Exceptional manifestation of Madelung's disease after liver transplantation

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Abstract

Unlike simple obesity, Madelung's disease (MD) is a rare disease characterized by symmetric accumulation of massive adipose tissue on the neck, the superior part of the trunk and limbs, leading to a pathognomonic cosmetic deformity. Here, we report an extremely rare case of MD associated with bilateral gynecomastia in a 61-year-old man, with a history of recent liver transplantation for alcoholic liver disease (ALD). (Acta gastroenterol. belg., **2022,** 85, **102-104**).

Keywords: Liver transplant, lipomatosis, alcohol abstinence.

Introduction

The development of several comorbidities after liver transplantation is frequent. Despite them, gain weight and metabolic disorders often occurs during the first post-operative year (1). However, some conditions may request a particular attention. Madelung's disease (MD) is a rare disease characterized by the accumulation of unencapsulated fat around the neck, shoulders and limbs (2). Frequently associated with alcoholism and hepatic disease, its etiology remains unresolved. We report the case of a 61-year-old man who developed a type 1 MD associated with bilateral gynecomastia, after he benefited from a liver transplantation.

Case report

A 61-year-old man complained about progressive and constant growing masses on both upper arms, shoulders and chest (Fig. 1). This condition started above 3 months after he had liver transplantation.

The patient's clinical history reported about 35 years of alcohol abuse. ALD was fortuitously diagnosed when he was 50. This led to a decompensated hepatic cirrhosis (Child Pugh B9) with portal hypertension, encephalopathy and ascites. He stopped alcohol abuse and had no other relevant health problem nor familial pathology. He was eligible psychologically and clinically to liver transplantation.

Abdominal perimeter was enlarged (95cm) because of ascites, but his body mass index (BMI) was on the normal range (21kg/m^2; 63kg for 170cm high). Two years after complete alcohol abstinence, he had a liver transplantation. The liver transplant was procured from a german donor free from any disease, including hepatitis B, hepatitis C and HIV.

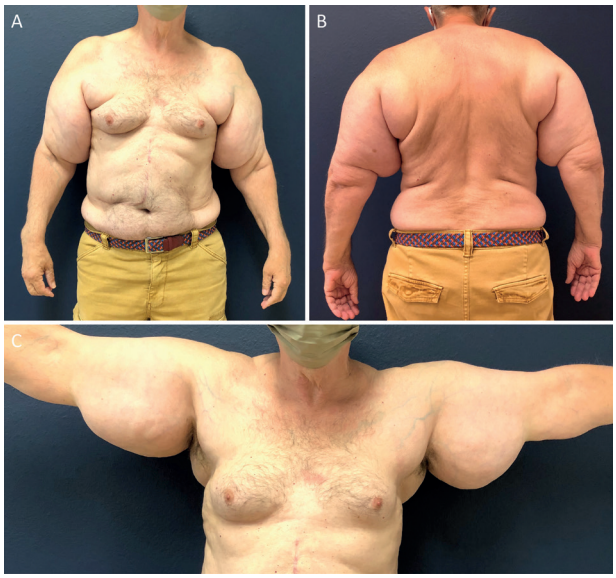

Figure 1 — A. Face view of bilateral fat deposition in the arm, shoulders and thorax associated with bilateral gynecomastia. B. Back view. C. Impressive fat deposition in the arms.

Post-transplant evolution was uncomplicated. The patient was compliant to immunosuppressive medication and follow-up. Treatment included tacrolimus 2mg/day, carvedilol, ursodesoxycholic acid and esomeprazol.

Physical examination showed bilateral symmetric soft and painless masses in all affected areas. Despite no changes in food habit and complete alcohol abstinence, the fatty masses grown before a progressive stabilization. The arm circumference, measured at 31cm before liver transplantation, reached to 53cm one year later, leading to difficulties for wearing clothes. Additionally, the patient had gained 22kg, developed overweight (85kg, BMI 29,4kg/m^2) and arterial hypertension.

Laboratory blood analysis revealed hyperuricemia (9,4mg/dL) and dyslipidemia (triglyceride 254mg/dL). Liver function (GPT 10 U/L, GOT 18 U/L, GT 30 U/L), renal function (GFR 63ml/min/1,73m^2), fasting blood

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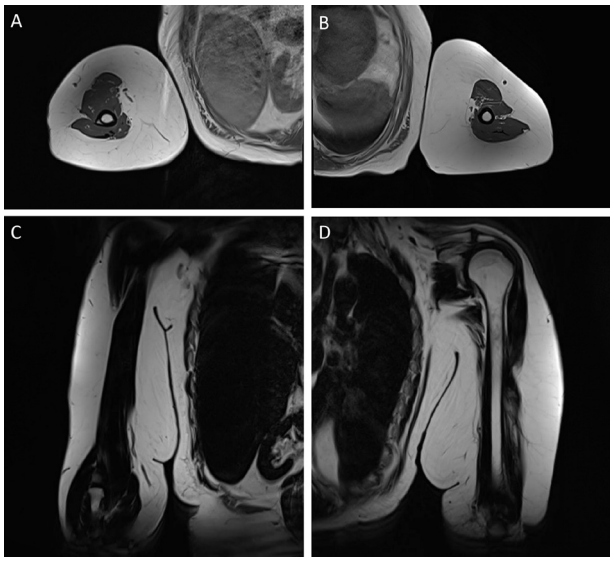

Figure 2. — MRI of the patient's arms showing the accumulation of adipose tissue circumferentially. A. Right arm, frontal view. B. Left arm, frontal view. C. Right arm, transverse view. D. Left arm, transverse view.

sugar (92 mg/dL) and total cholesterol (185mg/dL) were all within the reference range.

