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Case Report

A case report of Madelung's disease in China [☆]

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ABSTRACT

Madelung disease (MD) is a rare form of lipodystrophy, which refers to diffuse and symmetrical adipose tissue deposition in the superficial and deep subcutaneous fascial spaces, presenting as multiple painless masses throughout the body. The disease is most commonly seen in middle-aged men who have been drinking alcohol for a long time and has not been reported domestically. This article analyzed the clinical data with Madelung's disease, discussed its etiology, clinical manifestations, diagnosis, and treatment methods, and provided help for clinical diagnosis and treatment.

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Introduction

Madelung's disease, also known as multiple symmetric lipomatosis, benign symmetric lipomatosis, and Launois-Bensaude syndrome, is rare lipodystrophy [1]. It diffuses adipose tissue deposition in the superficial and deep subcutaneous fascial spaces and affects the neck, occiput, shoulders, upper arms, chest and back, and trunk. It is more commonly seen in middle-aged men who have been alcoholics for a long time [2]. At present, there are more than 400 cases of Madelung's disease reported in the world. The Mediterranean region ranks first globally, and Asia has the lowest incidence rate [3]. There are few reports of the disease in China. This ar-

ticle analyzed the clinical data of a case of Madelung's disease, discussed the etiology, clinical manifestations, diagnosis, and treatment of Madelung's disease. The report is as follows.

Case report

Clinical data

The patient, a 51-year-old male with a neck mass for more than 4 years, was admitted to the hospital on June 5, 2018. The patient had stumbled upon a neck mass four years earlier that had gradually grown in size. Recently, the patient noticed that the mass was significantly enlarged, affecting breathing and

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Fig. 1 – Patient's physical examination before surgery: 1. Front; 2. Back; 3. Left; 4. Right

approaching asphyxia, and went to the Stomatology Department of Inner Mongolia Medical University Hospital for treatment. At the same time, the patient had a 30-year history of alcohol consumption averaging 500 g/day and a 30-year history of smoking averaging 20 cigarettes/day. 5 years ago, the patient also had a history of neck tumor surgery unrelated to this disease.

Physical examination: the patient showed signs of obesity, with significantly elevated skin on both sides of the neck, soft mass, unclear border, no tenderness, low skin temperature, and no skin erythema. The upper boundary of the mass reached the mastoid process, the lower boundary reached the level of the clavicle, both the left and right sides reached the acromion, and the anterior boundary reached the anterior border of the sternocleidomastoid muscle. The left and right sides were basically symmetrical. The skin of the neck was elevated and attached to the neck. The upper border reached 2 cm above the hairline on the left and 5 cm above the hairline on the right. The lower border of the neck was flush with the seventh cervical vertebra, and the left and right sides were basically symmetrical. A bulge of the skin surface, 7 cm in diameter, was visible in front of the left midaxillary line (Fig. 1).

Auxiliary examination: ① Head and neck CT: Multiple symmetrical fat density shadows can be seen in bilateral neck, occipital bone, mandible, supraclavicular fossa and shoul-

der. Compression of adjacent tissues was consistent with Madelung's disease (Fig. 2). ② Chest radiograph: chronic bronchitis; old tuberculosis in both lungs; left pleurisy. ③ Lung function: severe obstructive ventilatory dysfunction, the slight decrease in ventilatory reserve, severe diffuse dysfunction. ④ Laboratory findings were not significantly abnormal.

Surgical methods

After admission to the hospital, all preoperative examinations were completed. After communication with the patient and family, the final decision was made to choose to remove the lipoma through two surgeries. Contraindications to surgery were ruled out, and "right cervical and right dorsal neck partial mass excision, right mandibular rim branch dissection, and right sternocleidomastoid muscle free flap transfer repair" was performed under general anesthesia on June 15, 2018 (Fig. 3). During the operation, the right external jugular vein, cervical intrathecal artery and vein, transverse cervical artery and vein, phrenic nerve and mandibular marginal branch of the facial nerve were protected. Two drainage tubes were pressed, and the wound was closed in layers. After the surgery, the patient returned to the ward safely, and the tumor was removed and sent to the pathology department for examination. After surgery, the dressing and negative pres-

