
Case report

Corticosteroid-induced myopathy mimicking therapy-resistant asthma

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Background: Therapy-resistant asthma is an important clinical problem. However, before considering asthma truly therapy resistant, it is essential to exclude diagnoses that may masquerade as therapy-resistant asthma, such as vocal cord dysfunction and recurrent aspiration, as well as factors related to loss of asthma control, including poor compliance, exposure to allergens, and sinusitis. Corticosteroid-induced myopathy may be an unrecognized but potentially important consideration in both settings.

Objectives: To describe a patient with corticosteroid-induced myopathy complicating recurrent exacerbations of asthma, which presented with persistently reduced airflow that mimicked therapy-resistant asthma.

Methods: A 20-year-old Japanese woman with severe intractable asthma who had a history of near-fatal attacks was admitted with recurrent asthma exacerbations that required long-term systemic corticosteroids.

Results: Wheezing episodes decreased but airflow limitation persisted, which was due to not only uncontrolled asthma but also corticosteroid-induced myopathy. Myopathy prevented the adequate use of inhalers, which in turn complicated the tapering of corticosteroids, leading to a vicious cycle. Careful and gradual reduction of corticosteroid dose, while continuing systemic administration of nonsteroidal antiasthma medications, resulted in a resolution of clinical and electromyographic signs of myopathy and pulmonary function abnormalities.

Conclusions: Corticosteroid-induced myopathy can masquerade as therapy-resistant asthma and can cause poor asthma control.

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INTRODUCTION

Systemic corticosteroids are essential in the treatment of acute asthma, but their long-term use at higher doses may cause adverse effects. Corticosteroid-induced myopathy complicating status asthmaticus was first reported in 1977,¹ followed by sporadic cases mostly associated with mechanical ventilation and muscle relaxant use, which likely aggravate myopathy.^{2–4} We report a case of corticosteroid-induced myopathy complicating recurrent exacerbations of asthma and presenting with persistently reduced airflow that mimicked therapy-resistant asthma.

CASE REPORT

A 20-year-old Japanese woman had asthma since the age of 2 years. The patient was admitted more than 10 times during

adolescence because of severe exacerbations, including a near-fatal attack that required mechanical ventilation. Precipitating factors of asthma were unclear, except for nonsteroidal anti-inflammatory drugs and intravenous succinate-containing corticosteroid preparations such as hydrocortisone, prednisolone, and methylprednisolone. Peak expiratory flow (PEF) monitored when the patient was ambulatory was 350 to 400 L/min when the patient was stable. The patient had never smoked cigarettes. The patient was sensitized to house dust mite and Japanese cedar pollen.

Asthma had worsened in March 1999 despite daily doses of inhaled fluticasone propionate, 800 μ g via a Diskhaler; pranlukast hydrate, 450 mg; and slow-release theophylline, 400 mg. Inhaled long-acting β -agonists were unavailable in Japan at that time. The patient was first admitted to our hospital because of acute asthma on April 19, 1999 (Fig 1). The results of chest x-ray examination were normal. The total IgE level was 37 IU/mL. Inhaled salbutamol via a metered-dose inhaler and intravenous betamethasone were given, successfully leading to discharge on April 27, 1999, while continuing treatment with oral prednisolone, 20 mg/d. However, the patient was readmitted on May 24, 1999, because of severe persistent wheezing and cough, with a decrease in the PEF to 180 L/min, which were unresponsive to initial ambu-

