Case Report

Idiopathic Central Sleep Apnoea: An Indian Case with Polysomnographic Findings

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Abstract

Patients with idiopathic central sleep apnoea (ICSA) usually complain of poor quality sleep; yet many of them do not receive appropriate treatment because of poor recognition of ICSA by health professionals. We report the case of a patient with ICSA who was misdiagnosed and received treatment for seizures, depression or anxiety for a number of years and discuss the differential diagnosis and treatment options for ICSA. **[Indian J Chest Dis Allied Sci 2014;56:41-44]**

Key words: Idiopathic central sleep apnoea, Polysomnography.

Introduction

Central sleep apnoea (CSA) is characterised by the absence of stimuli for breathing during sleep from respiratory-regulation centre for a period of at least 10 consecutive seconds.[1] Polysomnographically, it is seen as the absence of any signal in airflow, chest and abdominal channels.[1,2] Clinical diagnosis is made when central-sleep-apnoea-index is more than 5.[1] Clinically, it manifests as insomnia or poor quality sleep or difficulty in breathing during night.[1] International Classification of Sleep Disorders-2 (ICSD-2)[1] has classified CSA into the following subtypes, namely, infantile, idiopathic, Cheyne-Stokes breathing, high altitude periodic breathing, and CSA due to other medical conditions not Cheyne-Stokes breathing. In addition, other classifications systems for CSA have been described in reviews.[3,4]

We report the case of a patient with idiopathic CSA (ICSA) who was misdiagnosed and received treatment for seizures, depression or anxiety for a number of years.

Case Report

A 37-year-old male presented with history of poor quality sleep, drying of mouth during sleep and abnormal movements during sleep since past 17 years. Movement episodes were stereotyped. They were recurring at the interval of approximately one month. Each episode used to last for approximately 10 minutes and was occurring at around 1.30 AM. Each episode was characterised by feeling of chocking followed by awakening and struggle to breathe. It was associated with tremulousness in whole body along with twisting of both upper limbs in opposite directions without tonic-clonic movements. Patient could not speak until 15 minutes after termination of episode. However, he remained conscious during and after each episode.

His sleep schedule suggested that he usually went to bed at around 10.30 PM and falls asleep within 15 minutes. He wakes up 2-3 times in night to go to washroom to fall asleep again within 15 minutes each time. Usually, he wakes-up by 7.30 AM and leaves bed within 15 minutes. He does not feel fresh after waking up and remains lethargic and somnolent during the day.

There was no history suggestive of involuntary voiding or tongue bite during the episode; headache, weakness or confusion after the episode. He also denied snoring, restless legs, difficulty falling or staying asleep, shift working, regurgitation of food during sleep, or any dream associated with the event. Patient never consumed any psycho-active substance of abuse. Other medical or surgical history was non-remarkable. Family history was non-contributory to the diagnosis.

He sought advice from a number of specialists (physicians, neurosurgeons, neurologists, psychiatrists and chest-physicians) in the past 17 years. He underwent waking electroencephalogram (EEG) multiple times that did not reveal any abnormality. He was prescribed following anti-epileptic drugs during this period: tablet phenytoin 100 mg three times daily (December 1992 - May 1993); tablet carbamazapine 200 mg twice daily (May 1993 - July 2004) along with one of the proton-pump-inhibitors (PPI), namely, pantoprazole or omeprazole) in adequate doses regularly. In August, 2004 he was shifted to tablet oxcarbamazapine 300 mg twice daily, which he continued till March 2005 along with a PPI. Considering no change in his symptoms, then he was shifted to tablet valproate 300 mg once-a-day along with pantoprazole 40 mg per day. Since the

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symptoms kept recurring, he discontinued all anti-epileptic drugs in December 2007 but continued to use pantoprazole. Besides anti-epileptics and PPIs, he was also prescribed anti-emetics, benzodiazepines and antidepressants in between for short periods. However, he was never prescribed any opiate analgesic.

Patient was averagely built. His body mass index (BMI) was 23.3 Kg/m^2; neck circumference was 36 cm. Pulse rate was 58/min, regular in rhythm; blood pressure was 110/70 mmHg; respirations 12/min, regular. Chest was clear on auscultation and expansion was 5cm. Naso-oro-pharyngeal examination disclosed left-sided deviated nasal septum, however, airflow through both nares was adequate.

Considering the clinical information and examination following disorders were considered in the differential diagnosis: sleep-related seizures, sleep terrors, confusional arousals, central sleep apnoea, periodic limb movement disorder (PLMD), sleep-related gastroesophageal reflux disease, sleep associated laryngospasm, sleep-related choking, nocturnal asthma and sleep related abnormal swallowing.

