Madelung's Disease

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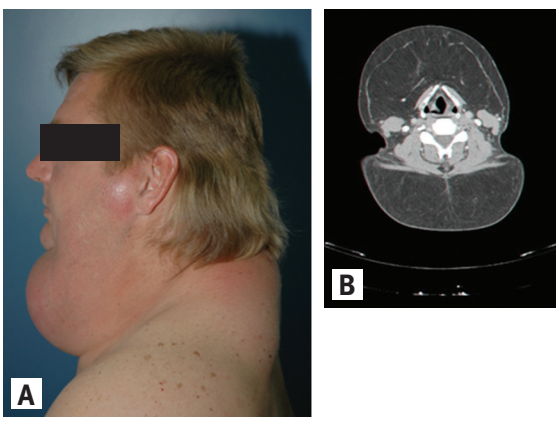
Madelung's disease is a rare condition whose pathophysiology is poorly understood. It is characterized by massive fatty deposits distributed in a symmetric pattern mainly in the face, neck, and nape of the neck. It usually affects middle-aged men with chronic alcohol abuse. The condition does not spontaneously regress and it may cause serious clinical, aesthetic and psychological dysfunction. We present a patient with Madelung's disease in order to familiarize the physician with this unusual condition.

PATIENT DESCRIPTION

A 37 year old man with a history of alcohol abuse and heavy smoking was admitted with bilateral thickening and enlargement of the neck, nuchal region and upper arms that began 3 years previously and had progressively enlarged. The patient had no history of dyspnea or dysphagia. He denied any associated pain or discomfort and stated that his main concern was cosmetic.

Fatty accumulation in the cervical and nucchal areas



Physical examination revealed extreme enlargement of the submandibular, parotid, cervical, and nuchal regions, bilaterally. The masses were freely movable, painless, and non-tender [Figure A]. Cardiovascular, respiratory and neurologic examinations were unremarkable.

Laboratory results, including complete blood count, liver function tests, electrolytes, fasting lipid profile, fasting glucose, and kidney function tests were within normal limits. Serology for human immunodeficiency virus antibodies was negative.

Cervical ultrasonography revealed bilateral fatty accumulations in the cervical and submandibular regions. Computed tomography scan showed extensive fatty accumulations in the cervical and upper thoracic region with no mediastinal involvement or blood vessel dislocation [Figure B].

Fine-needle aspiration showed nonspecific fibro-adipose tissue. Subcutaneous fat tissue biopsy obtained from the left lateral nuchal region showed normal fat tissue without malignant changes.

A definitive diagnosis of Madelung's disease was made on the basis of the patient's medical history of alcoholism, increased fatty tissue accumulation, and histologic examination. The patient was taken to surgery and the deep and superficial fatty masses of the neck were excised.

COMMENT

Madelung's disease, also known as benign symmetric lipomatosis and Launois-Bensaude syndrome, is a rare disorder. It was first described by Sir Benjamin Brodie In 1846. Madelung described the first series of 35 cases in 1888, and Launois and Bensaude presented a larger series of 65 patients in 1898. Since then, approximately 200 cases have been published in the medical literature [1].

This rare condition is characterized by the presence of multiple symmetric, non-encapsulated fatty deposits (unlike the usual lipoma), distributed in a symmetric pattern in the face, neck and the superior part of the trunk, and rarely in the lower limbs, mediastinum and larynx. The tumor masses are soft and usually asymptomatic. Although benign in nature, cases of deep infiltration of mediastinal structures with compression of major vessels, nerves, trachea, larynx, bronchi, and esophagus have been reported [2]. Involvement of the tongue has also been noted [3].

Middle-aged men with a history of excessive alcohol intake are affected more frequently. The general incidence is unknown, but the prevalence may be higher in Mediterranean countries, notably Italy, Spain and France.

Two types of Madelung's disease have been described. In type 1 disease, fat accumulates around the neck and the nape of the neck, shoulders, upper arms, and upper back, giving the patient a "pseudoathletic" appearance. In type 2 disease, lipomas extend over the body, including around the hips and thighs giving the patient a generalized obese appearance [3].

