

Case report of comorbid alcohol-induced psychotic disorder and Madelung's disease

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Summary: Madelung's disease, also known as benign symmetric lipomatosis (BSL), multiple symmetric lipomatosis (MSL), fatty neck syndrome or Launois-Bensaude syndrome, is a rare disease characterized by the presence of multiple, symmetric, loose adipose tissues distributed around the neck, occipitalis, shoulder, back or chest. The fat masses are non-encapsulated and therefore can move freely between adjacent areas. This disease is most commonly seen among middle-aged Caucasian men of Mediterranean origins; it is rarely reported in Asia. Among individuals with Madelung's syndrome, 60 to 90% have a history of chronic alcohol abuse. We report a case of a 51-year-old Chinese man with a history of alcohol use disorder who had fat masses in his neck which gradually enlarged over a period of three years. Based on the case history and the results of physical examination, neck CT and other routine tests, he was diagnosed with Madelung's syndrome.

Key words: alcohol use disorders, Madelung's syndrome, benign symmetric lipomatosis, China

1. Case history

A 51-year-old married male of Han ethnicity was admitted to our hospital for alcohol detoxification for the second time on December 28, 2013. He had been drinking heavily for 30 years. He had strange behaviors and irritability for the past six years. His neck had been thickening for the past three years.

The patient started drinking heavily (around 100-150 ml of strong liquor once a day or once every other day) in 1984. By 1986, his intake had increased to 250 ml of strong liquor twice a day. He became agitated when he stopped drinking, symptoms that resolved if he re-started drinking. His wife tried to help him cut down by taking money away from him, but he managed to buy alcohol with credit. Starting in June 2007, he became increasingly paranoid and hostile. He doubted his wife's fidelity, suspected that she was trying to poison him (refusing to eat anything she cooked), and became suspicious that people around them were bugging his house. He often lost his temper for no apparent reason, and frequently verbally abused and threatened to kill his wife.

He was first admitted to our hospital on August 6, 2007 and was diagnosed with alcohol-induced psychotic disorder. He was detoxed and after being treated with risperidone (maximum dosage of 4mg/d), his delusions disappeared. He was discharged on November 30, 2007 with a maintenance dosage (4mg/d) of Risperidone. After 2.5 years of abstinence, he relapsed and resumed drinking 500ml/d strong liquor in May 2010, following a stressful house relocation. His delusions reappeared in October 2010, believing that his wife was having an affair and that the village committee sent strangers to follow him. Sometimes his speech was disorganized or incoherent, such as calling himself the 'underground person' and his wife the 'aboveground person'. His personality changed and he became very agitated. A growing fatty mass was found on his neck in November 2010; it was not painful and did not interfere with his breathing.

He was readmitted to our hospital by the family for detoxification on December 28, 2013. On admission he was physically healthy with no history of major physical illnesses. He was not a smoker. He was 172 cm tall with

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a body mass index (BMI) of 20.2 kg/m². His vital signs were normal (body temperature= 36.6°C, pulse rate=84/minute, respiratory rate=17/minute, blood pressure=120/90 mm Hg). No abnormality was found in his ears or nose and there was no congestion in the pharynx or swelling in the tonsils. His neck was enlarged but soft. His trachea remained in the center and no swelling was seen in the thyroid. Above the suprasternal fossa, there was a 3cmx2cm lipoma with no clear edge. Two similar lipomas of 4cmx4cm were also found at the back of the neck. They appeared to be connected and free to move. No muscular atrophy or sensory dysfunction was found in the limbs, but both of his hands were slightly shaking. The patient was conscious and oriented. He had delusions of jealousy and persecution, unstable emotions and irritability. No hypobulia (i.e., lack of motivation) was found but the patient had a lack of insight.

His family reported that he was extroverted and outgoing before the onset of the psychosis. Since the onset of the most recent episode two months before admission, he had showed no symptoms of elevated mood, excessive talking, heightened self-esteem, irritability, suicide attempts or changes in appetite. There was no family history of alcohol abuse.

The results of his laboratory tests are shown in Table 1. With the exception of slightly elevated mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH), routine blood tests were normal. Serum chemistry showed abnormalities consistent with the liver dysfunction commonly seen with chronic alcohol abuse. And, with the exception of a slightly elevated thyroid-stimulating hormone (TSH), the thyroid function tests were normal. No abnormal results were found in his routine urine, electrocardiogram, or ultrasound of the thyroid. Computed tomography (CT) scan of his brain is shown in Figure 1: the third ventricle, the bilateral ventricle, the lateral fissure cistern and the cistern of the interhemispheric fissure were expanded and the sulci were broadened. CT scan of his neck is shown in Figure 2: it revealed extensive symmetric fat accumulation in his neck and submandibular regions in the spaces between adjacent subcutaneous or muscular structures. No capsule was seen around the fat tissue.

