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CASE REPORT

Restrictive Cardiomyopathy due to Secondary Haemochromatosis in a Patient with Beta Thalassaemia Major: A Rare Entity

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Abstract

Haemochromatsis occurs due to iron over load. Thalassaemia major is an inherited disorder that can cause secondary haemochromatosis due to haemolysis and repeated blood transfusion. The secondary haemochromatosis in thalassaemia patient can rarely present with restrictive cardiomyopathy. Here, we report a case, where a 30-year-old woman with thalassaemia major presented with shortness of breath with paroxysmal nocturnal dyspnea, orthopnoea , oedema, skin pigmentation, raised Jugular venous pressure(JVP), cyanosis and bilateral basal crepitation. After through investigations, she was diagnosed as a case of heart failure due to restrictive cardiomyopathy with secondary haemochromatosis as a complication of repeated blood transfusion. She was treated with iron chelation therapy, furosemide, beta-blockers, angiotensin receptor blocker (ARB) and discharged with follow up. Iron chelation therapy should be imitated early to prevent secondary haemochromatsosis and its complications in thalassaemia major patient.

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Introduction

The secondary haemochromatosis can be caused thalassaemia major, sideroblastic anaemia, chronic haemolysis, chronic liver disease hepatitis C, alcoholic cirrhosis, nonalcoholic steato-hepatitis.[1] Haemo-chromatosis is commonly presented as arthralgia, pigmented skin, diabetes mellitus and restrictive cardiomyopathy with heart failure.[2]

Beta thalassaemia major in inherited disorder with a global incidence approximated to be 1 in 100,000, with 1 in 10,000 persons living in the European Union. Approximately 1.5% of the people in the world has thalassemia. In Southeast Asia, the prevalence and carrier rates of -thalassemia are relatively high. According to recent surveys, between 300,000 and 400,000 newborns are born each year with a significant haemoglobin disease (23,000 with -thalassemia major), with up to 90% of these births taking place in underdeveloped countries.[2] It is estimated that 6–12% of the population, or roughly 10–19 million people, are carriers of â-thalassemia in Bangladesh.[3] Approximately 6000 to 8000 newborns with thalassemia are born in Bangladesh each year.[4]

The main step of treatment of thalassaemia major is repeated blood transfusion which might lead to iron deposition in various organ including heart muscle. The overall prevalence of iron overload in cardiac muscle in thalassaemia major patient is 25%.[5] Here, we report a case of thalassaemia major who was presented with heart failure due to restrictive cardiomyopathy due to secondary haemochromatosis.

Case report

A 30-year-old woman presented with shortness of breath with paroxysmal nocturnal dyspnea,orthopnoea for 7 days. She was a known case of thalassaemia major and she was receiving repeated blood transfusion of almost 5 to 10 unit

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every year for last 20 years. She occasionally received few doses of dose iron chelating agent but was not adequate. She also complains of generalized pigmentation and swelling of the legs, palpitation. Splenectomy was done at age of 14 years and was not on ay vaccination schedule thereafter. She had history of repeated chest infection and treated with several antibiotics. She had primary amenorrhoea. Two of her siblings are affected from thalassaemia and parents had history of consanguineous marriage. On general examination she was anaemic, moderately icteric, there was generalized pigmentation, raised JVP, bilateral pitting pedal oedema, pulse-50 beats per minute, blood pressure-100/70 mm of Hg with no postural drop, cyanosis was present, scanty pubic and axillary hair growth. The systemic examination revealed that there was a splenectomy scar mark over abdomen, moderate enlarged firm hepatomegaly, both heart sound were soft, presence of third heart sound, bilateral basal crepitation. After evaluation by investigations(table-1) she was diagnosed as a case of thalassaemia major with post-splenectomy status with secondary haemochromatsosis with restrictive cardiomyopathy.

