Diaphragmatic Paralysis: A Clinical Imitator of Cardiorespiratory Diseases

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Abstract

Diaphragmatic paralysis has a predictable effect on lung function. However, the symptoms depend on the preexisting heart-lung diseases and may mimic various cardiorespiratory processes. We describe the presentation in six patients. In a fit man, unilateral diaphragmatic paralysis caused dyspnea only at strenuous exercise. In a patient with emphysema it caused dyspnea mainly when carrying light weights. In another patient with emphysema it caused life-threatening hypoxemia simulating parenchymal lung disease. A patient with mild chronic obstructive lung disease and nocturnal wheezing following the onset of ULDP was believed for 15 years to have asthma. A patient with bilateral diaphragmatic weakness had severe choking sensation only in the supine position, simulating upper airway obstruction or heart failure. A female patient suffered nocturnal sweating due to ULDP. The clinical manifestations of diaphragmatic paralysis vary and can mimic a wide range of cardiorespiratory diseases.

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The normal diaphragm moves caudally as the muscle contracts and thereby facilitates inspiration. When a hemidiaphragm is paralyzed, the abdominal pressure together with the negative intrathoracic pressure cause proximal displacement of the muscle during inspiration. This paradoxical movement is associated with loss of inspiratory muscle power, reduces vital capacity and leads to mismatching of ventilation and perfusion [1-4].

Diaphragmatic palsy may be unilateral or bilateral. The etiology is unknown (idiopathic) in many cases. Unilateral paralysis is not rare following phrenic nerve injury during cardiac surgery, cervical spondylosis, pneumonia, neuritis of herpes zoster, or mediastinal compressive tumors. Bilateral paralysis is usually part of motor neuron disease, myopathies, muscular dystrophy, acid maltase deficiency, hypo or hyperthyroidism, amyloidosis, systemic lupus erythematosus and severe malnutrition [4,5]. The symptoms resulting from loss of diaphragmatic function are variable. While ULDP among healthy people is mostly asymptomatic, BLDP tends to cause marked morbidity [6].

Dyspnea is the main symptom and is often erroneously attributed to preexistent cardiorespiratory disease (orthopnea is

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* Deceased
ULDP = unilateral diaphragmatic paralysis
BLDP = bilateral diaphragmatic paralysis
$_{VE}$max = peak ventilation

often prominent). Daytime fatigue may be due to poor sleep. Hypoxemia is the result of mismatching of ventilation and perfusion secondary to hypoventilation or atelectasis, and hypercapnia is a sign of disease progression.

Once ULDP or BLDP is suspected, confirmation is mandatory. Chest radiography, fluoroscopy (the "sniff" test, especially in ULDP) and very likely ultrasonography may be diagnostic for paralysis if paradoxical movement (cephalic directed movement with inspiration) is seen. Dynamic magnetic resonance imaging may be helpful in equivocal situations [7].

For ULDP vital capacity is reduced by at least 10% particularly if measured in the supine position. Maximal inspiratory pressure is reduced. Electromyography is considered the ultimate proof for the presence of diaphragmatic paralysis but it requires expertise in the performance and interpretation. As mentioned, many patients with ULDP are asymptomatic and do not need therapy. In selected symptomatic ULDP patients, especially in the postoperative setting, surgical plication of the diseased hemidiaphragm may result in lung function improvement and facilitates extubation [8,9]. BLDP often requires ventilatory support either partially (bilevel positive airway pressure) or total. Diaphragmatic pacing may be considered when the phrenic nerves are intact, but this procedure has not yet gained popularity.

During a 2 year period we encountered among our patients with diaphragmatic paralysis six who demonstrated the wide clinical spectrum of this disease, indicating that the paralyzed diaphragm should be considered a clinical imitator.

