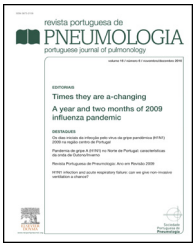
Rev Port Pneumol. 2014;20(1):42–45

revista portuguesa de
PNEUMOLOGIA
portuguese journal of pulmonology
www.revportpneumol.org



CASE REPORT

Successful treatment of atelectasis with Dornase alpha in a patient with congenital muscular dystrophy

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Received 15 October 2012; accepted 23 December 2012
Available online 2 October 2013

KEYWORDS
Dornase alpha;
Neuromuscular diseases;
Atelectasis

Abstract A 28-year-old neuromuscular patient chronically treated with nocturnal noninvasive ventilation developed pulmonary lobar atelectasis and daytime hypoxemia. Twenty four-hour 5 L/min oxygen was begun, while mechanical cough assist aids were applied for seven days. In the following three days, treatment with nebulized Dornase alpha (rhDNase) b.i.d. was tested, without any significant improvement. On 11 and 13th days rhDNase was instilled by flexible bronchoscopy. A rapid resolution of the atelectasis was observed with relief of hypoxemia, without significant side effects. On day 16 the patient was discharged without oxygen requirements. In non-intubated neuromuscular patients with atelectasis who do not respond successfully to non-invasive treatments intrabronchial instillation of rhDNase may safely help to improve airway clearance.

PALAVRAS-CHAVE
Dornase alfa;
Doenças neuromusculares;
Atelectasia

Tratamento bem sucedido de atelectasia com Dornase alfa num doente com distrofia muscular congénita

Resumo Um doente neuromuscular crónico de 28 anos de idade, tratado com ventilação noturna não invasiva, desenvolveu atelectasia lobar pulmonar e hipoxemia diurna. Foi iniciado suporte de oxigénio durante 24 horas, enquanto uma ajuda mecânica para a tosse era aplicada por 7 dias. Nos 3 dias seguintes o tratamento com Dornase alfa nebulizado (rgDNase) b.i.d. foi testado, sem qualquer melhoria significativa. No 11.° e 13.° dias rhDNase foi introduzido por broncoscopia flexível. Um restabelecimento rápido da atelectasia foi observado com alívio da hipoxemia, sem efeitos secundários significativos. No 16.° dia o doente teve alta sem necessidade de oxigénio. Em doentes neuromusculares não intubados, com atelectasia,

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0873-2159/$ – see front matter
http://dx.doi.org/10.1016/j.rppneu.2012.12.002

que não respondam positivamente a tratamentos não invasivos, a introdução intrabronquial de rhDNase pode com segurança ajudar a melhorar a abertura das vias respiratórias.

Introduction

In neuromuscular disease, impairment of cough mechanisms due to expiratory muscle weakness can favor the development of atelectasis after pulmonary infections.[1] This can lead to hypoxia with a life-threatening clinical situation. There is a lack of evidence-based studies on the management of infectious atelectasis.[2] Although chest physiotherapy, mechanical in-exsufflation (MI-E) and high-frequency chest wall oscillation (HFCWO) improve airway clearance,[3–6] they may not be sufficient, particularly when secretions become highly viscous due to accumulation of significant amounts of extracellular DNA.

Recombinant human Dornase alpha (rhDNase) may cleave and depolymerize extracellular DNA, and separate it from proteins: this allows endogenous proteolytic enzymes to break proteins and decrease viscoelasticity and surface tension of purulent sputum. In patients with cystic fibrosis rhDNase has proved extremely effective, with both aerosol administration[7] and bronchoscopic instillation.[8] Studies in newborns or in children have reported beneficial effects of rhDNase on atelectasis in non-cystic fibrosis patients,[9,10] and anecdotal reports have suggested a beneficial effect in respiratory syncytial virus bronchiolitis[11] and in atelectasis due to mucus plugs in newborns and children.[12]

