Madelung's Disease: Case Series and Literature Review

PEDAN H, BEHANOVA E, CALKOVSKY V, HAJTMAN A

Clinic of Otorhinolaryngology and Head and Neck Surgery, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, and Martin University Hospital, Martin, Slovakia

Abstract

Madelung's disease also called benign symmetric lipomatosis is a rare disorder of unknown etiology. The disease affects almost exclusively middle-aged men with a history of multi-year alcohol abuse. The major symptom is presence of non-encapsulated benign fat masses, especially in the area of the head and neck. Limited head and neck movement, dysphagia, and dyspnea may appear as well.

The diagnosis is clinical and is supported by imaging methods, often elevated hepatic enzymes in blood serum, and histological examination with finding of mature adipose tissue without signs of proliferation. Therapeutic methods involve liposuction or excision which is a method of choice nowadays.

In this article the authors review current knowledge, research state, and present five cases of the Madelung's disease occurring within the last 10 years at the Clinic of Otorhinolaryngology and Head and Neck Surgery in Martin, Slovakia.

Key words: Madelung's disease; lipomatosis; benign symmetric lipomatosis

INTRODUCTION

Madelung's disease is a rare disorder of lipid metabolism that is characterized by an unusual accumulation of fat masses around the neck and upper thorax with relative sparing of the trunk and extremities.

There are multiple synonyms for this disorder, such as Launois-Bensaude syndrome, Benign Symmetrical Lipomatosis, Multiple Symmetric Lipomatosis (MSL), or cephalothoracic lipodystrophy (1, 2). The disorder was first reported in 1846 by Brodie. In 1888 a German surgeon Otto Wilhelm Madelung called it "fat neck" (Fetthals) and gave a detailed description of the disorder. After that Launois and Bensaude in 1898 also characterized the disease. A similar phenotype was depicted 34 centuries ago in the carvings of the Queen of Punt (near Egypt) (1).

The incidence is about 1 in 25,000 and a male-to-female ratio of 15:1 to 30:1. Besides the fact that it is affecting mainly men in the age group of 30–60 years, it is more common in the Mediterranean area (2).

The pathoetiology of lipoma tissue in MSL remains unknown, but several theories have been proposed.

A defect in the adrenergic stimulated lipolysis that results in massive accumulation of lipomatous tissue is suggested (3). Another theory is related to an enzyme defect or a change in the cell surface which may prevent the breakdown of lipids leading to the characteristic signs (4). Recent findings suggest defective regulation of mitochondria in brown fat tissue with a mutation in mitochondrial DNA involving the MT-TK gene (5, 6, 7).

Address for correspondence:

Assoc. Prof. Vladimir Calkovsky, MD, PhD., Clinic of Otorhinolaryngology and Head and Neck Surgery, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, and Martin University Hospital, Kollarova 2, 036 01 Martin, Slovakia

Phone: +421-43 2633 714; E-mail: calkovsky@jfm.uniba.sk

In most cases there is no hereditary pattern, although in few cases more than one family member was affected by this condition, which suggests that it may be inherited (8).

Based on literary data, 90 % of cases is linked with alcoholism. The condition has also been associated with macrocytic anemia, diabetes mellitus, hyperlipoproteinemia, hypothyroidism, gout, and systemic mitochondrial diseases (1, 9).

The signs and symptoms of MSL may vary. There are two phenotypical variants of the disease: type 1 is common in males with protruding masses around the neck and upper thorax, type 2 is seen in females with predominant deposition over the proximal part of extremities and trunk (1).

MSL could be considered simple obesity due to the symmetry in the subcutaneous deposition of non-encapsulated fatty masses, but it usually causes cosmetic disfigurement such as hamster cheeks – collection of lipomas in the parotid region, horse collar – lipomas in cervical region, buffalo hump- posterior neck lipomatosis, or collection in the upper trunk can give the patient a “pseudoathletic appearance” (3, 8).

Majority of the patients develop the signs of peripheral neuropathy, autonomic nervous system manifestations and symptoms due to compression of the airways, esophagus, carotid artery, or vena cava (6, 10, 11). Malignant transformation of MSL is extremely rare (10, 12).

Diagnosis is based on physical examination, medical history, imaging studies such as CT, MRI or, in some cases, the diagnosis needs to be proved by biopsy (6). Currently, the recommended and the most effective method of treatment is excision or liposuction. (4, 6, 7). Each one has its own limitation like incomplete removal, scarring, or lipoma recurrence (7, 13, 14). In few cases patients have been successfully treated with salbutamol which increases the breakdown of fats. Abstaining from alcohol intake, weight loss, and correction of any associated metabolic/endocrine abnormalities are also recommended (4, 7).

