function tests were abnormal (bilirubin 17 IU/l, alkaline phosphatase 66 IU/l, aspartate transaminase 81 IU/l, gammaglutamyltranspeptidase 124 IU/l). The result of an intravenous pyelogram was normal. At operation the choledochus cyst was considerably shrunken, and was seen to have a definitely thickened wall. The gall bladder was not found and was therefore presumed to have been removed at the first laparotomy. The liver felt firm but was not obviously enlarged. There was considerable splenomegaly. A choledochocystojejunostomy with Roux-en-Y anastomosis was performed. Histological examination of an operative liver biopsy specimen showed the typical changes of congenital hepatic fibrosis, with an essentially normal liver parenchyma divided by broad bands of fibrous tissue containing strikingly dilated abnormal bile ducts. The postoperative course was satisfactory once post-transfusion hepatitis (HBsAg negative) had resolved.

Comment

Previous case reports of choledochus cysts have sometimes included reference to portal fibrosis and proliferation of the intrahepatic bile ductules,² occasionally in association with dilatation of intrahepatic ducts.³ The hepatic fibrosis has been attributed to obstructive biliary fibrosis, but we believe that some of these cases are, in fact, examples of classical congenital hepatic fibrosis. Since abnormalities of the intrahepatic biliary tree are well known in congenital hepatic fibrosis⁴ it might be expected that abnormalities of the extrahepatic biliary tree might also be found. We suggest that the occurrence of congenital hepatic fibrosis and a choledochal cyst is more than a chance relationship and that a choledochus cyst should be regarded as one of the congenital abnormalities associated with congenital hepatic fibrosis.

Our patient developed recurrent ascending cholangitis after an initially successful choledochocystoduodenostomy. This problem is well recognised and the long-term morbidity of this type of anastomosis may be as high as 65%.⁵ Trout and Longmire suggested that a Roux-en-Y choledochocystojejunostomy with concomitant cholecystectomy was the treatment of choice.

Reprint requests should be addressed to P M Smith.

¹ Kerr, D N S, *et al*, *Quarterly Journal of Medicine*, 1961, **30**, 91.

² *New England Journal of Medicine*, 1977, **296**, 328.

³ Tsuchida, Y, and Ishida, M, *Surgery*, 1971, **69**, 776.

⁴ Murray-Lyon, I M, *et al*, *Quarterly Journal of Medicine*, 1972, **41**, 477.

⁵ Trout, H H, and Longmire, W P, *American Journal of Surgery*, 1972, **121**, 68.

(Accepted 17 June 1977)

Departments of Surgery and Medicine, Llandough Hospital, nr Penarth, Cardiff

D N W LAKE, MB, FRCS, surgical registrar

P M SMITH, MD, MRCP, senior lecturer and consultant physician

M H WHEELER, MD, FRCS, senior lecturer and consultant surgeon

Opsoclonus in salmonella infection

Opsoclonus is a peculiar abnormal eye movement in many directions, distinguishable from nystagmus in being chaotic or non-rhythmic and tending to be more obvious during attempted fixation or refixation. Moreover, patients with opsoclonus are usually unaware of eye or environmental motion, because all movements are saccadic fast phase movements.¹ The sign was first described in patients with viral encephalitis by Orzechowski in 1913² and has also been known to occur in patients with polymyoclonia and neuroblastoma. We recently observed such a sign in a patient with salmonella infection.

Case history

A 21-year-old woman was admitted to Ramathibodi Hospital with high fever and abdominal pain. Her body temperature was 40°C, pulse rate 128 per minute, and blood pressure 100/70 mm Hg. There was slight tenderness in the right hypochondrium. She was drowsy and had generalised hyporeflexia. Relevant laboratory data showed normal haemoglobin and total and differential white cell count; SGOT, SGPT of 136 and 90 sigma units, respectively; blood culture grew *Salmonella* group A and Widal O agglutinin titre for *S paratyphi* A was greater than 1:320. The results of rectal swab cultures were negative. The patient was treated with 500 mg of chloramphenicol six-hourly on the eighth day after admission. Though her

body temperature dropped to below 38°C, she became more stuporous and confused. On the eighteenth day after admission we observed periodic, spontaneous, rapid, and irregular oscillations of both eyes in horizontal direction occurring several times per minute. Neurological examination showed no evidence of myoclonus or cerebellar signs. The results of cerebrospinal fluid examination and viral studies were normal. Electroencephalogram showed moderately diffuse slow wave abnormality. Opsoclonus lasted for four days, and then her general and mental condition steadily improved and fever subsided five days later. She was discharged after being in hospital for five weeks.

