months back but was not taking any medications. Patient had received iron supplementation for her complaints from local hospital few times in past 1 year. Patient did not give history of such similar complaints in the family members. On examination

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there was hyperpigmentation of skin which was more on the sun exposed areas gradually increasing since past one year (**Figure 1**). On general physical examination pallor was present and no icterus, lymphadenopathy and clubbing. On abdominal examination there was hepatosplenomegaly.

On investigation her haemogram were as follows Haemoglobin 8.4gm%, total leucocyte count 4630 cumm, platelet count 150000 cumm, MCV 64.9 fl, MCHC 33.5gm/dl, MCH 21.7 pg. Peripheral smear showed anisopoikilocytosis with microcytes, normocytes, elliptocytes, tear drop cells. Liver function test had following findings: total bilirubin 3.2mg%, direct bilirubin 1.1mg%, indirect bilirubin 2.1 mg%, total protein 7.6 gm%, albumin 3.9gm% , AST 90 U/L, ALT 130 U/L, ALP 140 U/L, LDH 242 U/L. On further evalution her iron profile showed following findings: serum iron 251ug/dl, TIBC 301ug/dl, transferrin saturation 83.39%, ferritin 842.51ng/ml. After the iron studies showed features of iron overload, patient blood was sent for haemoglobin electrophoresis which showed Hb A2 4.6% and Hb F < 1%, suggestive of beta thalassemia minor. Her ultrasound abdomen was suggestive of fatty liver with splenomegaly while fibroscan was suggestive of chronic liver disease. She was also evaluated for other causes of chronic liver disease with HbsAg, antihcv, autoimmune workup which all came negative. In order to rule out hereditary haemochromatosis HFE genotyping was done which did not detect any mutation. Liver biopsy was done which was suggestive of advanced chronic liver disease with iron overload consistent with haemochromatosis.

Figure 1: Skin pigmentation at the time of presentation

Figure 2: Improvement in pigmentation after iron chelation therapy

Patient is presently on oral iron chelation therapy with deferasirox 500mg BD and there has been symptomatic improvement as well as the pigmentation has reduced (**Figure 2**).

3. Discussion

Haemochromatosis is a condition where body accumulates excess of iron. Hereditary haemochromatosis is the most common type which is associated with genetic mutation of HFE gene. Secondary haemochromatosis is acquired condition that develops in people with anemia which often needs multiple blood transfusions. This can lead to excess iron build up. Secondary haemochromatosis can be caused by thalassemia or myelodysplastic syndrome if patients have received a large number of blood transfusions.[3] Each unit of transfused blood has approximately 250mg of iron. And human body has no active mechanism for the excretion of iron.[4] β-thalassemia can cause iron overload through repeated transfusion and increased intestinal iron absorption. β-thalassemia is classified as thalassemia major, thalassemia intermedia and thalassemia minor. Transfusion is usually not needed for thalassemia intermedia and thalassemia minor. Patients of thalassemia intermedia and minor are at risk of iron overload secondary to increased intestinal iron absorption but severe iron overload and target organ damage are not common in them.[5] These conditions have ineffective erythropoiesis, i.e., a high percentage of the erythropoietic precursor cells in the bone marrow do not survive and this ineffective erythropoiesis leads to compensatory erythroid hyperplasia leading to chronically increased iron uptake in the duodenum. Studies have shown that hepcidin and growth differentiation factor 15 (GDF15) play important roles in this process. Hepcidin is synthesized in the liver and it normally inhibits iron uptake in the duodenum. GDF15 belongs to the family of the transforming growth factor ß cytokines secreted by erythroblasts and suppresses the hepatic production of hepcidin. In thalassemia, the serum GDF15 level is extremely high which causes suppression of hepatic hepcidin production which is considered to be the cause of the increased intestinal iron uptake.[6] The increased intestinal iron resorption accompanying ineffective erythropoiesis is probably due to the lack of suppression by hepcidin.

If a patient with thalassemia presents with iron overload that is inconsistent with their transfusion history, genetic screening should be performed to detect a concomitant mutation in a second gene, either within the HFE gene or elsewhere, such as the genes encoding hepcidin, transferrin receptor 2 and ferroportin.[6]

In India studies initially did not find any association of primary iron overload and common HFE related mutations with cirrhosis.[7,8] But in recent few years there have been cases where chronic liver disease patients were evaluated for hereditary haemochromotosis and non HFE related mutations were found for HJV (hemojuvelin), HAMP (hepcidin) and TFR2(transferrin receptor 2).[9] Our patient was

diagnosed thalassemia minor while getting investigated for her raised iron stores. Patient had no history of blood transfusions and history of oral iron therapy was not significant to cause iron overload. We could not get her detailed genetic analysis done apart from HFE gene mutation due to financial limitations and availability which could have further helped in finding the cause of iron overload in patient of thalassemia minor. The explanation that we have for it in our patient is the increased duodenal absorption of iron due to ineffective erythropoiesis plus post menopause there is increased risk of rise in iron stores. Also non HFE related inherited factors needs to be evaluated when iron overload state cannot be fully explained by the drug and blood transfusion history. In women menstruation and pregnancy are important causes for iron loss hence they tend to have less of it than men. After menopause or a hysterectomy, the risk increases for rise of iron store women.

4. Conclusion

Patients of microcytic hypochromic anemia should be investigated with iron profile studies before starting on iron therapy as thalassemia patients may be misdiagnosed as iron deficiency anemia and will also raise concern of developing iron overload state.

5. Patient's Consent

An informed written consent was taken from patient before publication.

6. Source of Funding

None.

7. Conflict of interest

None.

References

1. Fleming RE, Britton RS, Waheed A, Sly WS, Bacon BR. Pathophysiology of hereditary hemochromatosis. *Semin Liver Dis*. 2005;25(4):411-9
2. Porter JL, Rawla P. Hemochromatosis. [Updated 2024 Oct 06]. In: Treasure Island (FL): StatPearls Publishing. 2023
3. Rotaru I, Gaman A, Gaman G. Secondary Haemochromatosis in a Patient with Thalassemia Intermedia. *Curr Health Sci J*. 2014;40(1):67-70.
4. Anderson GJ. Mechanisms of iron loading and toxicity. *Am J Hematol*. 2007;82(12):1128–31.
5. Sanctis VD, Tangerini A, Testa MR, Lauriola AL, Gamberini MR, Cavallini AR, et al. Final height and endocrine function in thalassaemia intermedia. *J Pediatr Endocrinol Metab*. 1998;11(Suppl 3):965–971
6. Tanno T, Bhanu NV, Oneal PA, Goh SH, Staker P, Lee YT, et al. High levels of GDF15 in thalassemia suppress expression of the iron regulatory protein hepcidin. *Nat Med*. 2007;13(9):1096–101.
7. Dhillon BK, Das R, Garewal G, Chawla Y, Dhiman RK, Das A, et al. Frequency of primary iron overload and HFE gene mutations (C282Y, H63D and S65C) in chronic liver disease patients in north India. *World J Gastroenterol*. 2007;13(21):2956–9.
8. Jain S, Agarwal S, Tamhankar P, Verma P, Choudhuri G. Lack of association of primary iron overload and common HFE gene mutations with liver cirrhosis in adult Indian population. *Indian J Gastroenterol*. 2011;30(4):161–5.
9. Dhillon BK, Chopra G, Jamwal M, Chandak GR, Duseja A, Malhotra P, et al. Adult onset hereditary hemochromatosis is associated with a novel recurrent Hemojuvelin (HJV) gene mutation in north Indians. *Blood Cells Mol Dis*. 2018;73:14–21.

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