Multiple system atrophy presenting with acute respiratory failure due to diaphragmatic dysfunction

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ÖZET

Diyafragmatik disfonksiyona bağlı akut solunum yetmezliği gelişen multisistem atrofi olgusu

Uykuyla ilişkili solunumsal disfonksiyon ve vokal kord paralizisi multisistem atrofi (MSA)'deki solunum yetmezliğinden sorumlu temel faktörlerdir. Biz başlangıçta alveoler hipoventilasyonla karakterize olan ve solunum yetmezliği gelişen, sonuçta MSA tanısı alan bir olguyu bildirdik. Bu olguda solunum yetmezliğinin olası nedeni solunum kas güçsüzlüğüydü. Bu olgu ile nedeni açıklanamayan hiperkapnik solunum yetmezliğinin ayırıcı tanısında MSA'nın göz önünde bulundurulması gerektiği vurgulanmak istendi.

Anahtar Kelimeler: *Multisistem atrofi, solunum yetmezliği.*

SUMMARY

Multiple system atrophy presenting with acute respiratory failure due to diaphragmatic dysfunction

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Sleep related respiratory dysfunction and vocal cord paralysis are considered to be the major factors responsible for respiratory failure in multiple system atrophy (MSA). We report a patient initially presenting with alveolar hypoventilation cul-

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minating in respiratory failure, ultimately diagnosed as MSA. No central sleep apnea or marked paralysis of the vocal cords was noted. The most likely cause for the respiratory failure was thought to be the weakness of respiratory musculature. This case emphasizes the need that MSA should be added to the differential diagnosis of unexplained hypercapnic respiratory failure.

Key Words: *Multiple system atrophy, respiratory failure.*

Multiple system atrophy (MSA) is a progressive neurodegenerative disorder that presents with parkinsonism. However, cerebellar signs can also be observed and untreated patients often have autonomic involvement in the form of orthostatic hypotension, impotence or lack of sexual stimulation, urinary urgency and incontinence. Bulbar involvement leading to stridor can occur, particularly at night, and sleep apnea is common. Apneic spells can lead to severe alveolar hypoventilation, warranting tracheostomy (1). We report a patient without sleep apnea on polysomnographic recordings, demonstrating no obvious vocal cord paralysis, who initially presented with unexplained hypercapnic respiratory failure and an ultimate diagnosis of MSA was reached.

CASE REPORT

Clinical Findings

A 66-year old nonsmoking male was admitted to the emergency department in August 2003, with the complaints of dsypnea, hypersomnolence and fatigue. He had a seven-year history of hypertension and type 2 diabetes mellitus. A transient weakness of the left arm developed in 1998, occurring twice on the same day and lasting for minutes, which was thought to be ischemic in origin and treated accordingly. In 2002, following transurethral prostatectomy, the patient experienced a severe laryngospasm leading to respiratory failure requiring emergent tracheostomy. An urgent tracheotomy was performed. A pneumonic infiltration, accompanied by an elevated diaphragm was noted in chest X-rays. When the pneumonia resolved, tracheotomy was closed. Since then, the patient was erroneously followed with the diagnosis of chronic obstructive lung disease (COPD) without regular treatment, although there was no history of smoking and pulmonary function tests (PFTs) were normal.

Physical examination revealed decreased breath sounds with otherwise normal findings. The patient was dysarthric. Limb movements were limited, while the muscle tone was slightly increased on both sides. Plantar reflexes were equivocal. A wide-based gait was present, with an inability to tandem walk. As the patient showed hypercapnic and hypoxic respiratory failure with a $PaCO_2$ of 57.5 mmHg and PaO_2 of 40.3 mmHg, the patient was transferred to the intensive care unit (ICU) of the department of pulmonary medicine and noninvasive positive pressure ventilation (NIPPV) was started.

