

CASE REPORT

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Family hypercholesterolemia revealed by myocardial infarction: Case report and literature data

Noël Maschell Mahoungou-Mackonia, A Fadoul, C Mahamadou, A Drighil, C Couderq, R Habbal

ABSTRACT

Introduction: Familial hypercholesterolemia is a monogenetic, autosomal dominant, heterozygous predominant disease that affects 1/500 births and only 20% of cases are diagnosed. Diagnosis is based on the MedPed score, which includes family history, clinical manifestations, complications, and hypercholesterolemia determined by biological tests with genetic confirmation of the mutation. Complications occur early, before the age of 55 in men and 60 in women, and are even more virulent in the homozygous form. Thus, we relate this clinical case to its underestimation, low prevalence, and especially its virulence.

Case Report: A 31-year-old, non-obese patient with a history of stroke in the mother at the age of 52 years, acute coronary syndrome on two occasions at the age of 44 years in the older brother. He was admitted to the hospital with a revascularized myocardial infarction in the right coronary artery by primary angioplasty. The clinical examination was normal, the lipid profile showed hypercholesterolemia (HCT) with low-density lipoprotein (LDL)-CT=3.64 g/L, high-density lipoprotein (HDL)-CT=0.32 g/L, and triglyceride (TG)=2.1 g/L. The MedPed score was 12 points with one copy of the LDL receptor gene on the genetic sample. The patient received high-dose lipid-lowering drugs combined with healthy dietary

measures. Genetic screening of the rest of the family was performed.

Conclusion: Familial hypercholesterolemia is a poorly understood disease, diagnosed late, usually after the onset of complications, requiring early family screening, drug treatment with very potent lipid-lowering drugs at a tolerated effective dose, as early as eight years of age if the diagnosis is confirmed based on the MedPed score.

Keywords: Familial hypercholesterolemia, MedPed score, Myocardial infarction, Right coronary

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INTRODUCTION

Familial hypercholesterolemia (FH) is a monogenetic, autosomal dominant disease, most often heterozygous and rarely homozygous, characterized by a very high virulence [1–3]. One in 200 to one in 300 people are affected in its heterozygous form, i.e., 1/500 births in France. Fifty percent of the children of affected parents have a risk of developing the disease. The homozygous form, most often composite, is much rarer (1 in 1,000,000 cases) [1, 4]. Familial hypercholesterolemia is due to the mutation of a single allele in the heterozygous form, resulting in a 50% reduction in hepatic clearance of low-density lipoproteins (LDL), producing LDL cholesterol (LDL-C) levels that are twice as high as usual from birth

and ten times higher if the mutation involves both alleles in the homozygous form [2]. The diagnosis is based on three basic characteristics: a family history, clinical manifestations related to hypercholesterolemia and its complications, and the presence of hypercholesterolemia in biology with genetic confirmation of the mutation after the MedPed score. Complications occur early, before the age of 55 in men and 60 in women [1]. It is therefore one of the most common genetic diseases but is under-diagnosed with only 20% of confirmed cases.

We present a case of myocardial infarction in a young patient, revealing familial hypercholesterolemia.

CASE REPORTS

We report the case of a 31-year-old non-obese patient, with no particular personal history, presenting with a notion of a stroke in the mother at the age of 52 and an acute coronary syndrome on two occasions at the age of 44 (Figures 1 and 2). He was hospitalized for a myocardial infarction in inferior left ventricular ejection fraction (LVEF) 62%, revascularized on the right coronary by primary angioplasty, at 96 minutes (Figure 3). Clinical examination was normal, including a blood pressure (BP) of 135/82 mmHg and a heart rate of 92 beats/min. The lipid profile showed hypercholesterolemia (HCT) with LDL-CT of 3.64 g/L, HDL-CT of 0.32 g/L, and TG of 2.1 g/L. The patient had a MedPed score of 12 points associated with genetic sampling, showing a copy of the LDL receptor gene.

The patient received high dose statin (Atorvastatin 80 mg/day and Ezetimibe 10 mg/day) combined with adherence to dietary hygiene measures, followed by further treatment of coronary syndrome: Ticagrelor 90 mg × 2/dr, Karegic 75 mg/day; Bisoprolol 2.5 mg/day, and Ramipril 2.5 mg/day. Family genetic screening was performed including those of the mother and brother. Progression on treatment after three months showed a reduction in LDL-CT to 1.80 g/L.

DISCUSSION

Familial hypercholesterolemia (FH) is by definition one of the most common autosomal dominant monogenic diseases, highly fatal but often unrecognised, accounting for only 20% of diagnosed patients [1–3]. There are two forms of familial hypercholesterolemia [5]:

- The homozygous form is much rarer (1 in 1,000,000 cases) with a very severe phenotypic expression that can lead to vascular accidents from adolescence. Its very specific management is only done in a specialised environment.
- The heterozygous form, which is much more frequent, affects 50% of children whose parents are affected.

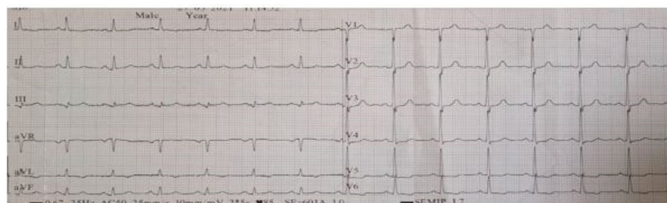


Figure 1: 12-Lead electrocardiogram (ECG) showing inferior shift.