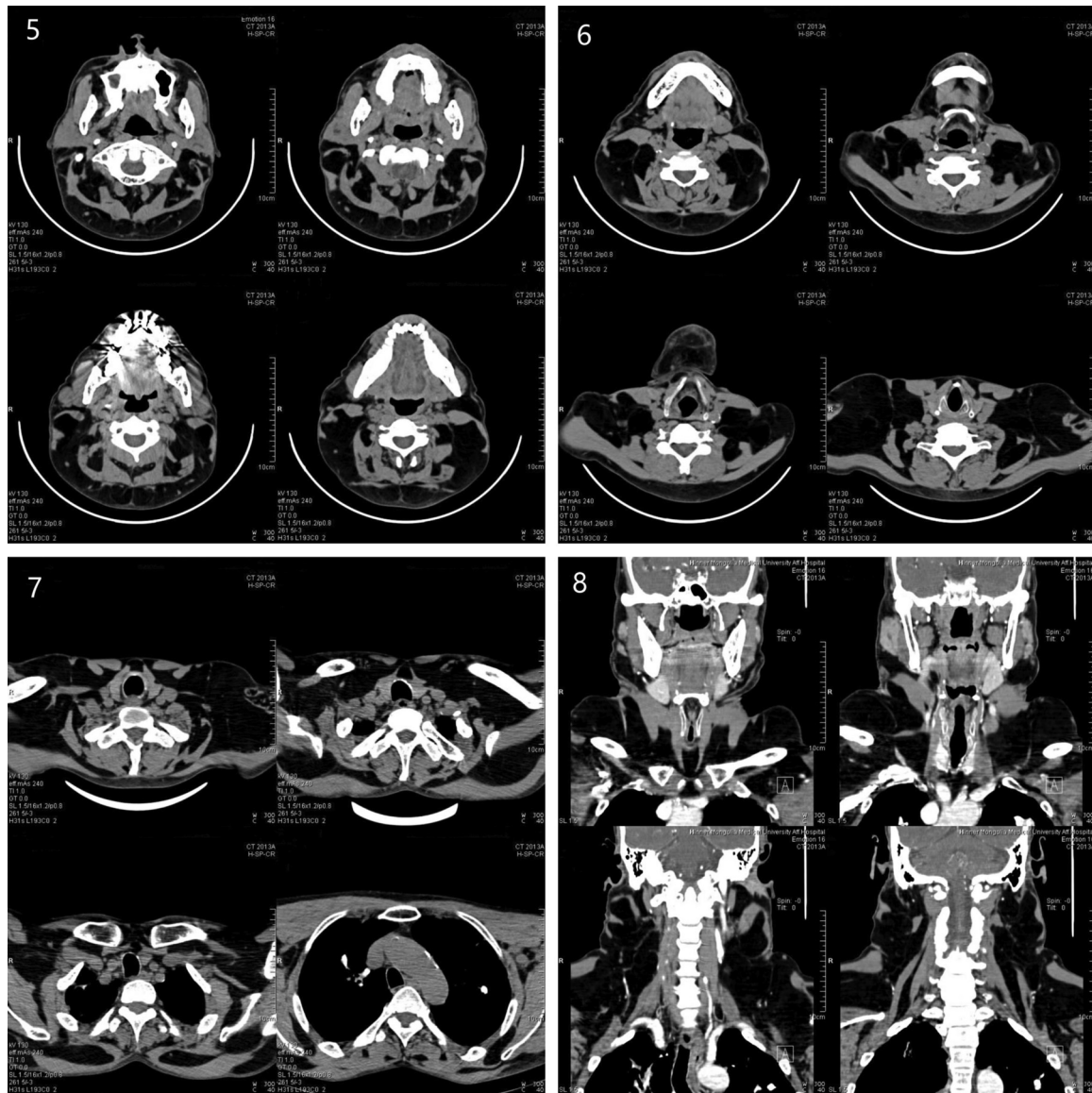


Fig 2 – CT of the head and neck: Multiple symmetrical fat density shadows in the neck, occiput, submandibular, supraclavicular fossa, and shoulder, and adjacent tissues are compressed

sure drainage device were changed regularly. After one week, the drains were removed, the sutures were removed on the 10 postoperative day, and the patient was discharged on the 11 postoperative day.

