Infective endocarditis complicating psittacosis: response to rifampicin

Endocarditis rarely complicates *Chlamydia psittaci* infection. 1, 2 We describe a patient who developed insidious progressive aortic valve regurgitation while the psittacosis/lymphogranuloma venereum complement fixation (LGVCVF) titres were rising. The infection responded to rifampicin after treatment with tetracycline had failed.

Case report

A previously healthy 43-year-old electrician was first admitted to hospital in August 1978 with a seven-day history of generalised aches, sweating, headache, muscle stiffness, diarrhea, vomiting, and frontal headaches. He kept pigeons but had had no contact with a parrot. There had been no ill health among his pigeons—as verified later by the public health authorities. He was feverish (40°C) with sinus tachycardia of 120/min. There were signs of left upper lobe consolidation. Cardiac auscultation was normal. Investigations: haemoglobin 14.4 g/dl; white cell count 3.4 x 10^9/l (3400/mm^3), 68% neutrophils, 22% lymphocytes, 10% monocytes; erythrocyte sedimentation rate 12 mm/h; arterial oxygen pressure 7.8 kPa (58 mm Hg) and arterial carbon dioxide pressure 3.1 kPa (23 mm Hg) on room air; urine microscopy showed numerous red cells, granular casts, and white cells; creatinine 197 μmol/1; serum sodium 123 mmol/l; potassium 3.8 mmol/l; blood urea 7 mmol/l (42 mg/100 ml); total serum protein 57 g/l, albumin 28 g/l; aspartate aminotransferase (AST) 174 IU/l (normal 5-32); gamma-glutamyltranspeptidase 49 IU/l (normal up to 45). Protein electrophoresis showed increases in α₁ and α₂ globulins. Chest x-ray examination confirmed left upper lobe consolidation. Tuberculin test, electrocardiogram (ECG), fluorescence antibody test against legionnaire's disease, immunglobulins, blood cultures, and aputum examination were normal.

He was initially thought to have a "bacterial" pneumonia and was given courses of amoxycillin, flucloxacillin, benzylpenicillin, and erythromycin. He failed to improve and was referred to a chest unit and developed fever and dry cough. Then a further and more pronounced development of pneumonia was noted. He was then seen at the respiratory unit where he was found to have a large right lower lobe consolidation. A chest x-ray showed that there were multiple opacities in both lower lobes and the right middle lobe. There was also a right-sided pleural effusion. He was kept pigeons and had kept pigeons in his youth. We suspected psittacosis and LGVCVF. He had given a history of being bitten by pigeons. He was immunised against Chlamydia psittaci. The patient had a history of exacerbation of reflux oesophagitis in the past.

He was then referred to our hospital. At the time of admission he was apyrexial with normal heart sounds and a soft right middle lobe crackles. The examination of the chest was otherwise normal. The haemoglobin was 10 g/dl and the white cell count was 11.2 x 10^9/l (11 200/mm^3), 56% neutrophils, 39% lymphocytes, 4% monocytes; erythrocyte sedimentation rate 104 mm/h.

Investigations: haemoglobin 11.5 g/dl; white cell count 11.2 x 10^9/l (11 200/mm^3), 56% neutrophils, 39% lymphocytes, 4% monocytes; erythrocyte sedimentation rate 104 mm/h; arterial oxygen pressure 7.8 kPa (58 mm Hg) and arterial carbon dioxide pressure 3.1 kPa (23 mm Hg) on room air; urine microscopy showed numerous red cells, fine granular casts, and white cells; creatinine 98 μmol/1; serum sodium 123 mmol/l; potassium 3.9 mmol/l; blood urea 17 mmol/l (97 mg/100 ml); total serum protein 55 g/l, albumin 28 g/l; aspartate aminotransferase (AST) 175 IU/l (normal 5-32); gamma-glutamyltranspeptidase 49 IU/l (normal up to 45). Protein electrophoresis showed increases in α₁ and α₂ globulins. Chest x-ray examination confirmed left upper lobe consolidation. Tuberculin test, electrocardiogram (ECG), fluorescence antibody test against legionnaire's disease, immunglobulins, blood cultures, and aputum examination were normal.

Problems with intravenous chlormethiazole (Heminevrin) in status epilepticus

Intravenous diazepam is a drug of first choice for status epilepticus. Administration is by either continuous intravenous infusion or bolus injection, and we have also used the rectal route successfully. For very resistant seizures, however, we have used instead a continuous intravenous infusion of chlormethiazole edisylate (Heminevrin) 8 g/l in an aqueous solution of 4%, dextrose, achieving control of fits in both major and minor status epilepticus with doses of 5-10 mg/kg/h by titrating fits with appropriate infusion rates. Respiratory depression and hypotension have not been serious hazards. Nevertheless, we report here several problems that we have encountered with this drug.

Recorded complications

**Reaction with plastics—**Intravenous chlormethiazole reacts with the plastic of giving sets and may soften the burette within four to six hours’ contact. No plastic packaging set is completely resistant to chlormethiazole, but certain sets—for example, Avon paediatric administration sets (Avon Medicals, Birmingham, UK)—seem more resistant than others. Chlormethiazole is apparently absorbed on plastics, and this is being investigated by the scientific and technical branch of the Department of Health and Social Security.

**Thrombophlebitis** has been a serious problem, especially with infusions of over 12 hours. Long Silastic tubes produce thrombophlebitis along the whole length of contact. Chlormethiazole apparently penetrates the walls of silicone tubing, so that the response may be due to a direct action of the drug on vessel walls or a product of interaction between drug and plastic.

**Fever—**All five children given the drug developed slight fever (table) (not reported before to the Committee on Safety of Medicines; personal communication), and we saw three children with hyperpyrexia—namely, temperatures of 39-40°C. There was no laboratory evidence of infection, and when chlormethiazole was stopped their temperatures fell. The manufacturers tested the solutions for pyrogens but with negative results.

**Severe headache occurred in all five children: the older ones complained, but the younger ones were irritable. Sixteen other cases have been reported to the Committee on Safety of Medicines (personal communication).**

**Effects of Chlormethiazole on five children with seizures resistant to diazepam**

<table>
<thead>
<tr>
<th>Case</th>
<th>No</th>
<th>Age</th>
<th>Duration in days</th>
<th>Headache</th>
<th>Thrombophlebitis</th>
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<tbody>
<tr>
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<td>1m</td>
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<tr>
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<td>1m</td>
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<td>5m</td>
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<tr>
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<td>+ +</td>
<td>+ + + + +</td>
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</tr>
</tbody>
</table>

We thank Dr A D Evans, consultant virologist, University Hospital of Wales, Cardiff, and his department for help in investigating this patient.


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Department of Medicine, University Hospital of Wales, Cardiff

A G JARIWALLA, MB, MRCP, senior medical registrar

Llandough Hospital, Penarth, Cardiff

B H DAVIES, MB, MRCP, consultant physician

J WHITE, MB, MRCP, medical registrar
Comment

Continuous intravenous chlorothiazide is an effective anti-
convulsant for status epilepticus, but because of the complications
mentioned should be used carefully, preferably for short periods only.

We thank the scientific and technical branch of the DHSS and the
Government Chemist for their interest and chemical analysis, and the
manufacturers of Heminevrin (Astra Chemicals), for their analysis and
pyrogen tests.

1 Harvey PKP, Higenbottam TW, Loh L. Chlorothiazide in treatment of

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The Hospital for Sick Children, Great Ormond Street, London
WCIN 3BH
S LINGAM, DCH, MRCP, neurological registrar
HELEN BERTWISTLE, BSCN, SRN, neurological ward sister
HEATHER M ELLISTON, MPS, group chief pharmacist
JOHN WILSON, BPH, consultant paediatric neurologist

Late displacement of central venous catheter resulting in vascular
obstruction

The introduction of large-calibre plastic catheters into the central
veins of patients has facilitated total parenteral nutrition and drug
administration. These two procedures may be of critical importance in
managing very sick people with bacterial endocarditis, acute
leukaemia during initial induction chemotherapy, or after bone
marrow transplantation. In each of these the peripheral vessels are
unsatisfactory routes for intravenous infusion, since large volumes
need to be given and also the high viscosity or hyperosmolality of
some of the materials may result in thrombophlebitis and thus
render small veins especially prone to occlusion. A number of
techniques are available for achieving access to the high-flow veins
within the thorax. To date these procedures have been relatively free
from serious problems, but the catheters may become dislocated
from the original desired site and then follow an abnormal route
within the thoracic vessels, leading to complications. In most reported
cases the unsatisfactory results arise during the introduction process
and we are not aware of late catheter migration, particularly against
venous flow, with resulting vascular occlusion.

Case report

A 49-year-old woman was hospitalised for cytotoxic chemotherapy for
stage IV lymphocytic lymphoma. In view of her poor physical state a
10-gauge Silastic catheter was introduced via the left subclavian line, using a
previously described technique. Postoperative chest x-ray examination
comfirmed that the end of the catheter was lying in the superior vena cava
with its end 1 cm above the right atrium. For the next three weeks the patient
received intravenous drugs, hyperalimentation, and daily fluid require-
ments by this route without any problems. During the same period blood
samples were collected from the catheter, since measurements in these
correlate well with those in samples simultaneously collected from peripheral
vessels. On day 23 after introduction of the catheter the patient’s left hand
and arm started to swell and this progressed slowly for two days. Careful
serial examination showed increasing tenderness and swelling of the left
arm, supraclavicular space, and axilla. Radiological studies showed that the
radio-opaque catheter had looped up inside the superior vena cava and
wedged into the axillary vein, obstructing blood flow. The catheter was
simply repositioned under x-ray control, and within two days all symptoms
had disappeared. No late complications have occurred.

