LETTERS TO THE EDITOR

CONCURRENCE OF FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY AND MYASTHENIA GRAVIS

We describe the diagnostic and management problems related to the association of facioscapulohumeral muscular dystrophy (FSHD) and myasthenia gravis (MG) in two unrelated patients in whom the diagnosis and hence treatment of myasthenia was delayed because progressive muscle weakness was ascribed erroneously to the underlying muscular dystrophy.

The first patient was a 69-year-old man who had been clinically diagnosed with FSHD, confirmed by deletion analysis (33 kb) 2 years prior to admission, who came to our attention because of the sudden onset of dyspnea, dysphagia, dysarthria, ptosis, and severe weakness of all limbs. Electromyography (EMG) revealed findings suggestive of myopathy. Repetitive nerve stimulation produced a decremental response suggestive of myasthenia gravis. Acetylcholine receptor-binding antibodies were present (12 pmol/L). Muscle biopsy of the biceps brachii demonstrated an increased variability of fiber size, fiber splitting, type II fiber predominance, and several necrotic fibers with cellular infiltrates (Fig. 1). Dystrophin, utrophin, and sarcoglycan antibody staining were normal. The patient was started on dexamethasone (25 mg daily), azathioprine (50 mg daily), and pyridostigmine (270 mg daily) with remarkable improvement.

The second patient was a 60-year-old man who presented for evaluation of fluctuating dysarthria that began 8 months earlier. On a few occasions he had choked while swallowing. For 5–10 years, he had noticed mild fluctuating difficulty in raising his arms over his head, carrying heavy items, and standing up straight. There was no family history of weakness. On examination there was mild dysarthria and facial and limb-girdle muscle weakness (MRC grade 4). Acetylcholine receptor-binding antibodies were present (4.1 pmol/L). Serum creatine kinase showed a 1.5-fold elevation. The FSHD diagnosis was confirmed by deletion analysis (33 kb). EMG showed short-duration motor unit potentials. Repetitive nerve stimulation produced a decremental response. Pyridostigmine produced modest benefit. Following treatment with mycophenolate mofetil (1000 mg twice daily), the dysarthria and dysphagia improved.

Previous authors have observed the concurrence of myasthenia gravis with myotonic dystrophy[5] or limb-girdle muscular dystrophy,[2] and in another family with familial FSHD.[6]

In our Case 1, the diagnosis of MG may have been delayed because at least part of the initial symptoms of fatigability and shortness of breath attributed to FSHD were probably due to untreated MG. Although rare (<1%), respiratory dysfunction alone may be the presenting symptom of MG.[4] Although atypical phenotypes, such as progressive external ophthalmoplegia, have been described in one family with FSHD,[3] the diagnosis of FSHD was questioned when ptosis and severe bulbar dysfunction developed. In Case 2, the diagnosis of MG and FSHD were made at the same time. It is possible, however, that the fluctuation of proximal weakness noticed prior to the onset of additional bulbar symptoms might have been due to untreated MG.

Up to 80% of muscle biopsies from patients with FSHD show some degree of mononuclear inflammatory cell infiltration.[1] It has been suggested that FSHD is an inflammatory myopathy, but biopsies do not contain non-necrotic muscle fibers focally invaded by T-cells,[1] patients do not benefit from prednisone treatment when assessed carefully by computerized muscle testing in controlled trials,[7] and the presence of abundant mononuclear infiltrates does not affect disease progression.[7] Although the usual diagnostic approach is to unify symptoms and findings under a single diagnosis, the association of myasthenia gravis with FSHD in our two patients is intriguing and raises the possibility that immune mechanisms may be operative in FSHD.[8]

V. Sansone, MD,[1]
D. S. Saperstein, MD,[2]
R. J. Barohn, MD,[2]
G. Meola, MD[1]

[1] Department of Neurology, University of Milan, Istituto Policlinico San Donato, Milan, Italy
[2] Department of Neurology, University of Kansas Medical Center, Kansas City, Kansas, USA

1. Arahata K, Ishimara T, Fukunaga H, Orimo S, Lee JH, Goto K, Nonaka I. Inflammatory response in facioscapulohumeral mus-

