International Journal of Contemporary Pediatrics
Hassan MA et al. Int J Contemp Pediatr. 2016 May;3(2):665-667
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20161061

Case Report

Two siblings with familial hyperchylomicronemis syndrome: disease presentation and diagnosis

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Received: 11 October 2015
Accepted: 17 December 2015

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ABSTRACT

Familial hyperchylomicronemic syndrome (FHS), Fat induced pancreatitis, Type 1 hyperlipoprotenemia (HPL) or exogenous hyperlipemia is a rare autosomal recessive disorder of lipoprotein metabolism ,with a prevalence of 1 in 1 million, it occurs due to congenital deficiency of lipoprotein lipase (LPL), congenital deficiency of apo-protein C-II, or the presence of LPL inhibitor (e.g., an anti-LPL autoantibody). This article reports 2 siblings: a male patient aged 7 years and a female aged 4 years with hyperchylmicronomic syndrome each had a different presentation of the same disease. The male presented with recurrent attacks of acute pancreatitis along with failure to thrive while his sister was asymptomatic.

Keywords: FHS, Recurrent pancreatitis, Lipoprotein lipase deficiency

INTRODUCTION

Hyperlipidaemia which is the elevation of triglyceride and/or cholesterol in plasma can be primary or secondary. Primary disorders are usually familial and transmitted genetically and more common in children, while secondary disorders are more common in adults due to high fat diet and sedentary lifestyle.[1] FHS, fat induced pancreatitis or Type 1 hyper lipoprotenemia (HPL) is a rare autosomal recessive disorder of lipoprotein metabolism, with a prevalence of 1 in 1 million, due to congenital deficiency of lipoprotein lipase (LPL), congenital deficiency of apo-protein C-II, or the presence of LPL inhibitor (e.g., an anti-LPL autoantibody). It is usually clinically manifested with TG levels exceeding 1000-2000 mg/dL, recurrent attacks of acute pancreatitis, loss of appetite, and failure to thrive. Infants may present with colicky abdominal pain, nausea and vomiting and finally death if undetected and untreated.[2]

CASE REPORT

A 7 year old male presented with epigastric pain, nausea, and vomiting of one day duration. The pain was epigastric, nonradiating, moderate in intensity and associated with multiple episodes of nonbilious vomiting that became bilious .Upon presentation, his pulse rate was 105/minute, blood pressure 110/60 mm Hg, respiratory rate 22/minute, and temperature 36.7°C. He was somnolent and dehydrated. Upon physical examination, patient had tender epigastrium, without hepatosplenomegaly. Initial laboratory findings were a total leukocyte count of 11000 with 73% neutrophils, platelets 470000, and C - reactive protein 0.08 mg/dl.
Serum electrolytes, calcium, liver, and renal function tests, and lactate dehydrogenase were normal. To be noticed that his serum was lipemic (Figure 1).

Other investigations showed lipase 22015 U/L, Amylase 2399U/L, total cholesterol 158 mg/dl, HDL16 mg/dl, triglycerides (TG) 381 mg / dl it should be noted here that

TG level was measured 3 days after admission. Fasting blood sugar was 109 mg/dl and HBA1C5.5%.

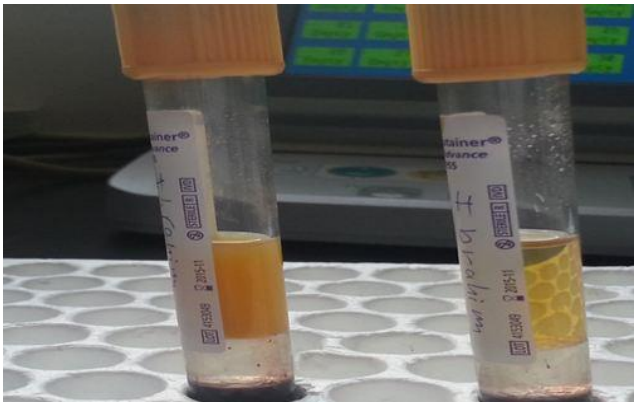

Figure 1: The lipemic serum of patient and his sister, to be noted patient's sister serum was more lipemic and this is manifested by her severe high TG level.

Past medical history revealed that he had 2 previous similar episodes, the first one was 6 months prior to his presentation (Table 1) and the other was one year ago, patient was diagnosed to have acute pancreatitis, managed supportively in outside hospital. Besides that, at 1 year of age patient experienced recurrent episodes of watery diarrhea with weight stagnation Investigations at that time revealed TG: 892 u/l-cholesterol: 242 u/l-lipase 345 u/l.

Table 1: Laboratory studies of the patient in the previous hospitalization.

Test done	6 months prior to this admission	2nd day of hospitalization	4 days after discharge
Lipase	10342 u/l	5054 u/l	58 u/l
Amylase		574 u/l	62 u/l
TG	870 u/l		90 u/l
Cholesterol	282 mg/dl		
HDL	25 mg/dl		
LDL	Undetectable	Undetectable	
HDL		232 u/l	
SGPT	140 u/l	32 u/l	
SGOT	36 u/l	33 u/l	
Imaging	Abdomen US was normal except for enlarged pancreas which showed increased reflectivity		

Family history showed that his grandparent had several attacks of acute pancreatitis and is currently suffering from chronic pancreatitis.