The patient recovered well after the first operation and was admitted to the hospital again on November 30, 2018, to treat the tumor on the left side of the neck. On physical examination, the patient's left neck skin was obviously raised, with soft texture, unclear borders, low skin temperature, no redness and swelling, the upper boundary of the mass reached the level of the mastoid, the lower boundary reached the level of the clavicle, and the front boundary reached the sternocleidomastoid muscle. The front edge, the outside reached the acromion. The skin on the nape was raised and connected to the neck. The scar from the last operation can be seen on the right side of the neck. On December 5, 2018, under gen-

eral anesthesia, "the left neck, posterior neck, subclavian and cervical sheath masses were removed, the mandibular border branch of the left facial nerve was removed, and the adjacent flap was transferred and repaired." During the operation, the left marginal mandibular branch of the facial nerve, submandibular gland capsule, greater auricular nerve, accessory nerve, and cervical arteries and veins were protected, a large area of hyperplastic fatty tissue was removed, and a negative pressure drainage tube was placed after the left submandibular and cervical sheaths. The wound was closed in layers, and the operation was successful. The tumor was cut out and sent to the pathology department for examination. Postoperatively, anti-inflammatory and symptomatic supportive treatment were given, dressings were changed regularly, negative pressure drainage device was replaced, the drainage tube was removed after one week, and stitches were removed intermit-

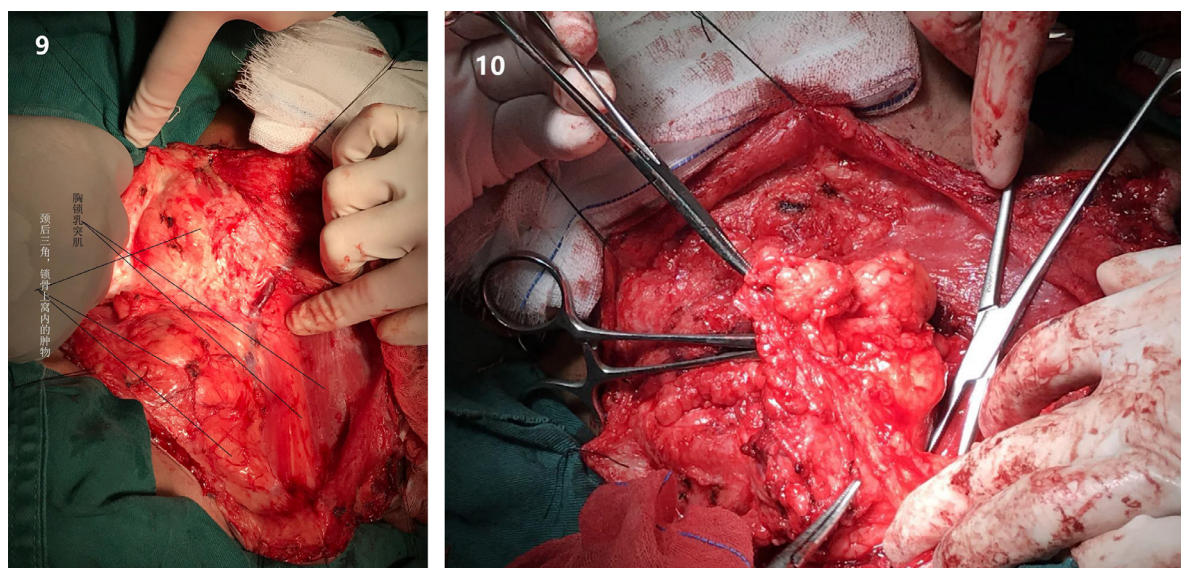


Fig. 3 – Surgical findings: The pictures 9 and 10 are lipomas seen during the operation



Fig. 4 – Lipoma was taken out by surgery: light yellow adipose tissue with envelope in some areas, lobulated, with a total volume of 11 × 11 × 4cm (Color version of figure is available online)

tently according to the wound healing. The patient's wound healed well, with no symptoms such as crookedness of the mouth, exudation, and redness or swelling of the skin around the wound. He was discharged from the hospital on the ninth postoperative day.