Patients and Methods

In our patients diaphragmatic paralysis was diagnosed by the sniff test under fluoroscopy in the supine and upright position [7]. Pulmonary functions were measured in the sitting and supine position using a water spirometer (Godart, Holland). Maximal breathing capacity was measured during 12 seconds and extrapolated to 1 minute. Respiratory pressures were measured using a face mask connected to a manometer. Maximal inspiratory and expiratory pressures were measured from functional residual capacity and from total lung capacity. Peak exercise O_2 uptake, peak ventilation and exercise hemoglobin saturation were measured during incremental maximal tests on a cycle ergometer. Exercise breathing reserve was defined as the difference between $_{VE}$max and maximal breathing capacity. These tests were performed using a breath-by-breath

cardiorespiratory system (MedGraphics, CPX, MN, USA) and a pulse oximeter (POET, Criticare, USA) as previously described [10].

Patient Descriptions

Patient 1. A 40 year old highly fit man underwent thoracotomy for a benign pericardial cyst. After the surgery he noticed that walking 5 km, an activity that he performed with ease before, became intolerable. He also noticed disproportional dyspnea while carrying his baby. Right ULDP was found after surgery. Lung functions are shown in Table 1. Peak O_2 uptake was 2.447 L/min, 93% of predicted, but breathing reserve was low, 6 L/min (normal > 15 L/min).

Comment: Exercise capacity was normal, but for this highly trained person the residual capacity represents deterioration. This deterioration was caused by the 30% loss of vital capacity [Table 1]. Had lung function been normal, his breathing capacity and peak O_2 uptake would have been 30 L/min and 0.5–0.75 L/min higher. A sedentary person who rarely expends highly demanding effort may feel no disability from ULDP. The disproportionate dyspnea when carrying his baby is characteristic for diaphragmatic paralysis (see comment on patient 2).

Patient 2. A 73 year old man, with 100 pack years of smoking, mild diabetes mellitus and adult-onset celiac sprue, noticed an abrupt onset of shortness of breath mainly in the supine position or when carrying a light weight. This sensation interfered with his ability to continue working in his profession. Effort tolerance was otherwise normal. Right ULDP was found and chest computed tomography revealed marked emphysema. Lung functions are shown in Table 1. Peak exercise O_2 uptake was 0.666 L/min, 46% of predicted with exercise desaturation [Table 1]. After 1 year of follow-up all the findings remained unchanged.

Comment: The complaint of dyspnea during weight carrying was in marked discrepancy with the otherwise preserved exercise tolerance. The symptom emerged during recovery from severe malabsorption and coincided with the onset of ULDP. Diaphragmatic paralysis has not been reported in association with celiac disease. Whether the paralysis resulted from diabetic or autoimmune neuropathy is unknown. When a diaphragm is paralyzed, the accessory and abdominal wall muscles adapt to assist inspiration [1-3]. Carrying weight interferes with the function of the accessory muscles and with the timed relaxation of the abdominal wall muscles [3]. The symptoms were probably caused by the combination of ULDP and emphysema, the latter further aggravating the dependency on accessory muscles. Difficulty in weight carrying has been described in BLDP [5].

Patient 3. A 69 year old man who smoked 20 packs/day x years had a history of pulmonary tuberculosis for which he had not received drug therapy. At the age of 66 the patient noticed shortness of breath on daily activities. Lung functions are shown in Table 1 (3a). Chest X-ray and CT demonstrated evidence of old TB, bilateral bullous disease and increased interstitial markings

TB = tuberculosis

Table 1. Pulmonary function tests in six patients with diaphragmatic paralysis

Patient no.	Max. O_2 uptake L (%)	HbS % rest/exercise	MIP/MEP (mmHg)	RV/TLC L (%)	FEV1/FVC L (%)
1	2.447 (93)	98/94	50/80	2.05 (108)/ 4.95 (73)	2.78 (71)/ 3.34 (68)
2	0.666 (46)	95/94	40/40	1.5 (83)/ 4.3 (78)	1.9 (72)/ 2.6 (77)
3a	NM	93/NM	NM	3.18 (154)/ 5.95 (101)	1.7 (69)/ 2.35 (72)
3b		80/NM	50/70		1.06 (41)/ 1.55 (50)
3c		97/NM	70/90		1.65 (66)/ 2.4 (75)
4	1.778 (102)	97/90	90/50	2.81 (142) 6.03 (115)	1.19 (40)/ 1.52 (39)
5a	NM	95/NM	40/80	2.16 (109)/ 3.82 (68)	1.19 (40)/ 1.52 (39)
5b		92/NM	20/60		1.02 (34)/ 1.16 (29)
6	NM	92/NM	60/70	NM	1.56 (77)/ 1.98 (74)

