

# Dramatic loss of weight in an obese patient with heart failure: a mighty heart in a big man

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## Abstract

Obesity has reached global epidemic proportions and has been associated with numerous comorbidities, including major cardiovascular diseases and heart failure. It has many adverse effects on hemodynamics and cardiovascular structure and function; it increases total blood volume and cardiac output, and also activates several neurohumoral systems that play an important role in causing cardiac dysfunction. Typically, obese patients have a higher cardiac output but a lower level of total peripheral resistance at any given level of arterial pressure. Over the past few years, experimental evidence has unraveled some important pathogenetic mechanisms that may underlie a specific form of “obesity cardiomyopathy”. However, many unanswered questions remain regarding the pathophysiological interactions between obesity and the heart. ■ Heart Metab; 2013;61:29–31

**Keywords:** Echocardiography; heart failure; natriuretic peptides; obesity.

## Clinical case

We present the case of P.M., a 50-year-old man with a history of progressive weight gain from the age of 18 years, up to the weight of 188 kg (body mass index [BMI] 61 kg/m<sup>2</sup>; obesity stage VI).

This patient attended the emergency department for worsening dyspnea. He presented with severe anasarca, with elephantiasis and trophic lesions of the lower limbs, tachycardia, tachypnea, and blood pressure within normal limits (120/70 mm Hg).

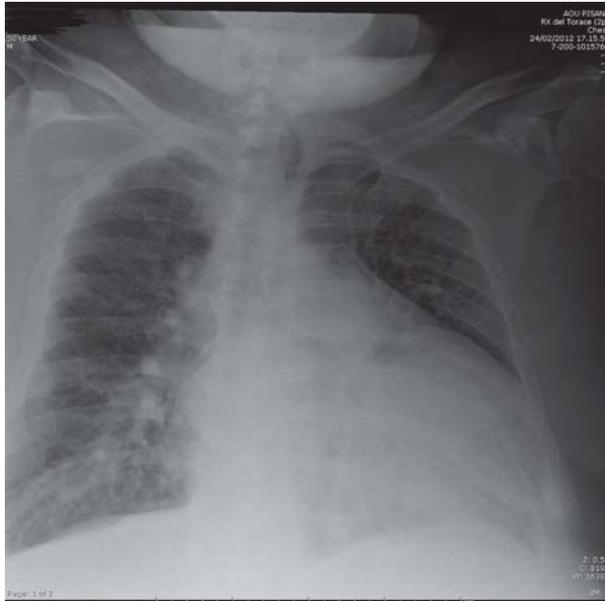
Blood gas analysis revealed respiratory failure type 2 (pH 7.38, PO<sub>2</sub> 49.6 mm Hg, PCO<sub>2</sub> 44.7 mm Hg). Blood tests showed advanced renal insufficiency (serum creatinine 4.4 mg/dL, estimated glomerular filtration rate 40 mL/min), liver dysfunction (severe coagu-

lation deficiency, cholinesterase 2900 U/l) and severe anemia (hemoglobin 9 g/dL). At recovery B-type natriuretic peptide [BNP] was 663 pg/mL and pro-BNP was 2317 pg/mL. Urgent chest X-ray showed severe cardiomegaly and severe pulmonary congestion (*Figure 1*). The echocardiogram displayed left ventricular dilation with end-diastolic volume (EDV) 280 mL, with diffuse parietal hypokinesis and reduction of global ejection fraction (EF) 32%. ECG recordings revealed tachycardial atrial fibrillation with right bundle branch block and low voltages of QRS in the peripheral derivations. The diagnosis was congestive heart failure (CHF) complicated by respiratory, renal and hepatic failure.

The patient was therefore hospitalized and treated with furosemide, first intravenously (mean 500 mg/

### Abbreviations

**BMI:** body mass index; **BNP:** B-type natriuretic peptide; **CHF:** congestive heart failure; **EDV:** end-diastolic volume; **EF:** ejection fraction



**Fig. 1** Chest X-ray

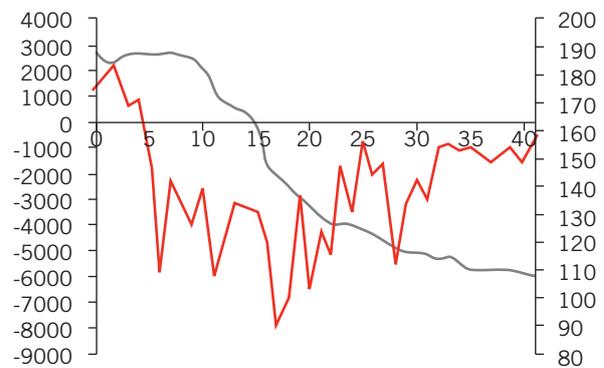
day) and then oral therapy (125 mg/day), angiotensin-converting enzyme inhibitor therapy (ramipril 5 mg/day), potassium canrenoate 50 mg twice a day, digitalis (0.250 mg/day), intravenous albumin, adequate water restriction and the introduction of a low-calorie diet.

