MARKERS OF INSULIN RESISTANCE IN A CASE OF LAUNOIS-BENSAUDE SYNDROME

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MARKERS OF INSULIN RESISTANCE IN A CASE OF LAUNOIS-BENSAUDE SYNDROME (Abstract): Launois-Bensaude syndrome (benign symmetric lipomatosis) is a rare disease characterized by symmetric fat deposits localized in the cervical region, shoulders and proximal parts of upper and lower limbs. We present the case of a 63-year-old male who presented the typical location of fatty masses and a history of chronic alcoholism associated with elements defining the metabolic syndrome. The biological profile indicated high-atherogenic mixed dyslipidemia, high basal insulinemia (30 μU/ml), and multiple markers of insulin resistance (Reaven index, lipid accumulation product, homeostatic model, insulin sensitivity index, and modified glycemic curve following oral glucose load). The particularity of the presented case is the discordance between the severity of metabolic disturbances and their clinical expression, raising the question whether this patient's cardiometabolic risk is increased or rather lowered by the association of benign symmetric lipomatosis. Keywords: LAUNOIS-BENSAUDE SYNDROME, INSULIN RESISTANCE.

Launois-Bensaude syndrome (benign symmetric lipomatosis, Madelung’s disease) is a rare disease of unknown prevalence, characterized by symmetric fat deposits prevalently localized around the cervical region, in the shoulders and proximal part of the arms and legs. The name of this disease is chronologically disputed by Sir Benjamin Brodie (1846), the first who described this deformity, followed by Otto W. Madelung (1888), a German surgeon, his name being particularly related to the disease eponymous with prevalently cervical location (“Madelung’s collar or neck”); in 1898, Raoul Bensaude and Pierre-Emile Launois published the first series of 75 cases and provided a full description of the characteristic features of the disease, adopting the term symmetric lipomatosis (1,2).

Middle-aged (30-60 years) males are most commonly affected, developing the characteristic distribution of body fat after at least 10 years of abusive ethanol consumption. The etiopathogenesis of benign symmetric lipomatosis is not fully known, the hypertrophy of malfunctioning brown fat and the decreased activity of mitochondrial respiratory enzymes that may result in lipolytic pathway depression being incriminated. In all these processes, alcohol is a
possible co-factor. The only effective treatment is surgery, through lipectomy and/or liposuction of fat masses (2, 3).

CASE PRESENTATION

A 63-year-old male from a rural area presented to the Pulmonary Rehabilitation Clinic of the Iasi Rehabilitation Clinic Hospital complaining of dyspnea, mMRC (modified Medical Research Council) breathlessness scale grade 2, intermittent productive cough and mild fatigability.

The patient presented to our clinic for entering a respiratory rehabilitation program having a previous diagnosis of moderate chronic obstructive pulmonary disease (COPD), the symptoms of this chronic lung disease being well controlled with inhaled tiotropium 18 µg/day. He also presented grade 2 essential hypertension, blood pressure being optimally controlled with amlodipine 10 mg daily.

What drew our attention during physical examination were the pseudotumoral subcutaneous masses: relatively symmetrical, located mainly in the proximal parts of the upper and lower limbs, with a pseudohypertrophic appearance, and under the chin, behind the ear, and in the nuchal region, resembling a Madelung’s collar (fig. 1).

On palpation, multiple mobile and painless small abdominal lipomas, like the masses in the upper body, were detected (fig. 2). Family history revealed that two patient’s brothers present a similar appearance; from personal history we found out that the fat masses with a typical location for Launois-Bensaude syndrome developed progressively over the last 20 years. Surgical removal of one mass located behind the right ear that became painful confirmed its benign nature, lipoma, but resulted in local recurrence.

The patient was a smoker (35 pack-years) and had a history of chronic ethanol consumption (70 international units/week, abstinent for about 6 months); clinically, stigmata of chronic alcoholism persisted, represented by retraction of palmar aponeurosis (Dupuytren’s contracture), bilat-
eral parotid gland hypertrophy, telangiectasias on the nose and cheekbone, but laboratory tests confirmed abstinence, serum transaminases, gamma-glutamyltranspeptidase and mean corpuscular volume being normal.

Patient’s anthropometric data showed a body mass index of 30.14 kg/m², corresponding to grade I obesity, and a pathological waist circumference of 115 cm, measured in standing position halfway between the costal margin and iliac crest line.

