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Diaphragmatic Paralysis - Symptoms, Evaluation, Therapy and Outcome

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1. Introduction

The diaphragm has a major role in inspiration. The muscle separates the mostly negative pressure chest cavity, from the positive pressure abdomen. The displacement of the muscle with inspiration expands the chest, augmenting the negative pleural pressure, thereby forcing air flow into the lung. However paralysis of the muscle, unilaterally or even bilaterally, is compatible with life in most cases due to effective adaptation of the other muscles of respiration. Patients with diaphragmatic paralysis may experience a wide range of symptoms: from being asymptomatic, symptomatic only with exercise, or respiratory insufficiency and death. Symptoms depends on the pre existing cardiorespiratory status, the extent of paralysis, unilateral or bilateral and on the nature of the paralysis, acute or chronic. Some symptoms are distinct and should always raise the diagnosis of diaphragmatic paralysis. The wide range of symptoms will be described, as well as the anatomical and physiological aspects in the normal and in the disease state, etiologies, work up and therapy. Unilateral and bilateral paralysis will be discussed together, despite differences in the prevalence, causes and course.

2.1 Structure and function of the normal diaphragm

The diaphragm, the most important contributor to inspiration, is one confluent uninterrupted structure, composed of a central tendon, surrounded by muscle fibers. The structure is relatively symmetric and each hemidiaphragm is innervated by the ipsilateral phrenic nerve. The muscle fibers are inserted to the sternum, lower ribs and the arcuate ligaments (Roussos & Macklem, 1982; Fell, 1998).

Due to this orientation, contraction of the fibers leads not only to a piston shape caudal displacement of the muscle, but also to elevation and expansion of the rib cage, expanding the chest cavity caudally and circumferentially, thereby forcing airflow into the lungs.

2.2 Diaphragmatic innervations and anatomy of the phrenic nerve

Each side of the diaphragm is innervated by contralateral upper motor neurons, but in some subjects it has bilateral cortical contribution. Therefore, in unilateral hemispheric stroke, muscle function is often partially preserved.

The phrenic nerve originates in the neck from cervical, C₃₋₅ roots, then takes a tortuous course, penetrates the posterior chest, behind the Sternomastoid muscle, between the subclavian vessels. The left phrenic nerve runs close to the thoracic duct, crossing the internal mammary arteries anteriorly, in front of the aortic arch and main pulmonary artery, approaching the anterior aspect of the pericardium between the mediastinal pleura and the pericardium. The right phrenic nerve follows the superior vena cava and the right side of the pericardium and pierces the diaphragm lateral to the vena cava hiatus and the left nerve pierces lateral to the left heart border. Each nerve divides on the surface of the diaphragm into 4 branches. After branching, the trunks penetrate and spread along the abdominal side of the muscle. The right phrenic nerve is shorter and less tortuous. Therefore, the nerves can be interrupted or damaged along this long course, within the neck, chest and even abdomen (Roussos & Macklem, 1982; Fell, 1998). Due to this unique anatomy, low cervical (below C₅) processes spare the phrenic nerves and the diaphragmatic function is preserved, despite paralysis of the intercostal muscles.

3.1 Physiology of breathing in diaphragmatic paralysis

When paralyzed, caudal displacement of the muscle with contraction is abolished or diminished, limiting chest expansion. Furthermore, due to more negative pleural pressure with inspiration, the muscle is displaced cephalad, further compromising lung inflation. The forced displacement of the diaphragm compresses the adjacent lung, thereby limiting regional ventilation. The more negative pressure that is maintained in the contralateral hemithorax causes wasted airflow from the affected to the unaffected lung. The reduced regional ventilation is often associated with reduced perfusion, but matching is not always optimal and relatively lower ventilation leads to deranged gas exchange and resting hypoxemia.

In the supine position, and in other postures when abdominal pressure rises, such as while bending forwards, the weight of the abdominal viscera or the pressure generated in the abdomen enhance cephalad displacement of the muscle, thereby further limiting lung expansion, causing dyspnea and aggravating hypoxemia (Gibson, 1989).

3.2 Causes of diaphragmatic paralysis and diaphragmatic weakness with emphasis on unique or rare causes

Diaphragmatic paralysis is in many, up to 2/3 of the cases, idiopathic. Common causes for unilateral as for bilateral paralysis are neurologic, such as peripheral phrenic nerve injuries, motor neuron disease, neuropathies and myopathies (including metabolic and endocrine) and to some extent hemispheric stroke (Gibson, GJ; Maish, 2010). In rare situations, diaphragmatic paralysis is the presenting or the predominant symptom of motor neuron disease or myopathy. Infection (viral), tumors, trauma, or inflammation can damage the

nerve throughout the long course. Even subdiaphragmatic processes and operations may damage the nerve along the branches.

