Case 143: Madelung Disease[1]

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History

A 49-year-old woman was referred to the internal medicine outpatient clinic for work-up of nonpitting edema. Her history was remarkable for a substantial weight gain (75 lbs [33.75 kg]) in the 6 months before presentation; this weight was distributed mainly in her thighs and upper arms.

Her medical history was remarkable for mild essential hypertension and rheumatoid arthritis, both of which were controlled effectively with medication. She denied increasing her caloric intake. Her alcohol intake was excessive, with consumption of more than 1.5 L of wine per day; however, there was nothing to suggest cirrhosis of the liver.

At physical examination, there was evidence of swelling in her upper limbs, with bilateral proximal arm circumference of 54 cm. According to the patient, her arm circumference was 39 cm 6 months earlier. Swelling was present but less impressive in the forearms. Swelling was also present across her upper chest, at the base of her neck, and in her upper thighs. There was no evidence of pitting edema. The findings of routine screening blood work, including complete blood count and electrolyte analysis, were normal. Thyroid-stimulating hormone levels and 24-hour urine cortisol concentrations were also normal. Subsequently, this patient underwent computed tomography (CT) of the head, neck, chest, abdomen, and pelvis.

Imaging Findings

There was symmetric distribution of subcutaneous fat in the upper arms, back of the neck, back of the torso, anterior chest wall, and upper thighs, with relative sparing of the abdomen (Figure). An incidental retroaortic left renal vein was seen. The solid organs and hollow viscera were normal, and there was no adenopathy, soft-tissue mass, or vascular or lymphatic anomaly.

Discussion

This was a challenging case, with a broad differential diagnosis that included *(a)* Madelung disease, also known as benign symmetric lipomatosis, multiple symmetric lipomatosis, and Launois-Bensaude syndrome; *(b)* generalized lipomatosis in association with other conditions, such as Bannayan-Zonana syndrome, Cowden syndrome, Proteus syndrome, and Dercum disease (adiposis dolorosa); *(c)* drug-induced lipomatosis (from steroidal or antiretroviral agent use); and *(d)* multiple familial lipomatosis.

The correct diagnosis was Madelung disease. The clues to this diagnosis came from a review of this patient's clinical history, particularly her alcohol consumption (> 1.5 L of wine per day), her relatively rapid weight gain over the course of 6 months, and the imaging findings of symmetric fat distribution throughout the neck, upper extremities, trunk, and legs. Biopsy of these lesions enabled us to confirm that they were benign subcutaneous fat.

To our knowledge, benign symmetric lipomatosis was first described in

Part one of this case appeared 4 months previously and may contain larger images.

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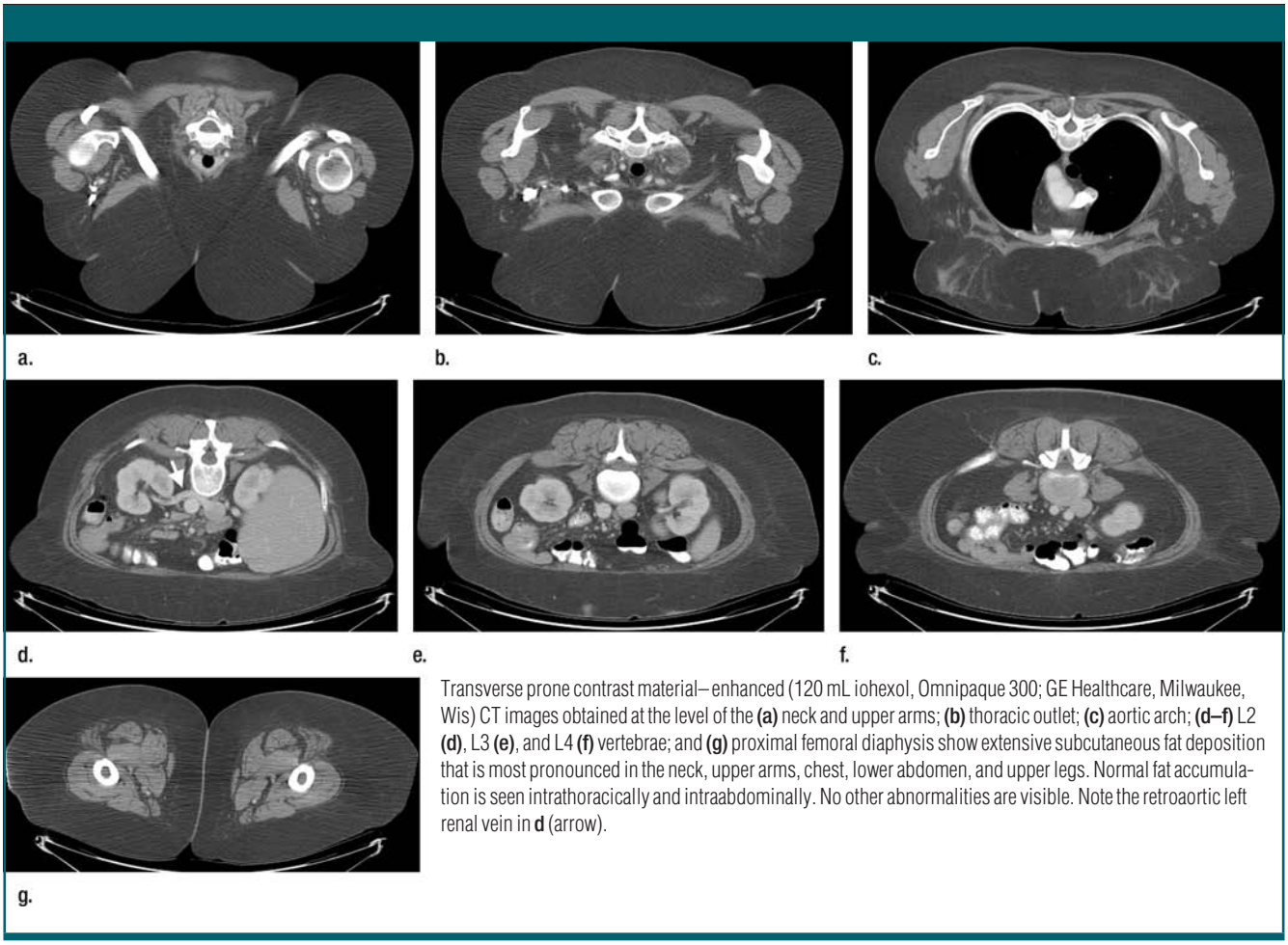

