Unusual presentation of more common disease/injury

Paediatric type III dyslipidaemia: a case of vanishing hyperlipidaemia

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Summary

An 11-year-old girl presented with palmar and tuberoeruptive xanthomas, and elevated triglycerides and total cholesterol levels. She had an apolipoprotein E2/E2 genotype. A diagnosis of type III dyslipidaemia was made and the patient started on niacin, fenofibrate and salmon oil. At age 18, her lipid levels were well controlled with fenofibrate once weekly. At age 21, the fenofibrate was discontinued and her lipid profile has been normal for the last 4 years. This case history may be consistent with a transient dyslipidaemia.

BACKGROUND

Type III dyslipidaemia (familial dysbetalipoproteinaemia) is an autosomal recessive disorder of lipid metabolism with a frequency of approximately 1:5000. It is characterised by the presence of two apoE2 alleles. An additional genetic or environmental factor, such as complete or partial Lipoprotein lipase (LPL) deficiency, obesity, gout, hypothyroidism or diabetes mellitus, is required for full clinical expression of this condition. Physical findings include palmar and tuberoeruptive xanthomas. Laboratory findings include elevated triglycerides, total cholesterol and low-to-normal apolipoprotein B (apoB).^{1,2} Type III dyslipidaemia is treated with low-fat diet and lipid-lowering medications. In this case, fenofibrate with a low-fat diet controlled her dyslipidaemia. Interestingly, over the next 10 years, fenofibrate dose was decreased and then discontinued and over the last 4 years, her lipids normalised without medications despite failing to adhere strictly to a low-fat diet.

CASE PRESENTATION

The patient was referred to our lipid clinic at age 11 with a family history of premature cardiovascular disease. Her past medical history was unremarkable.

On physical examination, in addition to palmar xanthomas there were bilateral tuberoeruptive xanthomas on her elbows. There was no arcus cornealis, xanthelasmas or tendon xanthomas. There was no hepatomegaly or splenomegaly.

INVESTIGATIONS

The baseline lipid profile and follow-up lipid levels are presented in table 1. The patient's baseline fasting triglycerides and total cholesterol were elevated at 4.9 mmol/l and 12.0 mmol/l, respectively. A thyroid-stimulating hormone (TSH) level was elevated at 80 but she denied symptoms of hypothyroidism, and she has not been treated for hypothyroidism. The antithyroid peroxidase antibodies were within the normal range. The TSH subsequently normalised without treatment.

She had an E2/E2 genotype and normal LPL and hepatic lipase activity.

DIFFERENTIAL DIAGNOSIS

The above findings are consistent with type III dyslipidaemia, which, as previously reported,³ rarely presents in childhood.

TREATMENT

A low-fat diet and 4 g of omega 3 fatty acids daily were prescribed. At a 6-month follow-up, her palmar xanthomas were disappearing despite her blood lipid profile not changing significantly. Subsequently, a low-dose niacin (250 mg twice daily) was added. However, the lipid values remained outside the target levels and the niacin was increased to 2 g four times daily and later to 3g four times daily.

Over the next 4 years, her lipids were much improved but not ideal. Although her physical findings also improved, the xanthomas were still, on occasion, visible, particularly when her diet had slipped. She was then started on Lipidil Supra 160 mg four times daily monotherapy. A year later, her lipids were well within the target. Subsequently, she used fenofibrate every second day and continued with it into her puberty. Later, the fibrates was reduced to once weekly.

Table 1 Laboratory findings before and after a low-fat diet and Lipidil Supra: baseline, 160 mg daily, 160 mg weekly and cessation of therapy

Analyte (units)	Baseline	On Lipidil QD	On Lipidil Q7 days	No Rx
Total Cholesterol (mmol/l)	12.0	6.3	5.3	5.3
LDL-C (mmol/l)	—	3.6	2.9	2.4
Triglycerides (mmol/l)	4.9	3.3	1.9	2.0
HDL-C (mmol/l)	1.2	1.1	1.5	2.0
Chol/HDL ratio (mmol/l)	10.3	5.5	3.5	2.6
Apo B (mmol/l)	1.2	1.0	—	0.7

OUTCOME AND FOLLOW-UP

Over the last 4 years, her lipid values have been well within the target, despite not being entirely compliant with the dietary instructions and not taking any lipid-lowering medications.

DISCUSSION

Patients with type III dyslipidaemia are responsive to therapy and fibrates are the most commonly used drugs.^{2 4 5} However, most patients are maintained on long-term therapy to reduce the risk of uncontrolled hypertriglyceridaemia and acute pancreatitis.^{6 7} In the case of our patient with a transitory hyperlipidaemia, she responded well to fenofibrate daily and maintained her target levels after discontinuing therapy, despite failing to adhere strictly to a low-fat diet.

