An unusual cause of orthopnoea-hashimoto's thyroiditis presenting as bilateral diaphragmatic palsy

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Abstract
We report a case of 36 yr old male without any comorbidities, who presented with a history of gradually progressive dyspnoea and orthopnoea for 6 months. Physical examination revealed bradycardia, paradoxical respiration suggestive of bilateral diaphragmatic palsy. Fluoroscopy demonstrated the presence of bilateral diaphragmatic paralysis. Etiological work up showed evidence of autoimmune hypothyroidism due to hashimoto's thyroiditis. Other possibilities were ruled out with appropriate tests. He was started on thyroxine and showed symptomatic improvement.

1. Introduction
Diaphragm is the pillar of respiration. Apart from respiratory symptoms, diaphragmatic dysfunction is associated with, exercise intolerance, sleep disturbances and, in the more severe cases, have a negative impact on survival. Diagnosis and treatment of Unilateral and bilateral diaphragm dysfunction may be challenging for the clinician because of its relative rarity and subtle clinical manifestations. Diaphragmatic dysfunction is probably underdiagnosed, but should not be neglected, as it is a disease marker, marker of severity and a prognostic indicator in intensive care units.

2. Case report
A 36 year old gentleman, carpenter by occupation without any comorbid illnesses, presented with insidious onset breathlessness for 6 months. He became markedly short of breath while lying down. There was no history of paroxysmal nocturnal dyspnoea, pedal edema, angina, palpitations, fever, cough. On clinical examination his pulse was 48/minute, regular in rhythm, normal volume. Blood pressure-120/80 mmHg.His respiration was normal in the upright position, but he became tachypnoeic in supine position and exhibited paradoxical (thoracoabdominal) breathing. On Auscultation, normal vesicular breath sounds were audible with clear lung fields. Rest of the examination, including neurological examination was unremarkable. His BMI was 22.8 kg/m². His hemogram, renal and liver function tests were within normal limits. Electrocardiogram showed sinus bradycardia. Chest xray showed elevation of both hemidiaphragms (in Fig. 1 below). Sonological assessment of diaphragmatic movements demonstrated reduced movement of both sides of diaphragm. A fluoroscopy was done to confirm the physical examination finding which demonstrated absent bilateral diaphragmatic movement. There was no movement on sniff test. Maximal transdiaphragmatic pressure (Pdimax) was significantly reduced (pdimax of 2 cm H20, normal 35–95 cm H20). Arterial

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blood gas values obtained in the sitting position were: a pH of 7.36; arterial carbon dioxide tension (PaCO₂) 44 mmHg; arterial oxygen tension (PaO₂) 94 mmHg; and HCO₃ - 23 mEq/L Pulse oximetry showed an oxygen saturation of 96% in the sitting position and that it dropped to 84% in the supine position. Spirometry in the sitting position showed a forced vital capacity (FVC) of 2.01 L (74% of predicted), forced expiratory volume in one second (FEV₁) of 1.04 (48%), and FEV₁/FVC of 91% consistent with a restrictive ventilator impairment. The diffusion capacity (DLCO) was normal. Magnetic resonance imaging of the cervical spine and brachial plexus was normal. High resolution computerised tomography of the chest revealed bilateral basilar atelectasis. Phrenic nerve stimulation at neck showed an absent response of the diaphragm bilaterally with preserved conduction through phrenic nerves. Electromyography of diaphragm showed a myopathic pattern. Neostigmine test was negative. Repetitive nerve stimulation study of the diaphragm was normal. Thyroid profile displayed a pattern suggestive of primary hypothyroidism. TSH was 86.1 (0.846–4.5 milliU/L), FT₃ was 1.05 pg/ml (Normal range – 2.5 – 3.9 pg/ml), FT₄ was 0.40 ng/dl (Normal range – 0.6 – 1.7 ng/dl), Anti thyroid peroxidase antibody (Anti TPO) was 600 IU (normal<80 IU). Ultrasound guided fine needle aspiration of the thyroid was done, which was consistent with Hashimoto’s (lymphocytic) thyroiditis. Thus a diagnosis of bilateral diaphragmatic paralysis due to hypothyroidism, as a result of Hashimoto’s thyroiditis was made. He was begun on thyroxine. After 3 months of treatment with thyroxine, he became euthyroid, his orthopnoea subsided, pdimax had improved. Maximal respiratory pressure, maximal voluntary ventilation and vital capacity improved dramatically on treatment.

3. Discussion

Bilateral diaphragmatic paralysis is often an anticipated consequence of a known neuromuscular disease. Patients with bilateral diaphragmatic paralysis as the primary manifestation of their disease typically present with dyspnoea that worsens in the supine position [1,2]. This symptom is frequently misinterpreted as a sign of heart failure but the evaluation for cardiac disease is negative. The most characteristic physical sign of diaphragmatic dysfunction is the paradoxical inward motion of the abdomen as the rib cage expands during inspiration. This disordered breathing pattern results from compensatory use of the accessory inspiratory muscles of the rib cage and neck. When these muscles contract and lower pleural pressure, the weakened or flaccid diaphragm moves in a cephalad direction and the abdominal wall moves inward. The abdominal paradox is typically observed when the maximum transdiaphragmatic pressure that the patient can generate against a closed airway is less than 30 cm of water; it rarely occurs in unilateral diaphragmatic paralysis. The onset of orthopnoea due to bilateral diaphragmatic paralysis is dramatic occurring within minutes of recumbency. Bilateral diaphragmatic paralysis is usually seen in the context of severe generalized muscle weakness. In some cases however, diaphragm is the initial or the only muscle involved. The most common causes of bilateral diaphragmatic paralysis are listed below [1–4].