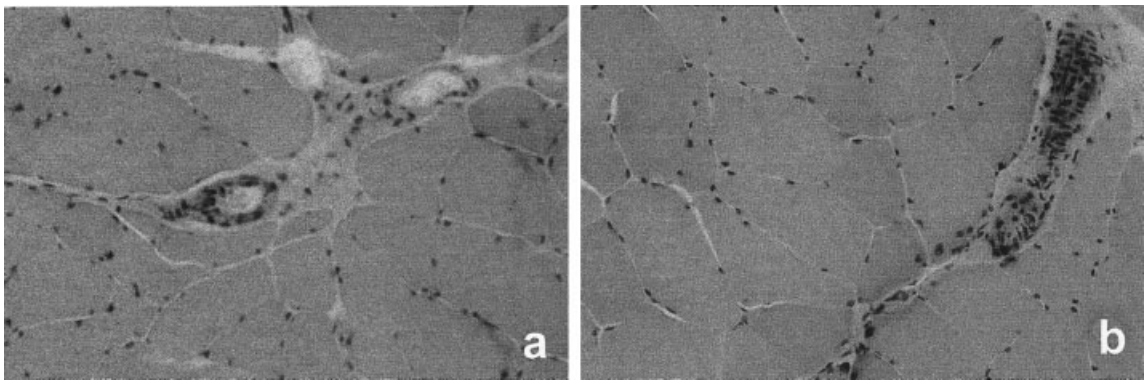

FIGURE 1. Biceps muscle biopsy from case 1, hematoxylin and eosin, ×20. (**a**) Note the variability in fiber size, fiber splittings, and mild increase of perifascicular tissue. (**b**) Note the enlarged blood vessel infiltrated with inflammatory cells.

cular dystrophy (FSHD): immunocytochemical and genetic analyses. Muscle Nerve 1995;S2:S56–S66.
2. Husain F, Ryan NJ, Hogan GR. Concurrence of limb girdle muscular dystrophy and myasthenia gravis. Arch Neurol 1989; 46:1047–1048.
3. Krasnianski M, Eger K, Neudecker S, Jakubiczka S, Zierz S. Atypical phenotypes in patients with facioscapulohumeral muscular dystrophy 4q35 deletion. Arch Neurol 2003;60:1421–1425.
4. Mantegazza R, Baggi F, Antozzi C, Confalonieri P, Morandi L, Bernasconi P, Andretta F, Simoncini O, Campanella A, Beghi E, Cornelio F. Myasthenia gravis (MG): epidemiological data and prognostic factors. Ann NY Acad Sci 2003;998: 413–423.
5. Maytal J, Spiro AJ, Sinnar S, Moshe SL. The coexistence of myasthenia gravis and myotonic dystrophy in one family. Neuropediatrics 1987;18:8–10.
6. McConigal A, Thomas AM, Petty RKH. Facioscapulohumeral muscular dystrophy and myasthenia gravis co-existing in the same patient: a case report. J Neurol 2002;249:219–220.
7. The FSH-DY Group. A prospective, quantitative study of the natural history of facioscapulohumeral muscular dystrophy (FSHD): implications for therapeutic trials. Neurology 1997; 48:38–46.
8. Tupler R, Barbierato L, Memmi M, Sewry CA, De Grandis D, Maraschio P, Tiepolo L, Ferlini A. Identical de novo mutation at the D4F104S1 locus in monozygotic male twins affected by facioscapulohumeral muscular dystrophy (FSHD) with different clinical expression. J Med Genet 1998;35:778–783.

Published online 18 August 2004 in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/mus.20118

AIR STACKING FOR COUGH ASSISTANCE

I read with interest the review by Perrin et al.[6] and found it comprehensive except for one important omission. The authors failed to note "air stacking" or the importance of maximal lung insufflations prior to attempts at manually assisted coughing.[4] Likewise, they recommended using mechanical insufflation–exsufflation (CoughAssist; J. H. Emerson Co., Cambridge, MA) at insufflation pressures of 20 cm H_2O, essentially the pressure required for normal tidal volumes in normally compliant lungs. However, the principal reason that we are able to manage patients with neuromuscular diseases without needing to resort to tracheotomy (with the sole exception of patients with advanced bulbar ALS)[2,3] is the effective airway secretion elimination afforded by optimal assisted coughing, that is, manual cough assist from the deep lung volumes of maximally insufflated lungs.[4] Undoubtedly, the reticence to expand lungs to the 60–70 cm H_2O pressures that we use routinely stems from the fear of barotrauma so common in patients with primarily lung disease and yet clinically nonexistent in our 800 noninvasive ventilation users. Indeed, our patients invariably find insufflation pressures of less than 35 cm H_2O to be ineffective or minimally effective at best. Although an average tidal volume may be 600 ml, an average effective cough volume is 2300 ml.[5] It is no surprise that studies that employ nocturnal-only nasal ventilation and ignore effective assisted coughing methods result in minimal benefits to patient longevity.[1] Any review article on long-term noninvasive ventilation is incomplete without recommendations for optimally effective assisted coughing.

