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Case Report

Acute onset sleep apnea with severe transient hyperglycemia in young adult: the diagnostic dilemma and management controversy

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ABSTRACT

Sleep disordered breathing and obstructive sleep apnea are frequently associated with hyperglycemic disorders. The common pathophysiological factors that link these disorders have been a matter of debate and current research. Abdominal adiposity and high body mass index are considered to predispose individuals to early onset of type 2 diabetes and related metabolic disorders. A young adult presenting with symptoms of obstructive sleep apnea often poses a diagnostic challenge for clinicians especially when multiple risk factors coexist. It is essential to establish the exact diagnosis so that specific treatment can be initiated. The role of a non-aggressive approach in management of severe hyperglycemic conditions has been doubted. We report a case of a 33 year old man presenting to the respiratory outdoor clinic for recent onset loud snoring and increased daytime sleepiness. Routine biochemistry reports revealed hyperlipidemia and severe hyperglycemia. The patient was ambulatory and stable throughout. The subsequent investigations identified multiple stressors and the possibility of a single cause was analysed. A rapid glycemic control and amelioration of symptoms were observed based on consistent monitoring and a conservative clinical approach. The key findings and relevant review of literature are discussed in this article.

Keywords: Sleep disordered breathing, Obstructive sleep apnea, Metabolic syndrome, Syndrome Z, Snoring, Severe hyperglycemia

INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by repetitive upper airway obstruction causing intermittent hypoxia and sleep fragmentation leading to symptoms like Snoring and excessive daytime sleepiness.[1] Sleep disordered breathing including OSA is frequently associated with obesity, type 2 diabetes and metabolic syndrome.[2-4] Studies have shown that severity of OSA is independently associated with levels of blood glucose, HbA1c and insulin resistance.[5,6] Besides these, many other risk factors like oxidative stress, systemic inflammation and hypertension are considered to be associated with OSA.[2,7] Treating OSA by continuous positive airway pressure (CPAP) have shown to significantly improved insulin sensitivity in individuals, but whether improving hyperglycemia can improve symptoms of OSA is still a matter of debate.[1,5] Lifestyle modification including weight reduction through exercise also improves symptoms of OSA. Diagnosis and management of OSA becomes a challenge when symptoms are vague and a number of risk factors co-exist.[8]

New-onset severe hyperglycemia in young adult (18-35 years of age) has been a diagnostic challenge, especially when it is transient or fluctuating. Hyperglycemia in young adults can be caused by conditions like young-

onset type 2 diabetes, MODY (Maturity Onset Diabetes of the Young), MMDM (Malnutrition Modulated Diabetes Mellitus), drug induced diabetes, stress hyperglycemia, metabolic syndrome, transient diabetes mellitus and Latent autoimmune diabetes of adults (LADA).[9] New onset type 2 diabetes mellitus and metabolic syndrome are becoming increasingly common in young adults.[10] There are a number of factors that link the pathogenesis of OSA and insulin resistance.[5,11] Finding the cause and establishing the exact diagnosis for hyperglycemia in young is important so that proper treatment can be initiated early. Whether lifestyle modification and conservative approach can help in management of severe transient hyperglycemia and related sleep disordered breathing without risks is doubted.[12]

CASE REPORT

A 33 year old man presented to the pulmonary out-patient clinic with complaint of mild cough, disturbed sleep at night with increased daytime sleepiness, tiredness and increased thirst for past one week. His family members reported that he has been snoring loudly for last few days and stayed irritated and un-focussed at work. The patient is an educated businessman, smoker and occasional drinker having a well built stature. He also reported being stressed by family and financial matters. Detailed history revealed that he had mild cough for past two weeks for which he took homeopathic medication, "Dulcamara" five days back, for three days on a friend's recommendation. He denies any overdosing of the homeopathic drug. He was non- diabetic, non-hypertensive (as per previous year's medical records) and apparently symptom free before, two weeks back and had no family history of diabetes and/or hypertension.

Relevant findings on examination: height= 166 cm, weight= 85 kgs, waist circumference= 91.5 cm, BMI= 30 kg/m^2, Pulse=80/min, Blood pressure= 130/90 mm of Hg, Respiratory Rate= 50/min. Auscultation revealed nothing significant. Assessment of excessive daytime sleepiness done by "Epworth Sleepiness Scale" produced a score of 12.

Considering a short onset and duration of symptoms the pulmonologist recommended routine biochemical investigations including diabetes screening and blood lipid profile before doing further investigations for obstructive sleep apnea.