CASES PRESENTATION

Case 1

50-year-old male with a history of approximately one-year growing soft occipital tumor without limited neck mobility, negative family history, permanently unmedicated for any disease. There was a history of several years lasting alcohol and nicotine abuse. Laboratory results showed a slight gamma-glutamyltransferase (GGT) elevation. Magnetic resonance imaging (MRI) displayed masses of unbound proliferated soft tissue, particularly in the occipital region and simultaneously in the ventral area of the neck prelaryngeally. By means of surgical treatment soft tissues of the front of the neck were removed. A significant improvement in the cosmetic effect was achieved. Histopathologically an image of enlarged mature adipose tissue was confirmed, which promotes the clinical diagnosis of the Madelung's disease. Outpatient control of the patient revealed partial recurrence of the disease, which required no further surgical treatment.

Case 2

A 34-year-old male observing for about half a year increasing elastic masses on the left side of his neck. He had no symptoms such as dysphagia or dyspnea. There was no family history of lipomatosis. Chronically unmedicated for any disease so far. He admitted an occasional alcohol abuse and long-term smoking. Laboratory results with elevations of hepatic enzymes indicated liver disorder. Computed tomography (CT) examination revealed increased soft tissue in the front neck area of an approximate size of $4 \times 2 \times 2$ cm. As a therapeutic method surgical treatment was chosen. Excision of masses of adipose tissue had satisfactory cosmetic results. During outpatient control one month after the treatment a recurrence of the disease was observed. Surgical re-treatment was indicated. After the second surgery the patient was controlled for 12 months without the need for further treatment. The diagnosis of Madelung's disease was supported by histopathological examination with the finding of increased mature fat tissue.

Case 3

56-year-old male complaining for nearly 5 years about growing soft, painless tumor on the front part of the neck. At the same time, he suffered from slight head movement problems. No breathing or swallowing difficulties were reported by the patient. He admitted excessive drinking and smoking in the last 10 years. He remembered no such disease in the family. Laboratory results showed signs of mild hepatopathy. MRI identified subcutaneous, oval, circumscribed tumor in the form of horizontal hourglasses, with an approximate size of $8 \times 4.5 \times 3.5$ cm. Lobular adipose tumor with a histologically confirmed diagnosis of mature enlarged fat tissue was surgically removed. Outpatient in the next 12 months without signs of recurrence.

Case 4

47-year-old male with a progressively increasing tumor in the front of the neck and upper back area over a period of 6 months. Except of the cosmetic defect he did not complain of other problems. Chronically treated for organic psycho-syndrome of toxic-alcoholic etiology. He confessed a history of 5-year alcohol abuse and smoking. No occurrence of Madelung's disease in the family history. No signs of liver damage on laboratory examination. On MRI enlarged soft tissues in the front of the neck reaching bilateral to sternocleidomastoid muscle were observed. Soft fat tissues present also in the parotid gland bilateral, occipitally on the left side and upper back. In treatment a large amount of subcutaneous fat tissue was surgically removed with a good cosmetic effect. In the following outpatient period recurrence of the disease was detected. Reoperation 3 months after the primary surgery was necessary. In biopsy specimens mature fat tissue was histologically confirmed supporting the diagnosis of Madelung's disease.

Case 5

49-year-old male with approximately 2-year growing large lipomatous tumor at the front of the neck (Fig. 1). In addition to cosmetic change the feeling of pressure and tension below the neck was present as well. The patient was chronically medicated for arterial hypertension and gastro-esophageal reflux disease (GERD). Family history of the disease was negative. Patient admitted excessive drinking and smoking over the last 10 years. Laboratory results showed a slight elevation of hepatic enzymes in the serum. MRI displayed a lobulized soft tissue tumor in the front of the neck extending bilaterally to sternocleidomastoid muscle and cranially to the mandible body. Fat connective tissue of an approximate size of $10 \times 10 \times 15$ cm from the neck area was removed by means of excision (Fig. 2, 3). Histology confirmed mature fat tissue without signs of proliferation. During the control period of 3 months the patient is so far without signs of disease recurrence.

Fig. 1 Pre-operative findings

Fig. 2 Operative findings **Fig. 3** Biopsy specimen

DISCUSSION

Madelung's disease is a disease of unknown etiology characterized by non-encapsulated benign fat masses especially in the area of the head and neck, the torso, and the upper limbs (1).

