Intractable Uraemic Pericardial Effusion

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INTRODUCTION

Intractable pericardial effusion can be a major problem (Bright, 1836; Goodner & Brown, 1965; Beaudry et al, 1966; Bailey et al, 1968; Cohen et al, 1970; Comty et al, 1971) in some chronic dialysis patients, and may not respond to frequent dialysis. High dosage systemic steroid administration has been helpful occasionally (Comty et al, 1971). The more commonly employed therapy of pericardectomy or fenestration (Comty et al, 1971) requires thoracotomy with its attendant risks.

We have combined 48 to 72 hour indwelling catheter drainage of the pericardial fluid and localised non-absorbable steroid instillation as an alternative to previous treatment methods.

PATIENTS

Case 1: A 52 year old male with a primary diagnosis of chronic pyelonephritis had been on dialysis for 2 months. Presenting problems were (1) mild upper respiratory infection for 2 weeks; (2) mild fever; (3) nondescript midthoracic chest pain radiating to the throat; (4) peripheral oedema; (5) shortness of breath, and (6) hypotension between dialyses and during attempts at ultrafiltration while on daily dialysis. Six days after admission to the University Hospital the patient became severely hypotensive and short of breath. A friction rub was noted. X-ray confirmed the diagnosis of pericardial effusion and pericardiocentesis was performed with placement of an indwelling pericardial catheter. Fungal, bacterial and viral cultures were negative. Three hundred ml of straw-coloured turbid fluid was withdrawn initially and, over the following 38 hours another 800ml were removed. Triamcinolone hexacetoneide* 50mg was instilled into the indwelling pericardial catheter at 8 hourly

*Aristospan, Lederle Laboratories, Pearl River, New York
intervals for two administrations and before the removal of the pericardial catheter 38 hours later. The chest pain totally resolved and the pericardial effusion has not recurred during the following 9 months of follow-up while he has been on chronic dialysis.

Case 2: A 19 year old male with a primary diagnosis of chronic glomerulonephritis had been on dialysis 2 months following transplant nephrectomy for rejection. The presenting problems were those of (1) weakness; (2) mild fever; (3) a full feeling in the chest and very mild midsternal chest pain; (4) gross peripheral oedema; (5) extreme shortness of breath, and (6) hypotension between dialysis and especially during attempts at ultrafiltration while on daily dialysis. A friction rub was noted. Seven days after admission the patient became severely hypotensive and short of breath. X-ray confirmed the diagnosis of pericardial effusion, and a pericardiocentesis was performed with placement of an indwelling pericardial catheter. Cultures taken for bacteria, fungus and virus were negative. Four hundred ml of sanguinous fluid were removed with subsequent removal of another 2800ml over the following 60 hours. Triamcinolone hexacetonide 100mg was instilled into the pericardial space initially, and 4 hours later. Four more 50mg instillations were administered before catheter removal. The pericardial effusion resolved and did not recur during the subsequent 2 weeks of normal dialysis prior to successful renal transplantation and there has been no recurrent pericardial problem for the subsequent one and a half years.

Case 3: A 35 year old male with a primary diagnosis of chronic glomerulonephritis had been on dialysis 3 weeks. The presenting problems were (1) a two to three week history of upper respiratory tract infection, nausea and vomiting; (2) fever; (3) midsternal chest pain radiating to the back and to the throat; (4) some shortness of breath and mild oedema; (5) extreme hypotension during and between dialysis; (6) cardiac arrhythmias, and (7) seizures while on dialysis. The electrocardiogram showed changes of pericarditis. All fungal, viral and bacterial cultures were negative. Intensive daily dialysis was initiated and he was started on prednisone, which continued for 6 days (20mg p.o., t.i.d) with relief of chest pain, but staphylococcal septicaemia necessitated its discontinuance. Treatment was begun with intravenous antibiotics, but one week after withdrawal of prednisone a friction rub was noted and X-ray confirmed the diagnosis of pericardial effusion. Pericardiocentesis was performed via an indwelling pericardial catheter. Samples taken for fungal, bacterial and viral cultures were reported as sterile. One hundred and fifty ml of straw-coloured fluid was withdrawn and another 400ml was withdrawn over the following 24 hours. Methylprednisolone 100mg was instilled into the pericardium and repeated 12 hours later, and again 24 hours later at the time of withdrawal of the pericardial catheter. Effusion recurred
19 days later and systemic antibiotics were started. During the following 20
days he had orthostatic hypotension, extreme hypotensive episodes, and res-
piratory distress. During these 20 days he underwent daily 6 hour dialysis
on two Gambro-Lundia 17 layer dialysers in series without decreasing the
size of the effusion. Pericardiocentesis was again performed with placement
on an indwelling pericardial catheter. Cultures were sterile. Two hundred
ml of straw-coloured liquid were withdrawn and another 800ml were removed
over the following 48 hours. Triamcinolone hexacetone 50mg was admini-
stered through the pericardial catheter initially, at 6 hourly intervals (7 ad-
ministrations) and finally before catheter removal. He has had no recur-
rence of his pericardial effusion in the subsequent two and a half months.

