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Case report

From Ancient Enigmas to Novel Paradigms: A Depiction of Multiple Symmetric Lipomatosis

Vlatka Pandžić Jakšić and Velimir Božikov

Department of Endocrinology, Diabetes and Metabolic Diseases, University Hospital »Dubrava«, Zagreb, Croatia

A B S T R A C T

A rare case of multiple symmetric lipomatosis type 2 in a female patient was presented. New possible iconographic representations of multiple symmetric lipomatosis were considered and some metabolic aspects of this disease were reviewed.

Key words: *multiple symmetric lipomatosis, paleopathology, obesity*

Introduction

Since ancient times morbid conditions were portrayed by artists, most often without intention and any medical knowledge. They anticipated and sometimes surpassed descriptions in scientific world. This unique expressiveness of art objects contributed to the paleopathology as much as written medical scripts, pathography of historical persons or study of human remains[1,2]. The importance and richness of particular iconographic sources leaded in 1983 to the introduction of the term iconodiagnosis[3].

Being a disfiguring disease, the wide spectrum of iconographic representation of obesity exists in figurative arts and archaeological findings through the time. A different perception of obesity in particular civilization was reflected through the artist's eye: for instance, in Greek figures as grotesque and despised, or in Etruscans as a symbol of wealth and well-being[4,2]. Particularly interesting have been figures from illiterate populations, statuettes of women, so called »stone-age Venuses«. They allowed Pontius, the founder of the term »iconodiagnosis«, to depict and differentiate between two main types of obesity: abdominal and gluteal[5]. On the other hand, archaeologists interpreted the most famous early image of a human, a woman called »Venus of Willendorf« as an ideal of beauty and fertility of this age. However, from the medical point of view this might be contested because such abdominal type of obesity is supposed to interfere with reproduction[2].

Recently, going further in depicting some ancient representations of obesity, a rare syndrome, multiple symmetric lipomatosis (MLS) was recognized[6]. This particular disorder with characteristic distribution of fat should be considered in differential diagnosis of obesity. This is a disease of massive fat accumulation under the skin and presents in at least two different clinical phenotypes: type 1 with fat deposits mainly around the neck and upper trunk and type 2 with fat deposits mainly in proximal limbs, saving the distal segments, creating in such a way a pseudoathletic, massive aspect[7].

Case Report

We present a case of a 48 years old female patient who presented with characteristic clinical phenotype of type 2 MSL. She attended our endocrinology outpatient unit complaining on large masses on both her arms. The enlargement has especially increased in the last 3 months, but has appeared and has been slowly accumulating for at least 3 years, the time coinciding with the onset of her menopause. She had no other complaints relating to the excess of adipose tissue, but her weight increased since then 20 kg, reaching 83 kg with body mass index of 36 and waist circumference of 98 cm. The rest of her past history was unremarkable besides alcohol intake of about 40 g daily. Physical examination revealed obvious symmetrical fat deposits in upper arms and shoulders (Figure 1). She presented a characteristic pseudoathletic appearance but also exhibited prominent abdominal and lower part of the body obesity.

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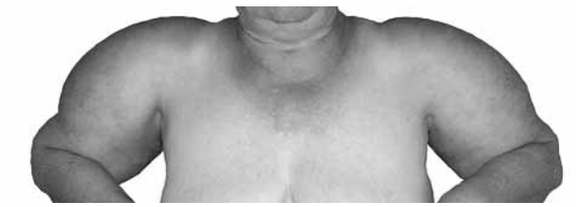

Fig. 1. Upper torso of our patient with multiple symmetric lipomatosis.

Routine laboratory evaluation disclosed evidence of chronic liver disease with two-fold increase of transaminases. Fasting cholesterol and its subfractions, as well as fasting triglycerides, were within the normal range. By performing oral glucose tolerance test and measuring hemoglobin A1c, we found no laboratory signs for diabetes mellitus. The measurement of fasting thyroid-stimulating hormone, cortisol, adrenocorticotropic hormone, IGF-1, prolactin, testosterone, luteinizing and follicle-stimulating hormone revealed no abnormalities but she had a relatively low estradiol level.

Microscopy of the sample obtained by cytological puncture revealed benign adipose tissue with normal cell diameter. Further examinations consisted of magnetic resonance that described the nonencapsulated adipose tissue in shoulder region with the largest diameter of 7 cm. Body composition determined by densitometry showed that she had 47.6 % body fat. Abdominal ultrasound confirmed hepatic steatosis. Electromyoneurography showed a beginning of motoric neuronal lesion in cervical and lumbal segment. The patient still considers whether to be operated and the method of choice would be liposuction[8].

Discussion

The first studies of MSL go back to 1846 by B. C. Brodie, who described a picture of symmetrical lipomatosis, particularly in the neck[9]. In 1888 Otto W. Madelung clearly described the syndrome in 33 cases in his work »Ueber den Fetthals«[10]. In 1898 P. E. Launois and R. Bensaude wrote »De adénolipomatose simmétrique« and accurately presented 75 cases of such a rare disease[11].

Besides being rare in clinical setting, the possible recognition of this disease in following archaeological findings engaged vivid discussions[12,13].

An ancient relief from Deir el-Bahri shows Queen of Punt offering gifts to the Queen Egyptian Hatshepsut (1473–1458 B.C.). Discerning the alleged pathological appearance of Queen of Punt, syndromologists found hyperlordosis, gluteofemoral obesity and symmetrically distributed deposits on the trunk, arms and thighs, sparing her face, neck, hands and feet. In the absence of her mummy, differential diagnosis of the Queen's phenotype resulted in a puzzle of several pathologic entities, among others: steatopygy, myxoedema, rickets, bilateral congenital hip dislocations, achondroplasia, neurofibromatosis and finally MSL[14].

