CHEST

Treatment of Idiopathic Diaphragm Flutter
A Case Study

Michael Chiou, BA; María Victoria Herrero; John R. Bach, MD; Jeffrey L. Cole, MD; and Enrique Luis Gonzales, AAS, CRT, RRT

Diaphragm flutter is a rare disorder defined by dyspnea and often thoracoabdominal pain associated with rapid rhythmic involuntary contractions of the diaphragm with no effective treatment. A 35-year-old woman's flutter was triggered by increasing the depth of breathing and by (electrical) stimulation of the diaphragm. Medical therapy, phrenic nerve crush, and diaphragm pacer stimulation were ineffective. Since increasing diaphragm activity was a trigger, resting the diaphragm was tried. A manual resuscitator and, subsequently, mouthpiece and nasal noninvasive ventilatory support (NVS) instantaneously halted the flutter for 3 months and almost instantaneously for another 6 months. For 16 months, it has continued to halt flutter with rare episodes when getting out of bed that resolve with up to 40 minutes of NVS. To our knowledge, this is the first case of idiopathic diaphragmatic flutter for which diaphragm rest was used as successful treatment with no adverse effects. This should be tried for future cases.

CHEST 2017; 151(4):e69-e71

KEY WORDS: diaphragm pacing; diaphragmatic flutter; noninvasive ventilatory support; treatment

Diaphragmatic flutter was described and named after Antonie van Leeuwenhoek in 1723. He self-reported attacks of epigastric pulsations and dyspnea. At least 68 cases were subsequently reported and characterized by rapid rhythmic involuntary contractions of the diaphragm accompanied by dyspnea and sometimes thoracoabdominal pain.[1,2] Treatment attempts have been largely ineffective.[1]

Case Report

In May 2008, a 35-year-old woman had sudden-onset chest tightness followed by left abdominal wall pulsations of about three per s ("flutter") and dyspnea for 3 weeks that was relieved only by sleep. The flutter was documented in June 2008, with myokymia and complex repetitive discharges on electromyography, and by video fluoroscopy.[3,4] Over the following years, she consulted pulmonologists, surgeons, gastroenterologists, neurologists, and pain specialists and received levetiracetam, clonazepam, IV immunoglobulin, plasmapheresis, rituximab, diazepam, baclofen, cyclobenzaprine, lorazepam, gabapentin, mycophenolic acid, and topiramate without benefit and with side effects that included allergies, skin rashes, and nausea. Cellulitis developed concomitant with plasmapheresis treatment. IV immunoglobulin therapy eliminated the flutter for 2 years, at which point it returned,

ABBREVIATIONS: NVS = noninvasive ventilatory support; VC = vital capacity

AFFILIATIONS: From the Department of Physical Medicine and Rehabilitation (Drs Bach and Cole and Messrs Chiou and Gonzales), Rutgers New Jersey Medical School, Newark, NJ; and Petrona Villegas de Cordero Hospital (Ms Herrero), San Fernando, Buenos Aires, Argentina.

CORRESPONDENCE TO: John R. Bach, MD, Department of Physical Medicine and Rehabilitation, University Hospital B-403, 150 Bergen St, Newark, NJ 07103; e-mail: bachjr@njms.rutgers.edu

DOI: http://dx.doi.org/10.1016/j.chest.2017.01.034

but repeated therapy was ineffective. She then underwent a left phrenic nerve crush, and two lower right intercostal nerves were implanted into the diaphragm. However, as phrenic function returned over the next 6 months, so did the flutter accompanied by constant left lower intercostal tenderness and pain from the sternum to the back. In September 2011, diaphragm pacemakers were implanted bilaterally, but their activation triggered flutter. After multiple skin infections and no efficacy from the external wires, they were removed in May 2016.

In July 2015, she presented to us with orthopnea and $>$ 30 episodes of flutter per day triggered by deep breathing, coughing, walking, and talking, each episode lasting minutes to up to 3 hours. Each episode was accompanied by thoracoabdominal pain rated at 6 of 10. Her vital capacity (VC) in a sitting position was 3,260 mL (81% predicted), and in a supine position it was 2,150 mL (54% predicted); oxygen saturation was 99%, and end-tidal carbon dioxide was 35 mm Hg. Flutter began during VC measurements. Since episodes were triggered by diaphragm pacing and exacerbated by increasing diaphragm activity, we considered resting the diaphragm. A manual resuscitator was used through a mouthpiece to ventilate her lungs for 1 min ("bagging"), and with the first insufflation, flutter stopped for several minutes. It then suddenly reappeared, and bagging again immediately resolved three further episodes during the 90-min visit. Therefore, a manual resuscitator with a 15-mm angled mouthpiece was prescribed for home use. She reported using it throughout the day and while at work as a civil engineer for a few minutes at a time to relieve flutter. Six weeks later, complaining of being unable to work while bagging her lungs to abort flutter, a portable ventilator (volume preset at 800-1,400 mL and a rate of 22 on assist/control mode) with nasal and 15-mm angled mouthpiece interfaces was prescribed to facilitate her employment. On occasion, she used the ventilator to relieve orthopnea and permit supine sleeping.