Case 4: A 26 year old white male with a primary renal diagnosis of chronic
glomerulonephritis had been on dialysis 5 months. He presented to hospital
having been called in for cadaveric renal transplantation. There were no pre-
senting complaints, but on examination and questioning he complained of (1)
a history of gastroenteritis with nausea and vomiting 3 weeks prior to ad-
mission; (2) a cough with shortness of breath 1 week prior to admission; (3) a
vague full feeling in the chest radiating to the shoulders and throat; (4) gross
peripheral oedema; (5) increasing shortness of breath, and (6) recent hyper-
tension of 250/140. Since the cadaveric kidney was available, he was dialysed
for removal of fluid and control of his hypertension. During dialysis a friction
rub was noted, and X-ray confirmed the diagnosis of a pericardial effusion.
Pericardiocentesis was performed and an indwelling pericardial catheter was
inserted. Cultures were sterile. Two hundred and sixty ml of fluid were
aspirated, and 450ml over the next 72 hours. Triamcinolone hexactetone
50mg was placed in the pericardial space initially every 6 hours for 10 doses,
and finally before the removal of the catheter at 72 hours. The patient was
transplanted from a cadaveric donor 2 hours after initial prophylactic peri-
cardiocentesis. The chest pain and symptoms of effusion subsided. During
the 10 days post transplant the patient had 5 dialyses until the kidney regained
normal function (creatinine 1.1mg/100ml) and during the total 8 week follow-
up there has been no evidence of recurrent effusion.

METHODS

The pericardiocentesis is done via a subxyphoid approach. The patient is
placed in the supine position. The upper abdomen and lower chest are pre-
pared with betadine solution. Atropine 2mg is administered subcutaneously.
Local anaesthetic is instilled one inch below the xyphoid and along the peri-
cardiocentesis track. The Number 14 gauge pericardiocentesis needle is
directed toward the left shoulder in a plane directly below the inner rib mar-
gins. The chest lead of the electrocardiograph is attached to the needle and
monitored for injury current as the needle is advanced one centimetre at a
time until a slight give is noted as the needle transverses the pericardial sac.
The stylet is removed and, after fluid drainage, a 30cm polyethylene catheter
is advanced into the pericardial space. The needle is withdrawn and the
catheter sutured in place. One hundred to 500ml of pericardial fluid are with-
drawn and 50mg of triamcinolone hexacetonide is instilled into the pericardial
space. A 50ml syringe with a three-way stopcock is inserted into the catheter
and used for repeated drainage and triamcinolone hexacetonide administration
at 4 to 6 hourly intervals. The catheter may be withdrawn 1 to 2cm at a time
if drainage becomes inefficient. When drainage stops a final 50mg of tri-
amcinolone hexacetonide is instilled and the catheter is removed. The catheter
tip is cultured.

RESULTS

Four dialysis patients with symptomatic pericardial effusions were treated
by indwelling polyethylene catheter drainage and local steroid instillation.
The two corticosteroids used were methylprednisolone and triamcinolone
hexacetonide (non-absorbable). The four effusions treated with the localised
triamcinolone hexacetonide did not reaccumulate while the effusion treated
with localised methylprednisolone recurred. The presenting symptoms, dura-
tion and volume of drainage, steroid dosage, and eventual outcome are inclu-
ded in Table I and Table II.

DISCUSSION

These four cases constitute a pilot study. However, the preliminary evidence
seems to indicate that a specific group of patients with intractable pericardial
effusion preceded by upper respiratory infection, symptoms of chest pain,
respiratory distress, hypotension, and fluid overload may be assisted by the
treatment described.

Several observations seemed significant. Chief among these was the fact
that case 3, who was treated with an absorbable steroid (methylprednisolone),
did well initially but reaccumulated his effusion. This was in direct contrast
to the lack of recurrence in this patient and in the other three cases where
non-absorbable steroid (triamcinolone hexacetonide) was used.

