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Suppresion of chronic nocturnal cough during continuous positive airway pressure (CPAP) treatment in a patient with asthma and obstructive sleep apnoea syndrome

Abstract

Sleep disruption may develop in patients suffering from chronic cough and in patients with obstructive sleep apnoea syndrome (OSAS). An increasing number of reports are being published that suggest a relationship between chronic nocturnal cough and the occurrence of breathing disorders during sleep characteristic of OSAS.

We report a case of a 59-year-old obese male (BMI 38.6 kg/m^2) suffering from asthma and chronic nocturnal cough irresponsive to optimal asthma treatment. Based on an examination of the patient's breathing function during sleep we established the diagnosis of moderate OSAS and initiated continuous positive airway pressure (CPAP) treatment, as a result of which the cough resolved. The successful outcome of using CPAP in preventing episodes of nocturnal cough was further confirmed after a year of CPAP use. This case report justifies the inclusion of OSAS in the differential diagnosis of nocturnal cough, including nocturnal cough in asthma patients. The use of CPAP, which prevents the development of apnoeas and hypopnoeas, may also lead to the resolution of chronic nocturnal cough.

Key words: chronic nocturnal cough, obstructive sleep apnoea syndrome, CPAP, asthma

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Introduction

The typical manifestations of obstructive sleep apnoea syndrome (OSAS) during sleep include snoring and interruptions in breathing [1]. Patients may complain of brief paroxysmal nocturnal dyspnoea, choking during sleep, restless and non-refreshing sleep, headache during sleep or upon arousal and nycturia. Sometimes, during polysomnography cough at the end of apnoeas may be observed. However, nocturnal cough is a rare complaint among patients with OSAS.

We report a case of a patient in whom we used a continuous positive airway pressure (CPAP) device due to very severe symptoms, which principally included nocturnal cough, and due to breathing disorders during sleep observed at a frequency indicative of moderate OSAS. The initiation of CPAP not only resulted in the resolution of sleep apnoeas and hypopnoeas but also in the resolution of the nocturnal cough.

Case presentation

A 59-year-old ex-smoker who ceased smoking 8 years before and had smoked about 20 cigarettes a day for the 32 years previously presented to the Polysomnography Laboratory of the Izerskie Mo-

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untains Centre of Pneumonology and Chemiotherapy Centre in Szklarska Poręba, Poland, with a history of snoring since his young adult years. He also complained about episodes of brief shortness of breath developing during sleep for the past several years, usually in the supine position, which he described as brief periods of choking. The patient was also suffering from morning fatigue and excessive daytime sleepiness that was score at 13 points on the 24-point Epworth Sleepiness Scale (ESS). He usually fell asleep right after going to bed but the sleep was often interrupted by arousals caused by coughing attacks. The cough was generally dry. The coughing attacks were difficult to control, most commonly occurred during sleep in the supine position and when they developed the patient assumed the sitting or kneeling position. The coughing attacks appeared each night and during some nights they recurred several times. Chronic nocturnal cough was the principal complaint reported by this patient.

For many years the patient had been under the care of internal medicine specialists due to asthma and had been on long-term treatment with inhalation glucocorticosteroids and bronchodilators. The patient periodically experienced episodes of dyspnoea with coughing and expectoration of mucous sputum accompanied by physical and spirometric signs of bronchial obstruction. At such times the patient received nebulised bronchodilators and parenteral glucocorticosteroids. The nocturnal cough was, however, persistent and was not related to the periodical exacerbations of asthma. On admission it was established that the patient had been taking, for a long time, twice-daily fluticasone 500 μg/inhalation and salmeterol 50 μg/inhalation. No skin tests for allergy were performed during the patient's stay at the Centre.

The patient had been receiving antihypertensives for many years, including a diuretic and an angiotensin-converting enzyme (ACE) inhibitor.

Before the hospital admission the patient had undergone upper gastrointestinal (GI) endoscopy, which showed no pathologies in the GI mucosa suggestive of gastrooesophageal reflux disease. No antireflux medications were therefore used. The patient did not undergo a 24-hour oesophageal pH-monitoring test.