Among the unique etiologies for diaphragmatic paralysis that should be considered are systemic lupus erythematosus (rarely presented with diaphragmatic weakness), neck trauma or chiropractic manipulation, central vein cannulation, occult thoracic malignancy and adverse event following bronchial arteries embolization. A relatively common cause is nerve damage, thermal, vascular or direct interruption during heart or mediastinal surgery. These postsurgical patients are often difficult to wean and the diagnosis can and should be made immediately. Diaphragmatic paralysis is also common following liver transplantation. In general, unilateral or bilateral disease share similar causes, but bilateral disease is more common in systemic processes such as myopathies or metabolic diseases.

4.1 Symptoms of diaphragmatic paralysis

Loss of part or all diaphragmatic contribution to breathing has predictable effects that cause a wide range of symptoms. The symptoms depend on several factors including: the stage of the paralysis, acute or chronic, on severity; whether the paralysis is unilateral or bilateral and on the presence (and severity) or absence of pre existing lung disease. Diaphragmatic paralysis is associated with reduced vital capacity at rest, more in the supine position. The accessory muscles of ventilation face greater load and gas exchange is deranged due to poor matching of ventilation to perfusion in the affected areas, leading to hypoxemia, at rest, and more so during sleep and exercise.

Therefore, subjects may be asymptomatic, complain of dyspnea only with effort, or complain of specific symptoms, such as orthopnea (its onset is immediate after regaining the recumbent position, in contrast with the delayed orthopnea of left heart failure), dyspnea with bending, immersion or carrying even light objects. Abdominal pain due to excessive load on the abdominal muscle was the presenting symptoms of bilateral diaphragmatic paralysis (Molho et al., 1987). Abnormal gas exchange is most important if lung disease preexists. These patients may develop respiratory insufficiency, severe hypoxia and CO₂ retention. Night sweats and other symptoms have also been reported (Ben-Dov et al, 2008) .

In acute onset paralysis, patient may feel acute distress, severe orthopnea, shoulder pain and fatigue, but symptoms usually diminish, due to either desensitization, adaptation of accessory muscles of respiration or due to full or partial recovery of the phrenic nerve itself. Therefore, diaphragmatic paralysis may imitate various cardiovascular diseases (Ben-Dov et al, 2008) and symptom are often unrecognized or attributed to pre existing lung disease (i.e., COPD), thereby avoiding further evaluation, or attributed to other organ disease (i.e., CHF), thereby subjecting the patients to unnecessary evaluation.

4.2 Acute diaphragmatic paralysis

The symptoms in acute disease are more severe. Patients describe acute onset of dyspnea and orthopnea. In the post surgical and post trauma cases, weaning from mechanical

ventilation may be difficult and the symptoms are often attributed to the surgery or trauma. Patients with acute onset idiopathic paralysis may be subject to extensive work up until diagnosis is appreciated. An acute syndrome has been described, neuralgic amyotrophy (not rare among idiopathic isolated phrenic nerve neuropathy), in which following a viral disease or surgery, patients feel abrupt onset of shoulder and neck pain, preceding dyspnea and orthopnea, the outcome of unilateral or bilateral phrenic nerve neuropathy. The paralysis persists in most patients but in some it resolves or relapses (Tsao et al., 2000).

Since a viral prodrome is not rare in acute onset disease, some authors attempted antiviral therapy with Valacyclovir with some positive responses. These authors consider isolated diaphragmatic paralysis as a "Bells palsy" of the phrenic nerve (Crausman et al., 2009).

4.3 Diaphragmatic paralysis in neonates

Birth injury, nerve damage during cardiothoracic surgery or cannulation of central veins and rarely neuromuscular diseases may cause unilateral and rarely bilateral paralysis (Sivan & Galvis, 1990; Simansky et al., 2002).

Diagnosis is often made only after failure to wean following surgery. Symptoms may be severe, but most are not specific, beside paradoxical movement of the abdomen. Diaphragmatic paralysis should be considered in any respiratory distress under these circumstances. Echocardiography with demonstration poor or paradoxical movement of the affected hemidiaphragm, while the infant breaths spontaneously, is considered the preferred method for diagnosis. Other methods are rarely used.

Fortunately, many infants with birth trauma associated paralysis recover spontaneously within 6-12 months, with or without restoration of diaphragmatic function. Electromyography (EMG) signals and phrenic nerve conduction following nerve stimulation provide prognostic information. If supportive care is not sufficient and mechanical ventilation is prolonged, diaphragmatic plication may lead to rapid improvement. Some authors believe that plication, in the post trauma cases is in general more effective in neonate than in adults (Simansky et al., 2002).