The metabolic profile revealed mixed dyslipidemia at high atherogenic risk (total cholesterol = 6 mmol/l, HDL-cholesterol = 0.9 mmol/l, triglycerides = 1.64 mmol/l, LDL-cholesterol = 4.32 mmol/l), normal glucose levels (4.93 mmol/l, and high basal insulinaemia (30 μU/ml), indicator of insulin resistance. Given the presence of basal hyperinsulinemia, we calculated the markers of insulin resistance derived from previous biological and anthropometric measurements (tab. I).

Also a 3-hour 75-gram oral glucose tolerance test was performed (fig. 3).

**TABLE I**

<table>
<thead>
<tr>
<th>MARKERS OF INSULIN RESISTANCE</th>
<th>RESULTS</th>
<th>COMMENTS</th>
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<tbody>
<tr>
<td><strong>TG/HDL ratio (Reaven index)</strong></td>
<td>4.17</td>
<td>Reaven index ≥ 3.5 indicates insulin resistance (4)</td>
</tr>
<tr>
<td><strong>LAP (lipid accumulation product)</strong></td>
<td>82 cm. mmol/l</td>
<td>Lipid accumulation product correlates well with insulin resistance and metabolic syndrome (5)</td>
</tr>
<tr>
<td><strong>HOMA-IR (homeostatic model assessment of insulin resistance)</strong></td>
<td>5.33</td>
<td>Values ≥ 2.6 indicate insulin resistance status; ≥ 4 it is considered prediabetic status (6)</td>
</tr>
<tr>
<td><strong>QUICKI (quantitative insulin sensitivity check index)</strong></td>
<td>0.29</td>
<td>Low values (&lt; 0.45) suggest insulin resistance ; &lt; 0.3 in diabetics (7)</td>
</tr>
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</table>
DISCUSSION

The patient presented a rare disease, benign symmetric lipomatosis, associated with metabolic syndrome, defined in this case by three factors: hypertension, abdominal obesity and low HDL-cholesterol, serum triglycerides being at the limit of diagnostic significance and basal glycemia levels within normal range (8). Simultaneous determination of basal insulinemia and calculation of some markers of insulin resistance (tab. I) revealed frankly pathological values, allowing the assertion of a hyperinsulinemic status associated with insulin resistance.

Remarkable is the discordance between the severity of metabolic disturbances and their clinical expression: the associated pathological conditions (hypertension, COPD) were easily controlled therapeutically and glucose metabolism disturbances were not very obvious. Thus, basal glycemia and the values of oral glucose tolerance test (fig. 3) were normal at fasting or at 2 hours, but prolonged monitoring for three hours revealed a late hypoglycemic dip, result of an abnormal overproduction of insulin in response to glucose load.

The particularity of this case is related to whether the patient's cardiometabolic risk, consequence of the accumulation of risk factors - male, smoking status, hypertension, chronic alcohol consumption, obesity - is increased or rather lowered by the association of Launois-Bensaude syndrome, having in view the mild clinical course despite the severity of underlying metabolic changes?

Review of literature data on Launois-Bensaude syndrome reveals a quite wide phenotypic and clinical variability in this category of patients, ranging from a type of "metabolically innocent" obesity with increased insulin sensitivity by decreased visceral adiposity ascertained by computer tomography (9), to a metabolic picture dominated by insulin resistance, particularly in those patients associating cervical lipomatose deposits and an obstructive sleep apnea syndrome, in its turn generating insulin resistance (10).

The presented case seems to be halfway between these two extremes, but the lack of large studies and validation of any of the models does not allow drawing an indisputable conclusion.
REFERENCES


**PELTOPHORUM AFRICANUM: ANTIMICROBIAL POTENTIAL AND HEPATOTOXICITY**

The antimicrobial activity and hepatotoxicity of *Peltophorum africanum* were evaluated in a study by Okeleye et al. Agar well and macrodilution methods were used for antimicrobial activity testing, as well as CellTiter-Blue cell viability assay to assess the toxicity on human liver cells. The results showed both bactericidal and bacteriostatic or fungistatic activity of the extract. The researchers observed good activity against *Plesiomonas shigelloides*. Despite its antimicrobial activity, the extract was toxic to human liver cell lines. Lethal dose at 50 revealed 82.64 ± 1.40 degree of toxicity at 24 hrs, while 95 percentile of cell death dose activity varied between log 3.12 and 4.59. (Okeleye BI, Mkwetshana NT, Ndip RN. Evaluation of the Antibacterial and Antifungal Potential of *Peltophorum africanum*: Toxicological Effect on Human Chang Liver Cell Line. *ScientificWorldJournal* 2013; 2013: 878735. doi: 10.1155/2013/878735).

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