CASE REPORT

Primary Hemochromatosis as Isolated Dilated Cardiomyopathy

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SUMMARY

Heredity hemochromatosis often presents with a restrictive cardiomyopathy and usually heart involvement is a very rare presentation. A 35 year old male with non-significant family history presented to Emergency Room in state of cardiogenic shock. After initial resuscitation he complained of ongoing SOB, Jaundice and palpitations for past few weeks. Initially he was treated as a case of systolic heart failure but later studies revealed HFE gene negative hemochromatosis presenting only as Dilated Cardiomyopathy with no evidence of restrictive pattern on ECHO.

Keywords: Dilated Cardiomyopathy, Hemochromatosis, Systolic Heart failure, HFE gene.

INTRODUCTION

Hemochromatosisis an autosomal recessive hereditary disease characterized by excessive intestinal absorption of dietary iron resulting in a pathological increase in total body iron stores. Humans, like most animals, have no means to excrete excess iron. Excess iron accumulates among various tissues and organs disrupting their normal function. The most susceptible organs include the liver, adrenal glands, heart, skin, gonads, joints, and the pancreas[1].

Juvenile hemochromatosis is a rare form of HH occurs in childhood is, also an autosomal recessive disorder. It is earlier in onset and more severe than typical HH and appears genetically distinct, not being due to the abnormal HFE gene that is responsible for HH. Defects of the HFE gene (located on the short arm of chromosome 6) cause the majority of cases of inherited hemochromatosis, which is therefore often referred to as HFE hemochromatosis (HFE-HC). HFE was the only known gene associated with hemochromatosis but it is now known that there are other genetic associations[2,3].

A systematic review has shown that about 0.4% of people of northern European descent have the genetic mutation that increases the risk of developing hemochromatosis but the clinical penetrance of the mutation is much lower than the genetic prevalence[4].

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CASE REPORT

A 35 years old male presented in emergency with complaints of worsening of shortness of breath in 1 month, yellow discoloration of eyes in 7 days and palpitations in 1 day. The patient was in his usual state of health 6 months back when he developed shortness of breath. Initially, breathlessness was of NYHA class 1 and then progressed to (NYHA class 3). He complained of dyspnea, orthopnea, PND

Table: 1. Hematological and other biochemical Laboratory findings

Parameters	Patients values	Reference range
WBC	6.4x103/mcl	4000 - 11000/mcl
RBC	4.64(x 10^6 /ml)	4.5 - 5.5 (x 10^6/ml)
Hb	12.2 g/dl	13.5 - 16.5 g/dL
HCT	36.4%,	41 – 50%
MCV	78.4fl	80 – 100fl
MCH	26.3pg	26 – 34 pg
MCHC	33.5 g/dl	31 – 37 g/dL
PLT	137x103/ul	100,000 to 450,000
CPK	99U/L	60 and 174 IU/L
LDH	128 U/ml	150-450 U/ml
CK-MB	12U/L	5-35 µg/ml
Cholesterol	172mg/dl	<200 mg/dl
Triglycerides	88.8mg/dl	<150 mg/dl
PT	13 sec	13 sec
APTT	37sec	31 sec
INR	1.0	1.0
Repeat (04/03/14)		
PT	22sec	14sec
APTT	34sec	31sec
Ferritin	2501.68ng/ml	21.81-274.66ng/ml
Iron	154ug/dl	65-175ug/ml
TIBC	160ug/dl	250-400ug/dl
Transferrin saturation	96.3%	12-36%

It was gradual in onset, progressive, associated with nausea, discomfort in epigastrium and deep yellow urine. The abdominal discomforts was gradual in onset, mild in intensity, dull in character, localized, no accompanied progressive swelling of feet and palpitations. He has also developed yellow discoloration of eyes for the last 1 week, aggravating factor and relieved spontaneously. For the last 1 day, he has developed palpitations and cold, clammy skin. He was taken to DHQ Bahawalnagar where he was found BP less and pulseless. Initially he was managed there and was referred to Mayo Hospital, Lahore. Further workup revealed Hemochromatosis and its treatment was started but he was tested negative for HFE gene mutation. ECHO report showed Dilated Cardiomyopathy but there was no evidence of Restrictive Cardiomyopathy. This is really surprising as hemochromatosis at this stage is supposed to cause restrictive cardiomyopathy first and then leads to dilated cardiomyopathy because of iron overload.