Laboratory Findings

At the initial evaluation in the emergency department, arterial blood gas (ABG) analysis on room air revealed an acute on chronic hypercapnic respiratory acidosis, with a pH of 7.30, PaO_2 of 40.3 mmHg, $PaCO_2$ of 57.5 mmHg, and HCO_3 32.6 mEq. Hemogram and serum biochemistry were within normal limits, except for elevated glucose levels. Erythrocyte sedimentation rate was 3 mm/hour A mild proteinuria was present. Thyroid function tests and vitamin B12 levels were normal. Antinuclear antibody was negative. An electroencephalogram was normal. Snoring and a $PaCO_2$ level that reached 85 mmHg was observed during sleep. A full night polysomnography revealed periodic respiration without marked apnea (Figure 1). The total hypopnea index was 8.1. Sleep efficiency was 44%. The total percentage of awakenings was 10.6%. Percent of total sleep time in REM was 1.9. Simple spirometry was normal, with forced vital capacity (FVC) of 3.81 L (93% of predicted), forced expiratory volume in one second (FEV_1) of 3.07 L (96% of predicted), and FEV_1/FVC of 81%. Maximal inspiratory pressure (PiMax) was 47 cmH_2O (57% of predicted) and maximal expiratory pressure (PeMax) was 102 cmH_2O (95% of predicted).

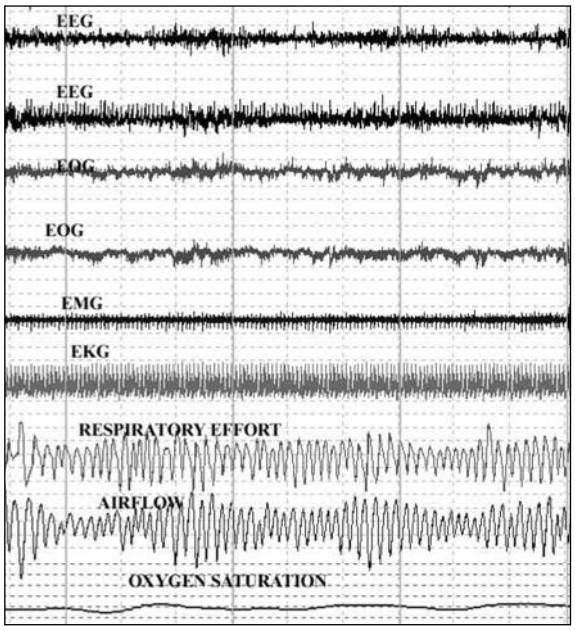

Figure 1. A full night polysomnography revealed periodic respiration without marked apnea.

Nerve conduction studies performed in the ICU revealed a sensori-motor peripheral neuropathy with some demyelinating features, in the form of markedly prolonged terminal and F-wave latencies. Needle electromyography (EMG) was normal. Repetitive nerve stimulation test performed on abductor digiti minimi, orbicularis oculi and serratus anterior muscles, failed to show a significant decrement response. Heart rate (R-R) interval variation analysis revealed abnormal findings on deep breathing. Sympathetic skin responses were unobtainable from both palms and soles. A quantitative EMG of the external anal sphincter showed an excessive prolongation of the motor units, indicative of a neurogenic involvement of the muscle. Terminal latencies of both phrenic nerves were prolonged and compound muscle action potential amplitudes were reduced, more marked on the left. Cranial magnetic resonance imaging showed millimetric ischemic signal abnormalities at the level of lateral ventricles and right striatum, as well as a mild brainstem and cerebellar atrophy. Acetylcholine receptor antibody assay was negative. The chest X-ray and thorax computerized tomography showed an elevated left diaphragm (Figure 2). However, both diaphragmatic movements were normal on fluoroscopy.

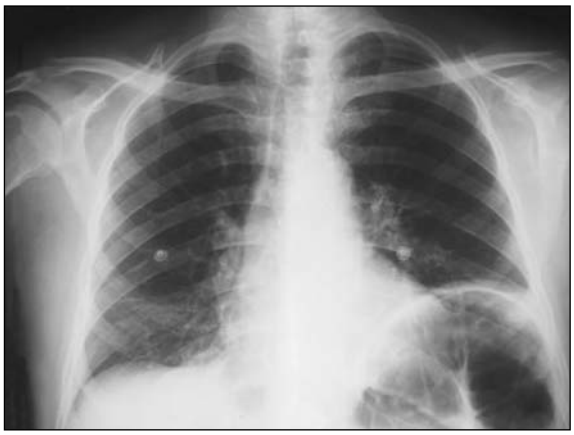

Figure 2. Posteroanterior chest X-ray shows left diaphragmatic elevation.

