Case report

A 66-year-old man presented in April 1979 with a flu-like illness and pleuritic chest pain. He was referred for investigation four months later because of persisting fatigue and lassitude. He had developed pain and stiffness of the neck and shoulders but no other symptoms.

Examination showed a blood pressure of 220/110 mm Hg, an exudative retinopathy, and albuminuria. The liver was moderately enlarged. Haemoglobin concentration and white cell and platelet counts were normal. Erythrocyte sedimentation rate was 106 mm in first hour. Blood urea concentration was 6.8 mmol/l (41 mg/100 ml), plasma sodium 141 mmol (mEq)/l, potassium 4.1 mmol(mEq)/l, and creatinine 73 μ mol/l (0.82 mg/100 ml). Creatinine clearance was 68 ml/min and urinary protein 6 g/24 h, and red and white cell casts were seen in the urinary deposit. An intravenous pyelogram was normal.

A renal biopsy specimen showed focal glomerulonephritis (figure). There

Single glomerulus showing focal glomerulonephritis with capsular epithelial proliferation. (Haematoxylin and eosin $\times 480$ (original magnification).)

was focal lobular obliteration and fibrinoid deposition, with focal thickening of the peripheral capillary loops, occasional epithelial crescent formation, and a diffuse increase in mesangium. Immunofluorescence staining of fresh material showed heavy granular deposition of IgG, IgA, IgM, C3, and C1q in both the capillary loops and mesangium. Ultrastructural examination of glutaraldehyde-fixed material showed electron-dense immune deposits in the mesangium and beneath the epithelial cells in the capillary loops. There were no subendothelial deposits. The morphological features, except for the absence of subendothelial deposits, were suggestive of systemic lupus erythematosus. Antinuclear factor was subsequently detected in the serum at a dilution of 1 in 128, but DNA binding was only 5% (thus he had four of the American Rheumatism Association criteria for systemic lupus erythematosus).

Several tests of liver function were abnormal. Serum alkaline phosphatase activity was 560 U/l (normal 21-94 U/l), aspartate transferase activity 52 U/l (normal 8-40 U/l), and albumin concentration 31 g/l (normal 35-53 g/l). A liver biopsy specimen showed moderate infiltration of mononuclear cells in the portal tracts with considerable fibrosis and focal mild piecemeal necrosis. There were no granulomas, but the bile duct showed considerable periductal inflammation and epithelial damage. The features were consistent with primary biliary cirrhosis. Tests for antimitochondrial antibody were positive and serum IgM was 360 IU/ml (normal 69-322 IU/ml).

Comment

Thomas *et al*¹ suggested that the liver damage in primary biliary cirrhosis may be mediated by immune complex deposition. Immune complexes certainly occur in the serum of patients with the disease,³ and the deposition of these complexes in the vicinity of bile ducts might account for the observed histological changes. Furthermore, primary biliary cirrhosis has been reported in association with systemic lupus erythematosus,⁴ rheumatoid arthritis,⁵ and glomerulonephritis,² diseases in which immune complex deposition is thought to have an important pathogenic role. In only one case, however, has immune complex deposition been clearly shown: Rai *et al*² reported the association of primary biliary cirrhosis and diffuse membranous glomerulonephritis and showed, by immunofluorescence, IgG and IgM contained in immune deposits in the glomeruli. In our case

immunofluorescence and electron microscopy showed complexes containing IgG, IgA, and IgM, which had induced a focal glomerulonephritis.

Thus, with this second case, evidence linking primary biliary cirrhosis and immune complex disease is slowly accumulating, but more case reports are needed before the association is established.

We thank Professor P J Scheuer, of the Royal Free Hospital, London, for his help in interpreting the liver biopsy.

- 1 Thomas HC, Potter BJ, Sherlock S. Is primary biliary cirrhosis an immune complex disease? *Lancet* 1977;ii:1261-3.
- 2 Rai GS, Hamlyn AN, Dahl MGC, Morley AR, Wilkinson R. Primary biliary cirrhosis, cutaneous capillaritis, and IgM-associated membranous glomerulonephritis. *Br Med J* 1977;i:817.
- 3 Wands JR, Dienstag JL, Bhan AK, Feller ER, Isselbacher KJ. Circulating immune complexes and complement activation in primary biliary cirrhosis. *N Engl J Med* 1978;298:233-7.
- 4 Runyan BA, LaBrecque DR, Anuras S. The spectrum of liver disease in systemic lupus erythematosus. *Am J Med* 1980;69:187-94.
- 5 Golding PL, Smith M, Williams R. Multisystem involvement in chronic liver disease. Studies on the incidence and pathogenesis. *Am J Med* 1973;55:772-82.

