Malays J Pathol 2023; 45(2) : 293 – 296

CASE REPORT

Lipaemic serum in Hb E-Beta thalassaemia major: A rare case of hypertriglyceridaemia thalassaemia syndrome

Noor Alicezah MOHD KASIM[1,2], Noor Shafina MOHD NOR[1,2*], Mang Teen WEN[3], Sharifah Khairul Atikah SYED KAMARUDDIN[3], Siti Hamimah SHEIKH ABDUL KADIR[1,4]

[1]Department of Pathology, Department of Paediatrics & Department of Biochemistry & Molecular Medicine, Faculty of Medicine UiTM Sungai Buloh,47000 Sungai Buloh, Selangor, Malaysia; [2]Institute of Pathology, Laboratory and Forensic Medicine (I-PPerForM), Universiti Teknologi MARA (UiTM), Selangor, Malaysia; [3]Department of Pathology `& Department of Paediatric, Hospital Sungai Buloh, Ministry of Health, 47000 Sungai Buloh, Selangor, Malaysia; [4]Institute of Medical Molecular Biotechnology(IMMB), Faculty of Medicine UiTM, Selangor, Malaysia.

Abstract

Introduction: A 1-year-old Malay girl presented with pallor, failure to thrive and hepatosplenomegaly. Her blood was sent for thalassaemia screening and it was incidentally found that her blood appeared lipaemic. *Case Report:* Primary and secondary causes of hyperlipidaemia were investigated. Her blood was sent for fasting lipid profile, thyroid function test (TFT), fasting plasma glucose (FPG), liver function test (LFT), renal profile (RP) and HIV screening. Lipaemic interference was removed by high-speed centrifugation. She is a product of non-consanguineous marriage. She is staying together with her stepfather who is HIV positive. Her mother's infective status was negative with no dyslipidaemic features and a normal lipid profile. Lipid profile of her biological father was not known. No other lipid stigmata such as eruptive xanthoma or lipaemia retinalis was seen in the patient. Haemoglobin analysis showed Hb E-Beta thalassaemia major. Her triglycerides was 9.05 mmol/L with normal total cholesterol, 2.85 mmol/L and high-density lipoprotein cholesterol (HDL-c), 0.26 mmol/L. Calculated low-density lipoprotein cholesterol (LDL-c) was invalid as triglycerides was >4.5 mmol/L. TFT, RP, FPG, LFT were normal and HIV status was negative. She was transfused with 10 ml/kg packed cell and her blood post transfusion appeared non lipaemic. *Conclusion:* Primary hypertriglyceridaemia was excluded based on insignificant family history of dyslipidaemia. Secondary causes of hypertriglyceridaemia were ruled out based on unremarkable laboratory investigations. Thus, we conclude that this patient is having hypertriglyceridaemia thalassaemia syndrome (HTS) which is a rare disorder with unknown pathogenesis. Further research may be required to explore this unknown association.

Keywords: Lipaemia, thalassaemia, hypertriglyceridaemia

INTRODUCTION

Hypertriglyceridaemia refers to elevated levels of serum triglyceride (TG) carrying lipoprotein. It may be familial or acquired.[1] The levels may rise due to increased synthesis in the liver or decreased catabolism. A secondary rise of hypertriglyceridaemia may occur in hypothyroidism, nephrotic syndrome, biliary atresia, storage disorders, and drug-induced disorders (isotretinoin, steroids, thiazide diuretics etc). Apart from the known secondary causes of hypertriglyceridaemia, thalassaemia major infants have been reported to have elevated TG levels although a rare phenomenon, thus presenting with lipaemic serum.[2] Here, we report a rare case of a thalassaemic infant who presented with hypertriglyceridaemia.

CASE REPORT

A 1-year-old Malay girl who is the first born of a non-consanguineous marriage presented with pallor and failure to thrive. She was on formula milk and took a normal balanced diet. She has completed her immunisation schedule up to

**Address for correspondence:* Assoc Prof Dr Noor Shafina Mohd Nor, Department of Paediatrics & Institute of Pathology, Laboratory and Forensic Medicine (I-PPerForM), Faculty of Medicine, Universiti Teknologi MARA, 47000 Sungai Buloh, Selangor, Malaysia. Telephone: +603-6126 5000. Handphone No.: +6012-5882756. Fax: +603-6126 7465. Email: *shafinamohdnor@yahoo.com*