Upper gastrointestinal (GI) endoscopy, magnetic resonance imaging (MRI) brain and cervical spine, nasopharyngeal endoscopy, two-dimensional (2-D) echocardiography of heart, spirometry and level-1 polysomnography were ordered.

Duodenitis was found on upper GI endoscopy; MRI cervical spine showed postero-central disc protrusion at C5-C6 and mild postero-central disc bulge at C6-C7, however, without neural impingement. Posterior fossa was normal. Naso-pharyngeal endoscopy revealed mild left-sided deflected nasal septum. Cardiac 2-D echocardiography was unremarkable. Spirometery and morning peak expiratory flow rate (PEFR) were normal.

Diagnostic sleep study was performed with the help of standard attended 17-channel polysomnography with video monitoring using Cadwell III Sleep Easy acquisition system (Cadwell Laboratories, Inc, Kennewick WA). Electrophysiologic sleep parameters studied included frontal, central and occipital electroencephalogram, right and left electrooculogram, and submentalis electromyogram. Anterior tibialis electromyogram was recorded to assess limb movement activity. Airflow was detected by thermistors and respiratory effort was determined by measurement of chest and abdomen motion with respiratory inductive plethysmography transducers. The arterial oxygen saturation was measured by the Cadwell oximeter with a 4-beat averaging mode. Raw data were manually scored in 30-second epochs for sleep stages using standard criteria.[5] Results showed that CSA were not associated with arousals. The cycle time for repetitive CSA was 40 sec and arousal was seen at the termination of few CSA (Figure). Other polysomnographic findings are shown in the table.

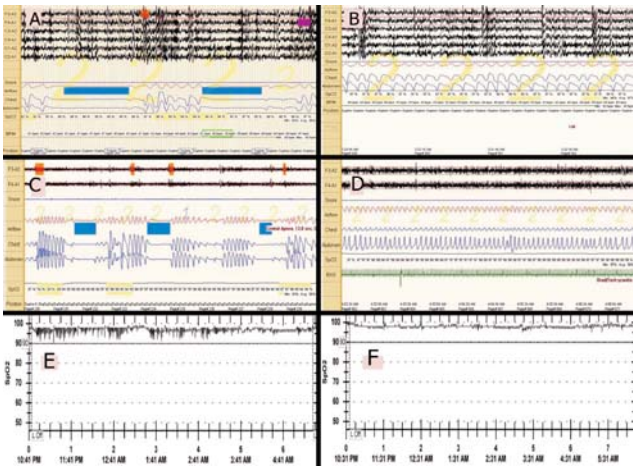

Figure. Polysomnographic findings of ICSA before and after CPAP therapy: (A) 60-second ep-och showing CSA and consequent microarousals; (B) 60-second epoch showing remission of CSA and microarousals following CPAP therapy; (C) 120-second epoch showing respiratory pattern before CPAP; (D) 120-second epoch showing respiratory pattern after CPAP; (E) overnight oxymetry showing mild desaturations before CPAP; and (F) overnight oxymetry showing resolution of desaturations after CPAP.

***Definition of abbreviations*: ICSA=Idiopathic central sleep apnoea; CSA=Central sleep apnoea; CPAP=Continuous positive airway pressure.**

CPAP titration study was done using same machine and montage. CPAP was kept at the pressure of 4 cmH_2O with oro-nasal medium size mask. Analysis of data suggested increased sleep latency due to discomfort of the mask. Mask was also the reason for frequent arousals during the night resulting in increased "wake after sleep onset" time. However, despite recurrent arousals, subjective sleep quality was better on this night. Results of titration study are shown in the table.

Discussion

We are presenting a case of ICSA who responded well to an increase in dead space. This is an uncommonly reported problem, which can be mimicked by many conditions as described below. In such cases, these diagnoses should be considered.

In the present case, sleep-related seizures were ruled out based upon the history, normal wake EEG, absence of seizure activity in diagnostic polysomnography, normal brain MRI study and poor response to anti-epileptic drugs for a long time.[1] Sleep terrors are seen during arousals from non-rapid eye movement (NREM) sleep and characterised by sudden onset screaming episodes during which patient is often unconsolable.[1] This patient did not meet the criteria for sleep terrors. Confusional arousals is another disorder of awakening and is commonly seen in children.[1] Considering the clinical presentation and age of patient, this was also