Lancaster Moor Hospital and Royal Lancaster Infirmary, Lancaster

J A MORRIS, MA, MRCPATH, consultant histopathologist
M B MCILLMURRAY, DM, MRCP, consultant physician

Addiction to temazepam

Growing awareness of the addictive properties of diazepam and nitrazepam has led doctors to switch to the shorter-acting benzodiazepine hypnotics, such as temazepam, in the belief that they are safer.¹ Although cases of dependence to lorazepam have been reported it is widely assumed that this group of benzodiazepine hypnotics are not as addictive as nitrazepam or flurazepam. Because the short-acting benzodiazepine hypnotics are being prescribed more often, doctors should be aware of the risks.

Case history

A 22-year-old unmarried factory worker presented with a direct request for help in withdrawing from the sleeping pills on which he had become dependent. He gave a two-year history of taking temazepam (Normison, Euhypnos) in association with alcohol. He had a history of depressive episodes, beginning at the age of 16, when his parents separated. Depression had been treated by his general practitioner with tricyclic drugs. He had had four courses of treatment lasting from three to six months in the last six years. Temazepam was prescribed initially for insomnia during a depressive episode and continued as a repeat prescription. He also drew on a repeat prescription made out for his mother. His job record was steady, but he had on three occasions abruptly abandoned work, usually after a domestic crisis. He was also addicted to nicotine, smoking 20-25 cigarettes a day, and alcohol, with an average intake of 2-4 pints of beer a day. His addiction to temazepam began as a means of augmenting the psychic effects of alcohol. He appears to have achieved optimal effects by taking the drug one hour before going out drinking. His initial dose was 10-20 mg but within a period of eight months he had on occasions increased his intake to as much as 100 mg. He had also found it necessary after the first six months occasionally to take a tablet during the day to abolish withdrawal symptoms, mainly a tremor in his hands. He had read a great deal of the published information on barbiturates but, interestingly, he considered barbiturates too dangerous. There was no other evidence of drug abuse.

At the time of the interview he had been taking 8-10 tablets a day for six months but had stopped them three days before the interview in an attempt to "kick the habit." He showed moderate withdrawal symptoms, mainly subjective anxiety and tension, restlessness, inability to sleep, and loss of appetite. Physical examination showed nothing abnormal other than a tremor of the outstretched hands. He refused admission because he feared loss of his job, and withdrawal was done on an outpatient basis, under cover of chlormethiazole, which was continued for 12 weeks. His continued presence at work in the early days was facilitated by short-time working owing to the recession. Withdrawal was relatively uneventful, the main complaint being difficulty in sleeping and vivid dreams. When the chlormethiazole was stopped he began having fluctuations of mood which stabilised on 25 mg of amitriptyline at night. Six months later he showed some depression of mood consistent with his life situation but was taking no drugs.

Comment

Addiction to benzodiazepines has been denied in some quarters on the basis that reported case histories do not fulfil the criteria of drug dependence.² This case illustrates dramatically the four main features of dependence—namely, use of a drug to achieve its psychic effects, increase of dosage with time to achieve the same effects, experience of withdrawal symptoms on stopping the drug or reducing the dose, and abolition of withdrawal symptoms when the drug is reinstated. Short-acting benzodiazepine hypnotics may have some advantage as regards hangover³ but they share the addiction potential of all benzodiazepines.

¹ Lader M. The present status of benzodiazepines in psychiatry and medicine. *Arzneim Forsch* 1980;**30**:910.

² Marks J. *The benzodiazepines: use, overuse, misuse, abuse*. Lancaster: MTP Press, 1978.

³ Committee on the Review of Medicines. Systematic review of benzodiazepines. *Br Med J* 1980;**280**:910-2.

(Accepted 11 March 1981)

Psychiatric Unit, Barnet General Hospital, Barnet EN5 3DJ

L RATNA, DPM, MRCPsych, consultant psychiatrist

Reducing risks from intravenous cannulae

Intravenous treatment is used increasingly in medical practice and accounts for the popularity of cannulae such as the Venflon, which allow continuous or intermittent intravenous access through a side port. Recently we studied the risks of such cannulae and showed local inflammation in 35% of cases, culture-positive cannula tips in 15%, and septicaemia in 1%.¹ In that study the technique of inserting the cannula was not standardised, and the skin was prepared with only a 70% isopropyl alcohol disposable swab (Medi-swab). We report here further studies on 260 cannulae to investigate practical ways of reducing such risks.

Methods and results

All Venflon cannulae studied were inserted on consecutive patients on two medical wards and an adjoining coronary care unit. The cannulae were removed when clinically indicated and were studied using the technique and methods previously described.¹ Before the cannula was removed a moistened swab was inserted into the side injection port, rotated vigorously, and cultured aerobically on blood agar.