The patient was diagnosed with alcohol-induced psychotic disorder and Madelung's disease. After he was admitted, alcohol intake was ceased and nutritional support was provided. He was treated with sodium valproate (1.2g/d), risperidone (4mg/d) and lofexidine (0.2mg/d). Psychological support was also provided to the patient by explaining the symptoms and harms of excessive drinking in order to promote his determination and confidence in alcohol cessation. His psychotic symptoms disappeared and insight recovered on January 19, 2014; he was discharged on February 20, 2014. The next day he had an operation in a general hospital to remove the fat tissues. At the outpatient follow-up one month after discharge the patient was adhering to the treatment of sodium valproate (1.2g/d) and risperidone (4mg/d). No psychotic symptoms were reported.

Table 1. Laboratory data on the patient

Indicators	Patient's result	Normal range
Routine blood tests		
(HGB) Hemoglobin	109g/L	120-172g/L
(WBC) White blood count	4.8×10 ⁹ /L	4-10×10 ⁹ /L
Neutrophils	54%	45-77%
Lymphocytes	34.3%	20-40%
Monocytes	9.2%	3-10%
Eosinophils	1.5%	0.5-5%
Basophils	1.0%	0-1%
(RBC) Red blood count	2.8×10 ¹² /L	4-5.5×10 ¹² /L
(PLT) Platelets	149×10 ⁹ /L	100-300×10 ⁹ /L
(HCT) Hematocrit	32.1%	38-50.8%
(MCV) Mean corpuscular volume	116.7fL	83.9-99.1fL
(MCH) Mean corpuscular hemoglobin	39.6pg	27.8-33.8pg
(MCHC) Mean corpuscular hemoglobin concentration	340g/L	322-362g/L
Serum metabolic panel		
(HBDH) Hydroxybutyrate dehydrogenase	194U/L	72-182U/L
(AST) Aspartate Aminotransferase	139U/L	5-40U/L
(TBIL) Total bilirubin	34.9umol/L	3.4-21.0umol/L
(DBIL) Direct (conjugated) bilirubin	16.9umol/L	0-6.8umol/L
(IBIL) Indirect (unconjugated) bilirubin	18.0umol/L	0-13.7umol/L
(TP) Total protein	53.2g/L	60-83g/L
(ALB) albumin	33.8g/L	34-55g/L
(GLO) l-gulono-γ-lactone oxidase	19.4g/L	20-45g/L
(GGT) Gamma-glutamyl transferase	927U/L	7-50U/L
Thyroid function tests		
(T3) triiodothyronine	1.54nmol/L	1.30-3.10nmol/L
(T4) thyroxine	103.8nmol/L	66.0-181.0nmol/L
(FT3) free triiodothyronine	4.69pmol/L	3.10-6.80pmol/L
(FT4) free thyroxine	17.49pmol/L	12.00-22.00pmol/L
(TSH) thyroid-stimulating hormone	6.54mIU/L	0.270-4.20mIU/L

Figure 1. Computed tomography (CT) of the brain

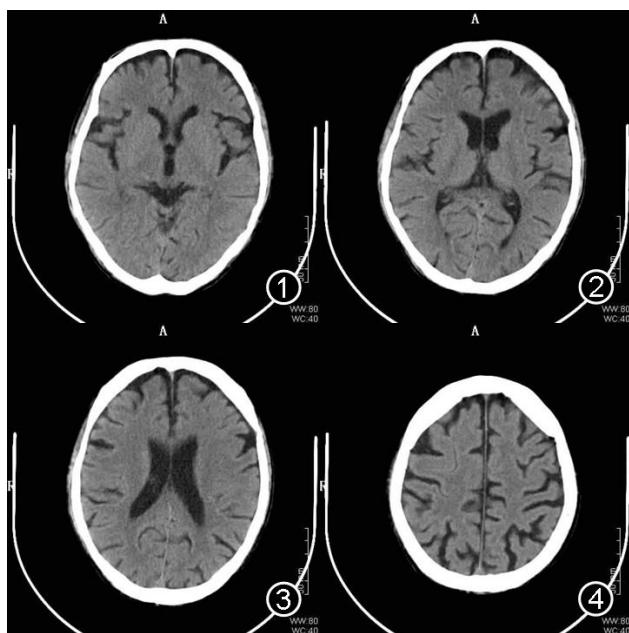
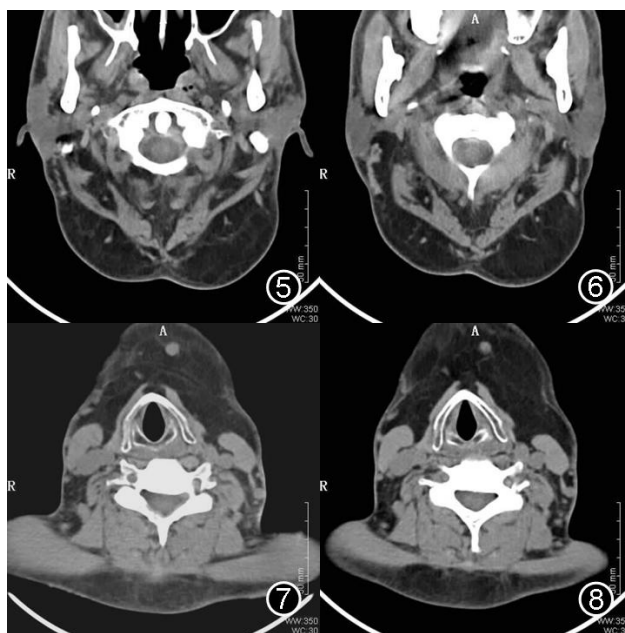