Most of these studies were performed by instillating the drug directly into the trachea in intubated patients. Although most patients showed an improvement within 24 h, in some of them direct instillation resulted in clinical deterioration, presumably due to a mucus mobilization that was too rapid.[10] This effect may be dangerous in neuromuscular patients if means for removal of the mucus are not immediately available, or if the rate of mobilization exceeds capacity of elimination. However, no studies reporting effects of rhDNase in neuromuscular patients have been published. In this article we describe the favorable clinical course of a non-intubated neuromuscular patient with infectious atelectasis treated with bronchoscopic instillation of rhDNase.

Case report

A female patient with a congenital muscular dystrophy had been treated with nocturnal nasal noninvasive positive pressure ventilation (NIV) since she was 20. At the age of 26 she was hospitalised for a complete atelectasis of the right lower lobe, and had recovered after more than a month with the application of an intensive combined protocol of HFCWO (The Vest Airway Clearance System, Hill-Rom St. Paul, MN, USA) plus manual and mechanical assist cough (In-Exsufflator, Cough-Assist®, Philips Respironics, Murrysville, PA, USA). Her clinical condition remained good until the age of 28, when her lung function tests showed the following values: vital capacity 0.55 L (16% of the predicted value), maximal inspiratory pressure 10 cmH_2O (11% of predicted), maximal expiratory pressure 14 cmH_2O (13% of predicted), and peak cough expiratory flow 80 L/min. A few months later, due to the appearance of fever and copious mucus production, she was treated with manual and mechanical chest physiotherapy plus antibiotics (ceftriaxone) initially. However, she still complained of dyspnea and a feeling of retained secretions, and was then admitted to hospital. She had a severe left convex scoliosis with a mean Cobb angle of over 70°. After a chest X-ray, a CT scan was performed (Fig. 1) which showed atelectasis of the right lower lobe. Her diurnal arterial oxygen saturation (SpO_2) fluctuated between 82 and 85% in room air, while $PaCO_2$ was normal. The patients showed minimal clinical signs of dehydration, namely dry mouth. She had good skin turgor and normal urine output. Haematocrit and electrolytes were normal except for potassium which was lower than normal. We began nutritional support and hydration because the patient was not able to eat and drink enough. Negative results were obtained from sputum cultures; however, intravenous antibiotics were administered. Twenty-four-hour NIV was begun, with the addition of oxygen (5 L/min), as NIV alone was not enough to maintain SpO_2 above 90%. Fifteen-twenty minutes sessions of HFCWO at a pressure of 5 cm H_2O and a frequency of 12 Hz were performed; each session was followed by five or six sessions of mechanical assist cough with an In-Exsufflator at pressures of +40/−45 cm H_2O, delivered respectively over 3 and over 2 s, with an abdominal thrust timed to the exsufflation cycle. This protocol was applied 4 times/day; additionally, In-Exsufflator

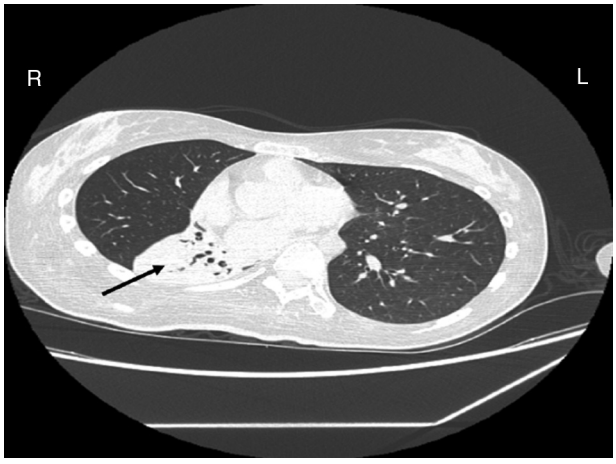

Figure 1 Chest CT scan at admission: atelectasis of the lower right lobe.