The cause of Madelung's disease is unknown. Many hypotheses have been proposed. Kodish et al. [4] suggested that the excess lipid accumulation results from hypertrophy of functionally defective

brown adipose tissue. The distribution of the fat masses and the ultrastructure of the adipose cells of the lipomas support this hypothesis. There is also increasing evidence that various mitochondrial dysfunctions underlie Madelung's disease. This hypothesis suggests that reduced activity of the mitochondrial respiratory enzymes might depress the lipolytic pathway. A familial form with a mitochondrial DNA abnormality has also been reported.

Alcohol seems to act as a cofactor, as 60–90% of Madelung's disease patients are chronic alcoholics. Chronic alcohol ingestion is known to promote lipogenesis and decrease lipolysis. In addition, alcohol is known to affect mitochondrial metabolism directly and can cause premature oxidative aging of mtDNA. However, patients with Madelung's disease and no history of alcohol consumption have also been reported [2].

Besides a strong association with chronic alcoholism, frequently associated findings include metabolic diseases like diabetes mellitus, lipid disorders, and systemic disorders such as liver disease and hypothyroidism [5]. Sensory, motor and autonomic polyneuropathy is noted in about 85% of patients, 80% of whom will develop a physical disability. The polyneuropathy occurs several years after the lipomas appear. Histologic studies show progressive axonal atrophy, which is in contrast to the demyelination and axonal degeneration produced by chronic alcohol intake [1].

The diagnosis of Madelung's disease is primarily established by physical examination and clinical history. The disorder can be defined as a "sight diagnosis" disease because of the typical distribution pattern of the masses that do not recede even with reduced calorie intake. Massive symmetric deposition of fat becomes cosmetically deforming in the parotid region ("hamster cheeks"), cervical region ("horse collar"), and posterior neck ("buffalo hump") [5].

Computed tomography and magnetic resonance imaging are helpful in assessing the distribution of excess fat. Sonography does not provide adequate preoperative information. Histologically, cells in the abnormal lipomatous areas are indistinguishable from those in normal fat, although ultrastructural investigations have shown that the adipocytes are smaller than expected and multivacuolated [1].

It is important to consider other entities such as "simple" truncal obesity, angiolipoma, neurofibroma, encapsulated lipomas, hibernoma, congenital infiltrating lipomatosis of the face, encephalo-craniocutaneous lipomatosis, liposarcoma, lipoblastomatosis, and salivary gland disorders in the differential diagnosis [3]. The lipomatosis observed in HIV-infected patients is also a differential diagnosis, thought to be related to the use of protease inhibitors [1].

The clinical course of the disease involves an initial period of fast growth followed by many years of slow progression. There is no report of spontaneous regression after cessation of alcohol consumption. Malignant transformation is extremely rare; only one case of malignant degeneration was reported in the literature [5].

The treatment for Madelung's disease is surgery. It is reserved for patients with aesthetic deformities, psychological problems, or aerodigestive dysfunction attributable to compression by fatty tissue. Recurrence of the lipomas is common. Medical treatment is not effective. Lipectomy and liposuction are the treatments of choice. Liposuction is a safe and easy method. It can be performed safely under local anesthesia, but it can be difficult in patients whose fatty tumors have a fibrous stroma. Open excision is more effective for patients with severe cosmetic deformities. It is also safer because nerves and major vessels can be identified. The risk of postoperative hematoma has been reported by many authors, emphasizing the need for careful hemostasis and vacuum drains [2].

HIV = human immunodeficiency virus

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"There is a crack in everything. That's how the light gets in"

Leonard Cohen (born 1934), Canadian singer-songwriter, musician, poet and novelist. His work explores religion, isolation, and interpersonal relationships. Famously reclusive, having once spent several years in a Zen Buddhist monastery, and possessing a persona frequently associated with mystique, he is extremely well regarded by critics for his literary accomplishments, for the richness of his lyrics, and for producing an output of work of high artistic quality over a five-decade career.

"The most radical revolutionary will become a conservative the day after the revolution"

Hannah Arendt (1906-1975), German Jewish political theorist