Figure 2. Computed tomography (CT) of the neck



2. Discussion

Madelung's disease is also known as benign symmetric lipomatosis (BSL), multiple symmetric lipomatosis (MSL), fatty neck syndrome or Launois-Bensaude syndrome.^[1] It was first reported by Brodie in 1846.^[2] In 1888, Madelung^[3] summarized 33 cases reported in the literature in 1888 and characterized the disease as "multiple, symmetric deposits of fatty tissue in the head, neck and upper trunk". It predominantly affects middle-aged men with a history of alcohol abuse^[4] and of Mediterranean or European origins.^[5] There are cases reported from around the world but it is very rare in Asian populations.^[6]

The main clinical feature of the Madelung's disease is the presence of multiple, symmetric, loose adipose tissue deposits mainly around the neck, occipitalis, shoulder, back and chest. Accumulations on the limbs, scrotum and tongue have also been reported. The fat masses are not encapsulated.^[7] Although Madelung's disease is usually free of dysfunction, compression of the trachea, esophagus, and nerves can occur with associated dyspnea, dysphagia and nerve compression related syndromes.^[7,8] This disease has been associated with multiple physical and neurological conditions including hyperlipidemia, hyperuricemia, gout, diabetes mellitus, hypertension, hypothyroidism, liver diseases, and nerve dysfunction.^[9,10] CT characteristics of Madelung's disease include fat accumulation and enlargement of the sides of the neck, the nape of the neck, the occipital area, and the upper back. In the sides of the neck spaces between the platysma muscles are often filled with fat; in the nape of the neck, occipital area, and upper back regions, spaces between the subcutaneous structures are often filled with fat. The

lipoma are usually symmetric with no clear boundaries. There may be linear or reticular fibers and calcification or ossification in the accumulated fat tissue. Muscles in the neck area can be stretched and vessels can be dislocated due to compression, but no fat is observed in the muscle tissue itself.^[11]

This case is a 51-year-old man with a 30-year history of heavy alcohol consumption. His tolerance to alcohol had substantially increased and he had clear withdrawal symptoms. Jointly considering his drinking history, laboratory tests, psychotic symptoms, personality change and social dysfunction, a diagnosis of alcohol-induced psychotic disorder was made. The slow growth of the fatty masses in his neck had lasted for three years and they were not associated with any pain or other associated symptoms. Combining his medical history, physical examination, CT scan and pathological tests, the diagnosis of Madelung's disease was made after consulting a surgeon.

The concurrence of alcoholism and Madelung's disease has been widely reported. Using 'Madelung's disease' as the key words to search in the China National Knowledge Infrastructure (CNKI), 82 case reports were found among which 67 (82%) reported a history of heavy alcohol consumption. We also searched PubMed using the following keywords: 'Alcoholism AND ((Madelung's syndrome) OR (Benign symmetric lipomatosis) OR (Multiple symmetric lipomatosis) OR (Fatty neck syndrome) OR (Launois-Bensaude syndrome)). A total of 33 cases were found among which three were Asians and the rest were Caucasians.

Although not seen in this case, there are other symptoms of Madelung's disease. Filgueiras and

colleagues^[12] reported a 42-year old male with alcohol intoxication who had lumps around the neck and the shoulder as well as purple, scaly, erythematous-violaceous lesions and bullous lesions on the limbs; the patient was diagnosed with chronic alcohol intoxication, Madelung's disease, and niacin deficiency. After detoxification and treatment with intravenous B complex replacement, the cutaneous lesions healed but the lipoma remained intact. Triantafyllou and colleagues^[13] reported two cases of co-occurring alcohol intoxication and Madelung's disease that had sensorimotor polyneuropathy with proximal predominance and neuropathic skin lesions; head CT showed decreased brain volume and psychological tests found that they had impaired memory, attention, cognition, logical thinking, and executive functioning. Grau Martín and colleagues^[14] found that the development of Madelung's disease is related to early onset of drinking and large alcohol consumption. It is unclear whether the prognosis differs between alcohol-induced psychosis with and without Madelung's syndrome.