On admission to the Centre the patient was found to be obese, his height was 171 cm, his body mass was 113 kg and his body mass index (BMI) was 38.6 kg/m^2. The unremarkable history, physical examination, chest radiogram and electrocardiogram did not suggest any potential circulatory failure. No echocardiogram was obtained. A routine ENT examination did not reveal any abnormalities in the upper respiratory tract. Blood pressure was 120/80 mm Hg. Spirometry revealed a decreased forced vital capacity (FVC) of 57% predicted (2360 ml) and a decreased forced expiratory volume in 1 second (FEV_1) of 53% predicted (1750 ml). FEV_1/FVC was normal (74%). Arterialised capillary blood gas analysis revealed the following values: pH 7.38, $PaCO_2$ 42 mm Hg, PaO_2 70 mm Hg, SaO_2 94%.

The patient underwent a study of breathing during sleep with the use of the EMBLETTA device (Resmed, Iceland), which recorded respiratory airflow with a nasal cannula, respiratory movements of the thoracic and abdominal wall by plethysmography, and the body position, arterial blood oxyhaemoglobin saturation (SaO_2) and pulse rate by pulse oximetry. The apnoea/hypopnoea index (AHI) was 26. The predominant breathing disorders were sleep hypopnoeas (accounting for 68% of breathing disorders) and obstructive sleep apnoeas (21%) with the less common mixed and central apnoeas (6% and 5%, respectively). Oxygen desaturation index was 39. Mean SaO_2 during sleep was 91.6%. During periods of arterial blood desaturation SaO_2 dropped to an average of 87% with the minimum value being 69%. Mean heart rate during sleep was 74 beats per minute (bpm).

Based on all the testing done in this patient the diagnosis of asthma, obesity and well-controlled hypertension was upheld and the diagnosis of moderate OSAS was added. The patient was qualified for CPAP. Initially an automated CPAP device was used and the optimal value of therapeutic pressure in the nasal mask was determined. Then a recommendation to continue treatment with the CPAP device at the pressure of 6.5 cm H_2O was made. The treatment was very well tolerated. The nocturnal cough, snoring, morning fatigue and daytime sleepiness all subsided. After 3 months of regular CPAP treatment the patient was readmitted for follow-up tests. During CPAP treatment the nocturnal cough had never recurred. The patient continued to take the same medication as during his first hospitalisation, in particular, the same ACE inhibitor at an unchanged dose, and the same inhalation bronchodilators. The study of breathing during sleep conducted during CPAP treatment (pressure in the nasal mask 6.5 cm H_2O) revealed the following: AHI 3, oxygen desaturation index 4, mean SaO_2 during sleep 95%. Mean heart rate during sleep was 60 bpm. Continued use of CPAP at home was recommended. Six months later the patient was readmitted with an exacerbation of asthma: attacks of dyspnoea and cough during

waking hours accompanied by auscultatory signs of bronchial obstruction. He was still using CPAP regularly and was not experiencing the nocturnal cough. Following a short course of parenteral glucocorticosteroids and nebulised short-acting bronchodilators the symptoms and the auscultatory signs resolved. A study of breathing during sleep while using CPAP conducted a year after the diagnosis of OSAS revealed the following: AHI 2, oxygen desaturation index 6, mean SaO_2 during sleep 93%, mean heart rate during sleep 66 bpm. No nocturnal cough occurred during the use of CPAP.

Discussion

The initiation of CPAP in our patient with OSAS and asthma, on long-term treatment with an ACE inhibitor for hypertension and complaining about persistent nocturnal dry cough unexpectedly resulted in the resolution of the most bothersome symptom, the chronic nocturnal cough.