The second example is the Capestrano Warrior discovered in Abruzzi region, a naturalistic monumental stone sculpture of the native Italic fighter being over two and one-half meters tall, from approximately sixth century B.C. The Warrior is sculpted with unnaturally big hips and wide shoulders and although some have considered it as eunuch, there has been undoubtedly striking resemblance with MSL[6],[13].

From nearly the same period and from Germany, »Warrior of Hirschlanden« shows stylistic similarities to the Capestrano one. This fact was used in argument against pathological interpretation of their features[13]. However, unproportionaly robust legs, slender upper body and tiny head of the »Warrior of Hirschlanden« might be characteristics of an other disorder, the acquired partial lipodistrophy (Barraquer-Simons syndrome) which consist of loss of fat from face, neck and trunk and accumulation of excess fat in the hips and the rest of lower limbs[15].

In our research, Queen of Punt and Capestrano Warrior haven't been the only possible iconographic representation of MSL. The well-known Gimbutas' book on »Goddesses and Gods of Old Europe« has been a rich collection of pictures of Neolithic figures. Pontius used it in differentiating types of obesity and it allowed us to go a step further[16,5]. Bearing in mind the type 2 MSL clinical phenotype, we have found several figures with unnaturally wide shoulders and large arms, for example, from Sesklo, Thessaly in Greece, from sixth millennium B.C (Figure 2). They might have been inspired by pseudoathletic appearance of MSL as well[16,5].

The enigma would remain whether these had been cases of MSL, other form of obesity or artistic pseudopathology. The reality of artist is not always a physical reality. The artistic regard originates from cultural and spiritual context and reflects broader aspects of the civilization[16]. Recognizing this nowadays-rare pathology in ancient sculptures might be burdened with controversies but even the occurrence of simple obesity in both Venuses from Paleolithic and Goddesses from Neolithic era is controversial. Obesity as a consequence of sedentary lifestyle is in contradiction with the actual way of life in that

Fig. 2. Upper torso of goddess with massive shoulders and arms, Sesklo, Thessaly, 6000 B.C. (photo: courtesy of the National Archaeological Museum, Athens).

time[17]. The contemporary incidence of MSL in countries around the Mediterranean is not unusual[18]. Authors have already speculated about genetic relation and possible inheritance of this disease from an ancient Mediterranean population[6]. Could it be that this phenotype was more common in ancient time? Possible answers lay in its future genetic dissection.

More than 400 hundreds cases have been reported since the first descriptions of MSL, but its etiology remains obscure. First hypotheses interpreted MSL as a defect in the adrenergic stimulated lipolysis[19]. The disease has also been suppose to originate from brown adipose tissue (BAT)[20]. The recent study of the genes' expression confirmed that MSL cells express the UCP-1 gene, the specific biochemical marker of BAT, although functionally deregulated BAT because of its defective lipolytic response to catecholmanines[21].

Mitochondrial dysfunction has been associated with alterations of fat metabolism in several disorders and it seems to be a crucial mechanism involved in the development of lipomatosis[22]. Cases with point mitochondrial DNA mutations were documented but those mutations do not occur in the typical disease[23,24]. However, patients with MSL, just as in our case, often suffer from chronic alcoholic hepatopathy. As alcohol has been admitted to interfere with mitochondrial metabolism, this is probably an important link to the pathogenesis of MSL[25].

Some results indicated decreased insulin resistance in patients with MSL[26,27]. Accumulation of subcutaneous fat leads to change of subcutaneous to visceral fat content ratio, reducing the insulin resistance analogous to the thiazolidinedione action. This was supposed to present a more metabolically benign mean of increasing energy stores and an attractive hypothesis that MSL might be a paradigm of metabolically innocent obesity appeared[26,27]. However, caution is suggested because the conclusion of good insulin sensitivity in MSL patients should not be generalized. There is a considerable clinical and phenotypic variability in patients with MSL, some being reported to have diabetes[28,29].

Conclusions

We have presented here a case of type 2 MSL, disorder especially rare in females. Considering its strong similarity with simple obesity, we think that it might be an under recognized syndrome as well among famous Gimbuta's »Goddesses of Old Europe« as in actual clinical practice[16]. The particular pathognomonic appearance might be concealed or become less evident when occurring together with simple obesity, especially in older individuals. Critical but not skeptical approach to ancient art and other paleopathological data might allow us to expect further contributions to iconodiagnosis[2,5].

Until recently adipose tissue was regarded as a passive depot of lipids, but increasing evidence points to an important role of adipocytes as a complex and active endocrine organ and adipocytokines play a major role in whole body metabolism. MSL might present a captivating paradigm for new concepts in this field.

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V. Pandžić Jakšić

Department of Endocrinology, Diabetes and Metabolic Diseases, University Hospital »Dubrava«, Av. Gojka Šuška 6, 10000 Zagreb, Croatia
e-mail: vpandzic@kbd.hr

OD DREVNIH ENIGMA DO NOVIH PARADIGMA: PRIKAZ MULTIPLE SIMETRIČNE LIPOMATOZE

S A Ž E T A K

Opisan je rijedak slučaj bolesnice s multiplom simetričnom lipomatozom tipa 2. Razmotreni su novi mogući ikonografski prikazi multiple simetrične lipomatoze te su iznijete spoznaje o metaboličkim aspektima te bolesti.