Comment

Neuropsychiatric manifestations of typhoid fever are well recognised. Though encountered encephalitic symptoms are protean, opsoclonus has not been reported. Besides, neurological complications have been reported in patients with *Salmonella typhi* infection. Opinion differs as to the site of lesion causing opsoclonus. Though cerebellar involvement in association with opsoclonus may be important,⁴ cases are on record with no evidence of cerebellar findings. Indeed, Orzechowski himself,² as well as other subsequent observers, suggested a mesencephalic lesion as the origin. Recently, isolated opsoclonus has been reported occurring in a patient with occult systemic malignancy.⁵ Our patient with paratyphoid infection presumably had transient inflammation of her brain stem or cerebellum which was responsible for the unique ocular movement similar to that occasionally seen in viral encephalitis.

¹ Gay, A J, *et al*, *Eye Movement Disorders*, chap 4, p 79. St Louis, Mosby, 1974.

² Orzechowski, C, *Journal Psychologie Neurologie*, 1927, **35**, 1.

³ Osuntokun, B O, *et al*, *Archives of Neurology*, 1972, **27**, 7.

⁴ Ellenberger, C, *et al*, *Neurology (Minneapolis)*, 1968, **18**, 1041.

⁵ Bellur, S N, *Neurology (Minneapolis)*, 1975, **25**, 502.

(Accepted 29 June 1977)

Department of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

ATHASIT VEJAJIVA, MB, FRCP, professor

PRAVIT LERDVERASIRIKUL, MD, lecturer

Rheumatoid factor in a patient with Reiter's disease and aortic incompetence

Aortic valve disease is a well-recognised complication of Reiter's disease.¹⁻³ We report a case in which the development of aortic incompetence was accompanied by a positive slide latex test to a high titre.

Case report

A 30-year-old man was admitted in November 1973 from the outpatient department. In December 1965 he had had an episode of urethritis, followed by conjunctivitis and arthritis of the left knee and ankle. The ESR (Westergren) was 82 mm in 1 hour, while the results of the antinuclear factor and latex tests were negative. Reiter's disease was diagnosed and in the next eight years he had recurrent episodes of conjunctivitis, anterior uveitis, urethritis, and arthritis. At no time was any cardiovascular abnormality noted, and his latex test remained negative. When he attended the outpatient department in 1973 he gave a six-week history of tightness across the chest, exertional dyspnoea, and a cough productive of green sputum. The symptoms had followed an influenza-like illness which had persisted for four months. He had passed a small clot of blood per urethram on one occasion only. There were no joint or eye symptoms. He was febrile (99.2°F; 37.3°C) and had a collapsing pulse with a blood pressure of 130/60 mm Hg. There was a harsh, mid-systolic murmur at the apex of the heart and a loud, blowing, decrescendo murmur at the left sternal edge. No other abnormality was noted. The results of relevant investigations were as follows. ESR: 14 mm; slide latex titre 1:1280, rising to 1:2560 10 days later; WR, Kahn, GCFT VDRL, LE cells, ANF, plasma proteins, liver function tests, immunoglobulins, and fibrin degradation products (FDP) were all negative or normal. Repeated blood cultures were sterile and antibody titres for the following were within normal limits: *Coxiella*, *Mycoplasma pneumoniae* and

influenza, sendai, psittacosis, adeno- and respiratory syncytial viruses. HLA typing showed the presence of B27 antigen.

His symptoms responded to oral corticosteroids and three months later he was well, with a normal ECG and negative latex test. In the last three years his ESR has never been higher than 26 but his latex test titres have been 1:640 (March 1975); 1:320 (July 1975), and negative (November 1975). Throughout this period he has remained well and his cardiac signs are unchanged.

Discussion

In our patient aortic incompetence presented eight years after the first episode of Reiter's disease and was associated with a positive slide latex test to a titre of 1:2560. That he was not one of the 2% of normal individuals with a positive slide latex test is shown by the two previous and two subsequent negative results. We have found 18 case reports in which aortic incompetence has occurred secondary to Reiter's disease. In only one of these has the disease been associated with a positive latex test for rheumatoid factor and this was only weakly positive.⁴ We have found only two other cases of Reiter's disease associated with the presence of rheumatoid factor, though in one of these the presence of rheumatoid nodules suggests the coincidence of rheumatoid arthritis with Reiter's disease.⁵

We have ruled out all the generally listed causes of a positive slide latex test. There was no clinical or biochemical evidence of chronic liver or respiratory disease, and the repeated negative blood cultures, normal FDP, and subsequent benign clinical course without any antibiotic treatment rule out subacute bacterial endocarditis. In addition the level of the positive titres (1:1280 rising to 1:2560) is much higher than is usually seen in non-rheumatic conditions.

The significance of the raised latex titre remains unexplained. Perhaps it is a marker, suggesting an autoimmune aetiology of aortic regurgitation in Reiter's disease. Perhaps serial measurements of latex titres in patients with aortic incompetence and Reiter's disease would have shown similar results in the other published accounts.

