Successful treatment of empyema thoracis with human recombinant deoxyribonuclease

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Empyema thoracis is a serious condition with a significant mortality. The importance of drainage of the pleural space was recognised by Hippocrates. Simple percutaneous tube drainage may fail in over 50% of patients, most of whom will then require surgical procedures. The overall mortality of pleural empyema is 10%. The use of intrapleural enzymes to aid drainage was first described in 1949 using a mixture of streptokinase and streptococcal DNase. In recent years purified streptokinase has come into widespread use, but recent evidence suggests that streptokinase has no effect on pus viscosity but that deoxyribonuclease (DNase) reduces the viscosity of pus. We report the first use of human recombinant DNase given intrapleurally to treat an empyema which had not resolved after standard treatment with streptokinase.

CASE REPORT

An 83 year white woman was admitted with a 4 day history of fevers and rigours with breathlessness and right sided pleurisy. On examination she was pyrexial and toxic with arterial desaturation (SpO2 89%) and signs of a right pleural effusion. She was in atrial fibrillation with a peripheral blood picture of neutrophilia and mild renal impairment (white cell count 14.8 x 10^9/l, creatinine 0.24 mmol/l).

The patient was treated with intravenous erythromycin, ceftriaxone, and metronidazole. Blood cultures grew Streptococcus pneumoniae sensitive to penicillin and treatment was changed to roxithromycin orally and benzyl penicillin intravenously. Two days after admission the pleural effusion had increased and 900 ml of purulent fluid were aspirated. This had a protein content of 35 g/l, glucose <0.3 mmol/l, and lactate dehydrogenase (LDH) of 9412 units/l. Gram stain showed Gram positive cocci. Two days later the fluid had re-accumulated and an intercostal catheter was inserted. After 1 week of continuous drainage yielding 1.4 l the patient remained systemically unwell and toxic and the chest radiograph had not improved. The patient was then referred to the thoracic team.

A second intercostal catheter was inserted lower down into the main body of the empyema and intrapleural streptokinase was given for 3 days at a daily dose of 250 000 units. There was further drainage of 330 ml on day 1, 110 ml on day 2, and 100 ml on day 3. At the end of this period the chest radiograph had improved, but there was still a substantial pleural collection and the patient remained unwell (fig 1).

The patient adamantly refused to consider thoracic surgical intervention and, after explanation of the experimental nature of the treatment, agreed to be treated with intrapleural human recombinant DNase (dornase alfa, Pulmozyme).

Five mg of dornase alfa and 50 ml of normal saline were thus instilled into the pleural space daily for 3 consecutive days with clamping of the tube for 4 hours after instillation. Suction at 20 cm H2O was applied as it had been throughout the period of intercostal drainage. On day 1 330 ml of thin pus drained, on day 2 a further 170 ml, and on day 3 300 ml drained with considerable improvement both in the radiograph (fig 2) and in the patient’s systemic symptoms. Her appetite and energy levels improved and she became afebrile. The chest drains were removed on day 23 of her admission.

The patient was discharged on oral clindamycin. Her chest radiograph 1 month after discharge had further improved. Antibiotics were discontinued and she remains well 3 years later with no systemic symptoms, no respiratory impairment, and a virtually normal chest radiograph.

DISCUSSION

Successful treatment of pleural empyema depends on adequate drainage of the pleural space. The two factors which seem likely to prevent successful drainage by intercostal tube are loculation of the fluid by formation of fibrinous strands within it and increasing viscosity and adherence of the pus to the pleural surfaces, possibly preventing lung expansion by coating the visceral pleura. It is over half a century since Tillett and Sherry demonstrated the beneficial effects of intrapleural enzyme treatment using fairly crude streptococcal extracts. A more refined version of the extracts was later marketed by Lederle & Co as Varidase and continued to be used, particularly in the UK, to treat empyema. Because of some worries regarding the antigenicity of this fairly crude preparation, there has been much interest in...
Figure 2: Posteroanterior radiograph of patient after 3 days of treatment with intrapleural DNase showing marked reduction in the size of the right sided empyema.

LUNG ALERT

US mortality statistics: the increasing importance of influenza and the role of RSV

Mortality attributable to influenza is difficult to estimate because death certificates do not often include relevant data. Thompson et al have developed a statistical model using national mortality and viral surveillance data to estimate influenza deaths by type and subtype from 1976 to 1999 and, for the first time, deaths from respiratory syncytial virus (RSV) from 1990 to 1999. Using a new technique, they looked at data for underlying respiratory and circulatory deaths as these figures were more likely to include influenza related deaths than if only pneumonia and influenza deaths were considered. There was a significant increase in influenza associated deaths over this period (p = 0.001). Influenza was estimated to be associated with a mean of 3.1% of underlying respiratory and circulatory deaths and RSV with 1%. Influenza A (H3N2) was associated with the most deaths, followed by RSV. The bulk of deaths from both viruses occurred among those aged over 65. Influenza caused more deaths in all age groups than RSV, except in children younger than 1 year.

This study underlines the importance of prevention measures against viral infections in our ageing population, and the need for development of an effective vaccine against RSV.

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