Learning from errors

Statin resistant dyslipidemia in a patient treated with amiodarone

Ahmad Al-Sarraf,^{1,2} Min Li,² Jiri Frohlich^{1,2}

¹Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, British Columbia, Canada;

²Healthy Heart Program, St Paul's Hospital, Vancouver, British Columbia, Canada

Correspondence to Professor Jiri Frohlich, jifr@mail.ubc.ca

Summary

The authors describe a patient treated with amiodarone presented with high low-density lipoprotein cholesterol (LDL-C) levels who did not respond to treatment with a statin. Both amiodarone and amiodarone induced hypothyroidism influence the synthesis of LDL-receptor which may explain the lack of effect of statin. This was confirmed by normalisation of LDL-C upon discontinuation of amiodarone and treatment with thyroxine.

BACKGROUND

Hyperlipidemias are either primary (familial) caused by specific genetic abnormalities or secondary resulting from other conditions that lead to alterations in lipid metabolism. Some of the most common causes of secondary hyperlipidemia include type 2 diabetes mellitus, hypothyroidism, cigarette smoking, cholestatic liver diseases, nephrotic syndrome, renal failure, alcohol ingestion, obesity and drugs such as diuretics, β blockers and oestrogens.¹ Treatment of the underlying condition or discontinuation of the drug usually corrects the hyperlipidemia. We describe a case of dyslipidemia induced by amiodarone, a potent antiarrhythmic drug, and further exacerbated by amiodarone induced hypothyroidism. While weight loss is generally associated with a decrease in low-density lipoprotein cholesterol (LDL-C) and triglyceride and an increase in high-density lipoprotein cholesterol² in our patient the reverse occurred: his LDL-C level was markedly elevated. This led to an incorrect diagnosis of primary dyslipidemia and inappropriate initiation of statin therapy.

CASE PRESENTATION

A 41-year-old man attended Bernstein's diet clinic for weight reduction in May 2010. Before starting the programme, his lipid profile was normal and thyroid function test (thyroid stimulating hormone) was not requested (table 1). His initial weight was 559 pounds; he lost 350

pounds over the course of 1 year on a regular exercise and low fat diet. Two months after starting the program, he had a pacemaker and defibrillator implanted because of bradycardia. One month later, he developed ventricular tachycardia and ventricular fibrillation and was started on amiodarone 200 mg daily. Two months later, his LDL-C increased from 2.6 to 6.4 mmol/l and he was treated with crestor 10 mg. One month later, this was increased to 20 mg daily. Interestingly, his LDL-C level continued to rise up to 8.4 mmol/l despite the treatment.

At this point, the patient was referred to a lipid clinic for further management. Physical examination was unremarkable with no signs of a primary dyslipidemia and there were no clinical signs of hypothyroidism. Laboratory investigations before and during amiodarone treatment are shown in table 1.

Crestor was stopped as his dyslipidemia was thought to be due to administration of amiodarone and concurrent hypothyroidism. This was confirmed by discontinuation of amiodarone after a cardiac ablation and administration of L-thyroxine which resulted in a markedly improved lipid profile (table 1).

DISCUSSION

Thyroid hormone is one of several hormones that control gene expression of the LDL receptor.^{3 4} Hypothyroidism a well-known cause of secondary dyslipidemia^{5 6}

Table 1 Laboratory investigations before and after amiodarone treatment

Analyte (reference range, units)	Before weight reduction	On amiodarone	On amiodarone and crestor 20 mg	On L-thyroxine and discontinuation of amiodarone
Total cholesterol (<5.20 mmol/l)	4.4	8.7	10.9	5.5
LDL-C mmol/l	2.6	6.4	8.4	2.3
Triglycerides (<1.50 mmol/l)	1.3	1.8	2.2	0.7
HDL-C (>0.90 mmol/l)	1.2	1.5	1.5	2.9
Chol/HDL ratio	3.7	5.8	7.3	1.9
Apo B (<1.25 g/l)			1.78	0.66
Fasting glucose (3.6–6.0 mmol/l)	5	4.7		5.2
TSH mU/l (0.3–5.5)			6.73	

HDL, high-density lipoprotein; LDL, low-density lipoprotein; TSH, thyroid stimulating hormone.

characterised by elevated circulating levels of the apolipoprotein B100 containing lipoproteins namely very LDLs and LDLs.⁷ Similar to hypothyroidism, administration of amiodarone also increases LDL levels which is the result of a decreased expression of the LDL-receptor gene.^{8,9} In the case of our patient, the unexpected increase in LDL-C could be explained by the synergistic effect of the hypothyroid state and amiodarone medication both of which reduce LDL-receptor promoter activity.¹⁰ What is also of interest is that, that under these circumstances, the HMG-CoA inhibition by the statin apparently did not influence the LDL-receptor synthesis. We conclude that in patients treated with amiodarone, thyroid status has to be examined prior to treatment with statins.

Learning points

- ▶ Important of distinguishing between primary and secondary hyperlipidemia: lesson learnt from a patient treated with amiodarone.
- ▶ Effects of amiodarone and thyroid hormone of LDL-receptor synthesis/possible interference with the mechanism of statin action.
- ▶ Not all patients with dyslipidemia require statin treatment.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Chait A**, Brunzell JD. Acquired hyperlipidemia (secondary dyslipoproteinemias). *Endocrinol Metab Clin North Am* 1990;**19**:259–78.
2. **Krauss RM**, Winston M, Fletcher BJ, *et al.* Obesity: impact on cardiovascular disease. *Circulation* 1998;**98**:1472–6.
3. **Bhattacharya S**, Balasubramaniam S, Simons LA. Regulation of low-density-lipoprotein metabolism in the rat. *Biochem J* 1986;**234**:493–6.
4. **Soutar AK**, Knight BL. Structure and regulation of the LDL-receptor and its gene. *Br Med Bull* 1990;**46**:891–916.
5. **Cappola AR**, Ladenson PW. Hypothyroidism and atherosclerosis. *J Clin Endocrinol Metab* 2003;**88**:2438–44.
6. **Morris MS**, Bostom AG, Jacques PF, *et al.* Hyperhomocysteinemia and hypercholesterolemia associated with hypothyroidism in the third US National Health and Nutrition Examination Survey. *Atherosclerosis* 2001;**155**:195–200.
7. **Abrams JJ**, Grundy SM. Cholesterol metabolism in hypothyroidism and hyperthyroidism in man. *J Lipid Res* 1981;**22**:323–38.
8. **Hudig F**, Bakker O, Wiersinga WM. Amiodarone-induced hypercholesterolemia is associated with a decrease in liver LDL receptor mRNA. *FEBS Lett* 1994;**341**:86–90.
9. **Hudig F**, Bakker O, Wiersinga WM. Amiodarone decreases gene expression of low-density lipoprotein receptor at both the mRNA and the protein level. *Metab Clin Exp* 1998;**47**:1052–7.
10. **Bakker O**, Hudig F, Meijssen S, *et al.* Effects of triiodothyronine and amiodarone on the promoter of the human LDL receptor gene. *Biochem Biophys Res Commun* 1998;**249**:517–21.

This pdf has been created automatically from the final edited text and images.

Copyright 2011 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Al-Sarraf A, Li M, Frohlich J. Statin resistant dyslipidemia in a patient treated with amiodarone. *BMJ Case Reports* 2011; 10.1136/bcr.08.2011.4620, date of publication

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow