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Case Report

A Patient with Sarcoidosis and Obstructive Sleep Apnea: A Case Report and Review of the Literature

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Abstract

Sarcoidosis is a multisystemic granulomatous disease that affects individuals worldwide. Patients with this disease, sometimes experience a decrease in quality of life and are at increased risk of disability and comorbidities. Several studies have reported correlations between sleep disorders and sarcoidosis, with an accompanying rise in pain perception and fatigue. Obstructive sleep apnoea (OSA) is the most common of sleep disorders and it contributes to increased cardiovascular morbidity and mortality. Although the true impact of OSA on patients with sarcoidosis remains to be defined with certainty, it is certain that both pathologies lead to a state of symptoms.

We present a case of OSA and sarcoidosis. PP was 62 years-old, nonsmoking male (BMI 29 Kg/m^2), who had suffered from sarcoidosis for 4 years, that was with immunosuppressive drugs, developing insomnia, restless legs syndrome and daytime symptoms, such as pain, stiffness and fatigue. The main comorbidities were ischemic cardiomyopathy, chronic atrial fibrillation with a left ventricular ejection fraction of 45% and main metabolic syndrome. Despite optimization of the immunosuppressive treatment, his symptoms remained unchanged. He underwent a pulmonary examination on suspicion of OSA, which was confirmed by nocturnal cardiorespiratory monitoring. The patient was diagnosed with moderate OSA and was administered automatic positive airway pressure therapy, which effected the disappearance of symptoms.

Recently, it has been demonstrated that OSA is rather common in sarcoidosis. This clinical case underscores the importance of the early identification of these diseases**.** Treatment might be beneficial with regard to future comorbidities such as cardiovascular dysfunction and improve measures of fatigue and pain, and the quality of life.

Keywords: *Obstructive Sleep Apnea; Sarcoidosis*

Introduction

Sarcoidosis is an inflammatory disease, which is characterized by granulomatous inflammation [1]. It is a systemic disease in which granulomas can develop on any sides of the body causing significant variability in the type and degree of presenting symptoms [2]. The lungs are most commonly involved but any organ can be affected by its manifestations (e.g. cardiac, neurological, skin and ocular, etc.) and clinical course can vary.

As reported at the 1991 World Congress on Sarcoidosis in Kyoto: "Sarcoidosis is a multisystem disorder of unknown cause. It commonly affects young and middle-aged adults and frequently presents with bilateral hilar lymphadenopathy, pulmonary infiltration, ocular and skin lesions. Other organs may also be involved. The diagnosis is established when clinico-radiological findings are supported by histological evidence of noncaseating epithelioid cell granulomas. Granulomas of known causes and local sarcoid reactions must be excluded. Frequently observed immunological features are depression of cutaneous delayed-type hypersensitivity and increased CD4/CD8 ratio at the site of involvement. Circulating immune complexes along with the signs of B-cell hyperactivity may also be detectable. The course and prognosis may correlate with the mode of the onset and the extent of the disease. An acute onset with erythema nodosum or asymptomatic bilateral hilar lymphadenopathy usually heralds a self-limiting course, whereas an insidious onset, especially with multiple extra-pulmonary lesions, may be followed by relentless progressive fibrosis of the lungs and other organs" [3].

The incidence of Sleep-disordered Breathing (SDB) and Obstructive Sleep Apnea (OSA) is higher in patients who are affected by sarcoidosis [4]. OSA has emerged as an important public health problem, it is characterized by repetitive partial or complete obstruction of the upper airway during sleep. These events can be categorized as *obstructive apneas*-complete obstruction of the upper airway for ≥ 10 seconds or hypopneas, which cause incomplete upper airway obstruction that results in a decline in oxygen levels (3% or 4% desaturation) or arousal from sleep. OSA is usually defined by an apnea-hypopnea index (AHI) (calculated as apneas + hypopneas/ hours of total sleep time) of ≥ 5 and symptoms of excessive daytime sleepiness, unrefreshing sleep, or chronic fatigue [5].

OSA is also being recognized as an independent risk factor for several clinical comorbidities, including systemic hypertension, cardiovascular disease, stroke, pulmonary embolism and abnormal glucose metabolism.

Repeated episodes of hypoxia and normoxia, which are reminiscent of ischemia–reperfusion events and are believed to promote the production of reactive oxygen species and inflammation - as in ischemia-reperfusion injury to the vascular wall - increase the risk for atherosclerosis and for comorbidities.

OSA can appear during the natural course of interstitial lung diseases, with a prevalence of 17 to 88%, compared with 2% to 4% in healthy adults [6-9].