The etiology and pathogenesis of Madelung's disease is not clear. Chronic alcohol intake has been found in 60 to 90% of the reported cases, so alcoholism is considered an important risk factor,^[15] as shown in the present case. One hypothesized mechanism is hypertrophy of the brown adipose tissue induced by a catecholamine disturbance; this hypothesis is based on the observation that the common areas where the fat tissues are found in Madelung's disease are also the main areas of the brown adipose.^[7] Ethanol can decrease the activities of the beta(3)-adrenergic receptors and disturb the catalytic unit of adenylyl cyclase, which interferes with the noradrenaline induced synthesis of intracellular cyclic adenosine monophosphate (cAMP) and, therefore, leads to a defect in adrenergic-stimulated lipolysis and could cause dysfunction of fat cells in benign symmetric lipomatosis.^[10] Chronic intake of ethanol can also trigger mitochondrial DNA mutations in the brown fat cells and lead to defective sympathetic-stimulated mitochondrial biogenesis and neoplastic-like proliferation of brown adipocytes.^[16] Madelung's disease may also be associated with changes of other lipometabolic factors, such as hypertension, abnormal insulin levels, hypothyroidism and so on.^[7]

The diagnosis of Madelung's disease should be differentiated from multiple neck tumors, familial lipomatosis, fat pad, dolorosa adiposis and liposarcoma.^[11]

The treatment of Madelung's disease requires comprehensive consideration of comorbid conditions. Surgical removal or liposuction are the most effective methods to remove the excessive fat tissue.^[17] The advantage of liposuction is that it is less evasive compared to surgical removal; the disadvantage is that it

may leave loose skin and the reoccurrence of fat tissue is common if the suction is not complete. Therefore, in cases where fat tissues are found in multiple areas, surgical removal should be considered first. Surgical removal should also be prioritized when there is compression of the respiratory tract or the digestive tract. Nonetheless, the fat tissues often grow along the blood vessels. Therefore, bleeding may be a concern when attempting surgical removal of the lipomas. Other measures include abstinence from alcohol and weight control in order to prevent recurrences,^[7] though diet and weight loss have shown limited effect for the treatment Madelung's disease.^[17]

After proper treatment, the recurrence of Madelung's disease is rare, although new lipoma may occur. It is also rare for the lipomas to become cancerous. Tizian and colleagues^[18] reported a case of malignant degeneration in Madelung's disease in 1983. Enzi and colleagues^[19] followed up 31 cases for 4 to 26 years and found that eight cases died (a case-fatality rate of 25.8%), three of which were sudden deaths attributed to severe autonomic nervous system conditions. None of the 31 cases had serious heart diseases but those with lipomas inside the mediastinum were more likely to die. This longitudinal study highlighted the importance of follow-up and the treatment of associated conditions in these individuals. At the time of this case report, we have only followed up this case for one month so it is too early to tell the long-term outcome.

This case again shows the importance for psychiatrists to increase their awareness of unusual medical conditions that can co-occur with mental and substance abuse disorders. Psychiatrists should consider the possibility of the Madelung's disease when patients with alcohol-related problems show changes in appearance. Similarly, physicians in general medical settings who identify patients with suspected Madelung's syndrome should ask about a history of drinking and look for signs of alcohol-induced mental problems.

Conflict of interest

The authors declare no conflict of interests related to this case report.

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酒精引起的精神病性障碍共病马德隆氏病的病例报告

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概述: 马德隆氏病是一种罕见的疾病, 也称为良性对称性脂肪过多症 (BSL), 多发性对称脂肪堆积症 (MSL), 肥颈综合征或 Launois-Bensaude 综合征, 其特征为多发性、对称性、脂肪组织松散地堆积在颈部、枕部、肩部、背部或胸部。脂肪组织是没有被包裹的, 因此在相邻区域之间可以自由移动。这种疾病在地中海中年白人男子中最常见; 在亚洲很少报道。马德隆氏综合征患者 60 ~ 90% 有慢性酗酒史。我们报告一例 51

岁中国男性酒精所致精神障碍患者, 发现颈部脂肪组织 3 年里逐步扩展。根据病史、体格检查, 颈部 CT 等常规检查结果, 他被确诊为马德隆氏综合征。

关键词: 酒精使用障碍, 马德隆氏综合征, 良性对称性脂肪瘤病, 中国

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