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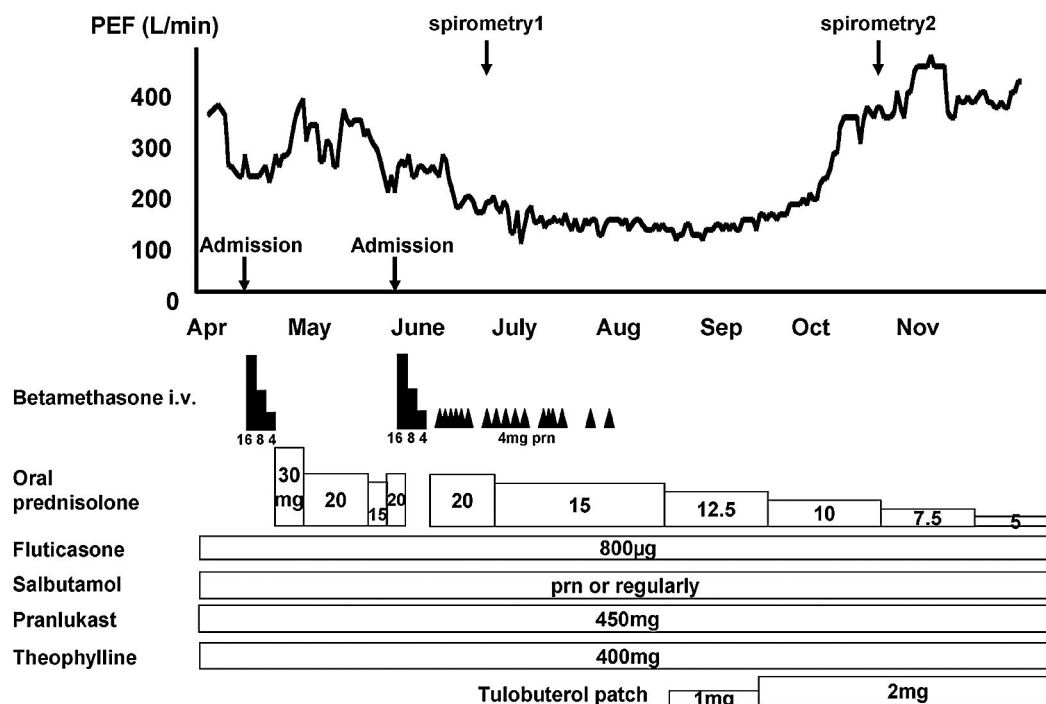


Figure 1. Summary of clinical course showing changes in peak expiratory flow and the main treatments and their doses.

latory treatment. On arterial blood gas analysis, the pH was 7.384, the P_{aO_2} was 59.3 mm Hg, and the P_{aCO_2} was 40.9 mm Hg while the patient was breathing room air. Use of a nebulizer was contraindicated because of paradoxical bronchoconstriction.

Despite additional treatment with salbutamol, 200 µg via a metered-dose inhaler, and 6-hourly intravenous injection of betamethasone, 4 mg, wheezing and airflow obstruction persisted and fluctuated. Use of systemic corticosteroids was continued at reduced doses, and wheezing episodes gradually decreased. However, 4 weeks after admission, PEF values decreased again to less than 200 L/min. The patient could not fully inspire fluticasone and had difficulties of walking. A chest x-ray film showed the elevation of bilateral diaphragms. Proximal muscle weakness was noted, but sensory and reflex abnormalities were absent. Pulmonary function was examined on June 29, 1999, when the patient was taking 15 mg/d of oral prednisolone and intermittent but still frequent courses of intravenous betamethasone. The results showed forced expiratory volume of 1 second of 0.80 L (27% of predicted), a vital capacity of 0.85 L (28%), a total lung capacity of 3.55 L (83%), a residual volume of 1.95 L (229%), a functional residual capacity of 2.36 L (115%), a maximal inspiratory pressure of -23 cm H₂O (25%), and a maximal expiratory pressure of 12.2 cm H₂O (15%). A combined restrictive and obstructive pattern of flow-volume loop was noted (Fig 2). Arterial blood gas analysis showed a pH of 7.355, a P_{aO_2} of 61.9 mm Hg, and a P_{aCO_2}

of 54.4 mm Hg while breathing oxygen at a rate of 0.5 L/min by nasal cannula. The serum creatine phosphokinase level was normal and myoglobinuria was absent. The results of a nerve conduction study were normal, but electromyography revealed myogenic abnormalities. Eosinophilia or cushingoid aspect was absent. Corticosteroid-induced myopathy was diagnosed.

