Treatment of Clotted Hemothorax with Fibrinolysin

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The lysis and aspiration of a clotted hemothorax by means of an effective enzymatic agent is highly desirable. Various enzymes have been used for this purpose but all have certain disadvantages. Trypsin has an irritative effect of pleural pain on injection and often shows a toxic reaction due to the enzyme or breakdown of protein products. The inhibitor (antitrypsin) normally present in the serum or exudates rapidly increases in concentration after the use of trypsin. This may require an increasing dosage of trypsin with successive treatments.

Streptokinase-streptodornase acts primarily as an activator and depends on plasminogen in the wound exudates. Occasional pyrogenic reactions are encountered with this enzyme. Inhibitors to streptokinase are also present in many patients who have had streptococcal infections.

The proenzyme, profibrinolysin, circulates in human and animal plasma. Proenzyme becomes activated during life or after death of the organism. Some of the known activators are streptokinase, staphylokinase, cytofibrinolysokinase, epinephrine, chloroform and potassium cyanide.

Dastre noted the proteolytic substance of blood serum and named this fibrinolysin. Loomis isolated the active proteinase in 1946. Fibrinolysin is an euglobin, soluble in saline and when mixed with antibiotics loses little activity. Fibrinolysin attacks only fibrin, fibrinogen or prothrombin.

The following animal experiments were done to simulate postoperative and traumatic clotted hemothorax and to assess the effectiveness of fibrinolysin solution.

Experimental Method

A standard hemothorax was produced in the following manner. Blood was drawn into sterile beakers from donor dogs, covered and allowed to clot. These clots were refrigerated for 24 hours. Well formed serum free clots weighing from 96 to 300 grams were obtained. These clots were then placed by a left thoracotomy into the pleural cavity of 16 dogs. At the time of death or sacrifice both chest cavities were explored for residual fluid or clot. Previous experimental studies show that air or fluid may often readily pass to the opposite side of a dog's pleural space. Preliminary in vitro studies were done to determine the proteolytic effect of bovine fibrinolysin solution on clotted dog's blood. Clots weighing 200 grams were incubated at 37°C. without agitation in 200 units of fibrinolysin solution and were reduced approximately by one-fourth in 24 hours. Control clots of the same weight under similar conditions but without fibrinolysin failed to show any liquefaction.

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Series I—Table I

Eleven dogs had left thoracotomy and left lower lobectomy. A preformed serum-free clot was placed in the pleural cavities of all these animals in order to simulate a postoperative clotted hemothorax. No attempt was made to pleuralize the bronchial stump after lobectomy. Daily intramuscular injections of 600,000 units of procaine penicillin were given up to one week. On the first postoperative day multiple site aspirations were done to determine if any spontaneous liquefaction had occurred. Fibrinolysin, 200 units diluted with saline to a volume of 20 cc., was then injected into the left lower chest, except in dog No. 69 where 400 units of fibrinolysin was used. Daily multiple site needle aspirations were then done until the animal died or was sacrificed.

One dog died seven days postoperatively from atelectasis and pneumonia. The remainder of the animals were serially sacrificed. In all animals the original clot was effectively reduced by the lytic action of fibrinolytic solution. None of the animals showed any impairment in wound healing. All of the unpleuralized bronchial stumps showed varying stages of healing. All the animals showed expanded functioning lungs with little pleural reaction except dogs No. 131 and No. 136 (atelectasis or pneumonia).

Series II—Table II

Five dogs had left thoracotomy performed with placement of a preformed serum free clot in order to simulate a standard traumatic hemothorax. Multiple serial aspirations were done on the first postoperative day up to the time of sacrifice. Fibrinolysin solution 200 units diluted to a volume of 10 cc. was injected into the left pleural space after the first thoracentesis. Fibrinolysin solution effectively lysed the clotted hemothorax in all these dogs. None of the animals in Series I or II showed any objective reactions or pleural pain to the injection of fibrinolysin.

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Wgt.of Clot in Gms.</th>
<th>Total Dosage of Fibrinolysin Units Vol in cc</th>
<th>No. of Daily Injections</th>
<th>Total Aspirated Vol in cc</th>
<th>Fate Post-operatively</th>
<th>Post-mortem Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>130</td>
<td>175</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>10</td>
<td>Killed 3 Days</td>
</tr>
<tr>
<td>131</td>
<td>200</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>50</td>
<td>Killed 3 Days</td>
</tr>
<tr>
<td>73</td>
<td>96</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>282</td>
<td>Killed 5 Days</td>
</tr>
<tr>
<td>48</td>
<td>186.5</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>71</td>
<td>Killed 5 Days</td>
</tr>
<tr>
<td>47</td>
<td>109.5</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>50</td>
<td>Killed 5 Days</td>
</tr>
<tr>
<td>136</td>
<td>105</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>50</td>
<td>Died 7 Days</td>
</tr>
<tr>
<td>98</td>
<td>170</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>68</td>
<td>Killed 8 Days</td>
</tr>
<tr>
<td>99</td>
<td>158</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>104</td>
<td>Killed 8 Days</td>
</tr>
<tr>
<td>69</td>
<td>150</td>
<td>400</td>
<td>40</td>
<td>1</td>
<td>42</td>
<td>Killed 12 Days</td>
</tr>
<tr>
<td>1</td>
<td>150</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>60</td>
<td>Killed 12 Days</td>
</tr>
<tr>
<td>126</td>
<td>120</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>68</td>
<td>Killed 28 Days</td>
</tr>
</tbody>
</table>

Table I

THORACOTOMY, LOBECTOMY, & INSTILLED CLOT TREATED WITH FIBRINOLYSIN

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CLOTTED HEMOTHORAX

The assay of antifibrinolysin levels in the blood of the pretreated animals was attempted but discontinued because of technical difficulties. The original thought being a more accurate estimation in determining the dosage of fibrinolysin needed to lyse the hemothorax.