¹ Csonka, G W, *et al*, *British Medical Journal*, 1961, **1**, 243.

² Good, A E, *Seminars in Arthritis and Rheumatism*, 1974, **3**, 253.

³ Paulus, H E, Pearson, C M, and Pitts, W, *American Journal of Medicine*, 1972, **53**, 464.

⁴ Block, S R, *Arthritis and Rheumatism*, 1972, **15**, 218.

⁵ Csonka, G W, *British Journal of Venereal Disease*, 1959, **35**, 84.

(Accepted 29 June 1977)

Enfield District Hospital, Enfield, Middx

R M DU BOIS, MB, MRCP, senior house officer
S FREEDMAN, PHD, MRCP, consultant physician

Suppression of serum testosterone concentrations in men by an oral contraceptive preparation

Synthetic oestrogens have been used to treat prostatic cancers for over 50 years. High doses have been necessary for adequate response, and long-term use has produced cardiovascular side effects as well as unpleasant feminising effects.¹ The effect of a combined administration of synthetic oestrogens and progestogens has been little studied so far. We have examined the effects of a combined injection of norgestrel and ethinyloestradiol on serum testosterone levels in normal men.

Methods and results

Five healthy men, aged 27-39, volunteered. They took one Eugynon 50 tablet (50 µg ethinyloestradiol + 500 µg norgestrel) between 0700 and 1100 each day for nine days. Venous blood samples were obtained three times a day (between 0900 and 1100, 1500 and 1700, and 2000 and 2300) at about six-hourly intervals on the day before starting the drug, the second, fourth, sixth, and ninth days on the drug, and on the third and seventh days after stopping the drug. Serum testosterone was assayed by a specific radioimmunoassay.²

The figure shows the effect of the drug ingestion on serum testosterone levels. Concentrations (mean of the three samples) fell rapidly for the first

Response of serum levels (mean of three sampling times) of testosterone in five men ingesting norgestrel 500 µg + ethinyloestradiol 50 µg/day for nine days. Vertical bars show standard error of mean.

four days and continued to fall at a slower rate during the 9 days of ingestion. On the ninth day concentrations had fallen to 8% of the initial levels (1.25 nmol/l (0.36 ng/ml)). After discontinuation of the drug concentrations rose quickly and had recovered fully within a week. All men experienced loss of libido during the latter half of the ingestion period.

The results show a powerful effect of the contraceptive preparation in depressing serum testosterone levels in men. Ethinyloestradiol ingestion alone does not produce this pronounced effect,³ which is therefore caused by the progestogen norgestrel. Our preliminary studies with norgestrel ingestion alone do in fact confirm that the effect is almost entirely due to the progestogen. This short-term study therefore indicates that norgestrel is a promising agent for trial in treating prostatic cancer.

Norgestrel has been classified by Edgren *et al*⁴ as a progestogen with androgenic effects and was given an androgenicity rating of 7.5% when compared with testosterone propionate by its effect on the ventral prostate in castrated rats. Later, however, Edgren *et al* administered up to 20 µg of norgestrel to castrated male rats weighing 50 g and found no increase in the weight of the ventral prostate or the seminal vesicles.⁵ A combination of norgestrel with ethinyloestradiol also had no trophic effect on the rat prostate. Whether these results are applicable to people or not, it seems unlikely that our small doses would have any trophic effects on the prostate.

When the present results are compared with the testosterone depressing effects reported for other synthetic steroids, progestogens, or oestrogens, it is clear that on a weight basis norgestrel has by far the strongest effect.

Comment

We suggest that norgestrel alone or combined with small doses of ethinyloestradiol warrants a trial in treating prostatic cancer. As a constituent of oral contraceptive preparations the drug has proved without major side effects in women, and the small doses needed keep the cost within reason.

We gratefully acknowledge support from the Cancer Research Campaign and the Kishinchand Chellaram Foundation.

¹ Byar, D P, *Cancer*, 1973, **32**, 1126.

² Kjeld, J M, *et al*, *British Medical Journal*, 1976, **2**, 1354.

³ Smals, A G H, *et al*, *Acta Endocrinologica*, 1974, **77**, 765.

⁴ Edgren, R A, *et al*, *Fertility and Sterility*, 1967, **18**, 238.

⁵ Edgren, R A, *et al*, *Journal of Reproduction and Fertility*, 1968, suppl 5, 13.

(Accepted 15 July, 1977)

Endocrine Unit, Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS

J M KJELD, MD, PHD, research fellow

C M PUAH, BSC, technical officer

B KAUFMAN, MRCP, consultant physician

S LOIZOU, BSC, technical officer

J VLOTIDES, MD, research fellow

G F JOPLIN, PHD, FRCP, consultant physician and senior lecturer in clinical endocrinology