A severe exacerbation of asthma recurred, with a decrease in the PEF to 120 L/min. The corticosteroid dose was increased transiently and was then gradually and carefully reduced. In addition to other systemic medications such as pranlukast and theophylline, tulobuterol patch, a transdermal

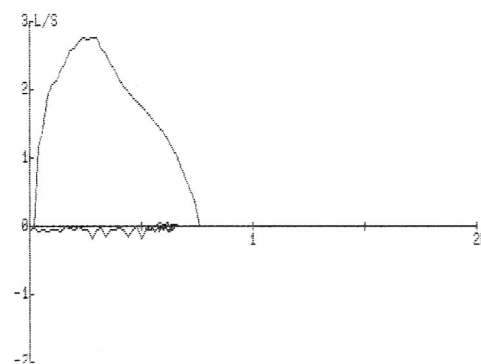


Figure 2. A flow-volume loop obtained at the diagnosis of corticosteroid-induced myopathy.

sustained-release β -agonist, was prescribed. When the prednisolone dose was tapered to 10 mg/d, the PEF values recovered to more than 300 L/min. Clinical and electromyographic signs of myopathy nearly resolved, and pulmonary function examined on October 19, 1999, improved to a forced expiratory volume of 1 second of 2.63 L (87%), a vital capacity of 3.50 L (116%), a total lung capacity of 4.67 L (111%), a residual volume of 1.31 L (160%), and a functional residual capacity of 2.37 L (125%). The flow-volume loop recovered to a simple pattern of mild airflow obstruction (Fig 3). The patient remained stable and was lost to follow-up when she moved the following year.

DISCUSSION

Prolonged treatment with systemic corticosteroids induced myopathy in a patient with intractable asthmatic with recurrent exacerbations. Reported cases of corticosteroid-induced myopathy complicating status asthmaticus have mostly been associated with mechanical ventilation and muscle relaxant use, which are likely to aggravate myopathy,²⁻⁴ whereas uncomplicated cases of corticosteroid-induced myopathy exist as well.⁵⁻⁷ Even a thorough review of such cases has not yielded a consensus with regard to the dose or duration of corticosteroid at which myopathy is likely to occur. Persistently low PEF values in our patient were attributed to both uncontrolled asthma and myopathy. Reduced inspiratory flow due to muscle weakness prevented the adequate use of inhaled medications, which precluded a prompt tapering of corticosteroid dose, leading to a vicious cycle. Systemic antiasthma drugs, such as the tulobuterol patch,^{8,9} might help the tapering of corticosteroids in such situations. Because the patient had experienced acute bronchospasm after intravenous succinate-containing corticosteroids,^{10,11} phosphate-containing corticosteroid betamethasone was used, although it may be more likely to induce myopathy than other compounds.^{1,12}

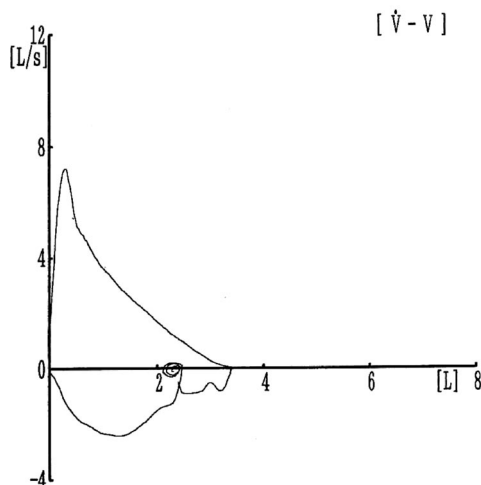


Figure 3. A flow-volume loop obtained at near resolution of myopathy.