J. Bach, MD

Department of Physical Medicine and Rehabilitation, University Hospital B-403, University of Medicine and Dentistry of New Jersey, 150 Bergen Street, Newark, New Jersey 07103-2406

1. Bach JR. Conventional approaches to managing neuromuscular ventilatory failure. In: Bach JR, editor. Pulmonary rehabilitation: the obstructive and paralytic conditions. Philadelphia: Hanley & Belfus; 1996. p 285-301.
2. Bach JR, Baird JS, Plosky D, Nevado J, Weaver B. Spinal muscular atrophy type 1: management and outcomes. Pediatr Pulmonol 2002;34:16–22.
3. Gomez-Merino E, Bach JR. Duchenne muscular dystrophy: prolongation of life by noninvasive respiratory muscle aids. Am J Phys Med Rehabil 2002;81:411—415.

4. Kang SW, Bach JR. Maximum insufflation capacity. Chest 2000; 118:61–65.
5. Leith DE. Lung biology in health and disease: respiratory defense mechanisms, part 2. In: Brain JD, Proctor D, Reid L, editors. Cough. New York: Marcel Dekker; 1977. p 545-592.
6. Perrin C, Unterborn JN, D'Ambosio C, Hill NS. Pulmonary complications of chronic neuromuscular diseases and their management. Muscle Nerve 2004;29:5–27.

Published online 18 August 2004 in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/mus.20116

Reply

We thank Dr. Bach for highlighting the importance of assisting cough in patients with respiratory insufficiency due to neuromuscular disease. This is a point we tried to emphasize in our review. Dr. Bach points out that we failed to mention "air stacking"; this was edited out of an earlier draft for the sake of brevity. However, we acknowledge that "air" or "breath" stacking can be a useful strategy to enhance cough effectiveness. The technique requires the use of a volume-limited (not bilevel) ventilator and intact glottic function. The patient retains several consecutive ventilator breaths by closing the glottis after each breath and achieves a total tidal volume that may exceed 2 L, depending on body size. The greater elastic force at these higher lung volumes enables the patient to attain greater airflow during cough, as found in earlier studies by Dr. Bach.[1]

With regard to his point about greater insufflation pressures during mechanical insufflation–exsufflation, we cannot entirely agree with Dr. Bach. We concur that an inspiratory pressure of 20 cm H_2O is on the low side, usually used only initially when patients are adapting to the technique. We most often use insufflation pressures closer to the upper end of the 20–40 cm H_2O range that we suggested in our review (i.e., 35–40 cm H_2O) for greater enhancement of cough. However, the 60–70 cm H_2O pressures suggested by Dr. Bach seem a bit high. In two recent articles on mechanical insufflation, the ranges given are closer to the range we gave in our article. In one by Sancho et al.[3] pressures used were +40 and −40 cm H_2O for insufflation and exsufflation, respectively, and in a second by Miske et al.[2] on children with neuromuscular disease, insufflation pressures ranged from 15 to 40 cm H_2O and exsufflation pressures from −30 to −50 cm H_2O. We would be reluctant to endorse the routine use of pressures as high as those suggested by Dr. Bach without better documentation of safety.

Nicholas S. Hill, MD

Division of Pulmonary, Critical Care, and Sleep Medicine, Tufts–New England Medical Center, Tufts University School of Medicine, 750 Washington Street, Room 257, Boston, Massachusetts 0211-1526

1. Bach JR. Mechanical insufflation-exsufflation: Comparison of peak expiratory flows with manually assisted and unassisted coughing techniques. Chest 1993;104:1553–1564.
2. Miske LJ, Hickey EM, Kolb SM, Weiner DJ, Panitch HB. Use of the mechanical in-exsufflator in pediatric patients with neuromuscular disease and impaired cough. Chest 2004;125:1406–1412.
3. Sancho J, Servera E, Diaz J, Marin J. Efficacy of mechanical insufflation-exsufflation in medically stable patients with amyotrophic lateral sclerosis. Chest 2004;125:1400–1405.

Published online 18 August 2004 in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/mus.20117