Clinical Examination: All vitals were normal, while in CVS: Apex beat is localized in 6th intercostal space, in anterior axillary line, of normal character. Heart rate is 90/min, rhythm regular, first heart sound S1 is reduced in intensity but audible, second heart sound S2 is normal, no added heart sounds, no murmur, and no pericardial rub. GIT: Liver is enlarged 2 fingers below costal margins, soft in consistency, surface is smooth, and edges are rounded, non-tender, and non-pulsatile. Liver span is 16 cm. No other viscera or mass palpable. Upper border of liver was in 5th intercostal space.

Table: 2. Biochemical Laboratory findings

Parameters	**Patients values**				**Reference range**
	24/02/14	**26/02/14**	**28/02/14**	**04/03/14**	
T.bilirubin	4.1	19.3	17.4	9.9	0.3 to 1.9 mg/dL
D.bilirubin	6.1	-	-	-	0 to 0.3 mg/dL
ALT	1475	1051	541	438	7 to 45 units per liter (U/L)
AST	1576	1209	366	197	8 to 40 U/L
Alk Phos	376	129.3	157	121	45 to 115 U/L
T.Protein	6.8			4.4	6.3 to 7.9 g/dL
Albumin	5.0			1.9	3.5 to 5.0 g/dL
RFTS	Normal				
Serum Electrolytes	Normal				
HbsAg	Positive(on screening)				
Anti-HBc antibodies	Negative				
Anti-HCV	Negative(on screening)				
Anti-HAV IgM	Not done				
Anti-HEV IgM	Not done				
Urine Bilirubin	+++				
ECHO Parameters	**ECHO findings of patient**				
LA and LV	Dilated				
LA	42mm				
LVIDS	76mm				
LVIDD	87mm				
IVS	9 mm				
EF	25%				
Global hypokinesia					
LV apex.	Organized clot in LV apex				
LV function	Poor				
MR	++				
TR	+				
Conclusion	DCMP , LV thrombus , poor LV systolic function , MR++ , TR +				

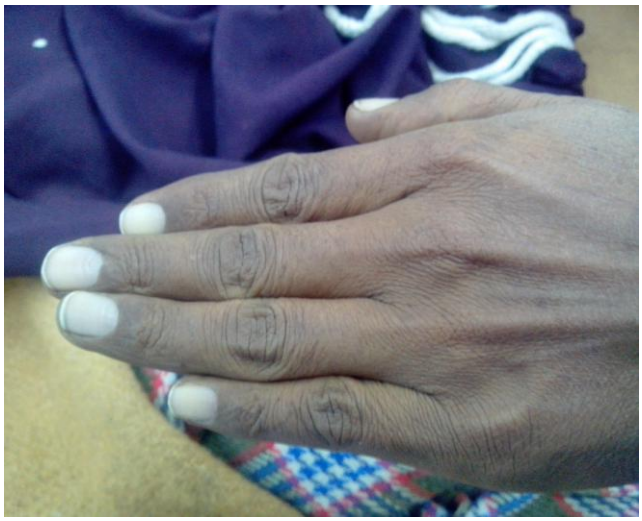

Fig 1. Nails findings of primary haemochrmatosis as isolated dilated cardiomyopathy koilonychia (spoon nails) due to anemia

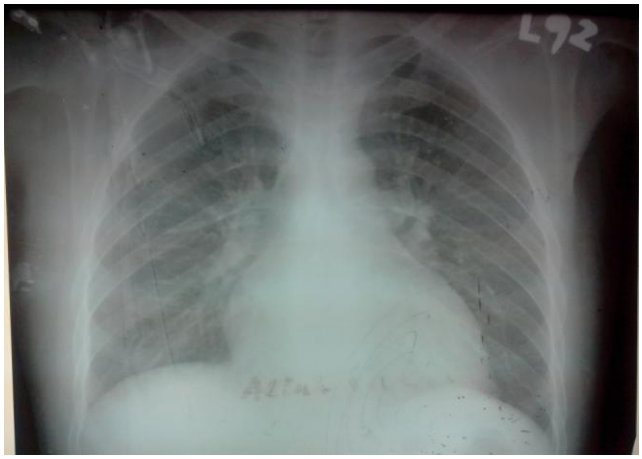

Fig. 2: Radiological finding of Primary Hemochromatosis as Isolated Dilated Cardiomyopathy Chest radiograph shows a enlarge heart size.