Several studies have reported a correlation between OSA and sarcoidosis (estimated from 17% to 67%) [4,10]; the co-presence of these pathologies increases several symptoms and leads to fatigue [11,12].

Fatigue has been reported in approximately 60% of OSA patients [4] due to fragmented sleep and hypoxemia; such rates in sarcoidosis are similar, ranging from of 50% to 70% [11,12], caused by granulomatous inflammatory mediators or adverse events of corticosteroid therapy. Regardless of its underlying cause, fatigue can significantly impact on a patient's quality of life.

Various hypotheses have been proposed to explain the association between OSA and sarcoidosis such as sarcoid neuropathy, including direct infiltration of the hypothalamus which is involved in regulating sleep and circadian function. Also obesity due to steroids and a high Body Mass Index (BMI) has been implicated with deposition of fat around the upper airways that can increase their collapsibility [13-16].

The overlap between sarcoidosis and OSA can also increase the risk of comorbidities in certain cardiovascular and cerebrovascular diseases, pulmonary hypertension and associated neurocognitive deficits.

Case Report

PP, a 62 years-old, nonsmoking male, who suffered from sarcoidosis for 4 years, was admitted to our sleep surgery department for a history of insomnia and snoring. He had restless legs syndrome and daytime symptoms, such as hypersomnolence, pain, stiffness and constant fatigue. His medical history included ischemic cardiomyopathy, chronic atrial fibrillation and metabolic syndrome.

The clinical examination findings revealed a BMI of 29.5 kg/m^2, neck circumference of 43 cm and an enlarged abdomen with adipose tissue (abdominal circumference 110 cm).

On evaluation, his pulse pressure was normal, regular and his blood pressure was 130/80 mmHg, The heart rate was 80/min, respiratory rate was 12 breaths/min, and SpO_2 was 95% in room air. The arterial blood gas analysis showed a pH of 7.45, PaO_2 72 mmHg, $PaCO_2$ 41 mmHg, pH 7,45, $SatO_2$ 95% and HCO_3 25 mmoli/L. The physical examination was negative. Muller maneuver was performed to identify any tracheal collapse.

The echocardiography showed LVEF of 45% moderate mitral aortic insufficiency and moderate pulmonary hypertension. The computed tomography (CT) scan of the lung showed lymph nodes at subcarinal level and symmetrically at the hilar level associated with the presence of micronodules with a typical perilymphatic distribution (Figure 1 and 2).

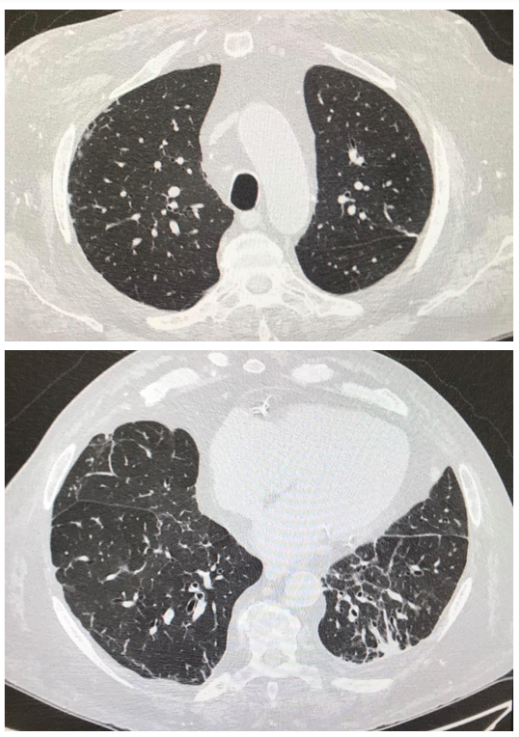

Figure 1 and 2: *CT scan of the patient.*

His pulmonary function testing (PFT) showed a moderate obstruction pattern: forced vital capacity (FVC) of 2.15 lt - 55% predicted, forced expiratory volume 1s (FEV1) of 2.09 lt - 68% predicted, and the FEV1- FVC ratio of 0.95.

Despite optimization of the immunosuppressive treatment, his symptoms remained unchanged at the one month of follow up.

To evaluate fatigue and hypersomnolence, we administered the fatigue assessment scale (FAS) [17] and Epworth scale Sleepiness Scale (ESS), which revealed a high degree of sleepiness, with a score of 16/24 [18] and the 6-point STOP Bang questionnaire, which led to a suspicion of OSA [19].

The patient took home sleep test in room air. The AHI was defined per current criteria [5]. Events of obstructive apneas (OA) and central apnea (CA), number and events of hypopnea (H) and average of arterial saturation (SpO_2 average%) with time of desaturation (T < 90%) were also analyzed.

