Madelung disease
A case report

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Abstract
Rationale: Madelung disease (MD), a rarely reported disease, also known as benign symmetric lipomatosis, a disorder resulting from alcoholic abuse. It’s largely under-recognized and under-reported, possibly because of unawareness of the condition by physicians.

Patient concerns: A 45-year-old Chinese man presented with intermittent fatigue and abdominal distension and progressive bilateral breast enlargement. He has been a heavy drinker for ten years before onset of the disease with an average daily alcohol intake of more than 120 g/day.

Diagnosis: Due to the patient’s symptoms, laboratory test results, radiographic findings, he was diagnosed with MD.

Interventions: We treated him with abstinence from alcohol and supportive therapy.

Outcomes: The patient is now in stable condition, with improvement in symptoms during follow-up.

Lessons: Doctors, confronted with progressive bilateral breast enlargement in a patient with alcoholic liver disease, should be aware of the underreported MD. Recognition of this syndrome could help doctors establish diagnosis and emphasize the importance of alcohol abstinence as the mainstay of management.

Abbreviations: ALT = alanine aminotransferase, AST = aspartate transaminase, BMI = body mass index, HIV = human immunodeficiency virus, MD = Madelung disease, MRI = magnetic resonance imaging, MSL = multiple symmetric lipomatosis, OGTT = oral glucose tolerance test.

Keywords: alcoholic liver disease, lipomatosis ; case report, madelung disease

1. Introduction

Madelung disease (MD) was 1st described by Brodie in 1846,[¹] and named by Madelung in 1888. The disease is relatively rare, and it is characterized by multiple, symmetric distribution of non-encapsulated fatty masses on the face, neck, shoulders, etc. There are other multiple synonyms, such as Launois-Bensaude syndrome, and multiple symmetrical lipomatosis (MSL).[²,³] The pathogenesis of MD is unclear. Abstinence from alcohol remains the most effective treatment. The disease is more common among people of Mediterranean descent, and there are few reports of Asian cases with typical breast enlargement. Surgical treatment can be sought for patients with changes in their appearance. Here we report a case of alcoholic cirrhosis with progressive fat deposition in breast, posterior neck and upper extremities, to improve the clinicians’ understanding of MD.

This case report was approved by the ethics committee of the First Hospital of Jilin University, Changchun, China, and the informed consent form was signed by patient.

2. Case presentation

A 45-year-old male was admitted to our hospital due to intermittent fatigue and abdominal distension for 4 years. Four years ago, the patient was diagnosed with decompensated alcoholic cirrhosis in our hospital. He was given anti-fibrosis, hepatoprotective, symptomatic and supportive treatment, and was discharged from the hospital after improvement of his condition. The patient was hospitalized several times during the recent 4 years due to fatigue and abdominal distention. In past 2 years, the patient experienced bilateral, painless, and progressive breasts enlargement accompanied by a 20 kg weight gain. The patient denied a history of viral hepatitis and hepatitis virus exposure, and denied a history of special medication use. There were no similar cases in the family. The patient had a > 10-year history of alcohol consumption equivalent to 120 g/day. According to the patient, the libido was normal, there was no erectile dysfunction.

The physical examination revealed the following: conscious; body mass index (BMI), 36.3 kg/m²; central obesity; facial telangiectasias; scattered spider angiomas across the upper chest,
face and neck; liver palms; bilateral breast enlargement; systemic scattered painless lumps distributed mainly on the upper back, deltoid areas, hips, and thighs (Fig. 1); a bulging, soft abdomen; a tender liver and spleen; and negative shifting dullness. The testes were normal and symmetric.

Notable laboratory tests on admission showed a reduced levels of cholinesterase (3398 U/L, reference: 4300–12000 U/L) and albumin (28.4 g/L, reference: 40–55 g/L) without jaundice, elevated levels of aspartate transaminase (AST) and alanine aminotransferase (ALT). The prothrombin time was 17.5 s (reference: 9.0–13.0 s) and prothrombin activity was 54% (reference: 80–120%). A reduced levels of platelet 91 × 10^9/L (reference: 125–350 × 10^9/L). Hepatitis B, hepatitis C, syphilis, and human immunodeficiency virus (HIV) serologic testing were all negative. All autoimmune liver disease antibodies tests were negative. The levels of copper and iron were normal. Oral glucose tolerance test (OGTT) and thyroid function were normal. Sex hormone test results showed that luteinizing hormone was 0.88 IU/L (reference: 1.24–8.62 IU/L), prolactin was 22 pg/L (reference: 2.64–13.13 pg/L) and testosterone, estradiol, and follicle stimulating hormone levels were normal. Uric acid was normal. Magnetic resonance imaging (MRI) examination of the liver and spleen showed evidence of cirrhosis, slight enlargement of the spleen and portal hypertension with collateral circulation. A breast ultrasound examination showed breast hyperplasia and fat deposition. An MRI of the head showed multiple focal ischemic lesions in the brain. An MRI of the neck and upper extremities suggested excessive fat deposition (Fig. 2). Combined with medical history, clinical symptoms and signs and auxiliary examinations, the patient was finally diagnosed with MD and was treated with abstinence, liver protection, and anti-fibrosis agents. This patient was followed up every 6-month and did not undergo surgical treatment. Fat deposits in various parts of the body were visualized using MRI (Fig. 2).