With the prevalence of 1: 25,000 this disease belongs to very rare diseases. It affects almost exclusively men and the majority (90 %) of cases is associated with a history of long-term alcohol abuse (2). The most common symptoms include the presence of deforming neck resistance, limited head and neck movement, dysphagia, and dyspnea. Occurrence is sporadic with peak incidence in the Mediterranean area and Eastern Europe (2).

Our group of patients for the past 10 years is represented by five men aged 34 to 56 with an average age of 47.2 years. The major and often the only symptom is at least 6-month-long period of enlarging soft neck tumor that disturbs the patient optically and occasionally limits head and neck movement of the patient. Dominant location of lipomatosis in the neck was the anterior part of the neck ranging bilaterally to sternocleidomastoid muscle (80 %). In one patient the main location was occipital area with enlarged fat tissue also in the front part of the neck.

Among all five men multi-year alcohol abuse was proven in the past history, which was also demonstrated in four men by elevation of hepatic enzymes, especially GMT and aspartate aminotransferase (AST). Nicotine abuse was observed in all five men as well.

All patients' biopsy specimens were subsequently examined with the identical result – mature adipose tissue without signs of proliferation. This result is substantial for Madelung's disease. The therapeutic method was excision of adipose tissue (Fig. 4) with a recurrence in two patients within a three-month horizon.

Fig. 4 Post-operative result

Despite of inter-individual differences, in case of unsuccessful alcohol abstinence the risk of recurrence is nearly 100 %.

CONCLUSION

Although surgical treatment is a method of choice, it has only a short-term effect. It remains only symptomatic and, therefore, it is necessary to search for causes and pathomechanisms of the disease.

REFERENCES

- 1) Suresh Chandran CJ, Godge YR, Oak PJ, Ravat SH. Madelung's disease with myopathy. *Ann Indian Acad Neurol* 2009;12: 131–132.
- 2) González-García R, Rodríguez-Campo FJ, Sastre-Pérez J, Muñoz-Guerra MF. "Benign symmetric lipomatosis (Madelung's disease): case reports and current management". *Aesthetic Plast Surg* 2004; 28 (2): 108–113.
- 3) Josephson GD, Sclafani AP, Stern J. Benign symmetric lipomatosis (Madelung's disease). *Otolaryngol Head Neck Surg* 1996; 115: 170–171.
- 4) Ramos S, Pinheiro S, Diogo C, Cabral L, Cruzeiro C. Madelung disease: a not-so-rare disorder. *Ann Plast Surg* 2010; 64(1): 122–124.
- 5) Plummer C, Spring PJ, Marotta R, Chin J, Taylor G, Sharpe D, Athanasou NA, Thyagarajan D, Berkovic SF. Multiple Symmetrical Lipomatosis — A mitochondrial disorder of brown fat. *Mitochondrion* 2013; 269–276.
- 6) Mimica M, Pravdic D, Nakas-Icindic E, Karin M, Babic E, Tomic M, Bevanda M. Multiple symmetric lipomatosis: a diagnostic dilemma. *Case Rep Med* 2013; 1–4.
- 7) Sia KJ, Tang IP, Tan TY. Multiple symmetrical lipomatosis: case report and literature review. *J Laryngol Otol* 2012; 126(7): 756–758.
- 8) Madelung's Disease. NORD. 2005; <http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/778/viewAbstract>
- 9) Becker-Wegerich P, Steuber M, Olbrisch R, Ruzicka T, Auburger G, Hofhaus G. Defects of mitochondrial respiratory chain in multiple symmetric lipomatosis. *Arch Dermatol Res* 1998; 290: 652–655.
- 10) Ramos S, Pinheiro S, Diogo C, Cabral L, Cruzeiro C. Madelung disease: a not-so-rare disorder. *Ann Plast Surg* 2010; 64(1): 122–124.
- 11) Alameda YA, Torres L, Perez-Mitchell C, Riera A. Madelung disease: A clinical diagnosis. *Otolaryngology – Head and Neck Surgery* 2009; 141(3): 418–419.
- 12) Guastella C, Borsi C, Gibelli S, Della Berta LG. Madelung's lipomatosis associated with head and neck malignant neoplasia: a study of 2 cases. *Otolaryngol Head Neck Surg* 2002; 126: 191–192.
- 13) Zielinska-Kazmierska B, Lewicki M, Manowska B. Madelung disease. *Advances in Dermatology and Allergology/Post py Dermatologii i Alergologii* 2015; 32(5): 400–403.
- 14) Sharma N, Hunter-Smith DJ, Rizzitelli A, Rozen WM. A surgical view on the treatment of Madelung's disease. *Clin Obes* 2015; 5(5): 288–290.

Received: March, 31, 2018

Accepted: June, 18, 2018