Multiple symmetric lipomatosis with vulvar involvement: a rare case report associated with walking difficulty and urination disorder

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Abstract

Multiple symmetric lipomatosis (MSL)—a rare metabolic condition characterized by diffuse, nonencapsulated, painless fat deposits—remains a challenging condition to treat. In addition, the clinical manifestation of MSL in women has not been fully understood due to the male-dominated prevalence of the disease. Here, we report a rare case of MSL with vulvar involvement and provide a review of the literature to increase the understanding of both the diagnosis and treatment of the disease. A 46-year-old Japanese woman, who had a history of chronic alcohol consumption for over 20 years, presented with bilateral giant enlargement of the labia major and complained of difficulty in walking and urination. Magnetic resonance imaging revealed nonencapsulated fat deposits involving the vulvar region and extending around the rectum. The patient underwent pubic lipectomy followed by episio-perineoplasty, which resulted in a good esthetic outcome with sufficient patient satisfaction. The morphological presentation of MSL in women is different from that in men, and clinical expression of MSL in the vulvar region is rare but cannot be overlooked owing to the potential of serious sequelae such as walking difficulty, urination disorder, and sexual dysfunction. In such cases, lipectomy followed by episio-perineoplasty is indicated for the treatment of the condition and its sequelae, while ensuring less chance of relapse and better esthetic outcome compared with other treatment strategies. Level of evidence: Level V, therapeutic, diagnostic, risk/prognostic study.

Keywords Multiple symmetric lipomatosis · Female · Lipectomy · Alcoholism · Vulva

Introduction

Multiple symmetric lipomatosis (MSL), also known as Madelung disease, is a rare condition characterized by an accumulation of multiple nonencapsulated lipomatous tissues with a symmetric distribution that was first reported by Brodie [1], Madelung [2], and Launois [3]. The characteristic metabolic pattern of MSL is well described in men, including the very characteristic “buffalo hump” or “horse collar (Madelung collar).” However, the clinical expression of MSL in women is different from that in men; the typical morphologic presentation in women is characterized by fat

deposition in the proximal arms and legs, giving the patient a “football player” appearance [4]. Thus, such sex-related morphologic features could lead to the underdiagnosis of the disease in women.

There have been few reports of MSL involving external genital organs that play a role in the process of human reproduction. In men, only 8 cases of MSL affecting the scrotal region have been reported [5]. In women, MSL with vulvar involvement affecting the mons pubis was first described by Tan et al. [6] in 2008 and remains such a rare condition that no other cases have been reported in the English literature to date. The distribution of lipomatosis in the perineal region is not only rare but attracts clinical interest because it may create problems such as sexual dysfunction, urination disorders, and difficulty in walking. Here, we report a new case with vulvar involvement, which is also the first case of MSL affecting the labia majora, with a review of the literature to increase the understanding of both the diagnosis and treatment of the disease.

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Case report

A 46-year-old Japanese woman presented with a 3-year history of painless, soft, slow-growing swelling of the labia majora, which was causing difficulty in walking and urination (Fig. 1). She had a history of drinking both 1000 mL of beer (5% alcohol content) and 180 mL of spirits (20–25% alcohol content) at least every day for over 20 years, resulting in decompensated liver cirrhosis. Physical examination revealed bilateral giant masses affecting the labia majora, cheek, and upper arm, whereas there were no masses on the neck or shoulders. Magnetic resonance imaging (MRI) revealed non-encapsulated fat deposits in the labia majora and extending around the rectum (Fig. 2). Computed tomography (CT) revealed nonenhancement of the accumulated fat and no apparent enlargement of the inguinal or pelvic lymph nodes. Laboratory data showed both hyperbilirubinemia and hypoalbuminemia with thrombocytopenia. Excisional biopsy was performed, and the pathologic tissue demonstrated diffuse overgrowth of mature adipocytes, suggesting no malignancy.

The patient underwent pubic lipectomy followed by episiotomyplasty (Fig. 3). The lipomatous tissue lacked encapsulation and the transition between lipomatous and normal tissue was poorly demarcated. Two specimens, measuring $20 \times 17 \times 6$ cm (weighing 900 g) in the left and $17 \times 12 \times 7$ cm (weighing 640 g) in the right labia majora, were removed and subsequent esthetic reconstruction was performed by further reduction of the fatty tissue in the mons pubis and an additional surgical incision in the groin to resect excess skin (Fig. 4). Pathologic examination revealed no lipoblasts or atypical stromal cells but only mature adipocytes without nuclear atypia. Immunohistochemistry showed no expression of MDM2, CDK4, or p16 antigens. The patient's postoperative course was uneventful, and she was satisfied with her functional improvement, including walking and urination, as well as the esthetic outcome (Fig. 5).

Discussion

We described the case of a 46-year-old woman with bilateral giant lipomatosis in the vulvar region, which caused problems such as difficulty in walking and urination. MSL is so rare that the literature on this disease mainly comprises case reports and a small number of series. The incidence of MSL is approximately 1 in 25,000, and the male-to-female ratio is 15:1 to 30:1 [7, 8]. The disease mainly affects men between 30 and 60 years of age and develops within a few months or several years; not many women with MSL have been reported [9].

