CASE REPORT

Treatment of plastic bronchitis in acute chest syndrome of sickle cell disease with intratracheal rhDNase

S S Manna, J Shaw, S M Tibby, A Durward

Plastic bronchitis, a condition associated with widespread mucous plugging of the tracheobronchial tree, is an increasingly recognised bronchoscopic finding in acute chest syndrome of sickle cell disease. Removal of casts by bronchoscopy is technically challenging. We describe a child with acute chest syndrome where bronchoscopic removal of extensive tracheobronchial plastic casts was facilitated by intratracheal rhDNase.

Acute chest syndrome (ACS) in sickle cell disease, which is characterised by fever, respiratory distress, and new pulmonary infiltrates, is a common cause of hospitalisation and accounts for 25% of deaths in these patients. The underlying pathophysiological mechanisms may include pulmonary infection, infarction, sequestration, oedema, and bone marrow or fat embolism. Recently a high prevalence (72%) of pulmonary infection, infarction, sequestration, oedema, and bone marrow or fat embolism has been reported in patients with ACS following flexible bronchoscopy. The role of physiotherapy, mucolytics, and fibroptic bronchoscopy for removal of these “plastic” casts has not been established.

Nebulised recombinant human DNase (rhDNase) is effective in clearing thick respiratory secretions in patients with cystic fibrosis. Intratracheal rhDNase has also been used in the treatment of life threatening mucus plugging in asthma and lung atelectasis in neonates. Here we describe a ventilated child with ACS complicated by plastic bronchitis who had a significant and sustained improvement in oxygenation following intratracheal administration of rhDNase to facilitate bronchoscopic removal of the mucus plug.

CASE REPORT

A 7 year old boy with homozygous sickle cell disease, who had multiple previous hospital admissions for sickle crises, presented to a haematology unit with a short history of fever, cough, and dyspnoea. On presentation he was pyrexial (38.1°C), with a respiratory rate of 40 breaths per minute, and required oxygen therapy via nasal prongs to maintain oxygen saturations above 90%. Chest x-ray examination revealed bilateral streaky pulmonary infiltrates. The haemoglobin was 76 g/l, and the white cell count 8.2 × 10^9/l. Despite conventional medical treatment with morphine, intravenous hydration, antibiotics (ceftriaxone and clarithromycin), and a partial exchange transfusion (40 ml/kg of packed red cells) his respiratory condition deteriorated over 48 hours, requiring admission to our paediatric intensive care unit.

The patient required tracheal intubation and mechanical ventilation for hypoxaemic respiratory failure (oxygen saturations of 83% in 100% face mask oxygen, arterial blood gas: pH 7.43, pCO2 5.6 kPa, and pO2 7.1 kPa). A lung protective strategy was adopted accepting oxygen saturations of 90% with permissive hypercapnoea. Following a two hour period of conventional mechanical ventilation (FiO2 1.0, peak inspiratory pressure 32 cm H2O, PEEP 10 cm H2O), which included manual lung recruitment manoeuvres, muscle relaxation, and prone positioning, the patient deteriorated and required high frequency oscillatory ventilation (HFOV) using a Sensormedics 3100A oscillator. The arterial blood gas prior to HFOV was pH 7.22, pCO2 9.8 kPa, pO2 9.2 kPa and the oxygation index calculated at 21 (mean airway pressure × percentage oxygen / pO2, kPa × 7.5). The chest x-ray picture showed patchy consolidation and atelectasis bilaterally (fig 1). Our standard paediatric intensive care unit strategy for lung recruitment on HFOV was followed, with initial settings on HFOV set at a mean airway pressure of 28 cm H2O, amplitude 50 cm H2O, frequency 9 Hz, and bias flow 30 l/min. Over the first 24 hours on HFOV the oxygation index remained above 22 despite a further exchange transfusion (80 ml/kg of packed red cells) which reduced the sickle cell percentage from 38% to 14%. The haematocrit was maintained between 0.25 and 0.3. Inhaled nitric oxide was not used.