Clinical Experience

Experience in World War II indicated that from 15 to 20 per cent of hemothoraces clot.11 Organizing hemothorax occurs less frequently in civilian practice. Four clinical cases of clotted hemothorax were treated with fibrinolysin solution.

Case Reports

Case 1: A 34 year old white man was seen four days after injury with right hemopneumothorax. The upper six anterior ribs were fractured. Preliminary multiple level taps failed to aspirate blood. One hundred units of fibrinolysin was injected into the right pleural space the first and second days. Daily aspirations yielded 300, 250, 700, and 280 cc. of blood fluid. A total of 1530 cc. of lysed blood was aspirated with reexpansion of the lung.

Case 2: A 36 year old white man was seen five days after a penetrating wound of the right chest, with hemopneumothorax. Fibrinolysin solution 100 and 200 units was given on the first and third days. Daily aspirations yielded 150, 75, 150, 50 and 200 cc. lysed blood, a total of 525 cc. On the third day he had chills, fever 102°F. and pleural pain after fibrinolysis was injected. The pain lasted several hours and was relieved with intramuscular morphine sulphate grains 1/6. Decortication was done two weeks after admission. An organizing pleural peel and multiloculated cavities were present explaining in part the ineffectiveness of the fibrinolysin solution in dealing with the hemothorax.

Case 3: A 20 year old white man was seen 12 days after upper right anterior rib fracture with hemothorax. One injection of fibrinolysin 200 units was given on the first day. Daily aspirations yielded 850, 30, and 30 cc. A total of 910 cc. of bloody fluid was aspirated and the lung expanded.

Case 4: A 60 year old white man was seen two days after a penetrating wound with left hemopneumothorax. Fibrinolysin solution, 100 units was given on the first and third days. Daily aspirations obtained 200, 150, 750 and 300 cc. of bloody fluid. A total of 1,400 cc. of lysed blood was removed with expansion of the lung.

Fibrinolysin solution in three human hemothoraces proved to be an effective method of removing clotted hemothorax. Failure in Case 2 can probably be explained by the multiloculated cavities making the enzymatic action of fibrinolysin ineffectual. The fever and pleural pain after the intrapleural injection of fibrinolysin solution probably represents an antigenic reaction. Margulis et al12 have also reported on the effectiveness of fibrinolysin in the treatment of clotted hemothorax.

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Wgt. of Clot in Gms.</th>
<th>Total Dose of Fibrinolysin Units</th>
<th>No. of Daily Injections</th>
<th>Total Aspirated Vol. in cc.</th>
<th>Fate Post-Operatively</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>200</td>
<td>200</td>
<td>10</td>
<td>None</td>
<td>Killed 1 Day</td>
<td>No clot or fluid</td>
</tr>
<tr>
<td>123</td>
<td>300</td>
<td>200</td>
<td>10</td>
<td>None</td>
<td>Killed 3 Days</td>
<td>No clot or fluid</td>
</tr>
<tr>
<td>74</td>
<td>150</td>
<td>200</td>
<td>10</td>
<td>None</td>
<td>Killed 7 Days</td>
<td>10cc clot, 8cc fluid</td>
</tr>
<tr>
<td>55</td>
<td>100</td>
<td>200</td>
<td>10</td>
<td>None</td>
<td>Killed 15 Days</td>
<td>No clot or fluid</td>
</tr>
<tr>
<td>70</td>
<td>250</td>
<td>200</td>
<td>10</td>
<td>None</td>
<td>Killed 30 Days</td>
<td>No clot or fluid</td>
</tr>
</tbody>
</table>
SUMMARY

Intrapleural administration of fibrinolysin solution proved to be an effective agent in the treatment of experimental clotted pneumothorax. Clinical application similarly was effective in three of four patients.

RESUMEN

La administración intrapleural de fibrolisisina en solución ha mostrado ser un agente efectivo para tratar el neumotorax con coágulos hecho experimentalmente.

La aplicación clínica similarmente se mostró efectiva en tres enfermos.

RESUME

L'administration intrapleurale d'une solution de fibrinolysine s'est montrée être un agent efficace dans le traitement du pneumothorax expérimental.

L'application clinique fut également efficace chez trios malades sur quatre.

ZUSAMMENFASSUNG

Die intrapleurale Anwendung einer fibrinolytischen Lösung erwies sich als ein wirksames Mittel bei der Behandlung eines experimentell verklebten Pneumothorax. Die klinische Anwendung war ähnlich wirksam bei drei von vier Kranken.

REFERENCES