Table-I

Investigations with their results of the patient

Name of investigations	Results
Complete blood count	Haemoglobin- 8.4 gm/dl, ESR- 55 mm in 1st hourTotal WBC- 3.4x 10^{12}/L,Total platelet- 220x10^{9}/LMCV-71.8 fl, MCH-23.8 pg
Peripheral blood film	Microcytic hypochromic anaemia with lymphocytosis
C-reactive protein	11.8 mg/dl
Ferritin	12760ng/ml
Serum Bilirubin	0.33mg/dL
ALT(SGPT)	55U/L
HBsAg	Negative
Anti-HCV	Negative
Chest X -Ray PA view(figure-2)	-Bilateral inhomogeneous opacity upper and mid zone-Cardiac shadow is enlarged in transverse diameter with right ventricular type apex
Sputum for culture	Growth of normal flora
Sputum for Gene X-pert	MTB not detected
MT	2 mm in72 hours
Urine RME	Normal
Blood for culture & sensitivity	No growth
USG of whole abdomen	Hepatomegaly
HRCT chest	Non-specific pulmonary inflammatory lesion
Electrocardiogram(ECG)	Sinus rhythm with PAC, Tall R in v2 and hight of the r is more than s in v1Asymmetrical T wave inversion from v1 to v3 and lead III,AvF, Comment: Right ventricular hypertrophy with strain with PAC (figure-1)
Echocardiogram	Bi-atrial enlargement, Right ventricular hypertrophy, IVC dilated but lack of respiratory variation, Tricuspid and mitral regurgitation, E/A ratio> 2; E/e ratio>15(increased), E is below 10cm/sec, Motion medial and lateral mitral annulus is reduced (figure-3)

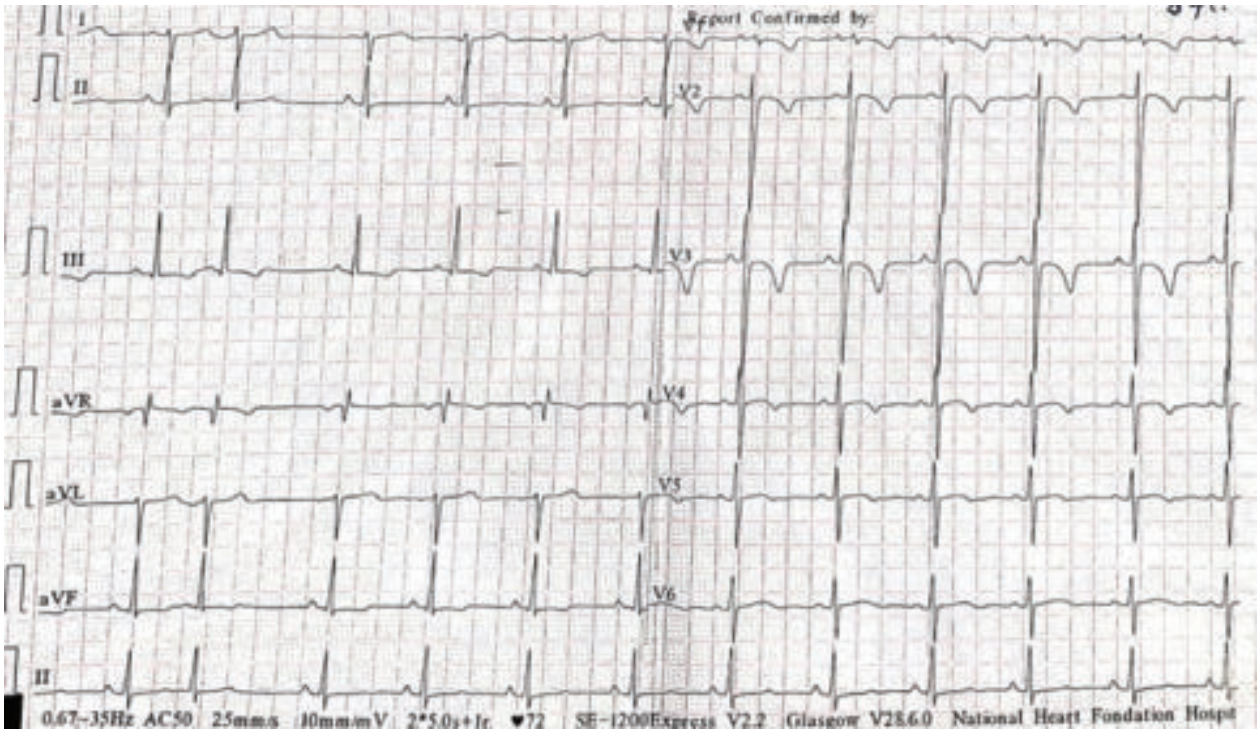

Figure-1: *Showing right ventricular hypertrophy with strain with premature atrial complex(PAC).*