3a, 3b and 3c refer to the findings in patient #3 before the onset of diaphragmatic paralysis, during the acute period and after recovery. 5a and 5b refer to the findings in patient #5 after the onset of unilateral and bilateral paralysis, respectively. Values in parenthesis are percent of expected values.
FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity, RV = residual volume, TLC = total lung capacity, MIP = maximal inspiratory pressure, MEP = maximal expiratory pressure, HbS% = hemoglobin saturation, NM = not measured.

consistent with interstitial disease. At age 67, following a coronary bypass graft surgery that was complicated by right ULDP, he developed severe hypoxemia (PaO_2 = 40 mmHg breathing room air), cor pulmonale and mental confusion. Chest radiography and CT revealed no other changes as compared with the earlier series. Pulmonary functions at that stage are shown in Table 1 (3b). Empiric anticoagulant, antibiotics, corticosteroids and anti-TB treatment were of no benefit. Within 3 months all symptoms and resting hypoxemia resolved with residual dyspnea only when the patient bent forward (lacing). Lung function returned to the preoperative level [Table 1, 3c]. This improvement coincided with recovery of the hemidiaphragmatic function.

Comment: ULDP is common following coronary bypass surgery, especially if hypothermia is applied, and it is often reversible [11,12]. This patient developed life-threatening hypoxemia, which was attributed to TB, pulmonary emboli or activation of the interstitial lung process. The recovery coincided with the restoration of the diaphragmatic function and not with any of the empiric trials. In the presence of severe preexisting lung disease, the mismatching of ventilation and perfusion caused by the ULDP led to marked hypoxemia. This course, in which the consequence of gas exchange abnormality dominated, imitating parenchymal disease, is uncommon in ULDP. Ventilatory failure with CO_2 retention has been described with BLDP [12] but hypoxic failure is very rare.

Patient 4. A 70 year old man who smoked 70 packs/day x years underwent right nephrectomy at the age of 55, and since the operation he felt nocturnal wheezing and episodic shortness of breath. Spirometry showed obstruction with some reversibility and the patient was placed on bronchodilators and intermittent oral steroids for apparent COPD. Right ULDP was found and dated to the time of the nephrectomy. Lung functions are shown in Table 1. Peak O_2 uptake was 102% predicted but the patient's ventilation was limited (breathing reserve 6 L/min). Oral steroids were withdrawn.

Comment: When a patient with a history of smoking complains of nocturnal cough and wheeze and lung function shows airway obstruction, it is tempting to attribute the symptoms to airway obstruction. The deterioration and the nocturnal symptoms following nephrectomy were the result of the ULDP and not the COPD. Exercise capacity was preserved, but ventilatory limitation to exercise was present, suggesting that pre-ULDP exercise tolerance was even higher, despite the COPD. Temporary loss of diaphragmatic function is common following upper abdominal surgery, but permanent paralysis is rare and the mechanism is unknown [13].

