Extremely low HDL-C in a patient with premature ovarian failure: case presentation

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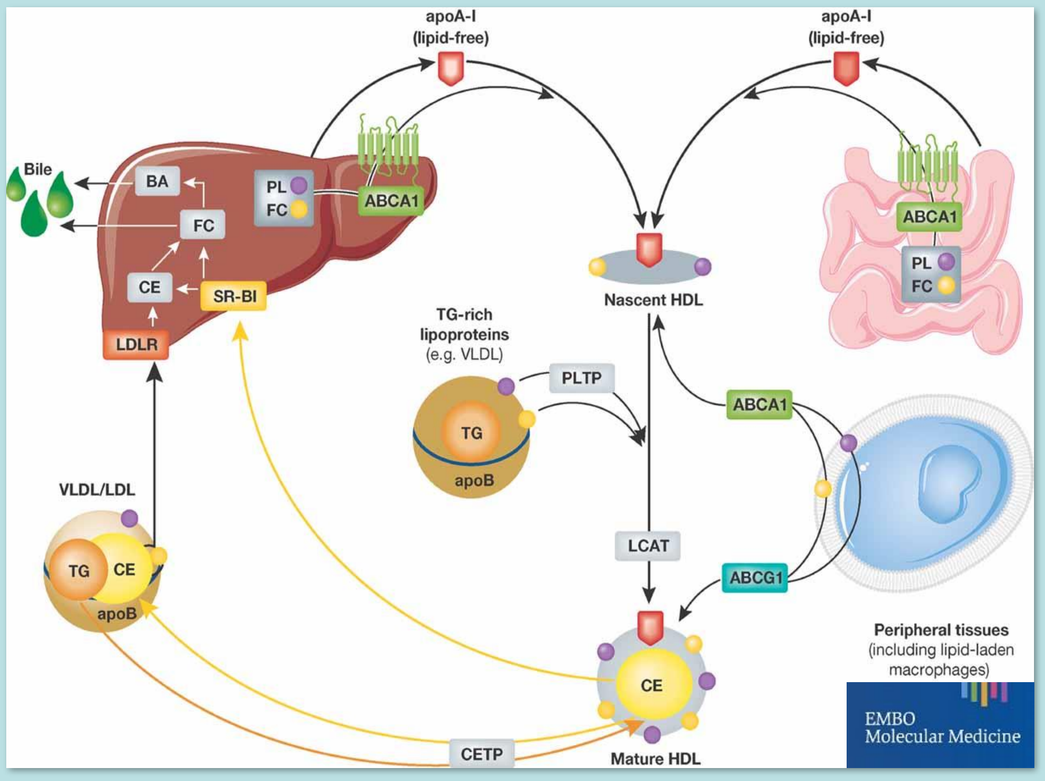
Introduction:

During menopause, plasma lipids change in an unfavourable way to a more atherogenic pattern, with increased total and LDL-cholesterol and decreased HDL-cholesterol concentrations.
Women with POI show increased cardiovascular morbidity and mortality regardless of the cause of the ovarian insufficiency. The treatment of premature ovarian failure in patients presenting extremely low HLD-C is a real challenge.

Case report:

Patient: 29 years old, smoker, history of contraceptive use, no pregnancies
Presenting for: secondary amenorrhoea, headaches and lower limb pain.
Clinical exam: normal (no xanthomas, no corneal opacities, normal tonsils)
Laboratory investigations:
•Thrombocytopenia 100000/ml
•FSH= 173 mUI/ml, LH= 92 mUI/ml, Estradiol <10 pg/ml
•Normal basal and stimulated cortisol
•Normal calcium and thyroid function
•Lipid panel: Cholesterol= 74 mg/dl (N.V.:<200)
- **HDL-C= nd/3.8/<3 mg/dl (N.V.:>50)**
- LDL-C= 48.6 mg/dl (N.V.:<160)
- Triglycerides= 108 mg/dl (N.V.:<150)
- Non-HDL= 70.2 mg/dl
- **ApoA1 <0.03 g/l- very low (N.V.: 1.08-2.25)**
- ApoB= 0.93 g/l- normal (V.N: 0.6-1.17).

ECG: normal. Effort ECG: 2-3 mm ST depression inferior leads.
Ultrasound: no signs of premature vascular/heart disease.
Haematology exam: no artifactual or secondary causes of low HDL-C. The thrombocytopenia was defined as essential.
Gynaecology exam: normal US of the uterus and ovaries.
Genetic testing: normal karyotype 46XX
Would have been useful: coronary multislice CT angiography, molecular genetic testing for specific mutations.
Family screening: a brother with similar lipid panel modifications.
Evolution: She was started on fibrates and oral contraceptive therapy with regular menstrual cycles but no improvement on the lipid panel (HDL-C remained <4mg/dl).



HDL pathway[3]: ApoA-I acquires phospholipids and free cholesterol resulting into nascent HDL, which takes up further phospholipids and free cholesterol via ABCA-1 from peripheral tissues (efflux) and VLDL. LCAT esterifies part of the free cholesterol to cholesterol esters, forming a mature HDL particle. It has an important role in the reverse cholesterol transport: HDL-associated cholesterol is either directly transferred to the liver via hepatic SR-BI or following CETP-mediated transfer to VLDL/LDL via the hepatic LDL receptor.

Causes of HDL-C below 20mg/dl in the absence of severe hypertriglyceridemia:
•primary monogenic disorders with **HDL-C <5 mg/dl**: ApoA1 deficiency: 11q23, Tangier disease[2]: 9q31.1, **HDL-C <10 mg/dl**: lecithin-cholesterol acyltransferase deficiency (16q22.1) and Fish eye disease, **HDL between 15 and 30 mg/dl**: apolipoprotein A-I mutations (Apo-A1 Milano), familial hypoalphalipoproteinemia.
•secondary causes (androgen use, malignancy)[1].
Causes of premature ovarian failure are wide ranging:
•chromosomal and genetic defects (Turner syndrome, fragile-X syndrome, autosomal gene defects: 9q33.3, 2p21)
•autoimmune disorders
•iatrogenic causes: surgery, radiotherapy, chemotherapy
•environmental factors.
Studies on SR-BI KO mice suggest a possible **correlation** between changes in HDL (structure/composition/abundance) and infertility, since HDL is the only lipoprotein present in substantial amounts in the follicular fluid surrounding the developing oocyte in humans[4].

Disscusions:

•Cardiovascular risk assessment is not well defined in this situations. The association between extremely low HDL-C levels and atherosclerosis still remains unclear in genetic conditions, as well as in the context of POI.
•HRT would be a better option than monophasic contraceptives because of the different effects of estrogens compared to progestins on the lipid panel; not indicated for cardiovascular risk prevention.
•Statin treatment must be individualised- not all patients have premature cardiovascular disease, even though in most studies, the cardiovascular risk usually increases with 2% for every 1% decrease in HDL-C. The main target remains lowering LDL-C.
•CETP inhibitors – may increase the cardiovascular risk; not studied in genetic HDL-C deficiency.
•The purpose of the treatment is prolonging the patient's life and improving it's quality.

References:

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