5 months old. Her developmental milestone was appropriate. She stays with her mother and stepfather. Her stepfather is HIV positive. Her mother's infective status was negative and she has a normal lipid profile. Lipid status of her biological father is unknown as he is uncontactable. She appeared pale and clinical assessment revealed hepatosplenomegaly with the liver and spleen palpable 4 cm below subcostal margin. No lipid stigmata such as eruptive xanthoma or lipaemia retinalis were seen. While taking her blood for further laboratory investigations, it was noted that her venous blood appeared grossly lipaemic (Fig. 1). Fasting serum lipid (FSL) was measured after serial dilution which showed markedly elevated TG of 9.05 mmol/L. Other lipid parameters which were total cholesterol and high-density lipoprotein cholesterol (HDL-C) were normal. The lipaemic serum was then removed by heavy centrifugation (Thermo Scientific, USA) at 25000 g for 5 minutes. The clear serum obtained was sent for liver function test, thyroid function test and renal profile to exclude all secondary causes of hypertriglyceridaemia and the results were all within normal range. Her haemoglobin (Hb) level was 7.2 g/dL and peripheral blood film showed hypochromic microcytic with many target cells seen. She was arranged for thalassaemia screening and chromatogram of Hb electrophoresis of the patient was suggestive of Hb E-β Thalassaemia as shown in Fig. 2. She was then transfused with 10 ml/kg of packed cells. Her blood was taken for a post-transfusion haemoglobin test, which showed a non-lipaemic plasma, as shown in Fig. 3. Unfortunately, post-transfusion lipid analysis was unable to obtain due to insufficient samples, and the patient did not turn up to repeat the analysis during the clinic follow-up. The lab results were tabulated in Table 1.

FIG. 1: Serum of the patient which showed grossly lipaemic serum.

DISCUSSION

Hypertriglyceridaemia is one of the most common lipid abnormalities encountered in clinical practice. However, in an infant, this phenomenon is rare. Hypertriglyceridaemia is defined as having fasting serum TG above the 95th percentile for age and sex.[3] A TG level greater than or equal to 1.13 mmol/L and a level greater than or equal to 130 mg/dL (1.47 mmol/L) is considered above the 95th percentile for children of ages 0 to 9 years and 10 to 19 years, respectively.[3]

Primary causes of hypertriglyceridaemia were ruled out based on history and the mother's normal lipid profile as well as the absence of primary hypertriglyceridaemia features like eruptive xanthoma and lipaemia retinalis. The common secondary causes of hypertriglyceridaemia such as hypothyroidism, diabetes mellitus, nephrotic syndrome, biliary atresia, storage disorders, drug-induced disorders for example isotretinoin, steroids, thiazide diuretics were also excluded making Hypertriglyceridaemia Thalassemia Syndrome (HTS) the most likely cause of the lipaemic serum. To the best of our knowledge, this is the first case of HTS reported from our country, Malaysia.

In most cases, the HTS is associated with β-Thalassemia Major and presents in the age group ranging from 4 months to 2.5 years while the TG level ranges from 9.04- 12.07 mmol/L.[1,4-6] Consistent with previously reported cases[5], the lipaemic serum disappears and TG normalises after blood transfusion. Various theories exist to explain this association. A study by Druml *et al*. showed that massive haemolysis might cause hypertriglyceridaemia.[7] They found that the elevation of serum TG occurs during or immediately after the haemolytic crisis and is only transient, with a fall within a few days if the cause of red cell destruction is eliminated. In massive haemolysis, catecholamine release might be increased and cause free fatty acid mobilisation. Thus, excess accumulation of free fatty acids induces secondary hepatic re-esterification into

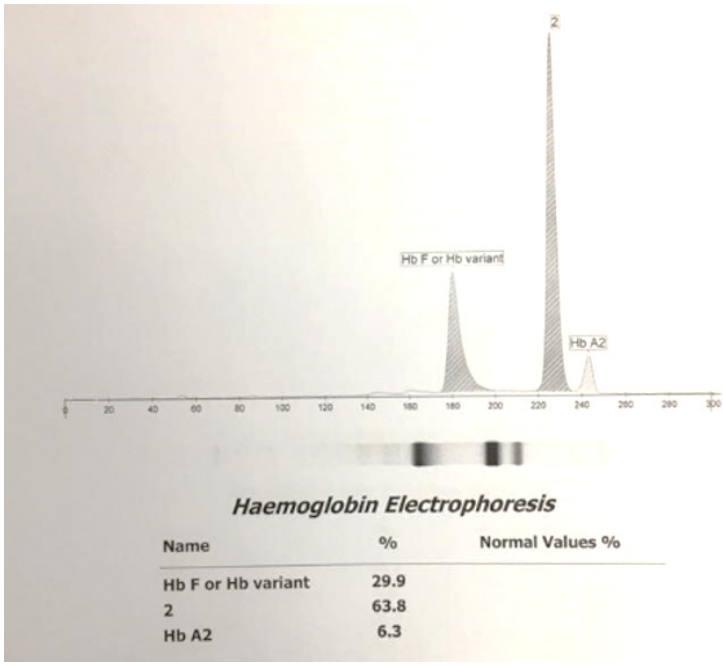

FIG. 2: Chromatogram of Hb electrophoresis of the patient suggestive of Hb E-β Thalassaemia.

TG. Apart from that, they hypothesised that haemolysis might cause hyperlipidaemia directly by affecting the microcirculation and indirectly by activation of the coagulation system. Both increased TG formation and impaired removal from the bloodstream may contribute to serum TG elevation. When blood is being transfused, the haemolysis effect gets diluted; thus, TG level normalises.