| Neurologic Causes                                      | Myopathic Causes                              |
|-------------------------------------------------------|-----------------------------------------------|
| Spinal cord transaction                               | Limb Girdle dystrophy                         |
| Multiple sclerosis                                     | Hyperthyroidism or Hypothryroidism            |
| Amyotrophic lateral sclerosis                         | Malnutrition                                  |
| Cervical spondylosis                                   | Acid Maltase deficiency                       |
| Poliomyelitis                                          | Connective tissue diseases                    |
| Gullian Barre Syndrome                                 | SLE                                           |
| Phrenic nerve dysfunction                              | Dermatomyositis, MCTD                         |
| Compression by tumour                                  | Amyloidosis                                   |
| Cardiac surgery                                        | Idiopathic                                    |
| Blunt trauma                                           |                                               |
| Idiopathic phrenic neuropathy                          |                                               |
| Posterior phrenic neuropathy                           |                                               |
| Radiation therapy                                      |                                               |

Disease progression is associated with progressive hypercapnea and hypoxemia which is more evident during sleep. Morning headaches, confusion, pulmonary artery hypertension, secondary erythrocytosis and signs of cor pulmonale can occur [5]. Fluoroscopy can be misleading in bilateral diaphragmatic paralysis because the cephalad movement of the rib may give a false appearance of caudal displacement of diaphragm [6]. A “sniff test” consists of assessing the motion of the diaphragm during a short, sharp inspiratory effort through the nostrils. Descent of the diaphragm will be seen in persons without the disorder. The gold standard for diagnosis of diaphragmatic paralysis is measurement of transdiaphragmatic pressure [7]. Treatable causes of diaphragmatic dysfunction include myopathies related to metabolic disturbances such as hypokalemia, hypomagnesemia, hypocalcemia, and hypophosphatemia. Hypothyroidism is also a treatable cause. The mechanism of thyroid myopathy is due to decreased activity of acid maltase (1,4 alpha glucosidase). Diaphragmatic paralysis due to neuralgic amyotrophy (parsonage turner syndrome) may improve spontaneously. When diaphragmatic dysfunction persists or progresses, ventilatory support, ranging from nocturnal to continuous, may be needed. Treatment of bilateral diaphragmatic paralysis depends on the etiology and severity [8,9]. The advent of small portable ventilator units capable of providing assistance with inspiratory as well as expiratory pressure has made non invasive positive pressure ventilation, an easily accessible and well accepted therapeutic tool of choice for symptomatic patients with bilateral diaphragmatic paralysis [10–12]. The use of phrenic nerve pacing with radiofrequency signalling is possible in patients with intact phrenic nerve function and no myopathy. In patients with bilateral diaphragmatic paralysis of acute onset,a one week of antiviral therapy may be considered [13,14].

Informed consent

Informed consent was obtained from the patient for publication of the report and accompanying images.
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References

[1] N. Kumar, W.L. Folger, C.F. Bolton, Dyspnoea as the predominant manifestation of bilateral phrenic neuropathy, Mayo Clin. Proc. 79 (2004) 1563.
[2] T. Stojkovic, P. Latour, G. Viet, et al., Vocal cord and diaphragm paralysis as clinical features of a French family with autosomal recessive charcot marie tooth disease, associated with a new mutation in the GDAP1 gene, Neuromuscul. Disord. 14 (2004) 261.
[3] J.M. Piehler, P.C. Pairolero, D.R. Gracey, P.E. Bernatez, Unexplained diaphragmatic paralysis: a harbinger of malignant disease? J. Thorac. Cardiovasc Surg. 84 (1982) 861.
[4] B.R. Celli, J. Rassulo, R. Corral, Ventilatory muscle dysfunction in patients with bilateral idiopathic diaphragmatic paralysis: reversal by intermittent external negative pressure ventilation, Am Rev. Respir. Dis. 136 (1987) 1276.
[5] A. Qureshi, Diaphragm paralysis, Semin. Respir. Crit. Care Med. 30 (2009) 315.
[6] C. Alexander, Diaphragm movements and the diagnosis of diaphragmatic paralysis, Clin. Radiol. 17 (1966) 79.
[7] ATS/ERS Statement on respiratory muscle testing, Am. J. Respir. Crit. Care Med. 166 (2002) 518.
[8] J. Davis, M. Goldman, L. Loh, M. Casson, Diaphragm function and alveolar hypoventilation, Q. J. Med. 45 (1976) 87.
[9] G.J. Gibson, Diaphragmatic paresis: pathophysiology, clinical features and investigations, Thorax 44 (1989) 960.
[10] K.A. Kleopa, M. Sherman, B. Neal, Bipap improves survival and rate of pulmonary function decline in patients with ALS, J. Neurol. Sci. 164 (1999) 82.
[11] P. Carratu, L. Spicuzza, A. Cassano, Early treatment with noninvasive positive pressure ventilation prolongs survival in amyotrophic lateral sclerosis patients with nocturnal respiratory insufficiency, Orphanet J. Rare Dis. 4 (2009) 10.
[12] N.S. Hill, Noninvasive ventilation. Does it work, for whom and how? Am. Rev. Respir. Dis. 147 (1993) 1050.
[13] R.S. Crausman, E.M. Summerhill, F.D. McCool, Idiopathic diaphragmatic paralysis: Bell’s palsy of the diaphragm? Lung 187 (2009) 153.
[14] F.J. Martinez, M. Bermudez-Gomez, B.R. Celli Chest, A reversible cause of diaphragmatic dysfunction, Hypothyroidism 96 (5) (1989 Nov) 1059–1063.