On observing polyclonal hypergammaglobulinemia with an increase in kappa and lambda light chains, leading to a suspicion of cardiac amyloidosis, the patient underwent biopsy of the periumbilical fat (which was negative for amyloidosis) and angiocardiac magnetic resonance imaging, which confirmed the echocardiographic findings and excluded the presence of subendocardial or diffuse hyperenhancement (typical of cardiac amyloidosis).

In the days after hospitalization, we observed a dramatic progressive weight loss (78 kg in 45 days), with a marked improvement in renal function (serum creatinine 0.82 mg/dL), gas exchange, liver function (cholinesterase 4300 U/L) and progressive resolution of trophic lesions in the inferior limbs.

One month after discharge the patient underwent a complete check-up. Blood sample tests showed normalization of hepatorenal function, a marked re-

duction in BNP levels (217 pg/mL) and reduced left ventricular volumes (EDV 200 mL) with improvement of left ventricular function (EF 42%). Cardioactive therapy was modified with the introduction of a  $\beta$ -blocker (carvedilol) and dose reduction of the diuretic and anti-aldosterone drug (Figure 2).



**Fig. 2** Body weight trend in relation to water balance

In order to complete the diagnosis and rule out the suspicion of secondary cardiomyopathy, the patient underwent myocardial perfusion scintigraphy, which showed reversible perfusion defects in the mid-distal anterior area and inferior area. Coronary angiography did not reveal the presence of significant coronary artery disease.

After 1 year, successive cardiologic controls confirmed the stability of the patient's clinical status (BNP 73 pg/mL) and further improvement of systolic left ventricular function (EF 46%, EDV 175 mL). The patient has currently reported significant improvement in symptoms and quality of life.

### Discussion

Obesity is one of the most prevalent diseases of our time. Severe obesity (BMI >40 kg/m<sup>2</sup>) is estimated to affect 5–10 million individuals in the USA [1,2]. Obesity induces several modifications in cardiac structure and function as a result of hemodynamic overload, and represents a risk factor for heart failure [3–6]. Adipose tissue is a metabolically active compartment, which requires 2–3 mL/min per 100 g of blood and constitutes an important blood reserve. With the accumulation of adipose tissue, blood flow at that level also increases (in patients with severe obesity it can reach half the cardiac output at rest) and blood volume expands in order to compensate for the increased oxygen demand. The expansion of

blood volume results in left ventricular dilation and is accompanied by eccentric hypertrophy of the myocardium even in normotensive individuals (ventricular cavity/ventricular diameter ratio remains almost unchanged). Moreover, the complex structural and functional alterations found in severely obese patients such as increased left ventricular mass, increased interstitial collagen content, left ventricular and left atrial dilatation, systolic and diastolic intramyocardial dysfunction (confirmed by different studies) would suggest the presence of a distinct typical form of “obese cardiomyopathy” that may be linked to insulin resistance, leptin and lipotoxicity [7–9].

The heart can tolerate this work overload for a very long period. However, over time cardiac function (both systolic and diastolic) deterioration is observed. During this phase reduced systolic function triggers a vicious circle, which leads to further dilatation of the heart chambers and activation of the noradrenergic system and renin angiotensin aldosterone system. These changes, together with the volume overload, further depresses cardiac function. Eventually, signs and symptoms of CHF appear.

A recent epidemiological study demonstrated that insulin resistance could represent a link between obesity and CHF. Insulin resistance, by an increase in circulating insulin, is capable of stimulating insulin-like growth factor 1 receptors, which are probably also implicated in the pathogenesis of myocardial hypertrophy observed in obese patients.

Hyperinsulinemia may lead to sodium retention that could cause subclinical myocardial dysfunction as a result of volume expansion. Furthermore, hyperinsulinemia may lead to sympathetic nervous system activation. Insulin resistance is related to an increased pressure response to angiotensin II, which stimulates left ventricular hypertrophy and interstitial fibrosis through its interaction with aldosterone.

Secretion of locally active molecules from fat cells like leptin (increased adiposity causes higher serum leptin concentrations) has been linked to ventricular hypertrophy in both animals and humans, independently from ventricular dilatation due to overload in obesity. Lipid accumulation in “non fat” cells results in cellular dysfunction with consequent lipotoxicity (low mitochondrial oxidative capacity, increased lipolysis) [9]. Over the past few years, experimental investigations have unraveled some important pathogenetic

mechanisms, such as cardiac steatosis, lipoapoptosis, and the activation of specific cardiac genes that may underlie a specific form of “obesity cardiomyopathy”. The integration between hemodynamic and metabolic models partly explains some differences observed in this particular patient population.

This case is pathognomonic of how obesity could be a determinant of myocardial dysfunction and could cause, when it is not rapidly recognized, severe CHF with secondary multiple organ failure. The rapid resolution of CHF is fundamental for this type of patient and can avoid severe complications; on the other hand, it allows recognition of the real obesity status clear of the volume overload induced by CHF itself. Once the problem of CHF is resolved, overweight treatment still remains, which we try to address by modifying the patient’s lifestyle nutritionally and with increased physical activity and, if necessary, when this approach fails, we resort to bariatric surgery. ■

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