Table. Polysomnographic findings on diagnostic and titration nights

Sleep Variables	Diagnostic	Titration
Sleep onset latency (min)	6	29.5
WASO (min)	12	87.5
REM latency (min)	146	253
Sleep efficiency (%)	98	94
N1 (% total sleep time)	14	9
N2 (% total sleep time)	66	71
N3 (% total sleep time)	5	10
REM (% total sleep time)	15	11
Arousal index total	10	6
NREM arousal index	12	7
REM arousal index	0	0
RDI total	19	0
RDI NREM	22	0
RDI REM	2	0
Total CSA index	12	0
REM	2	0
NREM	14	0
OSA index	0	0
MSA index	0	0
Hypopnoea index	1	0
Desaturation event index	8	0.3
REM	0	0
NREM	9.9	0
PLM index	5.1	6.7

Definitions of abbreviations: WASO=Wake after sleep onset; REM=Rapid eye movement; N3=Slow wave sleep; NREM=Non-rapid eye movement; RDI=Respiratory disturbance index; CSA=Central sleep apnoea; OSA=Obstruction sleep apnoea; MSA=Mixed sleep apnoea; PLM=Periodic limb movements

excluded. PLMD was excluded as we did not find periodic limb movements during sleep on either of night.[1] Sleep-related gastro-oesophageal reflux was ruled out as patient had been taking proton-pump-inhibitors for years, he denied reflux of food during night and laryngo-pharyngeal endoscopic examination did not show any sign of inflammation. Sleep associated laryngospasm, sleep-related choking and sleep related abnormal swallowing was ruled out based upon clinical history and polysomnography.[1] Spirometry and morning PEFR were done to rule out nocturnal bronchial asthma.

On polysomnography, CSAs predominantly appear during non-rapid eyemovement (NREM) sleep periods, these recur at an interval of approximately 20-40 seconds and are often terminated by arousal.[3] In contrast, Cheyne-Stokes breathing is characterised by typical crescendo-decrescendo pattern of breathing, longer cycle length with the arousal at the peak of respiration.[3] In contrast to obstructive sleep apnoea (OSA), overnight oximetery in CSA subjects shows milder desaturation.[3] Absence of persistent hypoxia ruled out sleep related hypoventilation syndromes.[1] Hence, this patient met the criteria for CSA.

CSA can develop owing to various causes.[1,4] In this case, brain related causes (trauma, cerebro-vascular accident, posterior fossa space occupying lesions) were excluded based upon clinical information and MRI of brain and cervical spine. There was no history of opiate intake. Furthermore, the breathing was not ataxic as seen in subjects with chronic opiate use.[6] Cheyne-Stokes breathing was not seen on either night. Clinical examination and 2D-echocardiography ruled out cardio-vascular conditions. High altitude periodic breathing is seen beyond heights of 4000 meters and our institute is situated at a height of 563 meters from sea-level.[1] Hence, the diagnosis of ICSA was considered.[1]

Pathophysiologically, CSA is characterised by an abnormality in the loop gain.[4] However, mechanism behind the ICSA is still unclear.[4] ICSAs are thought to develop in the setting of hyperventilation with hypocapnia.[1,7,8] This is important to understand while selecting treatment for ICSA.

Different approaches have been described to treat CSA depending upon its subtypes.[3] Evidences for therapeutic advantages and long-term safety regarding various modes of treatment, such as oxygen therapy, inhaled carbon dioxide (CO_2), addition of dead space, CPAP, atrial pacing device and acetazolamide for ICSA is limited.[3] Till date, no specific therapy for ICSA is available. However, a recent study demonstrated that zolpidem can improve ICSA by maintaining the sleep.[2]

CPAP is considered to be effective in ICSA by inhibiting lung reflex mechanisms and improving oxygenation.[3] Hence, we planned to titrate this patient with CPAP. The patient responded well to the mask ventilation at the pressure of 4 cmH_2O and further increment in the pressure was not required. This is a physiological pressure where CPAP only balances the intra-thoracic negative pressure without altering the airflow dynamics. In other words, CPAP at this pressure only adds to the dead space to increase CO_2 levels in blood. This approach has been found effective in the management of ICSA.[9] Addition of 400 mL of dead space has been found to reduce the fluctuation in oxygen saturation, apnoea-hypopnoea index (AHI) and arousals by keeping the partial pressure of CO_2 ($PaCO_2$) above apnic threshold.[9] In addition, an increase in end-tidal CO_2 and mean oxygen saturation were also observed.[9] Some of these findings were seen in the present case also.

The present case reiterates the fact that, in patients with chronic non-refreshing sleep, who are not improving to any treatment, the diagnosis of ICSA should be considered. Further, the addition of dead space needs to be explored as a scientifically acceptable and economical method to treat ICSA.

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