At this point a diagnostic flexible bronchoscopy (Olympus 2.8 mm) was performed which revealed extensive, thick, white adherent mucus plugs characteristic of plastic bronchitis obstructing the right middle lobe, right lower lobe, and left lower lobe bronchi. These could not be displaced with physiotherapy, intratracheal 0.9% saline, or negative pressure suction via the bronchoscope port. Intratracheal rhDNase (2.3 mg in 20 ml of 0.9% saline) was then instilled under direct bronchoscopic vision in each bronchus followed by chest physiotherapy. Adequate oxygation and ventilation was maintained throughout the bronchoscopic procedure as the

Figure 1 Chest x-ray picture during high frequency oscillation [pre-bronchoscopy] showing widespread bilateral patchy consolidation of the lungs.
bronchitis was passed via a sealed port in the endotracheal tube connector. Within 10 minutes, the fragmented mucus plugs had dislodged and were easily removed via the bronchoscopic suction port. Some of the casts showed distinctive branching bronchial patterns. Histology of the casts revealed bronchial epithelial cells, mature squamous cells, polymorphs, and fat laden macrophages. Cultures remained sterile after 48 hours and mycoplasma titres were also negative.

Following treatment with rhDNase there was an immediate and sustained improvement in oxygenation with a fall in the oxygenation index from 22 to 15 within four hours. This corresponded with an improvement in the appearance of the chest x-ray picture. Conventional ventilation was successfully re instituted 12 hours after rhDNase therapy. The clinical course was however complicated by neurological sequelae (cerebral infarction) and extubation had to be deferred another 12 days.

DISCUSSION

Plastic bronchitis is an increasingly recognised bronchoscopic finding in patients with ACS, with an incidence of 7% in the case series by Moser and colleagues. Although the clinical presentation of plastic bronchitis may vary, in severe cases the branching plastic casts may obstruct the airways, causing worsening respiratory failure. Since a quarter of the patients with sickle cell disease die from acute chest syndrome, removal of obstructive casts in ACS complicated by plastic bronchitis may offer a good therapeutic option.

Traditionally treatment of ACS includes hydration, analgesia, antibiotics, optimising tissue oxygenation, and in severe cases exchange blood transfusions. Recently the adoption of a lung protective strategy with low tidal volumes, permissive hypercarbia, and tolerance of lower arterial oxygen saturations has shown improved survival in patients with acute respiratory distress syndrome. However, adopting and maintaining such a strategy in patients with severe ACS is difficult as both hypoxia and hypercarbia may worsen the sickling phenomenon.

In this case report we demonstrate two important points. First, the diagnosis of plastic bronchitis with intrabronchial obstruction could only be made on flexible bronchoscopy, with the radiologic appearance showing widespread bilateral consolidation (fig 1). Second, mechanical removal of the obstructive plugs was successfully achieved by the administration of intratracheal rhDNase when other conventional methods (physiotherapy, saline lavage, and bronchoscopic suction) had failed. This was associated with a clinical and radiological improvement in oxygenation, allowing rapid weaning from the high frequency oscillator to conventional mechanical ventilation.

Recombinant human DNase is thought to reduce the viscoelasticity of purulent sputum from cystic fibrosis patients by hydrolysis of extracellular DNA. However, rhDNase may improve mucociliary clearance by altering the physical and rheological properties of sputum independent of its DNA content. Although the bronchial casts in our patient were cellular, one could postulate that rhDNase may be effective in cases of ACS associated with acellular casts.

Treatment of severe mucus plugging with rhDNase in other conditions associated with plastic bronchitis such as asthma and atelectasis is safe, well tolerated, and effective. In this subgroup of patients with marked airway obstruction secondary to mucus plugs the benefits of treatment outweigh the potential risk of blood streaking of the sputum that has been reported. This is particularly important when the cause for ongoing hypoxia may be caused by mechanical airway obstruction.

Considering the high frequency of plastic bronchitis in ACS, we believe it is reasonable to perform a diagnostic bronchoscopy early in the course of the disease, in those patients who show signs of respiratory deterioration. It is tempting to speculate the role of early bronchoscopic evaluation in these patients even prior to the requirement for mechanical ventilation. However, further studies to evaluate the role of rhDNase in patients with sickle cell disease are warranted.

References

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