We retrospectively reviewed 50 articles on this subject published between 2000 and 2019 to investigate the clinical manifestation of MSL in women. Using PubMed and the search terms “multiple symmetric lipomatosis” and “Madelung disease,” and excluding literature reviews without case reports, we found 106 cases in the English literature. As a result, 94 men (89%) and 12 women (11%) patients with MSL were identified, demonstrating a male-to-female ratio of 8:1. The mean age at presentation was 60.8 ± 16.4 years in women and 54.0 ± 10.2 years in men, while the mean age at onset was 54.6 ± 10.5 years in women and 46.6 ± 11.4 years in men. Of the patients, 67% of women and 87% of men had a history of chronic alcohol consumption. MSL was characterized by diffuse symmetric accumulation of adipose tissue, most commonly around the neck region (85.8%) followed by the shoulders (35.8%), upper extremities (22.6%), face (18.9%), back (11.3%), and chest (10.4%) (Table 1). Notably, women with MSL had lipomatous masses in the upper extremities, lower extremities, and axillae significantly more frequently than did men. As for MSL affecting the perineal region, only 10 men and 1 woman have been reported worldwide (Table 2).

MSL is classified into 3 types according to fat mass distribution [19]. Type I is characterized by a neck distribution; lipomatous tissue is located around the neck and deltoid region, giving the patient a “horse collar” or “buffalo hump” appearance. Type

Fig. 1 Frontal (a) and lateral (b) views of a 46-year-old woman with a symmetric distribution of fat masses involving the vulvar region

Fig. 2 Magnetic resonance imaging of the pubic area before surgery. T1-weighted axial images show high-signal intensity for fat deposition, which was diffuse and nonencapsulated in the labia majora (a) and extending around the rectum (b). c T2-weighted coronal images show high-signal intensity without a specific sign of liposarcoma, such as linear or nodular foci of hyperintensities, on short tau inversion recovery sequences (d)

Fig. 3 Perioperative images of lipomatous tissue excision in the labia majora and mons pubis. a A crescent-shaped skin incision was made in the expanded skin of the labia majora. Inner lines were designed at least 4 cm apart from the labia minora. En bloc resection of skin and subcutaneous lipomatous tissue was performed in the left (b) and right (c) of the labia majora, taking care not to damage the vaginal and rectal wall. d The

swelling in the mons pubis still remained after the reduction of fatty tissue in the labia majora. e Further reduction of fatty tissue in the mons pubis was performed to an extent that did not impair the cutaneous blood flow. f The excess skin produced by the reduction of fatty tissue was excised after an additional surgical incision in the groin

Fig. 4 Morphologic and pathologic images of the resected tissue. **a, b** Macroscopically, the excised tissue lacks encapsulation and the transition between lipomatous and normal tissue is poorly demarcated. **c, d** Histologically, hematoxylin and eosin staining reveals mature adipocytes without cell nuclear atypia, whereas lipoblasts and atypical stromal cells were not found. Degenerating findings, such as fibrosis, myxoid change, mild infiltration of inflammatory cells, and appearance of macrophages, were also seen occasionally. The scale bar represents 2.5 mm in **c** and 250 μ m in **d**

II is characterized by a pseudo-athletic appearance; lipomatous tissue is located throughout the body, including around the shoulders and upper extremities, and appears as simple obesity. Type III is characterized by a gynecoid appearance; lipomatous tissue is located in the lower body, including around the perineal region and lower extremities. However, some patients present with more than one type of distribution.

The diagnosis of MSL requires the presence of multiple non-encapsulated lipomatous tissues. Chronic alcohol consumption is a major risk factor, especially in men, and the disease may also be associated with certain internal diseases. Although MSL is

generally easily diagnosed on physical examination, it can be clinically misdiagnosed as certain other diseases. CT and MRI are important to confirm the diagnosis by excluding other soft tissue tumors, such as liposarcoma [20]. CT can consistently show nonenhanced accumulation of fat tissue within subcutaneous tissue or the spaces between muscles. MRI is superior to CT in showing the structure of soft tissue, including excess non-encapsulated fat tissue.

The cause of MSL remains controversial but is suggested to be associated with alcohol abuse because 90% of patients with MSL have a history of chronic alcohol consumption.