Initially we looked at 171 consecutive cannulae inserted with a sterile "no-touch" technique after spraying the insertion area with chlorhexidine gluconate 0.5% in 70% industrial methylated spirit (Dispray No 3, Stuart Pharmaceuticals) and allowing it to dry. Cannulae were secured with ad-

Correlations between cannula tip cultures, skin cultures, and side port cultures for 260 cannulae

No of cannulae	Infection found		
	Cannula tip	Skin	Side port
1	<i>S epidermidis</i> *	<i>S epidermidis</i> *	
1	<i>S epidermidis</i> *	<i>S epidermidis</i> *	<i>S epidermidis</i> †
2	<i>S epidermidis</i> †	<i>S epidermidis</i> *	<i>S epidermidis</i> *
2	<i>S epidermidis</i>		
1		<i>S epidermidis</i> †	<i>S epidermidis</i> †
3		<i>Pseudomonas aeruginosa</i> ‡	<i>Ps aeruginosa</i> ‡
1		<i>Klebsiella</i> sp*	<i>Klebsiella</i> sp*
12		Positive cultures	
4			Positive cultures

* Similar by phage-typing, biotyping, antibiograms.

† Dissimilar by phage-typing, biotyping, antibiograms.

‡ Non-typable.

hesive tape. The old Venflon model (n = 84), as previously studied,¹ was compared randomly with the current siliconised model (n = 87). Results were similar and were therefore combined. The mean duration of cannulation was 61.4 hours (range 8-330 hours). Six cannulae (3.5%) produced significant bacterial growth on roll-plate culture.² There were 20 (12%) positive skin cultures and 11 (6%) positive side port cultures (table). Local inflammation was present around 43 (25%) cannulae.

We also looked at a further 89 cannulae where the skin entry site was not occluded with the securing adhesive tape, but covered with a small sterile gauze. Forty-two (47%) of the cannula insertion sites were uncovered daily and sprayed with povidone-iodine dry powder (Stuart Pharmaceuticals). There was no difference in the complications observed and the results were therefore combined. The mean duration of cannulation was 65.5 hours (range 4-200 hours). No cannula tip was culture positive and in only one patient did skin and port cultures grow *Staphylococcus epidermidis* (see table). Local inflammation was present around 16 (18%) cannulae.

In all 260 cannulae there was no relation between cannula tip cultures or local inflammation and duration or site of cannulation, skin shaving, or use of the side port for giving medication. Medication had not been given through 73 (28%) cannulae. No cases of bacteraemia were found.

Comment

In both the cannulae secured with tape and those covered with sterile gauze the incidence of positive cultures from the cannula tip (3.5% and 0% respectively), local inflammation (25% and 18%), positive skin cultures (11.7% and 1%), and septicaemia (0%) was much lower than we previously reported.¹ This reduction is probably related to skin preparation with 0.5% chlorhexidine in spirit, careful cannula insertion, and an increased awareness of the problem. A separate gauze covering the insertion site appeared to reduce the incidence of positive cultures from the cannula tip and skin. Daily spraying with povidone-iodine did not reduce local inflammation or cannula infection.³

Although the side injection port is a useful device, it has been criticised as a possible harbour for infection.⁴ One small laboratory study found bacteria in 55% of 56 Venflon side ports.⁵ We noted a much lower incidence (4.6% of 260 side ports). On six occasions organisms shown to be similar by typing methods were found on skin culture and port culture, but on no occasion was the identical organism cultured from port and cannula tip.

Although this was not a controlled study, our findings suggest that risks from these intravenous devices may be reduced by limiting unnecessary cannulation (28% of our cannulae were not used for giving medication) and by using a careful sterile insertion and fixation technique.

We thank our medical and nursing colleagues for their co-operation, the Staphylococcus Reference Unit, Central Public Health Laboratories, London, for help in phage typing and biotyping our isolates, and British Viggo Ltd for support.

¹ Macfarlane JT, Ward MJ, Banks DC, Pilkington R, Finch RG. Risks from cannulae used to maintain intravenous access. *Br Med J* 1980;**281**:1395-6.

² Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying intravenous catheter related infection. *N Engl J Med* 1977;**296**:1305-9.

³ Noble CJ, Morgan-Capres P, Hammer M, et al. A trial of povidone iodine dry powder spray for the prevention of infusion thrombophlebitis. *Journal of Hospital Infection* 1980;**1**:47-51.

⁴ Peters JL, Fisher C, Mehtar S. Risks from cannulae used to maintain intravenous access. *Br Med J* 1981;**282**:223.

⁵ Oberhammer EP. Contamination of injection ports on intravenous cannulae. *Lancet* 1980;iii:1027-8.

(Accepted 13 March 1981)

Departments of Medicine, Therapeutics, and Microbial Diseases, City Hospital, Nottingham NG5 1PB

J T MACFARLANE, MRCP, senior registrar in medicine

M J WARD, MRCP, research registrar

D C BANKS, MD, FRCP, senior lecturer, university department of therapeutics

R PILKINGTON, FIMLS, senior laboratory scientific officer

R G FINCH, MRCP, MRCPATH, consultant and senior lecturer in microbial diseases