Table 1: Biochemistry reports on 3rd day of presentation.

Tests	Result	Reference range*	Method
Fasting plasma glucose(FPG)	252 mg/dL	70-100	Hexokinase
HbA1c	11.3 %	4.27-6.07	HPLC
Serum fasting insulin	8.0 µIU/mL	2-25	Chemiluminescent Microparticle Immunoassay(CMIA)
Serum insulin antibodies	0.7 U/mL	<12	ELISA
Serum C-peptide	1.34ng/mL	1.1-5.0	Chemiluminescence Immunoassay (CLIA)
Serum hs-CRP	3 mg/L	< 1	Immunoturbidometry
Serum uric acid	5.2 mg/dL	3.5-7.2	Uricase
Serum total cholesterol	208 mg/dL	< 200	spectrometry
Serum triglyceride	450 mg/dL	<150	Spectrometry
Serum HDL cholesterol	30 mg/dL	40-60	spectrometry
Serum LDL cholesterol	88 mg/dL	<100	(calculated)
Serum VLDL cholesterol	90 mg/dL	<30	(calculated)
*Reference ranges may vary for different labs			

Table 2: Biochemistry reports after 3 weeks of presentation.

Tests	Result	Reference range*	Method
Fasting plasma glucose	106 mg/dL	70-100	Hexokinase
HbA1c	6.8 %	4.27-6.07	HPLC
Serum total cholesterol	178 mg/dL	< 200	spectrometry
Serum triglyceride	240 mg/dL	<150	Spectrometry
Serum HDL cholesterol	34 mg/dL	40-60	spectrometry
Serum LDL cholesterol	96 mg/dL	<100	(calculated)
Serum VLDL cholesterol	48 mg/dL	<30	(calculated)
*Reference ranges may vary for different labs			

The next day lab reports showed fasting plasma glucose= 620 mg/dl, HbA1c= 11.4 %, serum total cholesterol= 214 mg/dl, triglycerides= 465 mg/dl, HDL cholesterol= 30 mg/dl, LDL cholesterol= 91 mg/dl, VLDL cholesterol= 93 mg/dl. After reports immediate urine sample chemistry showed presence of reducing sugar and ketone bodies in traces.

The patient was advised immediate hospital admission and the condition explained. Proper hydration was assured. The endocrinologist and the clinical biochemist were consulted to help establish the exact diagnosis. The patient was kept under observation and capillary blood glucose was monitored every two hours. The following sets of investigations were immediately advised to confirm the type of diabetes. Fasting plasma glucose, HbA1c, serum fasting insulin, serum insulin antibodies, serum C-peptide, serum hs-CRP, Serum uric acid, serum lipid profile and thyroid profile. The patient was stable & clinical features were improving on conservative management and insulin therapy was withheld till complete blood reports arrived. The third day blood reports are shown in Table 1.

Thyroid profile, serum electrolytes and arterial blood gas analyses reports were within normal limits. Insulin resistance, as estimated by the Homeostasis Model of Assessment - Insulin Resistance (HOMA-IR) was 4.98. The patient was advised to take a carbohydrate restricted diet with proper hydration and mild exercise. No insulin or oral hypoglycemics were given but blood glucose was monitored twice daily. There was rapid glycemic control and symptoms of sleep apnea also improved. After three weeks the following reports were obtained for blood biochemistry (Table 2).

Over the next two months of diet and exercise he lost a total of 8 kilograms of weight. BMI decreased to 27.8 Kg/m^2, Fasting plasma levels remained below 100 mg/dL and serum triglycerides were below 180 mg/dL. Snoring and other sleep symptoms also resolved and no further problems were reported. The patient is currently under regular follow-up.

DISCUSSION

An adult patient with high BMI presenting to the chest physician with complaints of loud snoring and excessive daytime sleepiness suggests the possibility of obstructive sleep apnea.[13] But in our case the history of tiredness and fatigue along with personal & professional stress and taking homeopathic medication for cough, raised more questions. There can be a number of conditions that could have led to the symptoms and the possibility of a serious underlying disorder could not be overlooked.[14,15] Besides, a combination of smoking and drinking can also lead to acute onset of loud snoring.[15]