A lipaemic serum can be detected through visual inspection, where the serum appears turbid when the TG level exceeds 4.6 mmol/L.[8] Apart from visual inspection, the lipaemic serum can be detected by using automatic detection L Index. In this method, the sample is diluted with saline or buffer, to which the spectra wavelength is measured. Lipaemia can cause interferences due to physical and chemical interference, spectrophotometric method interference, non-homogeneity of the sample, and volume displacement effect.[9] Therefore, the lipaemic sample needs to be identified, and all laboratory personnel should be trained to remove the lipaemia.

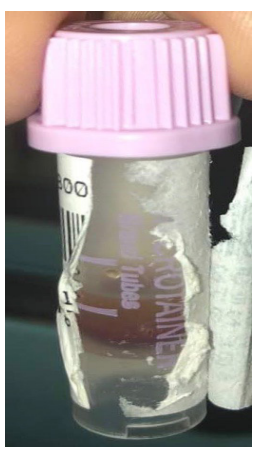

FIG. 3: Non-lipaemic plasma of the patient post blood transfusion.

In conclusion, although this is rare, HTS should be recognised early, after ruling out primary hypertriglyceridaemia and other secondary causes of hypertriglyceridaemia. Regular blood transfusions usually resolve the high serum TG levels. Early recognition is essential to prevent risk of complications such as acute pancreatitis and coronary disease. As, there is no clear theories on association of hypertriglyceridaemia with thalassaemia, further studies to elucidate whether there are other mutations or gene polymorphisms involved in lipid metabolism may be warranted.

Acknowledgement: The authors would like to thank the Director General of Health Malaysia for his permission to publish this article.

Conflict of interest: The authors declare no conflict of interest.

Table 1: Laboratory results

Test	Results		Reference range (unit)
	Pre blood transfusion	Post blood transfusion	
Hemoglobin	7.7	12.2	11.1 – 14.1 g/dL
White blood cell	10.9	21	6 – 18 x 10^9/L
Platelet	459	329	200 – 550 x 10^9/L
Total Cholesterol	2.85	Insufficient sample	0 – 5.2 mmol/L
Triglycerides	9.05	2.64	0 - 1.70 mmol/L
HDL-c	0.26	Insufficient sample	>1.2 mmol/L
LDL-c	-	-	< 3.0 mmol/L
Sodium	130	-	138-145 mmol/L
Potassium	3.9	-	98 – 107 mmol/L
Urea	1.2	-	3.2 – 7.4 mmol/L
Chloride	104	-	98 – 107 mmol/L
Creatinine	26	-	50 – 98 umol/L
Albumin	41	-	38 – 54 mg/dL
Total bilirubin	40.7	-	3.4 – 20.5 umol/L
Direct bilirubin	16.4	-	0 – 8.6 umol/L
Indirect bilirubin	24.3	-	3.42 – 13.68 umol/L
Aspartate transaminase (AST)	32	-	5 – 34 U/L
Alanine transaminase (ALT)	30	-	0 – 55 U/L
Alkaline phosphatase (ALP)	147	-	0 – 499 U/L
Lactate Dehydrogenase (LDH)	532	-	125 – 220 U/L
Free Thyroxine (FT4)	16.8	-	11.45 -17.63 pmol/L)
Thyroid Stimulating Hormone (TSH)	5.2	-	0.70 - 4.17 mIU/L)
Fasting plasma glucose	4.0	-	< 6.1 mmol/L)
Human Immunodeficiency Virus (HIV)	Non-reactive	-	-

Authors' contribution: All authors have contributed towards the preparation of the final manuscript.

REFERENCES

1. Khera R, Singh M, Goel G, Gupta P, Singh T, Dubey A. Hypertriglyceridemia thalassemia syndrome: a report of 4 cases. Indian Journal of Hematology and Blood Transfusion, 2014; 30:288-91.
2. Pandey S, Agrawal P, Rawat A, Gupta M, Khare P. Hypertriglyceridemia in a baby with thalassemia major. Indian Journal of Medical Specialities, 2020; 11:157.
3. Valaiyapathi B, Sunil B, Ashraf AP. Approach to hypertriglyceridemia in the pediatric population. Pediatrics in Review, 2017; 38:424-34.
4. Mohan BP, Prabhalekshmy K, Letha V, Nisha T. Idiopathic Hypertriglyceridemia in Thalassemia Major: A Case Report. National Journal of Laboratory Medicine, 2017; 6: PC04-PC06.
5. Das L, Samprathi M, Shukla U, Bandyopadhyay D, Das RR. Hypertriglyceridemia thalassemia syndrome: common disease, uncommon association. The Indian Journal of Pediatrics, 2016; 83:720-2.
6. Jain M, Ali W, Singh BB, Verma N, Kumar A. Hypertriglyceridemia thalassemia syndrome. Journal of Pediatric Endocrinology and Metabolism, 2018; 31:821-2.
7. Druml W, Grimm G, Laggner A, Schneeweiss B, Lenz K. Hyperlipidemia in acute hemolysis. Klinische Wochenschrift, 1991; 69:426-9.
8. McPherson RA, Pincus MR. Henry's clinical diagnosis and management by laboratory methods E-book, Elsevier Health Sciences, 2021.
9. Nikolac N. Lipemia: causes, interference mechanisms, detection and management. Biochemia medica, 2014; 24:57-67.