After this data TG level was taken for the parents and his 3 other siblings.

- Father: 117 u/l
- Mother: 76 u/l
- Sister aged 4years: 3846 u/l
- Sister aged 3 years: 97u/l
- Brother aged 11 month: 72 u/l

This brings up the second case to be presented which is his sister aged 4- year-old that has hypertriglyceridemia, but was completely asymptomatic.

Due to lack of facility to perform ultracentrifuge or genetic testing, lipid electrophoresis was performed to our patient and his sister (Table 2).

Table 2: Lipid electrophoresis of both patients.

Results of lipid electrophoresis	The boy	The girl
Chylomicron	Absence	Presence 3.3%
Alphalipoprotien	13.5%	13.5%
Prebetalipoprotien	86.5%	80.9%
Betalipoprotien	0%	0%
Appearance of serum	Clear	trouble
Decantation after 24h	Negative	negative

But here it should be noted that the condition for appropriate lipid testing were not present both of them had prolonged fasting 15 hours, and our patient was on extremely low fat diet, and was recently hospitalized less than 2 weeks which are all considered to be inappropriate conditions for lipid testing.

DISCUSSION

According to who Fredrickson classification of primary hyperlipidaemia there is 6 type I,IIA, IIB, III, IV and V, the most common dyslipidemias are types IIA, IIB, and IV. Type I and type III hyperlipoproteinemia (HLP) are extremely rare in pediatric patients, and type V is uncommon. Type 1 type 4 and type 5 all include hypertriglyceridemia and increase in VLDL.[3]

Our patient had the clinical findings of hyperchylomicronemic syndrome which included: Predominant increase in TG with slight increase in cholesterol, recurrent bouts of acute pancreatitis, failure to thrive, accumulation of triglycerides is generally proportional to the amount of dietary fat (so not constantly elevated and this explains the lipid fluctuations that our patient had from 870 u/l to 90 u/l in his previous admission, parents are cousins first degree consanguineous with a family history suggestive of autosomal dominant transmission, also the fact that 80% present before age 10 years, with 30% presenting before age one and the past medical history of this patient states that he was admitted for workup for hypertriglyceridemia with elevated lipase at the age of 11 month is also supportive of the diagnosis because maybe he was experiencing his first episode and finally

hypertriglyceridemia along with detection of chylomicron in his sister plasma. Here it should be noted that the inadequate condition for lipid testing which were mentioned early and lead to drop in lipoprotein levels especially that chylomicron is of exogenous source.[4] (disease also known as exogenous hyperlipemia so no fatty food no chylomicron).

The sister is of confirmed diagnosis despite of being asymptomatic since 3.3% chylomicrons were detected in herlipid electrophoresis even after prolonged fasting.

Regarding the etiology of hyperchylomicronemia whether it is LPL deficiency or LPL inhibitor or APO Protien C II deficiency according to the patients lipid profile it appears to be Apo lipoprotein C II deficiency since Apo lipoprotein C II deficiency shows elevated VLDL while LPL deficiency shows reduced to normal level VLDL (both show elevated Triglycerides and Chylomicron) but confirmative diagnosis with LPL assay and Apolipoprotien CII estimation was not performed.[5]

Here the question, why a diagnosis with a betalipoprotenemia was not considered even when both of them show 0 % betalipoprotien?

The response that the fact that neither the clinical findings nor the laboratory work up support the diagnosis. Clinically none of the 2 patients showed fat malabsorption, spinocerebellar degeneration, acanthocytic red blood cells, and pigmented retinopathy. In addition to that the laboratory workup showed that both patients show high VLDL while the lipoprotein profile of abetalipoprotenemia show absence of LDL and VLDL, this all stands against the diagnosis of abetalipoprotenemia.[6]

The absence of betalipoprotien in those two patients might be explained by the fact that VLDL interacts with LPL via apoprotein C-II to release TG, forming intermediate-density lipoprotein (IDL) particles, apoprotein C-II is transferred to HDL particles and the formed IDL particles are further metabolized to LDL by continued removal of TG by hepatic lipase So if these patients have Apo protein CII deficiency they will not be able to change VLDL into IDL consequently if no IDL eventually no LDL explaining the results of betalipoprotien level being 0 percent.[7]

CONCLUSION

Apoprotien C II deficiency can present earlier in life (LPL deficiency, 80% presented before age 10 years, with 30% presenting before age one. In contrast, apoprotein C-II deficiency is usually diagnosed later in life >13 years). The pediatrician should always take FHS with its different presentations into consideration when dealing with a case of pediatric recurrent pancreatitis.

ACKNOWLEDGEMENTS

The author would like to than the family members of both patients concerned for their collaboration.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Hassan MA, Anka M, Mneimneh S, Naous A, Rajab M. Two siblings with familial hyperchylomicronemis syndrome: disease presentation and diagnosis. Int J Contemp Pediatr 2016;3:665-7.