Fig. 5 Frontal (**a**) and lateral (**b**) view of the postoperative results 6 months after lipectomy

Table 1 Distribution of lipomatous masses in patients with MSL

Affected body areas	All patients, <i>n</i> (%)	Female, <i>n</i> (%)	Male, <i>n</i> (%)
Neck region	91 (85.8%)	9 (75.0%)	82 (87.2%)
Posterior neck/occipital	76 (71.7%)	7 (58.3%)	69 (73.4%)
Anterior neck/submandibular	56 (52.8%)	3 (25.0%)	53 (56.4%)
Trapezium region/shoulders	38 (35.8%)	4 (33.3%)	34 (36.2%)
Upper extremities	24 (22.6%)	7 (58.3%)	17 (18.1%)
Face/periauricular	20 (18.9%)	0 (0.0%)	20 (21.3%)
Back	12 (11.3%)	2 (16.7%)	10 (10.6%)
Pectoral region/chest	11 (10.4%)	0 (0.0%)	11 (11.7%)
Perineal region	7 (6.6%)	1 (8.3%)	6 (6.4%)
Abdomen	6 (5.7%)	1 (8.3%)	5 (5.3%)
Lower extremities	5 (4.7%)	2 (16.7%)	3 (3.2%)
Axillae	3 (2.8%)	2 (16.7%)	1 (1.1%)
Buttocks	1 (0.9%)	1 (8.3%)	0 (0.0%)

There is no evidence that the disease is hereditary, and malignant transformation is rare [21]. Many hypotheses have been proposed in previous studies. One suggestion is that alcohol directly affects mitochondrial metabolism by causing oxidative aging of mitochondrial DNA [22]. However, some patients with MSL have no history of alcohol intake. In another clinical and histologic investigation, molecular-uncoupling protein 1 mRNA and adipocyte fatty-acid protein-2 immunohistochemistry findings suggested that the lipomatous tissue observed in MSL originates from brown adipocytes [23]. However, this hypothesis is also unsatisfactory because some patients with MSL have lipomatous tissue in regions where brown adipose tissue is considered absent, such as the pubic area.

Treatment for MSL includes both surgical and nonsurgical procedures [24]. As there is no definitive etiologically targeted treatment, all treatments are palliative, with the goal of function recovery and improved appearance. Open excision (lipectomy) may proceed to an important demolition in nononcologic

diseases, but seems to be effective and safe because the vessels and nerves can be identified during the procedure. Liposuction is an easy method that can be performed safely under local anesthesia, but there is little clinical experience because it has not been widely used. A combined method of lipectomy and liposuction has also been reported [25]. When it is esthetically required to remove the skin as in the current case, lipectomy can provide a more desirable outcome compared with that with liposuction alone, which leaves sagging skin. Alternatively, liposuction of noncapsulated adipose tissue, with skin-only excision, would be an effective and less invasive option.

Intralipotherapy, a nonsurgical treatment, mainly limits growth of adipose masses and is not highly effective in reducing their volume. Alcohol withdrawal and weight loss may slow the enlargement of adipose masses and decrease the risk of recurrence after surgery, but cannot reverse the course of the disease. As for prognosis, patients with MSL who undergo lipectomy show a recurrence rate of 14% compared with 20% with

Table 2 List of MSL cases with involvement of the perineal region

Case no.	Authors	Age	Sex	Country	Alcoholism	Location
1	Grolleau et al. (1997) [10]	31	M	France	Severe	Scrotum
2	Soler et al. (1997) [11]	30	M	Spain	Severe	Scrotum, pubis
3	Soler et al. (1997) [11]	35	M	Spain	Moderate	Scrotum
4	Nounla et al. (2001) [12]	14	M	Germany	No	Perineum
5	Poggi et al. (2006) [13]	44	M	Italy	Severe	Scrotum
6	Tan et al. (2008) [6]	20	F	Turkey	No	Pubis
7	Penna et al. (2012) [14]	68	M	Germany	Severe	Scrotum, pubis
8	Alcantara et al. (2013) [15]	54	M	Brazil	Severe	Scrotum
9	Nikolić et al. (2013) [16]	51	M	Serbia	Severe	Scrotum
10	Turkan et al. (2015) [17]	34	M	Turkey	Unknown	Scrotum
11	Ndhlovu et al. (2015) [18]	58	M	Germany	No	Perineum
12	Costa et al. (2017) [5]	53	M	Portugal	Severe	Scrotum
13	Present case	46	F	Japan	Severe	Labia majora

liposuction procedures. Specifically, ultrasound-assisted liposuction has shown a relapse rate of 50% [19].

In conclusion, we described a rare case of a middle-aged woman with MSL affecting the vulvar region. She had a history of chronic alcohol consumption and presented with giant fat masses in the labia majora, causing functional problems, including difficulty in walking and urination. The morphologic presentation of MSL in women is different from that in men, showing increased occurrence in the upper extremities, lower extremities, and axillae. Understanding of its characteristics could be helpful in avoiding a certain degree of the underdiagnosis of the disease in women. Clinical expression of MSL in the vulvar region is rare but cannot be overlooked due to the potential of causing serious sequelae, such as sexual dysfunction, urination disorder, and difficulty in walking. Lipectomy followed by episioepineoplasty is indicated to treat the condition and its sequelae, while providing a low risk of relapse and good esthetic outcome. MSL is a rare disease, especially in women, but it is important for plastic surgeons to keep such knowledge in mind when treating female patients with similar symptoms.

Compliance with ethical standards

Conflict of interest Maiko Kiyama, Koji Kanayama, Solji Roh, Yoshitsugu Hattori, Jun Oba, Takuya Iida, Tetsuo Ushiku, and Mutsumi Okazaki declare that they have no conflict of interest.

Ethical approval No ethical approval was necessary for this case report.

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

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