Chronic cough is defined as cough persisting for more than 8 weeks [2]. The numerous causes of chronic nocturnal cough include, first of all: asthma, upper airway cough syndrome caused by chronic inflammation of the nasal mucosa and/or sinuses, and gastrooesophageal reflux disease [3–8]. The other common causes of chronic cough include smoking and chronic obstructive pulmonary disease [9], and treatment with ACE inhibitors [10]. Chronic nocturnal cough may also develop in the course of respiratory infections, particularly in the course of whooping cough [11]. Non-asthmatic eosinophilic bronchitis is a less frequent cause of chronic cough, including chronic nocturnal cough [8, 12]. In addition, chronic cough, which sometimes also occurs at night, is observed in numerous respiratory diseases whose manifestations include abnormal chest radiograms and in congestive heart failure [8]. It has recently been discovered that chronic nocturnal cough may also be caused by OSAS [13, 14].

The cough reported by our patient had been present for several years, thus satisfying the definition of chronic cough. It was a persistent dry and predominantly nocturnal cough. Initially, this nocturnal cough was considered one of the symptoms of previously diagnosed asthma. The severity of the nocturnal cough was not, however, affected by glucocorticosteroids or bronchodilators the patient was receiving.

Asthma is the cause of dry chronic cough in 24–29% of non-smokers [5] In asthma, cough may occur in patients during sleep, including patients who experience no symptoms of bronchial obstruction or cough while awake. For instance, nocturnal cough has been demonstrated in over a third of children with asthma during periods of stable disease [4]. The following factors may contribute to the development of nocturnal cough in patients with asthma: changes in the circadian binding of glucocorticosteroids with their receptors, stimulation of the parasympathetic system and the increased concentrations of proinflammatory leukotrienes during sleep [7]. Our patient had been suffering from asthma for more than a dozen years and the periodically developing symptoms of bronchial obstruction required dose increases and/or switching to another routes of administration of bronchodilators and glucocorticosteroids. The use of bronchodilator and anti-inflammatory treatment resulted in the resolution of bronchial obstruction and symptoms during waking hours but never reduced the severity of the nocturnal cough.

Nocturnal cough is often caused by cough-variant asthma [6, 12]. It is a mild form of asthma that usually responds to antiasthmatic treatment. Our patient was not, however, suffering from cough-variant asthma, as he periodically developed other manifestations that are typical of asthma and which were, for instance, observed during his hospitalisation.

The contribution of upper airway cough syndrome to the chronic nocturnal cough experienced by our patient cannot be ruled out, particularly since the syndrome may run a "silent" course, i.e. without any clinically overt manifestations of inflammation of the upper respiratory tract mucosa [8]. Sometimes in the course of upper airway cough syndrome, previously referred to as postnasal drip syndrome, nocturnal symptoms, such as cough and dyspnoea during sleep, predominate [15]. However, resolution of the nocturnal cough, the chief complaint in our patient, as a result of using CPAP rather than as a result using anti-inflammatory agents is the argument to support sleep apnoeas rather than upper airway cough syndrome as the cause of the nocturnal cough.

Contribution of gastrooesophageal reflux disease to the occurrence of the nocturnal cough in our patient also cannot be ruled out. Gastrooesophageal reflux disease may be the cause of nocturnal cough and the feeling of choking or burning in the chest during sleep, which leads to frequent arousals resulting in fragmentation of sleep, deterioration of the quality of sleep and chronic sleep deprivation [3]. Similarly to upper airway cough syndrome, gastrooesophageal reflux disease may not be accompanied by the typical gastrointestinal signs and symptoms and nocturnal cough may be

its only manifestation [16]. Gastrooesophageal reflux disease often co-exists with OSAS and the use of CPAP may beneficially affect gastrointestinal motility decreasing the number of reflux episodes during sleep [17]. Our patient did not have any symptoms suggestive of gastrooesophageal reflux disease and upper GI endoscopy revealed no findings that might suggest it. The presence of gastrooesophageal reflux disease cannot, however, be ruled out as no 24-hour oesophageal pH-monitoring test. Resolution of the nocturnal cough and sleep apnoeas indicates a causal relationship between the apnoeas and the cough, whether gastrooesophageal reflux disease, if any, was an additional contributing factor or not.