Patient 5. This 63 year old man had a history of diabetes mellitus, hypertension, ischemic heart disease and left hemiparesis. Concomitant with the onset of hemiparesis he noticed shoulder pain. Left ULDP was found, which had not existed earlier. Lung function at that stage is shown in Table 1 (5a). At a later date he noticed acute onset of a severe choking sensation in the supine position, although breathing was comfortable in the upright posture. After 30 seconds in the supine position the patient became extremely distressed, breath sounds diminished, vigorous suprasternal retractions were observed and the abdomen moved paradoxically (inwards during inspiration). The physiological findings during transitions from sitting to the supine position are shown in Table 2. During the sniff test both muscles moved opposite to the normal direction, confirming the presence of BLDP. Lung function is shown in Table 1 (5b). Forced expiratory vital capacity was reduced by 30% and maximal inspiratory pressure by 50%. Flow volume loop (sitting) showed reduced inspiratory flow rates at a constant level of 1.35 L/sec [Figure 1], consistent with inspiratory extrathoracic upper airway obstruction.

Comment: The diaphragmatic elevation coincided with the onset of hemiparesis. ULDP is rare in cerebral stroke and most textbooks do not mention cerebral event as a potential cause. The relative sparing of the diaphragm in cerebral stroke results from its bilateral cortical innervation. However, severe diaphragmatic weakness may follow a cerebrovascular accident [4]. The clinical history and the electroencephalogram were more consistent with brachial plexus neuritis (a common cause of isolated ULDP [14]). The findings described in Table 2 indicate that the supine distress was caused by diaphragmatic weakness and not by upper airway obstruction. The latter diagnosis could have been suspected based on the physical examination and the flow volume curve
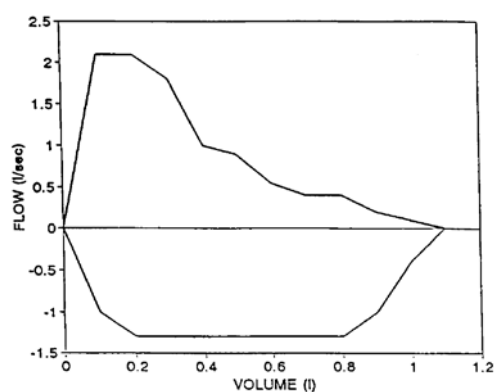
COPD = chronic obstructive pulmonary disease

Figure 1. Maximal inspiratory and expiratory flow volume loop of patient #5 with bilateral diaphragmatic paralysis. Note the relatively constant inspiratory flow rate during most of the inspiratory vital capacity.

Table 2. Respiratory parameters in a patient (#5) with bilateral diaphragmatic paralysis during positional changes

Symptoms	VE (L/min)	VC (L)	VT (L)	HbS% room air	HbS% high FiO$_2$	Position
None	10	1	0.5	90	98	Sitting
Distress	9.5	0.5	0.25	80	98	Supine*
Distress	NM	NM	NM	80	98	Supine intubated*

*After 1 minute in the supine position.
HbS% = hemoglobin saturation, VT = tidal volume, VC = vital capacity, VE = minute ventilation, NM = not measured.

[Figure 1]. Continuous nocturnal positive pressure ventilation relieved the supine symptomatology.

Patient 6. A 67 year old woman was referred for evaluation of nocturnal coughing and profuse sweating. She was asymptomatic in the upright position. Her history and a physical examination showed only ULDP described as idiopathic. Lung functions are shown in Table 1. Exercise capacity was normal. Workup for TB, thyroid disease, asthma, heart failure, angina and malignancy were negative and remained so during 2 years of follow-up.

Comment: The nocturnal sweating dated to the onset of ULDP. Extensive workup was negative. We believe that the night sweats represent an unusual somatic response to the sensation of dyspnea in the supine position. The causality between ULDP and sweating could have been supported had nocturnal positive pressure ventilation ameliorated the symptoms, but the patient refused to try this modality.

Discussion

Loss of diaphragmatic function has predictable consequences, each of which can lead to different symptoms. Vital capacity is reduced and limits breathing capacity. The accessory and abdominal muscles share a larger part in the inspiratory effort [1,3,5]. The deranged gas exchange in the under-ventilated lung can cause hypoxemia and the reduced respiratory muscle strength

may cause ventilatory failure [12]. Therefore, the symptoms of diaphragmatic paralysis vary widely and include among others: no symptoms, dyspnea, fatigue, orthopnea and chest pain [4]. The symptoms can be divided according to the physiological causes.

