

Review Article

Syndrome Z – The New Metabolic Syndrome

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ABSTRACT

The association of obstructive sleep apnea (OSA) and hypertension is well established. To recognize the clustering of nocturnal apnea with hypertension and cardiovascular risk factors, a specific syndrome called “Syndrome Z,” is being hypothesized. Clinical profile of a 43 year old male patient having features of syndrome X with coexisting OSA (“Syndrome Z”) is presented here with a short review of relevant literature.

INTRODUCTION

Nowadays, the focus is on primary prevention of coronary artery disease (CAD), which means risk factor modification. This often is a difficult medical task. “metabolic Syndrome” or “Syndrome X” constitutes one of the most important risk factors for CAD. The diagnosis of metabolic syndrome is made when an individual has three of the following five characteristics: increased waist circumference, high blood pressure, elevated fasting glucose, elevated triglycerides, and decreased high-density lipoprotein (HDL) cholesterol. Further to this “Syndrome Z” was introduced in medical practice by Ian Wilcox in 1996. Wilcox attached the respiratory partner for CAD risk, OSA, to syndrome X.

The importance lies in the fact that the medical fraternity is now challenging CAD by risk factor modification, but one of the major culprits, OSA, remains largely unnoticed and under treated.

CASE REPORT²:

A 43 year old male presented to Respiratory Medicine OPD with a one year history of habitual, loud snoring associated with excessive day time somnolence. Of late he has noticed weight gain. He is working as an accountant in Middle East. He experienced apneic spells in the night. He also has nocturia, impaired concentration and decreased sleep latency. He is a hypertensive on treatment for the last 12 years. No other significant illness in the past or in the family. His Epworth Sleepiness Score was 8/24. On examination he was obese (Fig 1) with Body Mass Index

(BMI) of 30, waist circumference of 42 inches and Neck circumference of 16.5 inches. His blood pressure was 160/100 mmHg,



Fig. 1-Photograph of the patient

Respiratory Rate was 16/minute, Pulse rate was 86/ minute and temperature recorded was 98.6°F. There was deviated nasal septum to right and Mallampati oropharyngeal score was Class II.

Routine blood examination showed hemoglobin of 11.8 gm%, Fasting Blood Sugar, 100mg%, and Post prandial Blood Sugar 144mg%. His chest X-ray (Fig.2) and ECG were normal. Fasting lipid profile showed total cholesterol

of 186mg%, Triglycerides - 243mg%, HDL - 36mg%, LDL - 101mg%, VLDL - 49mg%. His Serum uric acid was 7.6mg%, Serum TSH - 1.23mIU/l and arterial blood gas values were within normal limits.

Overnight Polysomnographic study with 7 hour sleep recording showed Apnea index - 8.8, Hypopnea index - 21.6 and a total Apnoea-Hypopnoea Index (AHI) of 30.4. Study showed total snore events of 588 with a Snore Index of 77.7. Mean saturation was 95.5% with lowest saturation of 77% and a desaturation index of 34. Mean heart rate was 68 per minute with no tachycardia or bradycardia.

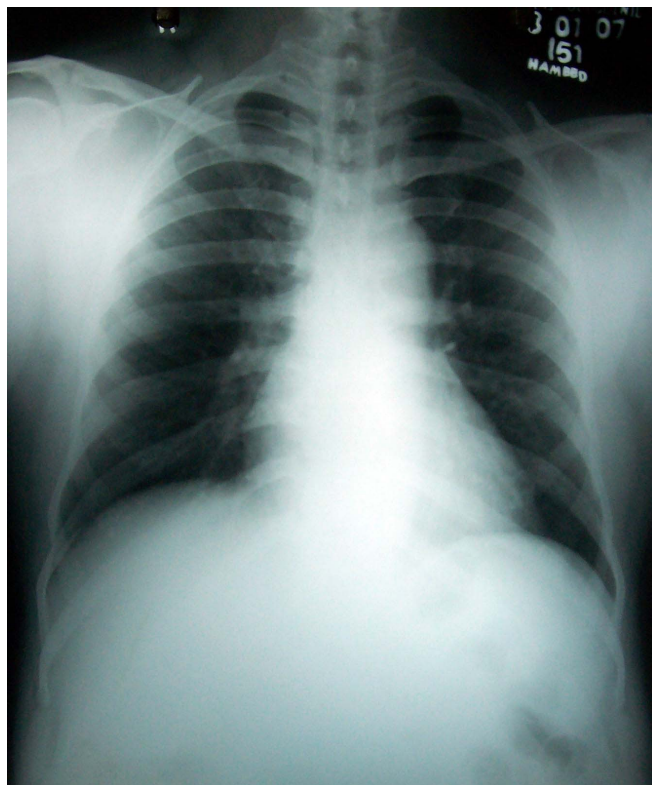


Fig. 2- Showing normal Chest X-ray

In brief he satisfies the criteria for Syndrome Z. Features suggesting Syndrome X for him are central obesity, high triglycerides, low HDL and hypertension along with which he has Severe OSA (AHI>30).

