

## Cushing's syndrome with mediastinal lipomatosis

*Pinaki Dutta, MD, DM.*

*Anil Bhansali, MD, DM.*

*Somashekara Reddy-KS, MD, DM.*

*Shariq R. Masoodi, MD, DM.*

**M**ediastinal lipomatosis is a rare benign condition characterized by deposition of a large amount of mature adipose tissue within the mediastinum. The common etiologies are obesity, exogenous or endogenous Cushing's syndrome, alcohol abuse and rarely it can be idiopathic.<sup>1</sup> It is more common now than thought previously, as imaging modalities like computerized tomography (CT) and magnetic resonance imaging (MRI) decisively diagnose this condition. Imaging features include smooth bilateral widening of the superior mediastinum with relative lucency and no definable mass in the lateral x-ray. It is usually asymptomatic, but may sometimes present with compressive symptoms, and often poses a diagnostic dilemma.

A 27-year-old male was admitted with excessive weight gain, typical purple striae on the abdomen, generalized increased pigmentation, proximal muscle weakness and psychotic behavior. He had no history of steroid abuse. On examination, he had centripetal obesity, buffalo hump, broad purple striae on the abdomen, pulp atrophy and generalized increased pigmentation. He was hypertensive with blood pressure of 190/110 mm Hg. Biochemical parameters were: serum sodium 135 meq/L; potassium 2.7 meq/L; fasting blood glucose 294 mg/dl; 0800h cortisol, 1000 nmol/L; 2100h cortisol, 640 nmol/L; and adrenocorticotropic hormone at 2100h 138 pg/ml. Cortisol levels after overnight in low dose and high dose dexamethasone suppression were 520, 960 nmol/L and 780 nmol/L; suggestive



Figure 1 - Computerized tomography scan of the chest, showing hypodense areas comparable to fat (HU-25) near aortopulmonary window.

of non-suppressibility of hypothalamic-pituitary-adrenal axis. Chest x-ray posteroanterior view showed mediastinal widening, but lateral x-ray was normal. Bone mineral density was reduced on quantitative CT. The result of the MRI sella was normal, CT adrenals showed bilateral enlargement and CT chest revealed diffuse mediastinal lipomatosis (**Figure 1**). As the primary tumor responsible for excess cortisol could not be localized with available investigations, he was managed for metabolic complications and subsequently underwent bilateral adrenalectomy. Presently, he is on replacement doses of prednisolone and fludrocortisone, and is doing well.

The factors responsible for distribution and quantity of adipose tissue in this patient could be multiple, such as, genetic background, diet, hormones, and exercise. Glucocorticoids redistribute adipose tissue from the peripheral to central region.<sup>2</sup> In Cushing's syndrome, characteristic features include buffalo hump, increased supraclavicular and truncal fat. Glucocorticoids have profound effects on the adipocyte, affecting both lipid accumulation and mobilization. Lipoprotein lipase activity, the main enzymatic determinant of triglyceride uptake, is increased by cortisol. Glucocorticoids also have a permissive effect on lipid mobilization stimulated by catecholamines,<sup>2</sup> and a synergistic role on lipid deposition when insulin levels are elevated, a frequent accompaniment of Cushing's syndrome. In this condition, an increased amount of fat is deposited in the peritoneum, subcutaneous sites, face and neck. The lipomatosis is better characterized by CT scan and MRI. The fat deposition in this syndrome rarely occurs in the mediastinum, popliteal fossa and spinal epidural space.<sup>3</sup> This peculiar distribution is partly explained by density of glucocorticoid receptors on adipocytes, which is one of the factors responsible for adipocyte differentiation, glucocorticoid receptor gene polymorphism and site specific regulation of set-point of 11- $\beta$  hydroxysteroid dehydrogenase-1 (11- $\beta$  HSD1).<sup>4,5</sup> In-vitro studies have found that omental and probably mediastinal adipose stromal cells (ASC) concentrate more active cortisol than inactive cortisone through the expression of 11- $\beta$  HSD1, which is increased further after exposure to cortisol and insulin. This mechanism ensures a constant exposure of glucocorticoids to central adipocytes.<sup>6</sup> It is also postulated that 11- $\beta$  HSD1 uncommitted ASC may facilitate proliferation. Once early differentiation is initiated, a switch to 11- $\beta$  HSD1 oxo-reductase activity generates cortisol, thus promoting central adipogenesis.<sup>7</sup> Lipomatosis as a component of symmetrical lipomatosis, is characterized by massive enlargement of the

## Clinical Note

abdomen (pseudo-ascites) due to intraperitoneal and retroperitoneal fat, exertional dyspnea due to compression of airway by lipomas of mediastinum, and abnormal glucose tolerance or diabetes mimicking Cushing's syndrome.<sup>8</sup> In our patient, the possibility of ectopic Cushing's syndrome was high for which the mediastinal widening on chest x-ray was interpreted as thymic enlargement which was subsequently resolved after CT scan. Therefore, the entity of mediastinal lipomatosis should always be kept in mind as a differential diagnosis in patients with ectopic Cushing's syndrome due to thymic carcinoid.

Received 27th January 2004. Accepted for publication in final form 7th April 2004.

From the Department of Endocrinology, Postgraduate Institute of Medical Education and Research, Chandigarh, India. Address correspondence and reprint requests to: Dr. Anil Bhansali, Department of Endocrinology, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India. Tel. +91 (172) 747585600 Ext. 6583. Fax. +91 (172) 744401/745078. E-mail: anilbhansali\_endocrine@rediffmail.com

### References

1. Pungarkar S, Sahn J, Patkar D, Varma R, Parmar H. Isolated symmetrical mediastinal lipomatosis. *J Assoc Physicians India* 2001; 49: 1026-1028.
2. Bjorntorp P, Ottosson M, Rebuffe-Scrive M, Xu X. Regional obesity and steroid hormone interactions in human adipose tissue. *UCLA Symp Mol Cell Biol* 1990; 132: 147-158.
3. Noel P, Pepersack T, Vanbinst A, Alle JL. Spinal epidural lipomatosis in Cushing's syndrome secondary to an adrenal tumor. *Neurology* 1992; 42: 1250-1251.
4. Rebuffe-Scrive M, Bronnegard M, Nilsson A, Eldh J, Gustafsson JA, Bjorntorp P. Steroid hormone receptors in human tissue. *J Clin Endocrinol Metab* 1990; 71: 1215-1219.
5. Di Blasio AM, van Rossum EF, Maestrini S, Berselli ME, Tagliaferri M, Podesta F et al. The relation between two polymorphisms in the glucocorticoid receptor gene and body mass index, blood pressure and cholesterol in obese patients. *Clin Endocrinology* 2003; 59: 68-74.
6. Bujalska IJ, Kumar S, Stewart PM. Does central obesity reflect "Cushing's disease of the Omentum". *Lancet* 1997; 349: 1210-1213.
7. Bujalska IJ, Walker EA, Hewison M, Stewart PM. A switch in dehydrogenase to reductase activity of 11- $\beta$  hydroxysteroid dehydrogenase type 1 upon differentiation of human omental adipose stromal cells. *J Clin Endocrinol Metab* 2002; 87: 1205-1210.
8. Zargar AH, Laway BA, Masoodi SR, Bhat MH, Bashir MI, Wani AI et al. Diffuse Abdominal Lipomatosis. *J Assoc Phys India* 2003; 51: 621-622.