Symptoms due to reduced maximal breathing capacity

The capacity of the respiratory system to ventilate the lung exceeds the ventilatory demand, even at peak exercise [15]. Therefore, many subjects with ULDP, which causes up to 25% loss of VC [16], are asymptomatic at rest. Surprisingly, even patients with BLDP (up to 50% loss of VC) are often only mildly symptomatic at rest if there is no other cardiorespiratory disease [7]. Patients with underlying lung or muscular disease are prone to be symptomatic when ULDP is present, since the processes may be additive. However, fit subjects whose cardiovascular system allows them to approach maximal breathing capacity (patient #1) will be symptomatic on exertion. The combination of good effort tolerance and orthopnea should suggest the diagnosis of ULDP.

Symptoms due to increased load on accessory muscles

Adaptation to missing diaphragmatic contribution depends on greater contribution by accessory, intercostal and abdominal muscles [1-3,5]. Excessive use of these muscles can lead to specific symptoms. When the tonus of these muscles is affected by other activity such as carrying a weight, the ability of the accessory and abdominal muscles to support ventilation is limited, causing shortness of breath disproportional to the task. Dyspnea during weight carrying has been described in BLDP. Marked dyspnea on water immersion with ULDP [17,18] is probably also due to neutralization of the supportive effect of the abdominal musculature on respiration. Excessive use of abdominal muscles leading to abdominal pain was the presenting symptom in twins with BLDP seen in our institute [19].

Symptoms due to gas exchange abnormalities

ULDP causes ventilation perfusion abnormalities mainly at the lung base. CO_2 retention is likely if severe underlying lung disease is aggravated by ULDP or BLDP. Cor pulmonale and respiratory failure have been described in BLDP [6,12,19]. In ULDP, hypoxemia is relatively common in the supine position and during exercise but is usually mild. In patient 3, postoperative ULDP caused severe hypoxemia. It is possible that hypoxemia and respiratory failure due to diaphragmatic paralysis may be more common than appreciated and symptoms may be attributed to other cardiorespiratory diseases.

Other symptoms and delayed diagnosis

Some patients with ULDP or BLDP undergo extensive workup including heart catheterization for evaluation of orthopnea and/or effort intolerance. Patients may be treated for pulmonary embolism or undergo evaluation for early interstitial disease (patient 3). Nocturnal wheezes and shortness of breath can be mistakenly attributed to preexisting asthma (patient 4). It is

VC = vital capacity

likely that the distress experienced in the supine position can in some individuals mimic other diseases. We believe that the night sweats (patient 6) also resulted from the ULDP. Diaphragmatic paralysis was not considered in most of our patients at presentation. Diagnosis was delayed from a few weeks (patient 5) to 15 years (patient 4). Common initial diagnoses have been pulmonary embolism, interstitial lung disease (for which lung biopsy was performed), acute exacerbation of COPD, and congestive heart failure [6,20-22].

In conclusion, diaphragmatic paralysis causes exertional dyspnea in otherwise healthy and fit individuals but can lead to various clinical symptoms especially in the presence of preexisting disease. These symptoms are caused by the loss of ventilatory reserve, loaded accessory muscles of respiration, and the abnormal gas exchange. The various presentations can mimic other cardiorespiratory diseases. Unexplained respiratory complaints in the absence of evident cardiovascular or parenchymal lung disease should raise the possibility of diaphragmatic paralysis, especially in clinical conditions associated with this disorder. Positional dyspnea (orthopnea, dyspnea when bending) and atypical exertional complaints (dyspnea on water immersion or while lifting weights) should also suggest this diagnosis. The sniff test under fluoroscopy and diaphragmatic ultrasonography are the standard diagnostic tools. Treatment is often unnecessary but nocturnal positive pressure ventilation, and rarely other modalities such as diaphragmatic pacing or diaphragmatic plication, should be considered.

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