Figure 2: Section of the four cavities, LVEF 62%.



Figure 3: On the left is a coronary angiography image showing a tight stenosis of the right coronary in its segment, while on the right is a revascularized right coronary.

Familial hypercholesterolemia leads to an increase in LDL-CT levels from birth. The atherosclerosis it causes begins in childhood and predisposes to premature coronary events in adulthood. For this reason, any late development of it in adult life is not suggestive of a familial form [1, 4].

The pathophysiology of FH is due to the mutation of a single allele (heterozygous state) of the LDLR genes, coding for the LDL receptor, APOB, responsible for the binding of LDL particles to their receptor, or PCSK9 coding for the “Protein convertase subtilisin/kexin type 9” which facilitates the lysosomal degradation of the LDL receptor [6]. A 50% reduction in hepatic clearance of LDL lipoproteins due to mutation of a single allele results in LDL cholesterol (LDL-C) levels twice as high as normal levels since birth.

The diagnosis of FH is based on a triad of MedPed scores combining [1, 7]:

- History:
 - o Family history:
 - Of premature coronary or vascular disease present in first-degree relatives (male < 55 years, female < 60 years) [1].
 - First-degree relative with LDL-C > 95th percentile [1].
 - First-degree relative with tendon xanthomas and/or corneal arc [2].
 - Child < 18 years with LDL-C > 95th percentile [2].
 - o Personal
 - Premature coronary artery disease (male < 55 years, female < 60 years) [2].
 - Premature cerebral or arterial occlusive disease of the lower limbs [1].
- Clinical signs
 - o Tendon Xanthomas [6]
 - o Corneal arc before 45 years [4]
- Biological data
 - o Biochemical:
 - LDL-C > 3.30 g/L (> 8.5 mmol/L) [8]
 - LDL-C: 2.50–3.29 g/L (6.5–8.4 mmol/L) [5]
 - LDL-C: 1.90–2.49 g/L (5.0–6.4 mmol/L) [3]
 - LDL-C: 1.55–1.89 g/L (4.0–4.9 mmol/L) [1]
 - o DNA analysis
 - Genetic mutations identified [8]

The MedPed score is classified into three:

- Possible (3–5 points)
- Probable (6–8 points)
- Certain (greater than 8 points)

In our case, our patient had a high MedPed score of 12, based on family history, clinic, and biochemistry, topped by the presence of an LDL receptor gene copy. Family screening should be done very early once the diagnosis is evoked because complications are early. In our case the notion of hypercholesterolemia was objectified in the brother and the mother with complications such as myocardial infarction and a stroke.

When the LDL-C level remains above 1.9 g/L in children and adolescents aged 8 to 10 years, management begins with dietary hygiene measures for a period of at least six months [1]. If hypercholesterolemia persists, a statin is recommended as first-line treatment in children, adolescents, and even adults at the lowest effective dose [3, 8]. This makes them the most important class of drugs for reducing LDL-C. Several molecules are marketed, allowing a reduction in LDL-C of 30–50% to be achieved. The latter depends on both the molecule chosen and the dose used [1]. In practice, the most potent statins, in particular atorvastatin or rosuvastatin, are used because of the significant increase in LDL-C. Ezetimibe, on the other hand, allows an average reduction of LDL-C of about 20%, as do anti-PCSK9 antibodies.

In our case, the patient received a high dose of statin and ezetimibe from the start.

CONCLUSION

Familial hypercholesterolemia is a common but very poorly understood genetic condition, usually objectified at the complication stage in developed countries where genetic testing can be performed. Management should be early once the diagnosis has been made and this should be done even in adolescence using statins at a lower effective dose.

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Author Contributions

Noël Maschell Mahoungou-Mackonia – Conception of the work, Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

A Fadoul – Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

C Mahamadou – Acquisition of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

A Drighil – Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

C Couderq – Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

R Habbal – Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be

accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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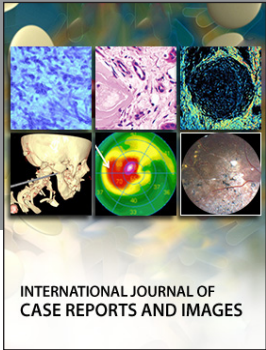
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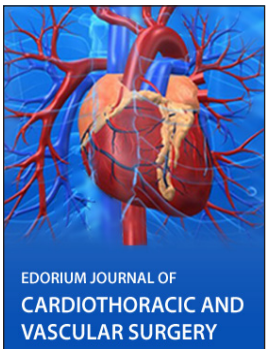
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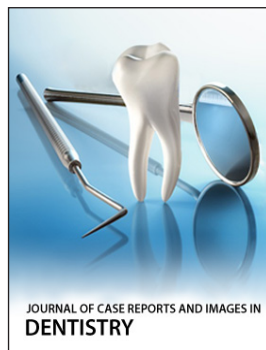
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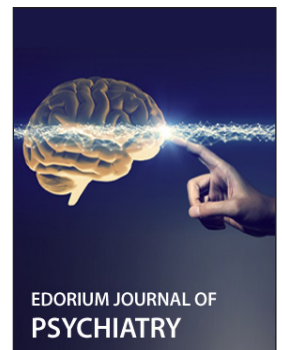
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