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EDITORIAL

Widespread xanthomas regression by personalized lipid lowering therapy in heterozygous familial hypercholesterolemia

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Cutaneous xanthomas;
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Abstract ''The lower, the better'' is the recommended approach in the management of high LDL cholesterol. Unfortunately, this does not always achieve as in the case of a 69-year-old woman referred to our Institute for her lipid profile (LDL cholesterol 412 mg/dl), bilateral xanthelasma and cutaneous xanthomas. With a maximized and personalized lipid-lowering therapies (rosuvastatin, ezetimibe, PCSK9i and lipoprotein apheresis), after only six months, the patient showed an impressive regression in her cutaneous xanthomas.

PALABRAS CLAVE
Xantomas cutáneos;
Hipercolesterolemia familiar heterocigótica;
Terapia hipolipemiante;
Xantomas tendinosos;
Xantelasma

Regresión generalizada de xantomas mediante terapia hipolipemiante personalizada en hipercolesterolemia familiar heterocigótica

Resumen «Cuanto más bajo, mejor» es el enfoque recomendado en el tratamiento del colesterol LDL alto. Lamentablemente esto no siempre se logra como en el caso de una mujer de 69 años remitida a nuestro Instituto por su perfil lipídico (colesterol LDL 412 mg/dL), xantelasma bilateral y xantomas cutáneos. Con terapias hipolipemiantes maximizadas y personalizadas (rosuvastatina, ezetimiba, iPCSK9 y aféresis de lipoproteínas), después de solo seis meses, la paciente mostró una regresión impresionante en sus xantomas cutáneos.

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Familial hypercholesterolemia (FH) is a genetic disease causing severe and premature atherosclerotic cardiovascular disease. ''*The lower, the better*'' is the recommended approach in the management of high LDL cholesterol. Unfortunately, this does not always achieve[1] as in the case of a 69-year-old woman referred to our Institute for her lipid profile [LDL-C 412 mg/dl, Lp(a) 119 mg/dl], bilateral xanthelasma and cutaneous xanthomas (Fig. 1 Panels A and B). At the age of 47, she undergone to PTCA/stenting on left anterior descending artery for effort angina. In the following twenty-two years, the patient did not experience any further cardiac event while self-discontinuing lipid-lowering therapies (LLT).

The physical examination was positive for Achilles tendon xanthomas (Fig. 2); CT coronary angiography showed diffuse non-critical calcific atherosclerotic disease and a 40% stenosis at the carotid bulb bilaterally was revealed. Genetic test confirmed the diagnosis of heterozygous familial hypercholesterolemia (HeFH). LLT with rosuvastatin/ezetimibe (20/10 mg OD), evolocumab (140 mg s.c. every 14 days) and lipoprotein apheresis (LA) was started (Liposorber®-LA MA-03 systems; Kaneka, Osaka, Japan) achieving a median inter-aphaeretic concentration of LDL-C and Lp(a) of 34 mg/dl and 40 mg/dl respectively.

With this maximized LLT, after six months, the patient showed an impressive regression in her cutaneous xanthomas (Fig. 1 Panels C and D).

Patients with HeFH with elevated lipoprotein(a) and previous cardiovascular events represent a comorbidity profile hard to manage and the current guidelines propose a more aggressive lowering in LDL-C and cholesterol-rich apolipoprotein B for their key role in the arterial wall atherogenesis.[1]

The singularity of the described case is represented by over-time stability of atherosclerotic disease in contrast of the widespread lipid deposits in the skin and tendons, even in the absence of LLT. The personalization of LLT becomes fundamental especially in patients affected by heterozygous FH and high Lp(a) in the light of their high cardiovascular risk.

FH patients are often characterized by age-related fat deposition on the Achilles tendon, showing thickening and fragility, and also related with the severity of coronary artery disease.[2,3] We know that short-term evolocumab is able to induce tendon xanthomas regression in a patient with homozygous FH,[4] that in HeFH the addition of a PCSK9 inhibitor to backbone LLT resulted in tendon xanthomas regression after 3 years of treatment[5] and that LA treatment allows the complete regression of lipid deposition[6] because accelerate the efficacy of LLT. In this case we combined all these therapies to maximize their effect.

