LATE MANIFESTATION OF HETEROZYGOUS H63D MUTATION AS HEREDITARY HEMOCHROMATOSIS IN 89-YEAR-OLD MAN

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Introduction

Hereditary hemochromatosis (HH) is an autosomal recessive disease that usually manifests in middle-aged people. In most patients, homozygous C282Y mutations in the HFE gene express the disease. But in some occurrences, compound heterozygous, including C282Y and H63D mutations, were also witnessed to manifest as HH. We present an atypical case where heterozygous H63D manifested as HH in an 89-year-old man.

Case Report

An 89-year-old Caucasian man of Italian descent presented with confusion, left-sided facial droop and slurring of speech. His past medical history includes end-stage renal disease on hemodialysis, atrial fibrillation and mild cognitive decline.

Physical examination: The patient had confusion but was alert & oriented to self and time. Facial droop and slurring of speech improved before evaluation. There was mild abdominal distension and positive for asterixis, and the skin was bronze in color.

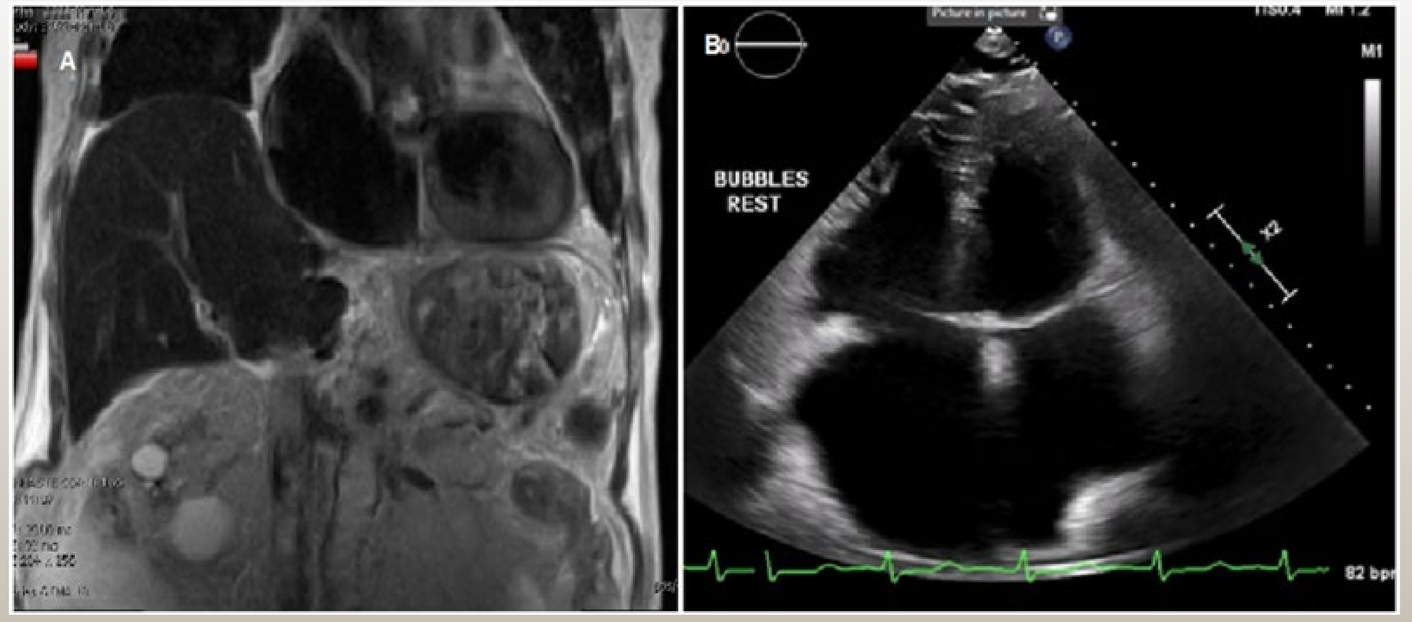
Work-up: The patient had persistent hypoglycemia and required intravenous glucose administration. Brain imaging was normal. CT scan of the abdomen, pelvis, and chest showed severe cardiomegaly and a moderate amount of ascites. Iron studies were abnormal (Table 1). Peritoneal fluid analysis was transudative. Ultrasound right upper quadrant was negative for any evidence of cirrhotic morphology. MRI showed hemosiderosis and two-dimensional transthoracic echocardiography showing severely dilated right ventricle and both atria (Figure A & B). The patient empirically underwent two sessions of phlebotomy. Genetic testing confirmed heterozygous H63D gene mutation. The patient followed up for the phlebotomy sessions and demonstrated significant improvement physically and well as cognitively.

	Day 1	Day 2	Day 3	Day 4	Day 15	Day 42
Hemoglobin (g/dL)	15.6	14.8	15.1	13.8	13.6	12.2
AST (U/L)	85	102	135	125	109	71
ALT (U/L)	56	57	70	74	72	46
Bilirubin (mg/dL)	3.0	2.9	2.6	2.9	2.6	2.1
INR	1.3	1.4	1.4	1.4	1.2	1.2
Ammonia (µmol/L)		99	45	46	42	31
Platelets (10^3/µL)	103	86	82	63	59	91
Ferritin (ng/ml)		1283				725
Iron (µg/dL)		187				130
Transferrin Saturation (%)		94				74

Discussion

This case highlights the consideration of HH in differential regardless of age if a patient presents with symptoms suspected of HH. Standard genetic testing includes testing C282Y and H63D mutations in the HFE gene on chromosome 6. Less frequently tested S65C, HFE4, TFR2-HHC, and FTH1 gene mutations also have the expression of HH in sporadic cases. Previously, heterozygous C282Y carriers with iron overload are assumed to have other genetic changes or influence by environmental factors, such as alcohol or liver disease, that increase disease expression. However, no such literature is available for heterozygous H63D carriers. Given the unusual age for phenotype expression and atypical disease, the presentation makes this unique case for learning the pathophysiology and genetics of HH.

Images



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