Transverse prone contrast material–enhanced (120 mL iohexol, Omnipaque 300; GE Healthcare, Milwaukee, Wis) CT images obtained at the level of the **(a)** neck and upper arms; **(b)** thoracic outlet; **(c)** aortic arch; **(d–f)** L2 **(d)**, L3 **(e)**, and L4 **(f)** vertebrae; and **(g)** proximal femoral diaphysis show extensive subcutaneous fat deposition that is most pronounced in the neck, upper arms, chest, lower abdomen, and upper legs. Normal fat accumulation is seen intrathoracically and intraabdominally. No other abnormalities are visible. Note the retroaortic left renal vein in **d** (arrow).

1846 (1). Otto Madelung reported a series of patients with this disease in 1888 (2). Shortly thereafter, Launois and Bensaude described a second series of patients with this disease in 1889 (3). Other cases have been reported since (4,5). This patient demonstrated both the classic history and the physical and imaging findings associated with this disease. Other imaging findings of Madelung disease include a relative paucity of fat in the mediastinum, pericardium, abdomen, and pelvis (4,6). Historically, Madelung disease has been seen most often in men (male-to-female ratio, 15:1) between 30 and 60 years of age (7). There is an increased prevalence of this disease in the Mediterranean population (the incidence in Italy has been reported to be as high as 1 in 25 000 men), and there is a relationship between this condition and excessive alcohol consumption, particularly red wine (8). Associated sequelae include liver disease with elevated liver transaminase levels and peripheral neuropathy, attributed largely to alcohol consumption and enlarged body habitus, respectively (5).

Clinical management of Madelung disease involves abstinence from alcohol; however, there is only a slight regression in the magnitude of lipomatous deposits (9). Surgery is the other component of treatment. Surgery is performed mostly for symptomatic relief because many patients develop upper respiratory problems, including snoring, dyspnea, and dysphagia. Obstructive sleep apnea is common, while more serious complications, such as superior vena cava obstruction and sudden death, are rare but have been documented (10).

The other diagnoses considered became exceedingly less likely in view of this patient's imaging findings and clinical history. The distribution of fat deposits made diet-related obesity unlikely. This patient was not taking any medications associated with fat deposition, such as steroidal or antiretroviral agents. She had never received steroids as part of her treatment for rheumatoid arthritis. She had never reported any abnormal skin lesions, nor did she have a history of intestinal polyps; thus, diseases such as Bannayan-Zonana syndrome or Cowden syndrome were unlikely (11). Indeed, imaging studies did not demonstrate any intestinal abnormalities. She had no dysmorphic features or apparent developmental delays, which made diseases such as Proteus syndrome or myoclonus, epilepsy, and ragged-red fiber (or MERRF) syn-

drome unlikely. Dercum disease (also known as adiposis dolorosa) was also unlikely, given the fact that this condition usually involves diffuse or localized painful fat deposits throughout the body, although the head and neck are spared, which was not the case in this patient (12). There was no family history of similar problems, which made familial lipomatosis unlikely. Thus, this patient's imaging findings showing the distribution of subcutaneous fat and her clinical history made Madelung disease the most likely diagnosis.

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Congratulations to the 109 individuals and four resident groups that submitted the most likely diagnosis (Madelung disease) for Diagnosis Please, Case 143. The names and locations of the individuals and resident groups, as submitted, are as follows:

Individual responses

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The following 52 individuals and two resident groups submitted the most likely diagnosis for Diagnosis Please, Case 138 (idiopathic spinal cord herniation) prior to the deadline for submissions for that case but were inadvertently left off the list. The names and locations of the individuals and resident groups, as submitted, are as follows:

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