All the patients had fever and symptoms suggestive of a mild viral infec-
tion (upper respiratory symptoms or gastroenteritis) as well as hypotension,
shortness of breath, and chest pain, except for case 4. (Capps, 1927; Goodner
& Brown, 1965; Hager, 1965). All the first three patients went on to develop
serious hypotension or respiratory distress requiring emergency pericardo-
centesis. The symptom complex and its progression identifies the condition
and emphasises the advisability of early pericardial drainage and non-absor-
ble steroid instillation.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Pericardial approach</th>
<th>Duration catheter drainage</th>
<th>Volume drainage</th>
<th>Type of pericardial steroid</th>
<th>Total pericardial steroid (mg)</th>
<th>Interval steroid doses (mg)†</th>
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<tbody>
<tr>
<td>Case 1</td>
<td>subxyphoid</td>
<td>36 hrs</td>
<td>1100ml</td>
<td>triamcinolone hexacetonide*</td>
<td>200</td>
<td>50 50 50 50 50</td>
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<tr>
<td>Case 2</td>
<td>subxyphoid</td>
<td>60 hrs</td>
<td>3200ml</td>
<td>triamcinolone hexacetonide</td>
<td>400</td>
<td>50 50 50 50 50</td>
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<tr>
<td>Case 3</td>
<td>subxyphoid</td>
<td>24 hrs</td>
<td>550ml</td>
<td>methylprednisolone sodium succinate**</td>
<td>300</td>
<td>100 100 100</td>
</tr>
<tr>
<td>Case 3‡‡</td>
<td>subxyphoid</td>
<td>48 hrs</td>
<td>1000ml</td>
<td>triamcinolone hexacetonide</td>
<td>450</td>
<td>50 50 50 50 50</td>
</tr>
<tr>
<td>Case 4</td>
<td>subxyphoid</td>
<td>72 hours</td>
<td>710ml</td>
<td>triamcinolone hexacetonide</td>
<td>600</td>
<td>50 50 50 50 50</td>
</tr>
</tbody>
</table>

* Triamcinolone hexacetonide is non-absorbable and therefore remains in the pericardial sac
** Methylprednisolone sodium succinate is absorbable steroid.
† Individual administrations were given after each pericardial drainage sample was taken.
‡‡ The single recurrent pericardial effusion which had previously been treated with methylprednisolone sodium succinate. It did not recur after triamcinolone hexoacetonide instillation.
Table II. Symptom Complex and Results of Therapy

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Symptom complex</th>
<th>Developed severe</th>
<th>Pericardiocentesis Required</th>
<th>Local pericardial steroid</th>
<th>Symptom relief</th>
<th>Duration of relief</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Symptom complex</td>
<td>Developed severe</td>
<td>Pericardiocentesis Required</td>
<td>Local pericardial steroid</td>
<td>Symptom relief</td>
<td>Duration of relief</td>
<td>Recurrence</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Clitoral pruritus,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>52</td>
<td>M</td>
<td>yes yes yes yes yes yes yes yes</td>
<td>yes yes yes yes yes yes yes</td>
<td>non-absorbable*</td>
<td>yes</td>
<td>9 months</td>
<td>none</td>
<td></td>
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<tr>
<td>Case 2</td>
<td>19</td>
<td>M</td>
<td>yes yes yes yes yes yes yes yes</td>
<td>yes yes yes yes yes yes yes</td>
<td>non-absorbable</td>
<td>yes</td>
<td>18 months</td>
<td>none</td>
<td></td>
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<tr>
<td>Case 3</td>
<td>35</td>
<td>M</td>
<td>yes yes yes yes yes yes yes yes</td>
<td>yes yes yes yes yes yes yes</td>
<td>absorbable**</td>
<td>yes</td>
<td>19 days</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Case 3</td>
<td>35</td>
<td>M</td>
<td>yes yes yes yes yes yes yes yes</td>
<td>yes yes yes yes yes yes yes</td>
<td>non-absorbable</td>
<td>yes</td>
<td>2½ months</td>
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<tr>
<td>Case 4</td>
<td>26</td>
<td>M</td>
<td>yes yes yes yes yes mild no no (yes)+</td>
<td>yes yes yes yes yes yes yes</td>
<td>non-absorbable</td>
<td>yes</td>
<td>2 months</td>
<td>none</td>
<td></td>
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</table>

* Triamcinolone hexocetonide (non-absorbable)
** Methylprednisolone sodium succinate (absorbable)
+ The requirement was prophylaxis of cardiac tamponade for immediate cadaveric renal transplantation
All cultures for bacteria, fungus, and known viruses, except rhinovirus, were negative as were viral titres. Particular efforts were made to isolate cytomegalovirus which can frequently be cultured from our patients after transplantation, but were unsuccessful.