Therapy-resistant asthma is an important clinical problem.^{13,14} Before asthma can be considered truly therapy resistant, however, conditions that can masquerade as therapy-resistant asthma, such as chronic obstructive pulmonary disease, vocal cord dysfunction, and recurrent aspiration, must be excluded.¹³⁻¹⁵ Factors related to loss of asthma control, including poor compliance or adherence to therapy, exposure to allergens, psychosocial and emotional factors, indoor or outdoor pollution, and sinusitis, should also be ascertained.¹³⁻¹⁵ Corticosteroid-induced myopathy is an important consideration in both settings. Putting too much confidence on airflow indices as the gold standard of asthma monitoring, as emphasized in recent asthma guidelines, may result in misdiagnosis. The essential therapeutic strategy is a reduction, not an increase, in corticosteroid dosage, in sharp contrast to purely uncontrolled asthma.^{13,14} This may be difficult, however, in patients such as ours who have intractable asthma.

REFERENCES

- MacFarlane IA, Rosenthal FD. Severe myopathy after status asthmaticus. *Lancet*. 1977;2:615.
- Shee CD. Risk factors of hydrocortisone myopathy in acute severe asthma. *Respir Med*. 1990;84:229-233.
- Lacomis D, Smith TW, Chad DA. Acute myopathy and neuropathy in status asthmaticus: case report and literature review. *Muscle Nerve*. 1993;16:91-98.
- Behbehani NA, Al-Mane F, D'yachkova Y, et al. Myopathy following mechanical ventilation for acute severe asthma. *Chest*. 1999;115:1627-1631.
- Knox AJ, Mascie-Taylor BH, Muers MF. Acute hydrocortisone myopathy in acute severe asthma. *Thorax*. 1986;41:411-412.
- Polsonetti BW, Joy SD, Laos LF. Steroid-induced myopathy in the ICU. *Ann Pharmacother*. 2002;36:1741-1744.
- Mitsui T, Umaki Y, Nagasawa M, Akaike M, Ohtsuka S, Odomi M, Aki K, Matsumoto T. Motor neuron involvement in a patient with long-term corticosteroid administration. *Intern Med*. 2003;42:862-866.
- Kume H, Kondo M, Ito Y, Suzuki R, Yamaki K, Takagi K. Effects of sustained-release tulobuterol on asthma control and beta-adrenoceptor function. *Clin Exp Pharmacol Physiol*. 2002;29:1076-1083.
- Fukuchi Y, Nagai A, Seyama K, et al. Clinical efficacy and safety of transdermal tulobuterol in the treatment of stable COPD: an open-label comparison with inhaled salmeterol. *Treat Respir Med*. 2005;4:447-455.
- Mendelson LM, Meltzer EO, Hamburger RN. Anaphylaxis-like reactions to corticosteroid therapy. *J Allergy Clin Immunol*. 1974;54:125-131.
- Nakamura H, Matsuse H, Obase Y, et al. Clinical evaluation of anaphylactic reactions to intravenous corticosteroids in adult asthmatics. *Respiration*. 2002;69:309-313.
- Thomas PK. Myopathy. *BMJ*. 1970;1:413-415.
- Chung KF, Godard P, Adelroth E, et al. Difficult/therapy-resistant asthma: the need for an integrated approach to define clinical phenotypes, evaluate risk factors, understand

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- pathophysiology and find novel therapies. ERS Task Force on Difficult/Therapy-Resistant Asthma. European Respiratory Society. *Eur Respir J*. 1999;13:1198–1208.
14. Wenzel SE, Fahy JV, Irvin CG, et al. Proceedings of the ATS workshop on refractory asthma: current understanding, recommendations, and unanswered questions. *Am J Respir Crit Care Med*. 2000;162:2341–2351.
15. Thomas P, Geddes DM, Barnes PJ. Pseudo-steroid resistant asthma. *Thorax*. 1999;54:352–356.

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