Figure 1. Fat deposition in different body parts. (A) Breast; (B) Back neck and upper extremity; (C) Trunk.

Figure 2. Fat depositions in different body parts examined by MRI. (A) MRI of the upper extremity and breast (white arrow); (B) MRI of the neck (white arrow); H: head, F: foot.
body are still progressing and weight gains are slow, but there are no other cirrhosis complications such as jaundice, ascites, gastrointestinal bleeding, liver cancer, etc. The condition is stable as of this writing.

3. Discussion and conclusions

The MD, also known as Launois-Bensaude syndrome, is a MSL or benign symmetric lipomatosis that is rare and with an unclear etiology. The disease is characterized by progressive, symmetric deposition of non-enveloped adipose tissue in typical locations.[4,5] According to previous foreign reports,[6,7] the dysfunction is more common in white males in Mediterranean or eastern European regions, and is more common in middle-ages adults (approximately 50 years of age), with a male-to-female ratio of 1:5. Among the 282 Chinese patients reported by Wang et al,[8] the ratio of men-to-women was 14.6:1, which is similar to that of foreign countries. According to the distribution of adipose tissue, MSL is divided into 2 types. Type I, also known as horse collar lipoma, the adipose tissue is mainly deposited in the upper body (neck, supraclavicular region, upper trunk, arms, and mediastinum), and often accompanied by weight loss. Type I MSL only occurs in males, and subcutaneous adipose tissue of uninvolved part is often decreased or lost. Type II MSL can also occur in females, and is often accompanied by weight gain, which is similar to obesity. Adipose tissue is deposited in the upper back, deltoid area, hips, and thighs (similar to the fat distribution in obese women), resulting in the so-called “false athlete’s sign.” Based on the fat distribution characteristics, the current patient had type II MSL.[4,9]

Although the pathogenesis remains unclear, some factors, such as defects in mitochondrial function of adipose tissues, decreases in cytochrome C oxidase activity, and catecholamine-induced fat deposition, may be involved in the development of the disease. Approximately 90% of MD patients have alcoholism. Alcohol can lead to a decrease in the number and activity of β-adrenergic receptors and promote fat synthesis.[9,10] Alcohol can also directly affect mitochondrial activity and cause premature oxidation of mitochondrial DNAs or the mutation of mitochondrial DNA (A8344G),[11] leading to the deposition of fat in different parts of the body. Many systemic diseases, such as primary hypothyroidism, Cushing’s syndrome, giant cell anemia, diabetes, epilepsy, cigarette smoking, and some malignant diseases,[12–14] may also be associated with the development of MD. During the follow-up, the patient had completed the relevant examinations in our hospital and Peking Union Medical College Hospital, basically excluding all other systemic diseases mentioned above.

The diagnosis of MD is mainly based on clinical and imaging examinations, especially MRI, to determine the deposition of fat in the involved areas. Enzi[15] reported that adipose tissue generally showed non-enveloped, symmetric deposition in the neck (83.3%), back (55%), and breast also in subcutaneous tissues of the abdomen (35%), upper extremities (54.1%), and lower extremities (28%) of male patients. The most commonly affected anatomic region is the neck, which is variably referred to as “horse neck,” “Popeye,” or “hump” signs, which often affects the patient’s appearance and even leads to neck deformities and severe breathing difficulties. Symmetric fat deposition can also happen in some rare parts such as tongue,[16] scrotum[17] and so on. The patient’s appearance had “Popeye” and “hump” signs; MRI indicated fat deposition in particular body parts; combined with his underlying disease of alcoholic liver disease, the diagnosis was clear.