These negative findings suggest that whether or not a virus or bacteria is involved, the basic problem is that of membrane inflammation (Bright, 1836; Comty et al., 1971; Hampers et al., 1968; Langendorf & Pirani, 1947) which should respond to steroid therapy. The patient who had a sanguinous pericardial effusion responded as readily as did the others, although a larger volume of effusion fluid was obtained. Thus, sterile sanguinous effusion may merely represent a more severe inflammation which happens to involve superficial blood vessels.

The patient who received systemic steroid therapy for treatment of pericarditis before the development of symptomatic effusion had resolution of chest pain, accompanying hypotension, and cardiac arrhythmias. The septicaemia during steroid therapy may have represented a complication of that therapy.

Increasing frequency and efficiency of dialysis appeared to have no beneficial effect. No patients had unusually poor erythropoiesis or neuropathy on electromyographic study, suggesting that once the symptom complex had presented, more intensive dialysis may not be helpful. Neuropathy or transfusion dependent anaemia do not necessarily accompany the development of intractable pericarditis with effusion.

CONCLUSION

Although our series is small, it offers preliminary evidence that the symptom complex of (1) upper respiratory tract or gastrointestinal symptoms; (2) chest pain; (3) respiratory distress; (4) fluid retention, and (5) hypotension during and between adequate dialysis should be taken as a warning that serious cardiac tamponade may follow. The pericardial fluid is sterile for bacteria, fungus, and virus though the effusion may be bloody or clear. Treatment is pericardiocentesis and 24 to 72 hour pericardial drainage with instillation of a non-absorbable steroid. The more radical intrathoracic surgical procedures of pericardiectomy and pericardial fenestration may be avoided while patients await renal transplantation or return to chronic dialysis.

REFERENCES

Bright, R. (1836) Guy's Hospital Report, 1, 338
Capps, J.A. (1927) Archives of Internal Medicine, 40, 715
OPEN DISCUSSION

T DRUEKE (Paris): At the Necker Hospital in Paris we have now drained 16 patients by the method you describe. The results of this were published last year in the Annal de Chirurgie. Only one recurrence has been seen, and despite the fact that we have never instilled corticosteroids into our patients, our results are the same as yours. It was interesting to see that in the patient who had a recurrence of pericardial effusion, there were no pericardial adhesions in the absence of soluble or non soluble corticosteroids.

BUSELMEIER: Had these cases on chronic dialysis whom you treated by daily dialysis or on steroid therapy proved previously that they were resistant or intractable?

DRUEKE: No, since we had not used corticosteroids before and we only treated patients with pericardial effusion and decompensation of cardiac function.

BUSELMEIER: Bright first described this problem 140 years ago. We found that conservative medical management helps in some patients and that others recovered with dialysis. Now we are trying to treat the very intractable or resistant cases with intense dialysis or with systemic steroids.

D HILTON (Stourbridge): Could you tell me if you had any complications from using heparin during dialysis, and whether you used regional heparinisation in these patients?

BUSELMEIER: We used infusion heparinisation. The dose was monitored from clotting times in the arterial line, and we have had no recurrent pericardial bleeding. The last patient had an acute bleed into the pericardium which I tapped. The man was drained for 70 hours and had been dialysed without any recurrence of his bleed.

HILTON: I have used the same method of heparinisation, but have seen a number of complications from bleeding into pericardial effusions — two of which have been fatal.
BUSELMEIER: I can only comment on our good luck in these cases. We have not had many other patients with chronic pericardial effusions. If we have more, we may have more trouble.

DRUEKE: If you did not find any bacterial growth in your pericardial effusion what could be the cause of the pericarditis?

BUSELMEIER: What a question! I am thinking of the number of people with an opinion on this. I think it could be a sympathetic response to a viro-bacterial infection. Whether antinuclear antibodies or specific heart antibodies or antimembrane antibodies are involved I do not know. We are now measuring antinuclear antibodies and antinuclear muscle antibodies in the effusion fluid which has been frozen for us, but I am afraid that I cannot at this stage answer your question. One point that I think is important is — is it safe to treat pericardial effusion which might be infected, with local steroid instillation?