At her 1-month follow-up, her VC had increased to 3,790 mL in a sitting position and 2,550 mL in a supine position. She no longer used nasal NVS overnight except when awakened by an occasional episode. Again, bagging stopped multiple episodes during the visit. A follow-up sleep study demonstrated normal oxygen saturation and blood carbon dioxide levels.

Diaphragm rest immediately halted the episodes for 3 months, almost immediately for another 6 months, and continues to be successful in relieving the flutter that is triggered by her getting out of bed in the morning more than one-half of the time. Her primary complaint became unremitting pain on a scale of 8 of 10 for which she takes oxycodone with minimal effect. More recently, as getting out of bed in the morning triggers flutter, it may now take up to 40 min of NVS for resolution. Some mornings, the NVS does not work and she must remain in bed all day; she then takes chlorpromazine to return to sleep, and on waking, tries again to use NVS to break the flutter episode. Ultrasonographic imaging of the hemidiaphragms performed in November 2016 demonstrated significant atrophy of the left side of the diaphragm, which is consistent with the paralytic elevation seen on chest radiography, her diminished VC, and sniff-test pressures.

Discussion

The findings of myokymia, myoclonus, and other irregular or rhythmic repetitive dystonic discharges in muscles, which are typically unilateral, can present as myalgias, cramps, spasms, weakness, stiffness, or twitching. They can be associated with stress, fatigue, excessive caffeine or alcohol intake, and demyelination and brainstem lesions. Myokymia typically refers to the slow nonfunctional undulating contraction of a muscle that is triggered from either proximal or distal motor nerve axonal pathologic conditions or from transaxonal ephaptic excitation from focal nerve injury along the length of the axon. In Isaacs' syndrome, myokymia generally responds well to phenytoin or carbamazepine, or both, suggesting a possible potassium channel irregularity.[5,6] Myoclonic twitches, jerks, or paroxysmal contractions can be caused by acute muscle contractions, such as when hiccups affect the diaphragm, which is referred to as positive myoclonus, or by brief lapses of contraction, which is called negative myoclonus, such as a hypnic jerk that occurs while falling asleep. Myoclonus may originate from lesions of the cerebral cortex, subcortex, or spinal cord. Although usually benign, they can be associated with ominous nervous system disorders such as multiple sclerosis, Parkinson's disease, Alzheimer's disease, Gaucher's disease, serotonin toxicity, some forms of epilepsy, subacute sclerosing panencephalitis, Creutzfeldt-Jakob disease, and occasionally intracranial hypotension. Complex repetitive discharges, such as

myotonia, are usually faster-firing (30-40 Hz) contractions than the frequency described as diaphragm flutter.

The myriad causes of involuntary muscle contraction suggest that treatment approaches depend on clinical presentation. However, no treatment has been effective permanently. Diaphragm flutter has been postulated to be caused by abnormal or increased excitation of the phrenic nerve associated with cardiomegaly, cervical disc herniation, cervical rib, lung disease, lymphadenitis, peritonitis, pleurisy, surgery, xiphoid fracture, psychogenic factors,[2,7-12] and, as in this case, physiologically and electrically increasing demand on the diaphragm. Besides the failure of this patient's medical therapies, others have reported failure using carbamazepine,[3,8] chlordiazepoxide,[13] chlorpromazine,[14] clonazepam,[1,15,16] clonidine patches,[17] diazepam,[8] diphenylhydantoin,[17-19] fluoxetine,[1] gabapentin,[1] haloperidol,[17] pimozide,[17] phenobarbital,[8] phenytoin,[1,3,15] trimethadione,[19] triphenylhexidyl,[16] valproic acid,[17,19] carbon dioxide therapy,[13] CPAP,[14,19] and phrenic nerve block with bupivacaine.[1,17,20] Phrenic nerve ablation surgery was reported to aid two of three patients for 6 and 12 months, respectively, with no further follow-up.[17,20]