Pathological examination: visible with the naked eye: light yellow adipose tissue was submitted for examination, with a total volume of 11 × 11 × 4cm. The cut surface of the tumor tissue was light yellow, solid, and soft, with capsules in some areas and lobulated (Fig. 4). Microscopically, the neoplastic tissue was composed of diffusely proliferating adipocytes that were mature and differentiated without atypia, which was consistent with lipoma. One lymph node was submitted for

reactive hyperplasia. Immunohistochemical results: CD3 (T area), CD20 (B area), Bc12 (germinal center one), Ki67 (germinal center), CD10 (), CD68 (-). Pathological diagnosis: Madelung's disease.

Results

The patients were reviewed regularly at 3, 6, and 12 months after surgery, with yearly check-ups 1 year after the surgery. There was no recurrence during 2 years follow-up. The symptoms of neck compression were relieved, and the symptoms of dyspnea, dysphagia, difficulty turning the head, difficulty shrugging, and weakness were all recovered.

Discussion

Madelung's disease was first reported by Brodie in 1846 [4]. In 1888, Madelung named the disease madelung's disease after a detailed summary and analysis of 33 cases reported in the literature at that time [5]. In 1898, Launois and Bensaude reported the data of 65 patients with the disease and conducted a more detailed discussion and summary, so the disease is also called Launois-Bensaude syndrome [6]. The incidence of Madelung's disease in China is relatively low, and it is mainly concentrated in areas where alcohol consumption is high., such as Inner Mongolia, Shandong, Guangxi, and Sichuan. At present, Madelung's disease is mainly divided into type I, type II, and type III [7]. Type I mainly occurs in men. The diseased adipose tissue is mainly concentrated in the parotid gland, neck, nape, submental area, upper back, shoulder, upper arm, neck deltoid area, and supraclavicular fossa. The incidence of type II madelung's disease is similar in men and women. Adipose tissue mainly accumulated in the extremities and upper torso, including the upper arms, upper back, inner thighs, abdomen and buttocks. Patients gained weight

and showed signs of obesity, resulting in signs of prosthesis [8]. Type III is the congenital accumulation of fat in children, mainly around the trunk of the bone. In this case, the patient was the type I, with fat accumulation on both sides of the neck, occiput, submandibular, supraclavicular fossa, and shoulder.

The etiology of Madelung's disease may be related to chronic alcohol consumption, endocrine disorders, liver disease, upper respiratory tract malignancies, chromosomal inheritance [9], and metabolic syndromes such as hyperuricemia and hyperlipidemia type 2 diabetes mellitus and hypothyroidism signs [10]. Although the pathogenesis of Madelung's disease is still unclear, it may be related to adipose tissue mitochondrial dysfunction, decreased cytochrome C oxidase activity, catecholamine-induced fat deposition, and reduced inducible nitric oxide synthase (iNOS) [11]. The distribution and types of adipocytes in Madelung's disease are similar to brown adipose tissue (BAT) [12]. The diseased tissue of Madelung's disease is not hypertrophy of existing adipose cells, but proliferation of adipose cells, which is involved in the formation of Madelung's disease. In lipomatous tissue, Sanna M [13] evidenced AKT, CK2, and ERK1/2 hyperactivation. Most literatures reported that the main cause of Madelung's disease is chronic alcoholism caused by long-term heavy alcohol consumption, which leads to mitochondrial cell dysfunction, premature oxidation of mitochondrial DNA or mitochondrial DNA mutation. Some patients can lead to abnormal liver function, resulting in lipid metabolism disorder, and further induce diseases. [14]. Alcohol can also cause a decrease in the number and activity of β -adrenergic receptors and promote the synthesis of triacylglycerols. If drinking a lot of fatty foods simultaneously, this phenomenon of fat accumulation will be more significant [15]. In this paper, all patients had bronchitis, old tuberculosis and pleurisy, which had no obvious relationship with the occurrence of Madelung's disease. Laboratory tests showed no significant abnormalities and no other related diseases that might cause Madelung's disease. The patient had been drinking heavily for a long time, which was deduced to be madelung's disease caused by alcohol poisoning.