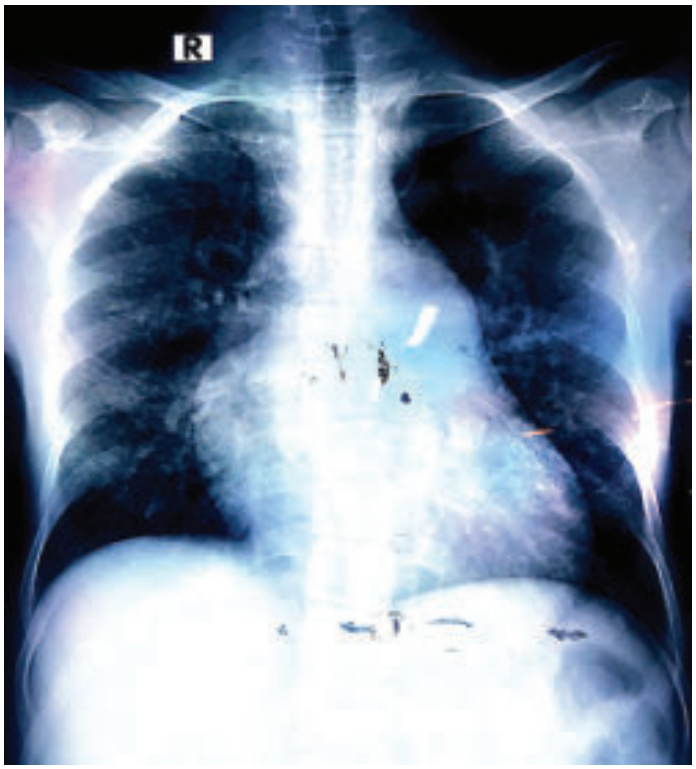

Figure-2: *Chest X-ray PA view is showing cardiomegaly with right ventricular type of apex and inhomogeneous opacity in both lung fields.*