The examination revealed moderate OSA (AHI 27/h) (Figure 3).

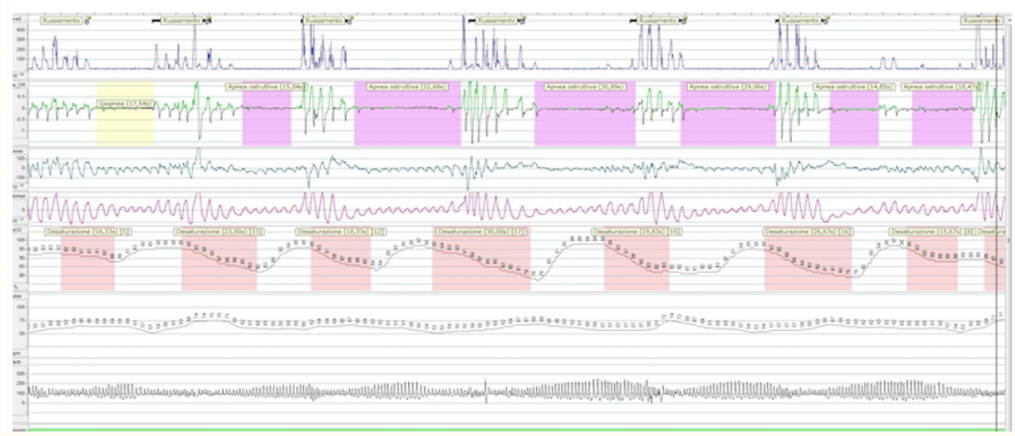

Figure 3: *Overnight HSAT at basal time.*

Consequently, the patient underwent automatic positive airway pressure (aPAP 4-13 cmH_2O) therapy which had a benefit.

At the 3 months follow-up the patient's quality of life had improved, accompanied by a reduction in pain and fatigue and a decline in the ESS to 9/24.

Discussion

Several studies have shown a high prevalence of sleep disorders (OSA, limb movements of sleep and restless legs syndrome) in patients with sarcoidosis.

In a prospective, observational study of 46 patients with sarcoidosis, Verbraecken., *et al*. observed sleep disturbances in 50% of patients [20]; in an other prospective, observational study by Pihtili., *et al*. the prevalence of OSA in patients with interstitial lung disease, including sarcoidosis, was 68% [21].

Mari., *et al*. examined 68 patients with sarcoidosis, noting a prevalence of OSA of 88.2%: 51.5% of their patients had a moderate-to-severe OSA [12].

Several conditions have been implicated in the development of OSA in patient with sarcoidosis.

In the study of Chiltra L., *et al*. BMI, lower lung volumes in pulmonary function tests and parenchymal involvement were independent predictors of OSA in sarcoidosis [4]. Sometimes the presence of sarcoidosis lesions in the upper respiratory tract (granulomas and nodules of the epiglottis and laryngeal sarcoids) can lead to life-threatening progressive airway obstruction [22].

Other theories suggest that obesity, due to corticosteroid intake, increases the circumference of the neck and, consequently, narrows the upper airways [4], as in our case report.

Potential associations with OSA and central apneas have also been seen in neurosarcoidosis (with lupus pernio) [4].

Although the true impact of OSA on patients with sarcoidosis remains to be defined, both pathologies lead to a state of fatigue. In our case report, the patient, affected by sarcoidosis, with significant comorbidities (ischemic cardiomyopathy, chronic atrial fibrillation and metabolic syndrome), continued to experience fatigue despite an increase in steroid therapy; the co-presence of snoring and hypersomnolence, led us to suspect the coexistence of OSA.

Treatment of our patients with automatic positive airway pressure in our patient, as reported [4], reduced his fatigue and sleepiness and improved his quality of life.

Several studies have hypothesized that sleep apnea, superimposed on sarcoidosis, increases the risk for comorbidities (cardiovascular and cerebrovascular diseases, pulmonary hypertension and associated neurocognitive deficits). Thus, the early diagnosis and treatment of sleep disturbances in the patient with sarcoidosis could improve their prognosis.

Conclusion

Several symptoms, such as fatigue, and manifestations of SDB are common in sarcoidosis. Moreover corticosteroids, the first-line drug that is offered in sarcoidosis, can cause significant weight gain and increase the risk of OSA.

The association between sarcoidosis and sleep apnea might significantly increase morbidity - particularly cardiovascular events - and mortality in patients who have both conditions.

This clinical case underscores the importance of the early recognition of OSA in the optimal management of sarcoidosis. An earlier diagnosis of OSA is needed for timely treatment and can improve quality of life (by reducing of fatigue) and the long-term clinical outcomes of sarcoidosis.

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