DISCUSSION:

Obstructive sleep apnea affects approximately 10% of middle aged men and 5% of women and is therefore a common condition³. Patients with OSA have many features in common with those with syndrome X, including systemic hypertension which is commonly reported.

Obstructive sleep apnea (OSA) has been linked to increased cardiovascular morbidity and mortality⁴ and can be considered an independent risk factor for CAD. Pathophysiologic mechanisms that are present in patients with OSA, including sympathetic activation, endothelial dysfunction, oxidative stress, systemic inflammation,

hypercoagulability, hyperleptinemia, and insulin resistance, may influence the development and progression of cardiac and vascular pathology. These mechanisms are found to be common for both metabolic syndrome and OSA. Also, OSA is widely prevalent in patients with obesity, diabetes, and hypertension.

Clustering of cardiovascular risk factors (termed metabolic Syndrome or "Syndrome X") was recognized as early as the 1920s and is currently thought to be related to the underlying pathophysiology of insulin resistance and hyperinsulinemia. The criteria proposed by the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) are the most current and widely used⁵.

According to the ATP III criteria, the metabolic syndrome is identified by the presence of three or more of these components:

- Central obesity as measured by waist circumference: In men greater than 40 inches and in women greater than 35 inches
- Fasting blood triglycerides greater than or equal to 150 mg/dL
- Blood HDL cholesterol: In men less than 40 mg/dL and in women less than 50 mg/dL
- Blood pressure greater than or equal to 130/85 mmHg
- Fasting blood glucose greater than or equal to 110 mg/dL

Other important features of the metabolic syndrome include microalbuminuria, hypercoagulability, increased inflammation, endothelial dysfunction, poor cardiorespiratory function and sympathetic activation. Cardiovascular metabolic syndrome X is becoming very common in India. It has even been suggested that the metabolic syndrome ("Syndrome X") may co exist with OSA ("Syndrome Z")¹. However, there is little information about the extent to which the cardinal features of the metabolic syndrome are present simultaneously in patients with OSA.

Coughlin and colleagues⁶ performed a cross-sectional study of 61 otherwise healthy subjects with OSA and 29 subjects without OSA. To mitigate confounding due to obesity, they also matched 34 of the OSA patients by body-mass index (BMI) to the 29 controls. Their results suggest that the prevalence of metabolic syndrome is about 40% greater in patients with OSA. The obesity epidemic and its impact on the prevalence of both metabolic syndrome and OSA make these data especially relevant and timely.

It is not clear whether OSA occur as part of the fundamental pathophysiology of metabolic syndrome, or does OSA, via repetitive nocturnal hypoxaemia and other mechanisms, promote the components of the metabolic syndrome.

OSA and the metabolic syndrome share a similar pathophysiologic milieu that would be expected to increase the risk of cardiovascular disease. Given the obesity epidemic at hand, the prevalence of both metabolic syndrome and OSA are rising. In patients with established

coronary artery disease, treatment of OSA may confer long term cardiovascular benefits. Our understanding of the relative importance and interactions of these cardiovascular disease mechanisms and risk factors in patients with OSA may have direct implications for the development of targeted preventive and therapeutic strategies². The results of various studies have undisputedly shown that appropriate treatment of OSA with Continuous Positive Airway Pressure (CPAP) therapy significantly reduces blood pressure⁷ and other cardiovascular complications like CAD, arrhythmias and stroke. Treatment of OSA also improves the altered metabolic physiology in patients with syndrome X. Also, proper management of syndrome X reduces the apnea hypopnea index in patients with co-existent OSA thus underlying the importance of simultaneous management of both the conditions.

CONCLUSION:

This case report of a classical case of Syndrome Z envisages the importance of OSA in CAD. OSA can modify the components of metabolic syndrome and vice versa. Early diagnosis and treatment of OSA is the cornerstone in the management of metabolic syndrome and hence CAD. Thus clinicians should keep high index of suspicion for OSA while dealing patients with known risk factors for cardiovascular complications.

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