The clinical manifestations of Madelung's disease are multiple painless masses all over the body, with diffuse and symmetrical deposition of subcutaneous fat tissue. Due to the complex anatomical structure of the maxillofacial region and neck, the face and neck are the most affected parts, and the recurrence rate is high [16]. It has been reported that with the increase of neck mass, patients may gradually develop symptoms such as limited head turning, throat compression, stenosis, and dysphagia. If adipose tissue invades the parotid gland, it will cause facial deformities. Invasion of the floor of the mouth leads to restricted tongue movement and dysphagia. Invasion of the tongue leads to the occurrence of megatongue [17]. Madelung's disease also involves the peripheral nervous system, manifested as limb weakness, and there have been a few reports of central nervous system involvement [18]. Madelung's disease is often associated with other diseases, such as liver disease, hypertension, hyperlipidemia, diabetes, hyperuricemia, abnormal renal function, hypothyroidism, and obstructive sleep apnea-hypopnea syndrome [19]. In this case, the patient had difficulty breathing, swallowing, turning his head, and lifting his shoulders due to the compression of the adipose tissue. Abnormal lung function, such as severe ob-

structive ventilation dysfunction caused by airway compression. Weakness of shoulder shrugging due to neurological involvement was present. No other complications were found.

Madelung's disease can be diagnosed based on the patient's long-term drinking history, clinical manifestations, physical signs, and imaging examinations such as CT and color Doppler ultrasound. The incidence of Madelung's disease is very low in China, and misdiagnosis and missed diagnosis still exist. Attention is needed to differentiate from other diseases, such as lipomatosis, liposarcoma, neurofibromas, diffuse thyroid enlargement, hypercortisolism, etc. [19]. The color Doppler ultrasound of Madelung's disease shows irregular and diffuse thickening of subcutaneous fat tissue, with or without apparent capsules and borders [20]. CT manifests as multiple subcutaneous, well-defined low-density fat accumulation, several scattered partitions in the tissue, and compressed and deformed adjacent normal tissues [21]. According to the patient's long-term drinking history, characteristic clinical manifestations, physical signs, and CT and pathological examination results, the diagnosis of Madelung's disease can be clearly established in this case.

The treatment of Madelung's disease includes adipose tissue resection, liposuction, or local drug injection lipolysis [22]. Alcohol cessation and weight loss will not reverse or prevent the continued development of Madelung's disease. Certain medications can degrade fat, such as salbutamol, vitamins and coenzymes. Although local drug injections for lipolysis are simple and can reduce patient pain, local fibrosis and adhesions can occur, with a high recurrence rate and increased difficulty in surgical excision or liposuction after recurrence [23]. Liposuction is generally suitable for those with small adipose tissue, and surgical resection is suitable for those with larger lesions [24]. Surgery is the most effective treatment, and staging excision is an option without increasing the recurrence rate. The surgical principle is mainly to improve local malformation and dysfunction, to avoid damage to important blood vessels and nerves, and complete surgical resection is not emphasized [25]. The primary purpose of the operation is to relieve the symptoms of compression, restore the appearance, and improve the quality of life of the patient. Due to the large lesion range of the patients in this group, the method of staging resection was adopted to avoid the increased bleeding during the operation and the intolerance caused by one-time resection. Moreover, the patient has been instructed to stop smoking and drinking and to eat a low-fat diet. After two years of follow-up, the patient had no recurrence of the disease.

Conclusion

Madelung's disease can be diagnosed based on its typical clinical manifestations and auxiliary examinations. Currently, the most effective treatment is the surgical removal of adipose tissue. Staging surgical excision is an effective way to reduce complications without increasing the recurrence rate. Furthermore, abstinence from alcohol and changing dietary habits are also effective factors to reduce recurrence.

Patient consent

Informed consent for publication of this case was obtained from the patient.

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