5.1 Diagnosis of diaphragmatic paralysis

An algorithm has been suggested for the diagnosis of diaphragmatic paralysis (Polkey et al., 1995). It is based on history, physical examination with emphasis on the presence or absence of paradoxical movement of the abdominal wall (posterior, instead of anterior displacement of the abdominal wall with inspiration). This sign is important and easily recognizable if the patient lays supine and relaxed. Paradoxical movement of the abdominal wall is almost always seen with bilateral paralysis, but common even with unilateral disease. Occasionally, no paradoxical movement of the abdominal wall, but limited or asymmetrical excursion of the affected side abdominal wall can be seen. However, paradoxical movement of the abdominal wall is occasionally present in healthy subjects, especially if not relaxed during the examination.

5.2 Imaging

Diaphragmatic paralysis is usually suspected when asymmetric diaphragmatic elevation is seen on plane chest radiograph. This finding is commonly associated with linear shadows or patchy atelectasis above the paralyzed diaphragm. Asymmetric level is absent in bilateral paralysis, rendering recognition more difficult. When suspected, diaphragmatic paralysis should be confirmed by the highly sensitive sniff test, using fluoroscopy or ultrasound (Tarver et al., 1989; Gotesman & McCool, 1997). During the sniff manoeuvre, the paradoxical movement of the paralyzed hemidiaphragm, cephalad with inspiration, in contrast with the rapid caudal movement of the unaffected muscle, can be seen with fluoroscopy, while failure of the thin muscle to thicken with contraction can be seen with ultrasonography.

5.3 Lung function

With unilateral diaphragmatic paralysis, lung function usually reveals mild restriction. Baseline upright vital capacity is mildly reduced (up to 80% of predicted). With bilateral disease, vital capacity may fall to 50% of predicted (Mier-Jedrzejowicz et al., 1988). Maximal inspiratory pressures fall to 80 and 30% of predict, with unilateral and bilateral paralysis, respectively (Steier et al., 2007). Vital capacity and oxygen saturation fall is augmented in the supine position; vital capacity is at least 10% lower than in the upright position. This postural effect is larger in right side and in bilateral paralysis. The larger effect of right paralysis is probably due to the right lung being larger and due to the weight of the liver, that in the supine position promotes cephalad displacement of the muscle. Oxygen saturation often falls markedly during sleep, mainly during the REM phase, as with exercise. Diffusion capacity may be near normal in diaphragmatic paralysis and if markedly abnormal, it justifies a search for an alternative cause.

5.4.1 Additional studies

The studies described above are usually sufficient to establish the diagnosis of diaphragmatic paralysis or of severe diaphragmatic dysfunction. However, in some cases more specific measures are needed.

5.4.2 Trans diaphragmatic pressure

During inspiration, pleural pressure, reflected by esophageal pressure, becomes more negative while the pressure in the abdomen, measured via a gastric balloon, becomes more positive (abdominal content is compressed by the descending diaphragm). In contrast, with paralysis, especially when bilateral, the diaphragms are displaced cephalad due to the negative pleural pressure, so that abdominal pressure decreases instead of increasing. Therefore, normally with inspiration, esophageal pressure (negative) and the gastric pressure (positive) will change to opposite directions. In contrast, with bilateral diaphragmatic paralysis, the pressure tracing in both organs will move to the negative direction and this is the gold standard finding to document paralysis. Transdiaphragmatic pressure can be measured during spontaneous tidal, maximal or sniff manoeuvre and or

following electrical phrenic nerve stimulation (using surface neck electrodes). These measurements however are difficult to standardize in bilateral disease and even more so with unilateral disease (Laporta & Grassino, 1985; American Thoracic Society/European Respiratory Society, 2002).

5.4.3 EMG

The EMG response of the diaphragm can be measured at the muscle insertion intercostal spaces with surface electrodes, with or without electrical phrenic nerve stimulation. Signals and nerve conduction velocity are studied for patterns indicating neuropathy, myopathy or show evidence of complete nerve interruption. However, these studies need expertise and are rarely performed, unless as a prerequisite for pacing.

6.1 Recommended further work up when the diagnosis of diaphragmatic paralysis is established

When diaphragmatic paralysis is confirmed, there is need to find the causal mechanism. There are no systematic studies assessing the yield of work up algorithms in an attempt to find the cause in the individual patient. However, even though most cases are idiopathic, in up to 5%, thoracic malignancy is present. Therefore, when the cause is not obvious, we recommend imaging studies, including CT scanning. Diaphragmatic paralysis, at all age groups, may be an early expression of systemic diseases, such as SLE, metabolic or endocrine disease and or of motor neuron disease, all of which justify specific evaluation, such as thyroid function and muscle enzymes and these diseases should be treated when possible.