Comment

A survey of central venous catheters used in our hospital over a
two-year period confirmed the finding of Fischer and his colleagues
that initial misplacement could occur and that intrathoracic complica-
tions may then arise. Nevertheless, once securely in position none of the catheters that we studied became displaced. Our case
was the first example of late dislocation we encountered over the
same two-year period, when catheters were routinely employed for
hyperalimentation, induction of cytotoxic chemotherapy in patients
with leukaemia, and long-term support after bone marrow trans-
plantation. The final resting place of the catheter is all the more
surprising in view of the retrograde course followed by the large
diameter and relative inflexibility of the plastic tubes. This com-
plication should be recognised as soon as it occurs since the hyper-
tonic and irritant solutions infused may lead to local endothelial
damage and thrombus formation. One way to check the patency is
by regular flushing, while direct determination of venous pressure is
an easy method of monitoring freedom from obstruction. While
radiological control is essential when introducing the catheter its
subsequent use is of lower priority in the complex management of a
critically ill patient. It is therefore not surprising that the symptoms
of mechanical obstruction may not be immediately evident. Since
delay in diagnosis is potentially serious we suggest that these patients
should be regularly examined, with particular emphasis on catheter
efficiency, and that x-ray studies should be undertaken whenever
anxiety arises. A dislocation may then be promptly corrected and
x-ray control will thus avoid venous complications.

1 Fischer J, Lundstrom J, Ottander H-G. Central venous cannulation: a
radiological determination of catheter positions and immediate intrathoracic
2 Jacobson P, Jacobson J. A practical method for ensuring long-term venous

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Department of Haematology, University of Cape Town Medical
School, Cape, South Africa
NICHOLAS NOVITSKY, MB, registrar
PETER JACOBS, MD, PhD, professor and head of department

Hydrallazine-induced cutaneous vasculitis

The commonest features of the hydrallazine-associated lupus syn-
drome are arthralgia and malaise. Erythematous rashes may occur but
vasculitis has not been reported. We have recently seen two patients
with ulcerating cutaneous vasculitis associated with hydrallazine
treatment.

Case reports

(1) A 63-year-old woman had been treated for hypertension and stable
renal impairment for 15 years. Hydrallazine was started in September 1979
and the daily dosage increased to 250 mg in addition to diuretic and beta-
blocking drugs and methylidopa. In July 1978 her serum antinuclear antibody
(ANA) was positive at a titre of 1/40 and her erythrocyte sedimentation rate
(ESR) 33 mm in 1 h. In July 1979 the ANA titre was 1/160 and the ESR
70 mm in 1 h. In August 1979 she was admitted to hospital with a 10 × 5 cm
ulcer on the lateral aspect of her left leg, which had developed over two weeks.
She gave a six-month history of arthralgia, myalgia, and weight loss of 3 kg.
Two days after admission she developed multiple vasculitic lesions over the
buttocks, thighs, and arms. Hydrallazine was withdrawn and the lesions began
to resolve. When one of them ulcerated, however, prednisone was
given for five days, with rapid disappearance of the lesions and healing of the
ulcer. Results of investigations included ESR 90 mm in 1 h; creatinine
clearance 25 ml/min; no proteinuria; haemoglobin 11.4 g/dl; white cell
count (WBC) 4.1 × 10^9/l (4100/mm^3), normal differential and platelets;
immunoglobulin IgG 13.6 g/l, IgA 1.75 g/l, IgM 2.60 g/l (normal IgM
0.5-1.8 g/l). IgG and IgM ANA titres were 1/2560, DNA binding 20%. No
other autoantibodies were found, complement screen was normal, C3,
c3q binding negative, and cryoglobulins were present in trace only. Sulpha-
metazine phenotyping showed her to be a slow acetylator and her total
intake of hydrallazine was estimated to be 120 g. Histology of a lesion from
her thigh showed allergic vasculitis with fibrinoid necrosis of small vessels.
Immunofluorescence microscopy showed deposits of IgM, fibrin, and C3
in small blood vessels.

(2) A 61-year-old woman with essential hypertension had received
hydrallazine, propranolol, and cyclopenthiazide K for two years. During
this time her maximum daily dose of hydrallazine was 100 mg and her
estimated total intake 95 g. In 1979 she presented with a six-month history of
pain and stiffness in her hands, wrists, elbows, shoulders, and knees