The MD has no specific treatment. Commonly used measures include abstinence, weight control, surgical treatment (fat resection and liposuction), and drug treatment with fenofibrate or phosphatidylcholine.[13] Surgical resection or liposuction can remove deposited fat tissue; however, patients often relapse after treatment. Liposuction is generally suitable for small volumes of fat deposition and surgical resection is suitable for patients with large volumes of fat deposition. Brea-García[13] reported an overall recurrence rate of 63% after surgery; the recurrence rates following open surgery, liposuction, and open surgery combined with liposuction were 51%, 95%, and 50%, respectively, suggesting a very high post-operative recurrence of the disease. It should be noted that abstinence cannot prevent further progression of the disease. Despite strict abstinence after the diagnosis of liver cirrhosis, the bilateral breast enlargement and weight increased progressively. Borriello et al[16] reported that MD may be cancerous. Therefore, regular follow-up of patients is very important.

The progression of MD is relatively slow, often complicated by other diseases and is easily misdiagnosed. The case we reported here had MD complicated by alcoholic cirrhosis. Laboratory testing revealed that the estrogen level was elevated. The breast enlargement was initially considered to be associated with the decreased ability of the liver to inactivate hormones. Therefore, it took 3 years from the occurrence of the signs to establish the diagnosis. Clinical practitioners should have increased awareness of MD and strive to make an early diagnosis.

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Author contributions

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References

[1] Lee MS, Lee MH, Hur KB. Multiple symmetric lipomatosis. J Korean Med Sci 1988;3:163–7.
[2] González-García R, Rodríguez-Campo FJ, Sastre-Pérez J, et al. Benign symmetric lipomatosis (Madelung’s disease): case reports and current management. Aesthetic Plast Surg 2004; 28:108–12.
[3] Zuber M, Pittasch D. Benign symmetric Lipomatosis (Launois-Bensaude syndrome). A rare cause of muscular weakness. Eur J Med Res 2006;11:74–7.
[4] Enzi G. Multiple symmetric lipomatosis: an updated clinical report. Medicine 1984;63:56–64.
[5] Mimica M, Pravdic D, Nakas-Kindic E, et al. Multiple symmetric lipomatosis: a diagnostic dilemma. Case Rep Med 2013;2013:836903.
[6] Hadjiev B, Stefanova P, Shipkov C, et al. Madelung disease: on the morphologic criteria for diagnosis and treatment. Ann Plast Surg 2010; 64:807–8.
[7] Mevzo E, Shrocca M, Mullace M, et al. Multiple symmetric lipomatosis: a review of 3 cases. Case Rep Otolaryngol 2012;2012:910526.
[8] Wang F, Wang BY. Infrequent manifestation of alcoholic liver disease: Madelung syndrome. J Pract Hepatol 2014;17:287–90. Chinese.
[9] Sayantant R, Partha PC, Subhopd P, et al. Bilateral breast enlargement in a chronic alcoholic: do not miss Madelung’s disease. BMJ Case Rep 2016;2016:bcr2016215082.
[10] Economides NG, Liddell HT. Benign symmetric lipomatosis (Madelung’s disease). South Med J 1986;79:1023–5.
[11] Gámez J, Playán A, Andreu AL, et al. Familial multiple symmetric lipomatosis associated with the A8344G mutation of mitochondrial DNA. Neurology 1998;51:258–60.
[12] Chalk CH, Mills KR, Jacobs JM, et al. Familial multiple symmetric lipomatosis with peripheral neuropathy. Neurology 1990;40:1246–50.

[13] Brea-Garcia B, Cameselle-Teijeiro J, Couto-González I, et al. Madelung’s disease: comorbidities, fatty mass distribution, and response to treatment of 22 patients. Aesthetic Plast Surg 2013;37:409–16.

[14] Heike Z, Gudrun UM, Frank RD, et al. Multiple benign symmetric lipomatosis—a differential diagnosis of obesity: is there a rationale for fibrate treatment? Obesity Surg 2008;18:240–2.

[15] Enzi G, Busetto L, Serqi G, et al. Multiple symmetric lipomatosis: a rare disease and its possible links to brown adipose tissue. Nutr Metab Cardiovasc Dis 2015;25:547–53.

[16] Kang JW, Kim JH. Symmetric lipomatosis of the tongue. New Engl J Med 2013;369:e5.

[17] Poggi G, Moro G, Toragni C, et al. Scrotal involvement in Madelung disease: clinical, ultrasound and MR findings. Abdom Imaging 2006;31:503–5.

[18] Borriello M, Lucidi A, Carbone A, et al. Malignant transformation of Madelung’s disease in a patient with a coincidental diagnosis of breast cancer: case report. Diagn Pathol 2012;7:1–4.