Transient dyslipidaemias may be secondary to systemic conditions^{8 9} including sepsis or medications (corticosteroids and atypical antipsychotics).^{10 11} Clinical awareness of this phenomenon can avoid misdiagnosis and continued treatment.

We speculate that there may be pubertal hormonal factors involved in modulating the factors that trigger dyslipidaemia in individuals with an E2/E2 genotype. It seems as though the functional impairment imparted by her apoE2 isoform has normalised during her transition from adolescence to young adulthood. Interestingly, in our patient, there are no obvious reasons for the early manifestation of the type III dyslipidaemia, as there are no usual factors such as LPL deficiency or hypothyroidism present that could have precipitated the early manifestation of this disorder.³ We do not believe that our patient was hypothyroid. The increased TSH had no associated laboratory or clinical features and normalised without any therapeutic intervention. Thus, we believe the high value was caused by the presence of heterophile antibodies.¹²

We conclude that not all patients with type III dyslipidaemia require long-term hypolipidaemic agents; in patients requiring pharmacotherapy, we recommend routine medication assessments as there may be a subset with transitory dyslipidaemia. However, although there was a clear clinical presentation of type III dyslipidaemia, there are several atypical features of this patient's presentation: manifestation in childhood, disproportion between the elevation in triglycerides (modest) and total cholesterol as well as uncharacteristically high apoB (1.2 mmol/l).

Learning points

- ▶ Type III dyslipidaemia is usually clinically silent in the paediatric population.
- ▶ When combined with additional genetic or environmental factors, the apoE2/E2 genotype can result in type III dyslipidaemia.
- ▶ Pharmacological treatment of type III disease is indicated if dietary modifications alone are insufficient in managing the dyslipidaemia.
- ▶ Fibrates are usually effective in treating this condition.
- ▶ Not all patients with type III dyslipidaemia require long-term lipid-lowering therapy due to the phenomenon of transitory dyslipidaemia.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Bari AU**, Hashim R, Rahman SB, *et al.* Familial Dysbetalipoproteinemia Pathophysiology. *J Coll Physicians Surg Pak* 2008;**18**:506–8.
2. **Blom DJ**, Byrnes P, Jones S, *et al.* Dysbetalipoproteinemia—clinical and pathophysiological features. *S Afr Med J* 2002;**92**:892–7.
3. **Fung M**, Hill J, Cook D, *et al.* Case series of type III hyperlipoproteinemia in children. *BMJ Case Reports* 2011; 10.1136/bcr.02.2011.3895, Published 9 June 2011.
4. **Keating GM**. Fenofibrate: a review of its lipid modifying effects in dyslipidemia and its vascular effects. *Am J Cardiovasc Drugs* 2011;**1**:227–47.
5. **Yuan G**, Al-Shali KZ, Hegele RA. Hypertriglyceridemia: its etiology, effects and treatment. *CMAJ* 2007;**176**:1113–20.
6. **Sandhu S**, Al-Sarraf A, Taraboanta C, *et al.* Incidence of pancreatitis, secondary causes, and treatment of patients referred to a specialty lipid clinic with severe hypertriglyceridemia: a retrospective cohort study. *Lipids Health Dis* 2011;**10**:157.
7. **Austin MA**, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. *Am J Cardiol* 1998;**81**:7B–12B.
8. **Palacio C**, Alexandraki L, Bertholf RL, *et al.* Transient dyslipidemia mimicking the lipid profile of Tangier's disease in a diabetic patient with gram negative sepsis. *Ann Clin Lab Sci* 2011;**41**:150–3.
9. **Garcia-Otin AL**, Civeira F, Peinado-Onsurbe J, *et al.* Acquired Lipoprotein Lipase deficiency associated with chronic urticaria: a new etiology for Type I Hyperlipoproteinemia. *Eur J Endocrinol* 1999;**141**:502–5.
10. **Stip E**, Tourjman V. Aripiprazole in Schizophrenia and Schizoaffective disorder: a review. *Clin Ther* 2010;**32**:S3–20.
11. **Steinherz PG**. Transient, severe hyperlipidemia in patients with Acute Lymphoblastic Leukemia treated with prednisone and asparaginase. *Cancer* 1994;**74**:3234–9.
12. **Despres N**, Grant AM. Antibody interference in thyroid assays: a potential for clinical misinformation. *Clin Chem* 1998;**44**:440–54.

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