CASE REPORT

Successful treatment of empyema thoracis with human recombinant deoxyribonuclease

G Simpson, D Roomes, B Reeves

Fibrinolytic enzymes, particularly streptokinase, are now widely used to treat empyema thoracis. Recent in vitro 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.

Empyema thoracic 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 pleura empyema is 10%. The use of intrapleural enzymes to aid drainage was first described in 1949 using a mixture of streptokinase and streptococcal DNase. A more refined version of this fairly crude preparation, there has been much interest in recombinant deoxyribonuclease (DNase) given intrapleurally to treat an empyema which had not resolved after standard treatment with streptokinase.

Empyema thoracic 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 pleura empyema is 10%. The use of intrapleural enzymes to aid drainage was first described in 1949 using a mixture of streptokinase and streptococcal DNase. A more refined version of this fairly crude preparation, there has been much interest in recombinant deoxyribonuclease (DNase) given intrapleurally to treat an empyema which had not resolved after standard treatment with streptokinase.

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 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 1 Posteroanterior radiograph of patient following 3 days of treatment with intrapleural streptokinase.
the use of highly purified streptokinase in this context. Results of controlled studies of this treatment have been mixed,2 7 and it was our clinical impression that the purified preparation was much less effective than the older preparation which contains a small proportion of streptococcal DNase. Subsequent studies showed that streptokinase alone has no effect on pus viscosity but that the inclusion of either streptococcal or human recombinant DNase reduced viscosity markedly.6 Similar results were obtained in an animal model using Varidase.7 DNase acts by depolymerisation of polymerised deoxribonucleoproteins and is a ubiquitous enzyme which will act on DNA of bacterial as well as mammalian origin, though the DNA in empyema pus is probably mainly derived from leucocytes.

In the case reported here fibrinolytic therapy failed and the patient was refusing surgical intervention. We believe this is the first reported use of human recombinant DNase to treat empyema thoracis and that the improvement in the patient’s condition was related to the reduction in viscosity and adherence of the pus by the DNase which thus aided drainage of the pleural cavity.

Human recombinant DNase seems to be extremely safe when given by nebulisation as it is in the treatment of cystic fibrosis. The experience with fibrinolytic agents suggests little absorption of enzymes from the pleural cavity when used to treat empyema.3 There were certainly no adverse reactions to the DNase used in this case. We would suggest that this clinical anecdote together with the in vitro evidence would support the inclusion of human recombinant DNase in future trials of intrapleural enzyme therapy in the treatment of empyema.

LUNG ALERT

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

Mo r tality 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.

Z Khaleelii
London Chest Hospital, London;
zhalekhkholeeli@hotmail.com
Successful treatment of empyema thoracis with human recombinant deoxyribonuclease

G Simpson, D Roomes and B Reeves

Thorax 2003 58: 365-366
doi: 10.1136/thorax.58.4.365

Updated information and services can be found at:
http://thorax.bmj.com/content/58/4/365

These include:

References
This article cites 6 articles, 1 of which you can access for free at:
http://thorax.bmj.com/content/58/4/365#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections
Inflammation (1020)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/