The initial biochemistry reports raised alarm and the detection of severe hyperglycemia with dyslipidemia shifted the focus to other possibilities. FPG=620 mg/dl and HbA1c=11.4% itself confirms the diagnosis of diabetes mellitus. Besides, a high BMI (>30) along with hypertriglyceridemia (465 mg/dl) and low HDL cholesterol (30 mg/dl) in this case qualifies for the diagnosis of metabolic syndrome as per the International Diabetes Federation (IDF) 2006 definition.[16] The association of metabolic syndrome with obstructive sleep apnea is now considered as separate disease entity called "syndrome Z".[3,11] We reviewed the past treatment history of the patient and the chances that the symptoms may be due to adverse effect of the self medication of 'Dulcamara'(Solanum Dulcamarum). Though Dulcamara, in high doses may cause drowsiness, sweating and anticholinergic symptoms but our review of literature could not establish any possibility of dulcamara causing such severe hyperglycemia or sleep disordered breathing in normal therapeutic doses.[17] Considering the stressful lifestyle of our patient we found that psychological or emotional stress has also been shown to raise blood sugar levels but whether it can cause severe hyperglycemia in absence of physical stress or an underlying metabolic derangement is still debatable.[18-21]

On the basis of multiple evidences and current diagnostic criteria diabetes mellitus was confirmed and the case could also qualify for the definition of metabolic

syndrome and syndrome Z.[3,11,16] It was essential to establish the cause and type of diabetes so that specific management could be initiated. The subsequent investigation reports showed normal levels of serum insulin, insulin antibodies and C-peptide, ruling out the possibility of type 1 diabetes or other forms of autoimmune diabetes.[22] Though glutamic acid decarboxylase antibodies (GADAs) could have been done to further exclude latent autoimmune diabetes of the adult (LADA) but seemed unnecessary considering the high BMI and evidence of insulin resistance reflected by HOMA-IR (4.98).[23] Besides, the presence of other cardiovascular risk factors like serum hs-CRP 3mg/L and dyslipidemia supported a chronic inflammatory pathology.[24,25]

Acute and severe hyperglycemia induced by multiple stress factors in a new onset type 2 diabetic patient is a therapeutic challenge.[11,26] Increased levels of stress hormones in acute illness can lead to hyperglycemia. In our case the patient had a recent history of cough and sleep disordered breathing which could have triggered a hyperglycemic episode. Though insulin therapy plays a central role in managing stress hyperglycemia in hospitalized patient it is not mandatory for ambulatory patients who are eating normally.[27] Adequate hydration and frequent blood glucose monitoring was done which further ruled out the need for insulin as there was rapid glycemic control using a conservative approach. As excess abdominal adiposity plays a key role in pathogenesis of metabolic syndrome, type 2 diabetes and obstructive sleep apnea, a conservative approach targeting at weight reduction by exercise and diet control lead to improvement in symptoms of all associated disorders.[28-30] Besides, as the acute stress factors subsided there was further improvement in symptoms and glycemic control. The reduction in HbA1c levels from 11.4% during acute hyperglycemia to 6.8% after three weeks was interesting but unanticipated. Though HbA1c reflects the glycemic status of an individual over the past 2-3 months, Kinetic studies have revealed that glycemia in the recent past influences the HbA1c values more than the remote past.[31] The mean blood glucose of past 1 month, 2 months and 3 months contributes 50%, 40% and 10% respectively to the final result. By mathematical modelling the t1/2 of HbA1c is estimated to be 35.2 days. This means that half of glycation seen during estimation has occurred in the previous 35.2 days.[32] This could partially explain the significant fall in Hba1c levels when there was quick glycemic control in our patient. There was also a notable improvement in the lipid profile over the three weeks period. It has been observed that modest weight loss (5-10%) is associated with significant improvement in overall lipid profile especially serum triglycerides. It is also observed that the improvement in the lipid profile is proportionate to the magnitude of weight lost.[33] The improvement in sleep disordered breathing symptoms can be qualitatively explained on the basis of their linked pathophysiologies.

CONCLUSION

This case enhances our understanding of the development and presentation of sleep disordered breathing and its frequent association with metabolic syndrome and type 2 diabetes. The underlying pathophysiologies are certainly linked and treating one disorder ameliorates the symptoms of the related conditions. Episodes of acute transient hyperglycemia can be triggered by coexistence of multiple stressors. Any condition of acute hyperglycemia must be investigated thoroughly and treated judiciously to prevent complications. But, if an underlying cause can be established and consistent monitoring is possible, then a holistic, non-aggressive approach including lifestyle modification and diet control can be remarkably effective in combating episodes of hyperglycemia and associated obstructive sleep apnea symptoms.

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