Treatment and Clinical Course

The patient underwent to NIPPV treatment with the highest value of inspiratory peak airway pressure (IPAP) and expiratory peak airway pressure (EPAP) of 10 cmH_2O and 5 cmH_2O respectively. After seven days of NIPPV therapy, the patient developed intractable respiratory acidosis with severe hypercapnia, accompanied by paradoxical thoracoabdominal movements and underwent intubation. A large amount of mucus was suctioned, implicating that the patient had impaired cough reflex and severe respiratory infection. A pulmonary infiltrate was present on chest X-ray. After initiating antibiotic therapy and mechanical ventilation for seven days, the patient was extubated and placed on NIPPV (BIPAP ST, Respironics; Murrysville, PA) (Settings: IPAP: 12 cmH_2O, EPAP: 4 cmH_2O). ABG analysis revealed pH of 7.46, PaO_2 of 75.3, $PaCO_2$ of 41.6 mmHg, HCO_3 30 mEq and SaO_2: 94% under NIPPV.

During follow-up, blood pressure measurements revealed a supine blood pressure of 113/56 mmHg, which fell to 88/40 mmHg on standing. Tachycardia was not present even in severe hypoxemic periods. He was unresponsive to Valsalva maneuver. An indirect laryngoscopic assessment revealed minimally impaired abduction of the right vocal fold. Rima glottis was sufficiently wide for the passage. The patient was started on levodopa and discharged with BIPAP therapy on October 2003. Twenty days later, he

had to be readmitted because of worsening fatigue and lassitude. The BIPAP settings were readjusted and levodopa was tapered. The patient was placed on dopamine agonist therapy.

DISCUSSION

Our patient is interesting, in view of the fact that MSA presented with respiratory failure, accompanied by subtle neurological findings, which were not debilitating enough to warrant an early neurological diagnosis. Previous reports commented on vocal cord paralysis and sleep apnea as presenting signs in MSA (2,3). The association of respiratory failure and MSA has been described mostly in conjunction with vocal fold paresis and sleep disorders (4-7). Vocal cord paresis often occurs bilaterally and is thought to arise from the neuronal denervation of posterior cricoarytenoid muscles, as a consequence of severe degeneration of the brainstem vagal centers. Abnormalities in the form of disorganized respiratory rhythm with central hypoventilation, sleep disturbance with frequent awakenings, Cheyne-Stokes respiration, and central apneas are thought to originate from a defect in brainstem regions regulating breathing. Pontine tegmental or the lateral pontomedullary junction lesions may produce the abnormal respiratory pattern (7-9). However, our patient neither had a significant upper airway obstruction, nor central sleep apnea. The previous episode of respiratory failure had been erroneously ascribed to COPD, but laboratory workup in this episode, suggested that the respiratory insufficiency was caused by respiratory muscle weakness.

Chester et al. described autopsy findings in a similar patient. They demonstrated that in the presence of pathological alterations of both central and peripheral nervous systems, there were no morphological changes in brainstem regions responsible for the respiratory rhythm. However, their case did not show sufficient evidence suggesting impaired neuromuscular apparatus. It was concluded that the respiratory failure resulted from impaired feedback control mechanisms stemming from the sensory afferents of the chest wall (10). Our patient shared the same features of severe hypercapnia, hemidiaphragmatic elevation and phrenic nerve dysfunction as the case described by Chester et al., but in contrast he had involvement of the neuromuscular system. The diminished Pimax, and severe paradoxical thoracoabdominal movements implicated diaphragmatic dysfunction. This probably resulted from the neuropathic involvement of the phrenic nerves and culminated in respiratory failure. This case emphasizes the fact that MSA should be included to the list of differential diagnosis in patients presenting with unexplained hypoxic and hypercapnic respiratory failure.

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