Sleep study should be considered, since disturbed sleep is a predictable consequence of diaphragmatic paralysis (Qureshi, 2009).

7.1 Differential diagnosis

Diaphragmatic elevation, dyspnea and orthopnea may result from many other causes. It is usually easy to differentiate subpulmonic effusion or subdiaphragmatic processes by appropriate imaging. Eventration of the diaphragm, mostly congenital, is a localized fibrous replacement of part of the musculature and the lateral chest x ray shows the localized nature of the defect. Patient with other diseases may experience symptoms mimicking to those induced by diaphragmatic paralysis. Orthopnea of cardiac origin has slow onset, while that of diaphragmatic paralysis is more abrupt and is relieved immediately after resuming the upright position.

8.1 Treatment options

Most patients with unilateral diaphragmatic paralysis need no specific therapy. Symptomatic patients or those with preexisting lung disease, or bilateral disease, especially if marked orthopnea exists, may benefit from non invasive nocturnal ventilatory support and this mode of therapy may offer improvement in sleep quality, day function and arterial

blood gases. The rationale for anti viral therapy for patient with acute onset disease following a "viral" prodrome has been discussed earlier.

8.2 Diaphragmatic plication

The loose, paralyzed diaphragm can be folded and sutured so that the compliance decreases following plication. The argument in favor of plication is that the less compliant stretched muscle limits the cephalad displacement with inspiration. The lung region adjacent to the paralyzed muscle is therefore not or less compressed and regional ventilation improves. Furthermore, airflow from the affected lung to the normal lung minimizes, leading to improved ventilatory efficiency. Plication can be offered to selected, symptomatic patients, whose symptoms affect their life style (Simansky et al., 2002). The exact indications have not been established. Following plication in selected patients, with 5 years follow up, lung function, upright and supine, have been shown to improve, sitting and supine Vital Capacity was 9% and 19%, or more, higher, respectively and the supine fall of FVC after plication was only 9% while it was 32% prior to surgery. Daily activities and dyspnea have also been improved (Versteeg et al., 2007; Freeman et al., 2009). However, this degree of improvement has not been consistently found (Higgs et al., 2002). Data on the effect of diaphragmatic plication on exercise tolerance, on peak exercise and on exercise gas exchange are anecdotal, in the adult as in the pediatric population.

8.3 Diaphragmatic pacing

Permanent phrenic nerve pacing is possible only if the phrenic nerve is fully intact and the muscle is functioning and even the deconditioned muscle fibers needs programmed gradual reconditioning. Ventilator dependent high cervical quadriplegics are candidates (Elefteriades et al., 1992). Pacing is rarely used in isolated, unilateral or bilateral diaphragmatic paralysis. There are inherent difficulties with pacing, such synchronization or lack of, with intercostal muscle.

9. Course and prognosis

Chronic unilateral diaphragmatic paralysis is usually asymptomatic or mildly symptomatic and the long term prognosis in the idiopathic and post traumatic cases is usually favorable. Even in the more symptomatic cases, symptoms gradually improve, either due to adaptation of the accessory muscles to the extra load of inspiration, or due to spontaneous recovery or improvement of the diaphragmatic function. Improvement has been described during follow up of months to years in various clinical settings (Gayan-Ramirez et al., 2008) and some authors believe that with time the compliance of the paralyzed muscle decreases, thereby limiting the cephalad displacement with inspiration (autoplication).

Bilateral disease carries worse prognosis, either because it is usually an expression of more severe disease and due to the marked impact of bilateral disease on respiratory mechanics. However, even patients with bilateral disease often improve, lose the dependency on ventilatory support, can live reasonable life and carry pregnancy and delivery. In some, adaptation is a result of one or more of the above mechanisms.

10. Conclusion

Diaphragmatic paralysis is a relatively common disease. In many cases it is mildly or not symptomatic. In many, the cause is idiopathic. Therefore, it is often undiagnosed or underappreciated. However, in some situations diaphragmatic paralysis causes severe, often unique symptoms (such as orthopnea and dyspnea with bending or immersion) that must direct to the appropriate work up. Diagnosis in most cases should be confirmed by the Sniff test with additional supportive tests such as upright and supine lung function and respiratory muscle forces. These tests are important for follow up. Correct diagnosis prevents unnecessary work up and facilitates recognition of various diseases (such as mediastinal tumors) some of them are treatable (such as inflammatory or endocrine diseases) and enhances work up for comorbidities, such as sleep abnormalities. In many patients no specific therapy is needed and in up to a quarter, paralysis or symptoms will improve spontaneously. The other may need nocturnal ventilatory assist. In selected cases diaphragmatic plication or pacing should be considered.

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