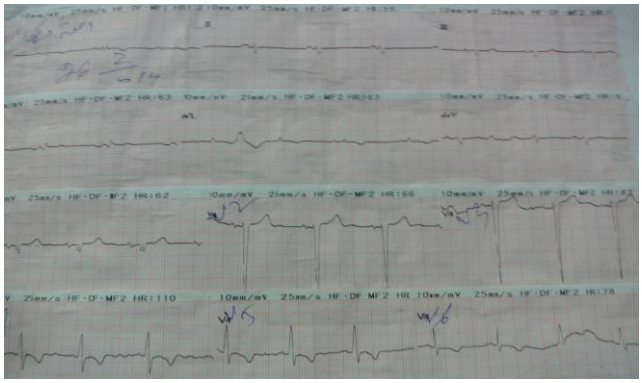

Fig: 3: Echocardiogram shows dilated and poorly contracting left ventricle in a patient with dilated cardiomyopathy.

DISCUSSION

Heredity Hemochromatosis usually involves various different systems of body and usually causes liver dysfunction, skin pigmentation, diabetes, arthopathy, and impotence, cardiac enlargement with or without heart failure or conduction defects.(6)

Hereditary hemochromatosis (HHC) is a heterogeneous group of disorders related to deficiency of the iron regulatory hormone hepcidin. HHC is an autosomal recessive genetic disease in which increased intestinal absorption of iron causes accumulation in tissues, especially the liver, which may lead to organ damage. Other organs that may be affected by iron deposits include the pancreas, joints, heart, skin and gonads.Liver fibrosis, cirrhosis and hepatocellular carcinoma are the most serious complications of iron overload. Early diagnosis and treatment are therefore essential[1,3].

Defects of the HFE gene (located on the short arm of chromosome 6) cause the majority of cases of inherited hemochromatosis, which is therefore often referred to as HFE hemochromatosis (HFE-HC). HFE was the only known gene associated with hemochromatosis but it is now known that there are other genetic associations[7].

A systematic review has shown that about 0.4% of people of northern European descent have the genetic mutation that increases the risk of developing hemochromatosis but the clinical penetrance of the mutation is much lower than the genetic prevalence[4].

The known mutations of the HFE gene are C282Y and H63D. The C282Y mutation is most common in white populations[5]. The prevalence of C282Y homozygosity in a meta-analysis of 2,802 hemochromatosis patients of European ancestry was 80.6%. HHC is a relatively common genetic disorder in northern European populations and is probably under-diagnosed[5].

Hemochromatosis is inherited in an autosomal recessive pattern, but the clinical picture is more complex because the expression (penetrance) of the gene varies. This means that not everyone who is homozygous for HHC genes will develop clinical disease. The variation in gene expression may be due to other factors affecting iron accumulation[8,9].

In our case this cardiomyopathy with iron overload was not seen in other visceras. The heart of this patient was dilated but there was no evidence of excessive iron deposit either in his heart. Biopsy was not taken in this case but was ruled out by radiological method. Cardiac enzymes were normal; therefore, there was no sign myocarditis in this case. No genetic investigation was performed on his family members but there was no history of such disease over there. To date, isolated hepatic hemosiderosis

like this case has not been reported without having disease in his family. There is absolutely no way to tell whether liver involvement in this patient was either due to acute hepatitis B infection or hemochromatosis .This case report definitely gives us idea that heart involvement is more common in HFE negative mutation patients but we need detailed studies to tell about the course of HFE gene negative mutation.

CONCLUSION

Our focus of discussion is that HFE mutation negative patients often present with more severe heart involvement as compared to liver involvement in patients with HFE positive HH as in this patient and lead to isolated dilated cardiomyopathy only instead of mixed pattern.

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