Treatment with ACE inhibitors is a fairly frequent cause of chronic cough. This adverse effect is seen in 24–31% of patients treated with this class of drugs with a male-to-female predominance [10]. In patients developing cough during treatment with ACE inhibitors the cough initially occurs at night and later also during waking hours, but it is still more severe during sleep than during wakefulness [10]. ACE inhibitors are used in patients with OSAS due to hypertension occurring in this syndrome. The cough in our patient was not, however, associated with treatment with the ACE inhibitor, as it subsided even though the drug had not been discontinued.

The diagnosis of non-asthmatic eosinophilic bronchitis was also not supported. Although nocturnal cough is present in about 9% of the patients with this type of bronchitis [12], this diagnosis cannot be made in asthma patients and cough in the course of non-asthmatic eosinophilic bronchitis resolves upon treatment with glucocorticosteroids, which was not the case with our patient.

Although cough during sleep is a typical manifestation of pertussis [11], there were no other clinical findings to support the diagnosis of this infectious disease in our patient.

Nocturnal cough, as a manifestation of repeated episodes of upper airway obstruction during sleep, was first reported in a female patient with severe OSAS and obesity hypoventilation syndrome with co-existent bulging of the membranous part of the trachea. The disordered breathing during sleep, including nocturnal cough, subsided as a result of CPAP [18].

Several years later a case of a 3-year-old child suffering from chronic nocturnal cough was reported. The child was diagnosed with obstructive hypoventilation during sleep and both upper airway obstruction and cough during sleep subsided upon treatment with a CPAP device [19].

A group of 4 non-smokers with OSAS in whom asthma, gastrooesophageal reflux disease, inflammation of the upper respiratory tract mucosa and ACE treatment as the possible causes of nocturnal cough had been ruled out was reported by Birring et al. in 2007 [20]. Treatment with a CPAP device resulted in a resolution of their chief complaint, namely cough. The authors therefore proved that OSAS was the cause of the cough in theses cases [20].

A year later Bauer et al. demonstrated the efficacy of CPAP in the treatment of a female patient complaining about chronic nocturnal cough in whom the diagnosis of OSAS was made [21].

The presence of chronic cough in patients without OSAS is often related to snoring [22–24]. Snoring is associated with increased respiratory effort and vibrations of the upper respiratory tract soft tissues. This may damage epithelial cells of the upper airways and lead to the formation of inflammatory infiltrates in the lamina propria of the mucous membrane [25]. The cellular infiltrates and the associated increases in the levels of inflammatory mediators in the upper respiratory tract mucosa may sensitise cough receptors and lead to increased cough reflex, similarly to what happens in patients with asthma or eosinophilic bronchitis [26, 27]. As snoring is the principal manifestation of OSAS, it may be assumed that the development of cough in patients with OSAS may be caused by damage to the epithelial cells of the upper airway mucosa and the associated inflammatory responses, in addition to the other causes described above.

In our patient, OSAS co-existed with asthma. Nocturnal cough was the chief complaint and was mainly attributed to asthma. The cough, however, failed to resolve following antiasthmatic treatment. The diagnosis of OSAS could not be made until the study of breathing during sleep was conducted and the nocturnal cough resolved upon treatment with CPAP, so reluctantly undertaken by the patient, who had lost all his hope for peaceful uninterrupted sleep.

The prevalence of chronic cough in patients with OSAS is currently estimated at up to 33% [13]. A study has recently been conducted to assess breathing disorders during sleep in patients with chronic cough. The diagnosis of OSAS was made in about a half of the patients and 93% achieved improvement or resolution of chronic cough with CPAP [14].

In the case of our patient we showed that the cause of his chronic nocturnal dry persistent cough irresponsive to optimal antiasthmatic treatment was sleep disordered breathing in the course

of OSAS. This case report indicates that it is justified to consider OSAS in the differential diagnosis of chronic nocturnal cough, including chronic nocturnal cough in patients with asthma. CPAP, which prevents sleep apnoeas and hypopnoeas, may also lead to resolution of chronic nocturnal cough.

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