Magnetic resonance imaging indicated subcutaneous non-encapsulated adipose tissue in all the hypertrophic regions (Fig 2). Breast ultrasonography indicated a bilateral benign dendritic gynecomastia.

Genetic search for mitochondrial disorders was negative: no mutations or pathogenic alterations in the MT-TL1gene (Mitochondrially Encoded TRNA-Leucine 1) and the MT-TK gene (Mitochondrially Encoded TRNA-Lysine) implicated in weight and height disorders were identified.

Based on clinical assessment, Madelung's disease was diagnosed. After complete informed consent, the patient undergo surgery, consisting in lipoaspiration associated with bilateral arms dermolipectomy. The 6-months follow-up showed stable result with arms circumference at 40 cm bilaterally.

Discussion

Mainly due to the immunosuppressive therapy, gain weight and development of metabolic disorders after liver transplantation is frequent, particularly in the first post-operative year (1). MD is an uncommon clinical condition characterized by multiple and symmetric accumulation of non-encapsulated adipose tissue. Also known as buffalo neck syndrome, Launois-Bensaude Syndrome, or Benign Symmetric Lipomatosis, Madelung *et al*. (3) followed by Launois and Bensaude (4) recorded many similar cases.

MD has been reported to occur most frequently in Mediterranean men ranging from 30 to 60 years old (2). Nowadays, more than 300 cases have been reported and the incidence is approximatively 1 in 25000 (5).

In 1984, Enzi described 2 types: type I characterized by fat deposition in the upper part of the body; whereas type II shows fat deposition all over the body, appearing as simple obesity (6).

The true etiology of MD remains unknown. Hepatic disease is frequently associated, rather ALD but also non-alcoholic fatty liver disease (NAFLD) have been described (6). Other conditions associated with MD are dyslipidemia, arterial hypertension, chronic obstructive pulmonary disease, hyperuricemia, hypothyroidism, diabetes mellitus type 2, carbohydrate intolerance (6, 7), presence of obesity and bilateral gynecomastia (6). Less frequent conditions include peripheral neuropathy of the lower limbs, MERRF syndrome (myoclonus epilepsy and ragged-red fibers), pain or dizziness of the involved limb (6). Also, autosomic dominant inherited transmission of MD has been reported and was associated with a mediastinal syndrome (8). Malignant transformation of these masses remains exceptional (9).

Alcohol appears to be a cofactor, and there is a history of alcohol abuse in nearly all the cases (60 to 100%) (2, 6, 10). Alcohol abstinence has no influence but is recommended (10). Our patient reported a complete abstinence since more than two years. Nevertheless, relapse after liver transplantation for ALD is frequent and must be screened by a socio-psychological evaluation (11).

The particularity of this case reported is that liver transplantation appears to act as a trigger. In 2008, Goetze *et al*. (12) described a similar case. A 49-year-old female observed growing masses shortly after liver transplantation, and gained 20 kg in few months. Nevertheless, she had no history of alcoholic consumption. The etiology of her liver disease was unclear and probably nutritive-toxic. Her medication consisted in prednisolone 20mg, tacrolimus 3mg and mycophenolate mofetil 1,5g twice a day. No information about weight, body mass index was indicated, nor comorbidities or evolution. Masses were situated in upper arms, neck and face.

Based on clinical examination, Madelung's disease was diagnosed but no relation to liver transplantation or immunosuppressive treatment has been proved (12). So further investigation is needed.

Differential diagnosis must be done with obesity (10). As reported by Lattanzi *et al*. (1), quickly after transplantation, weight gain and development of metabolic disorder is frequent, particularly due to the immunosuppressive treatment. Effectively, our patient presented a gain of 22 kg in the first year of follow-up and developed arterial hypertension, dyslipidemia and hyperuricemia. Moreover, the resurgence of a hepatic disease as NAFLD is difficult to exclude and remain possible in a patient who developed a metabolic syndrome (13). Hepatic biopsies should be redone in accordance with NASH CRN score criteria (13).

Nevertheless, the diagnosis of MD is mainly based on clinical examination: especially on type I as in this patient, pathognomonic masses growth on upper arms,

shoulders and chest, leading to a contrasting cosmetic deformity (2) that sometimes leads to a limitation of movements (5). Also, MRI emphasize the fat deposition in all involved areas, confirming the diagnose (6).

A biomolecular study revealed that MD fatty tissue is morphologically and histologically different from that of regular subcutaneous fat. Stem cells isolated from lipomatous tissue showed higher proliferative activity and alterations in expression of genes associated with proliferation, hormonal regulation, and mitochondria (14). In our case however, genetic testing was negative for a mitochondrial disorder. It has also been suggested that MD lipomas might be the result of a disorder of brown adipose tissue (15).

Unfortunately, there is no effective medication for MD. Weight loss or alcohol abstinence is not effective in reducing the size of fat deposits, but may help to stop the progression. The clinical course can be variable (10). Most frequently there is a period of rapid growth followed by a period of stabilization or quiescence. There is no spontaneous regression of the masses. All treatments are palliative. The goal is recovery of function and improved appearance (9).

Surgery is the only available option, despite high risks of recurrence (6). An open approach consisting in dermolipectomy, or a combination of lipoaspiration with dermolipectomy, is preferred than liposuction alone. The open approach provides an improved exposure of the fatty deposits and allows their removal down to the deep muscular fascia, with a better control of noble structures, such as vessels and nerves, resulting in a lower recurrence rate (5,6,7,9,10).

Conflicts of interest

The authors have no conflicts of interest to disclose.

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