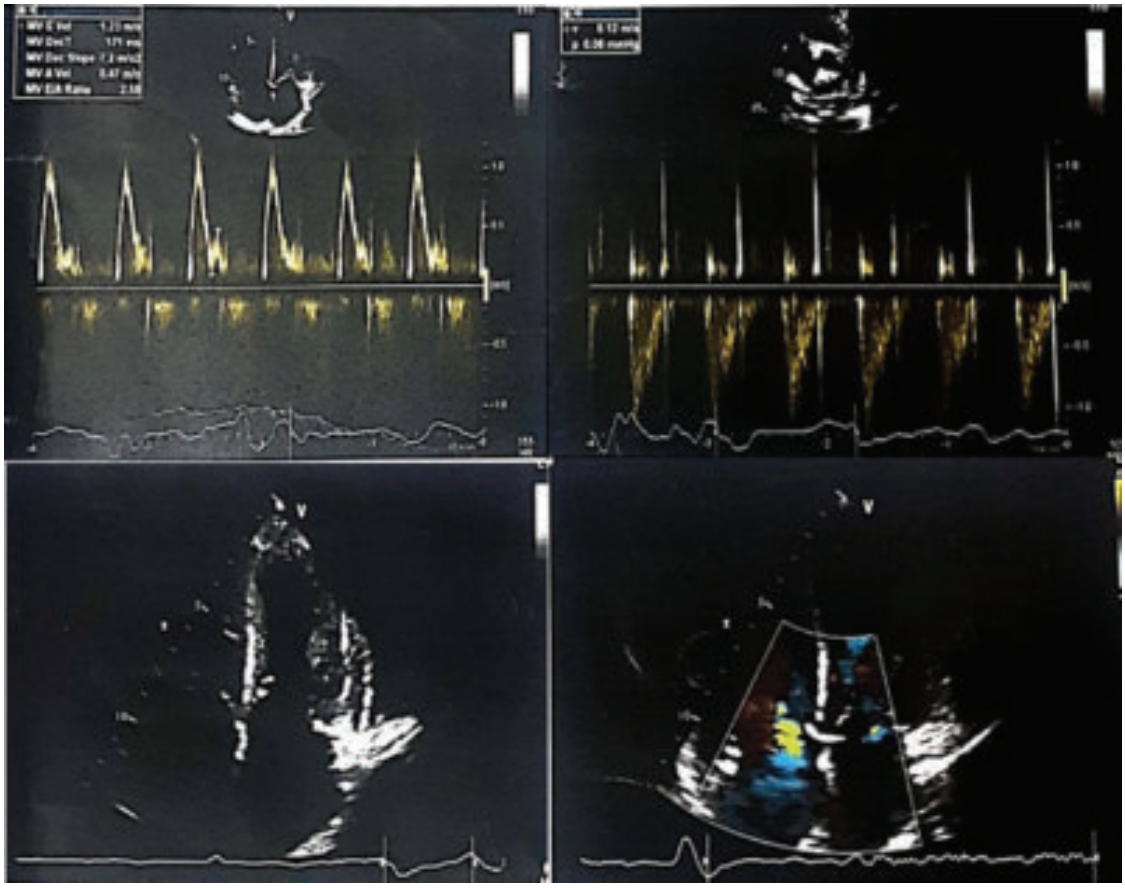

Figure-3: *Showing bi-atrial enlargement, right ventricular hypertrophy and tricuspid and mitral regurgitation*

Discussion

In haemochromatosis, iron absorption increases in intestinal mucosa more than body requires which in turn accumulates in different body organs. Though deposition in heart muscle is rare but can occur and patient may present with either dilated or restrictive cardiomyopathy or arrhythmias.[6]

Secondary haemochromatosis which occurs due to repeated blood transfusion in thalassaemia major patient and may become lethal by the age of 30 years.[7] The patient in this case report also came with heart failure due to restrictive cardiomyopathy around the age of 30 years.

Iron accumulation in the heart muscle causes tissue damage which results in restrictive or dilated cardiomyopathy leading to heart failure and pulmonary hypertension. In beta thalassemia, pulmonary arterial hypertension is the leading cause of heart failure.[8]

The pathogenesis of iron-over load cardiomyopathy is complex. Iron turn over in thalasaemia major patient is 10-15 times higher than the normal body iron due to ineffective erythropoiesis by marrow hyperplasia.[9] The unbound excess iron in ferrous form creates reactive oxygen species which is buffered by cytosolic ferritin turning into haemosiderin and deposited inside of lysozomes. The failure of the buffering system causes damage to cell membrane , ion channels and nucleic acid of the cardiac muscle which eventually leading to heart failure and arrhythmias. This cytosolic labile iron also alters genetic expression and signaling leading to apoptosis of the cardiac muscle and fibrosis.[10]

The joint pain, weakness, lethargy are the most common presenting complaints of haemochromatosis. But, patient may have other organ specific symptoms such as shortness of breath, oedema, ascites, jaundice, generalized skin pigmentation, arthralgia, raised jugular venous pressure, bilateral basal crepitation on auscultation.[10] This woman presented here also had similar kind of symptoms and signs on the background of thalassaemia major. In some study echocardiographic findings revealed that certain thalassaemia major patient may have left ventricular myocardial restriction, pulmonary hypertension and right sided heart failure. Around 40% older patient may present

atrial fibrillation and same amount of patient may have complete heart block over the age of 15 years.[11]

Cardiac magnetic resonance imaging(CMR) relaxation has immense role to diagnose a case of cardiac haemochomatosis. Iron chelating therapy plays a crucial role in preventing cardiomyopathy.[12] The serum ferritin >2500 μg/L, and liver iron concentration >15mg/kg dry weight can foresee heart failure in heamochromatosis patient. Unfortunately if subjects are not being detected on time for intervention, heart failure became outrageous leading to an increase in mortality rate.[13] In this patient, we could not do a CMR due to resource limitation. She also did not receive regular iron chelation therapy despite repeated blood transfusion and her serum ferritin level was more than 1,00,000 μg/L which was predictive of cardiac involvement.

Phlebotomy and chelating drugs are the first line of management and diuretics, cardiac glycosides, beta blockers, ACE inhibitors are helpful in treating congestive cardiac failure.[13] This patient was treated with chelation therapy, furosemide, beta blocker, Angiotensin receptor blocker and was followed up with improvement of the heart failure.

Conclusions

The secondary haemochromatosis is a rare complications thalassaemia major during the era of available iron chelation therapy. The mortality of secondary haemochromatosis increases due to cardiac involvement. High degree of suspicion is required to diagnosis. Adequate iron chelation should be initiated in patient with thalassaemia major patient who requires repeated blood transfusion to prevent theis serious complication.

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Data & Materials: Available from the corresponding author, on reasonable request.

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