This case of idiopathic diaphragmatic flutter is the first, to our knowledge, to be successfully treated by resting the diaphragm long-term without adverse effects. Phrenic nerve ablation did not resolve her flutter and either caused or apparently exacerbated her pain. The diaphragm pacemaker was detrimental initially and then was not adequately reapplied after the intercostal-phrenic nerve anastomoses were given enough time to heal. NVS rested the diaphragm and quickly eliminated the flutter. Thus, resting the diaphragm may be the first-line treatment strategy for this condition, but the permanence of its benefits remains in question.

Acknowledgments

Financial/nonfinancial disclosures: None declared.

References

1. Ramirez JD, Gonzales M, Hoyos JA, Grisales L. Diaphragmatic flutter: a case report and literature review. *Neurología*. 2015;30(4):249-251.
2. Samardhi H, Radford DJ, Fong KM. Leeuwenhoek's disease: diaphragmatic flutter in a cardiac patient. *Cardiol Young*. 2010;20(3):334-336.
3. Vantrappen G, Decramer M, Harlet R. High-frequency diaphragmatic flutter: symptoms and treatment by carbamazepine. *Lancet*. 1992;339(8788):265-267.
4. Larner AJ. Antony van Leeuwenhoek and the description of diaphragmatic flutter (respiratory myoclonus). *Mov Disord*. 2005;20(8):917-918.
5. Gutmann L, Gutmann L. Myokymia and neuromyotonia 2004. *J Neurol*. 2004;251(2):138-142.
6. Maddison P. Neuromyotonia. *Clin Neurophysiol*. 2006;117(10):2118-2127.
7. Rigatto M, De Medeiros NP. Diaphragmatic flutter. Report of a case and review of literature. *Am J Med*. 1962;32:103-109.
8. Jinnai K, Takahashi K, Shundo F, Komine Y, Gotoh K, Fujita T. Respiratory myoclonus. Report of a case with electromyographic study. *Jpn J Med*. 1986;25(3):288-292.
9. Philips JR, Eldridge FL. Respiratory myoclonus: Leeuwenhoek's disease. *N Engl J Med*. 1973;289:1390-1395.
10. Nakajima M, Hirayama K, Suzuki J, Shinotoh H, Yamada T. Diaphragmatic myoclonus of spinal origin. *Clin Neurol (Tokyo)*. 1986;26:13-18.
11. Scheifley CH, Saslaw MS. Diaphragmatic spasm associated with recurrent left pneumothorax. *Ann Intern Med*. 1947;26(1):129-133.
12. Soderstrom N. Clonic spasm of the diaphragm: observation in three cases with special attention to the ECG findings. *Acta Med Scand*. 1950;137(1):27-36.
13. Rigatto H, Castro Correa CE. Diaphragmatic flutter with an electromyographic study. *J Pediatr*. 1968;73(5):757-759.
14. Panigrahy N, Kumar PP, Chirla DK. Respiratory flutter syndrome in a neonate. *Indian Pediatr*. 2013;50(2):242-243.
15. Uzunhan TA, Çaliskan M, Nisli K, Orhan EK, Baslo B. Varicella-induced diaphragmatic flutter in a 12-year-old girl. *Pediatr Neurol*. 2013;49(5):385-386.
16. Iliceto G, Thompson PD, Day BL, Rothwell JC, Lees AJ, Marsden CD. Diaphragmatic flutter, the moving umbilicus syndrome, and "belly dancer's" dyskinesia. *Mov Disord*. 1990;5(1):15-22.
17. Cvietusa PJ, Nimmagadda SR, Wood R, Liu AH. Diaphragmatic flutter presenting as inspiratory Stridor. *Chest*. 1995;107(3):872-875.
18. Kobayashi I, Suzuki H, Kondo T, Yamauchi T, Ohta Y, Yamabayashi H. A case report of diaphragmatic flutter [in Japanese]. *Nihon Kyobu Shikkan Gakkai Zasshi*. 1990;28(5):777-780.
19. Kondo T, Tamaya S, Ohta Y, Yamabayashi H. Dual-respiratory rhythms: a key to diagnosis of diaphragmatic flutter in patients with HVS. *Chest*. 1989;96(1):196-209.
20. Corbett CL. Diaphragmatic flutter. *Postgrad Med J*. 1977;53(621):399-402.