Waiting for the new drugs on the way, as the antisense oligonucleotides against apolipoprotein (a), the first step is the personalization of the therapy safeguarding heterozygous FH patient's safety and quality of life, keeping in mind

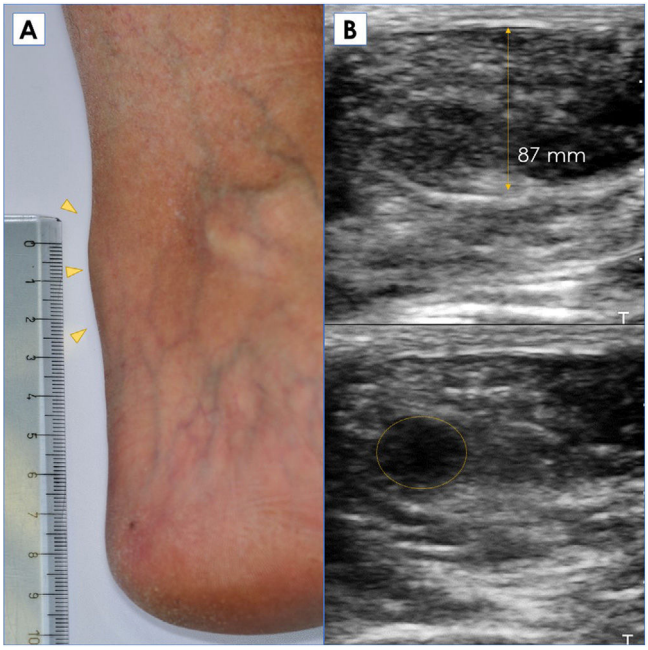

Figure 2 Panel A – Physical examination of Achilles tendon xanthomas (arrowhead). Panel B – Achilles tendon ultrasonography with increased thickness and irregular hypoechoic region (circle).

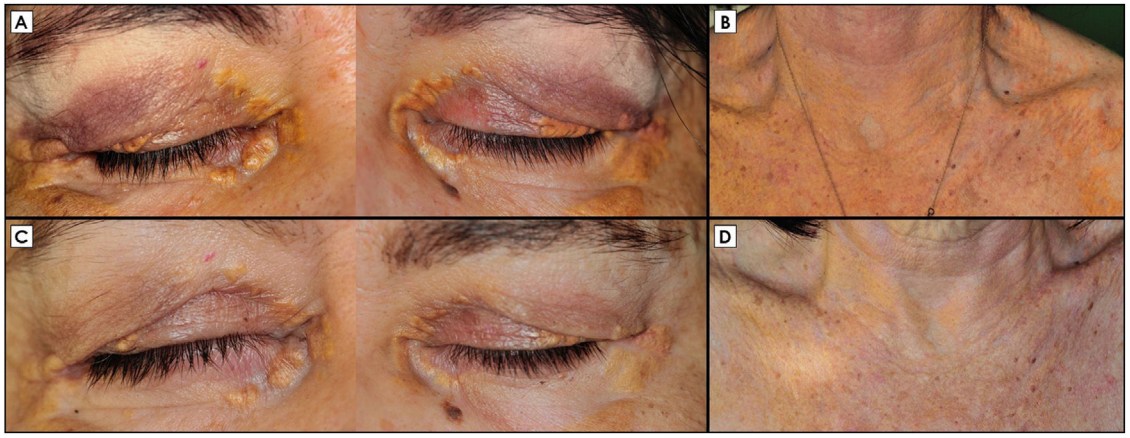

Figure 1 Baseline bilateral xanthelasma (Panel A) and extensive cutaneous xanthomas localized at the trunk (Panel B). Partial regression in xanthelasma (Panel C) and in cutaneous xanthomas hyperpigmentation (Panel D) obtained after six months of maximal lipid lowering therapy (rosuvastatin/ezetimibe 20/10 mg OD + evolocumab 140 mg s.c. every 14 days + lipoprotein apheresis).

that the correct diagnosis[1] and therapeutic adherence[7] are essential stages for patient's clinical management.

Authors' contribution

FS, BDP, FB and TS: contributed to conception or design, drafted and critically revised the manuscript. All authors read and approved the final version of the manuscript.

Authors' approval

All authors have seen and approved the study submitted.

No part of the submitted work has been published or is under consideration for publication elsewhere.

Notes

Data have not been presented at any congress.

Consent for publication

The patient signed the informed consent from form for anonymous medical data usage in our paper.

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Conflict of interest

No conflict of interest for each author.

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