halothane, and oxygen. The operation and anaesthesia were uneventful. Subsequent pain was controlled by the injection of a further 50 mg pethidine.

The next day she had only slight pain, which was well controlled by 30 mg doses of dihydrocodeine by mouth. On the second postoperative day, however, she became progressively drowsy with respiratory frequency slowing to four breaths/min. Her pulse became irregular with electrocardiographic evidence of ectopic beats and right bundle-branch block. She had no focal neurological signs, but her conscious level continued to deteriorate until she responded only to painful stimuli. Computed tomography of the brain showed no abnormality apart from carotid siphon calcification. Urine output was poor and plasma urea and creatinine concentrations rose to 14.5 mmol/l (87 mg/100 ml) and 250 μ mol/l (2.8 mg/100 ml) respectively despite apparently normal hydration (plasma sodium concentration 133 mmol(mEq)/l). Arterial blood gas analysis showed oxygen tension 7.9 kPa (59 mm Hg) and carbon dioxide tension 6.5 kPa (49 mm Hg); she was treated with an inspired oxygen concentration of 35%, and her arterial tension rose to 12.3 kPa (92 mm Hg). Her slow, deep breathing suggested opioid overdosage, and 0.4 mg of the opioid antagonist naloxone was given intravenously. She immediately woke and asked where she was, and respiratory frequency increased to 20 breaths/min. She became sleepy again over the next half hour, her respiratory frequency falling to 10/min. A further dose of naloxone had a good but less dramatic effect.

An infusion of doxapram was almost completely ineffective; she took only six breaths/min and remained drowsy. Lumbar puncture was performed; the pressure and appearance of the fluid were normal and a sample was taken for analysis. A continuous naloxone infusion was then started. As long as her respiratory frequency was greater than 10/min her conscious level remained satisfactory. The figure shows the respiratory frequency and doses of drugs used. The infusion was stopped on her sixth day in hospital; respiratory frequency fell but she no longer lapsed into unconsciousness. The respiratory rate was normal by the next day. For a few days after operation she was distinctly oliguric: this improved gradually with frusemide and fluid management.

Respiratory frequency during treatment, showing individual doses of naloxone, two periods of continuous infusion, and infusion of doxapram.

Control values for methionine-enkephalin and substance P in cerebrospinal fluid are in the range 0-10 pmol met-enkephalin/l and 20-100 pmol substance P/l (Y Hosobuchi, unpublished observations). The concentration of met-enkephalin in this sample was >9.0 nmol/l and of substance P at least 350 pmol/l. More detailed characterisation could not be attempted as all the available material had been used.

Comment

The extreme respiratory depression in this patient responded to the opioid antagonist naloxone. Naloxone is sufficiently specific that this response indicates the presence of opioid, and she had been fully conscious both on admission and after anaesthesia and had no evidence of brain injury. We conclude that her drowsiness and respiratory depression were opioid effects. A specific radioimmunoassay showed a high cerebrospinal fluid concentration of endorphin (met-enkephalin-like material). Although we could not determine the exact nature of the material, the specificity of the assay has been described¹ and the material must at least have contained the methionine-enkephalin sequence. The concentration of substance P in the cerebrospinal fluid was less abnormal and could not account for the observed symptoms.

The question arises where the opioid came from. She had received two 50 mg doses of pethidine on the day of admission. Neither caused drowsiness or respiratory depression, and after the first dose she could breathe spontaneously while under the anaesthetic. She subsequently received five doses of dihydrocodeine over 24 hours. Respiratory depression is not associated with use of this drug in moderate dosage.

Opioids may cause delayed respiratory depression; respiratory depression has occurred up to 24 hours after intrathecal injection of morphine.^{2,3} In our case the interval was about 36 hours and no drugs had been given intrathecally. The patient was still perceptibly drowsy seven days after her second dose of pethidine and six days after the last dose of dihydrocodeine. Neither pethidine nor dihydrocodeine show up in the radioimmunoassay used, which is specifically directed at peptides. The other striking feature was oliguria; no urine at all was passed on either the day of operation or the first postoperative day, and the next day she produced only 18 ml. Opioids are commonly regarded as potent stimulators of release of antidiuretic hormone,⁴ although this view has recently been challenged.⁵ Diuresis in our case coincided with the use of naloxone, although there were associated changes in central venous pressure, conscious level, and arterial gas tensions, which may have been contributory.

Given the radioimmunoassay data we must conclude that the high opioid concentrations found in her cerebrospinal fluid were caused by an endogenous met-enkephalin-like endorphin.

We thank Dr L L Iversen, director of the MRC Neurochemical Pharmacology Unit, for his help and advice in the investigation of this case and the preparation of this report, and Mr A G H Murley for permission to publish this case.

- Clement-Jones V, Lowry PJ, Rees LH, Besser GM. Development of a specific extracted radioimmunoassay for methionine-enkephalin in human plasma and cerebrospinal fluid. *J Endocrinol* 1980;**86**:231-43.
- Davies GK, Tolhurst-Cleaver CL, James TL. Respiratory depression after intrathecal narcotics. *Anaesthesia* 1980;**35**:1080-3.
- Gjessing J, Tomlin PJ. Postoperative pain control with intrathecal morphine. *Anaesthesia* 1980;**36**:268-76.
- Jaffe JH, Martin WR. Narcotic analgesics and antagonists. In: Goodman LS, Gilman A, eds. *Pharmacological basis of therapeutics*. 5th ed. New York: MacMillan, 1975:280.
- Grossman A, Besser GM, Milles JJ, Baylis PH. Inhibition of vasopressin release in many by an opiate peptide. *Lancet* 1980;iii:1108-10.

(Accepted 23 September 1981)

Addenbrooke's Hospital and MRC Neurochemical Pharmacology Unit, Cambridge CB2 2QQ

IRIS E SYMONS, MB, FFARCS, senior registrar in anaesthetics
PIERS C EMSON, MSC, PHD, senior scientist
JOHN V FARMAN, MB, FFARCS, consultant anaesthetist

Serum sickness due to hair straightener

Serum sickness, a delayed reaction to the administration of foreign protein, has been shown to be due to immune-complex deposition and inflammation mediated via the classical complement pathway.¹ Clinical manifestations generally become apparent within three to 14 days after exposure to the relevant agent.

Case report

A previously fit 31-year-old West Indian woman used a proprietary hair-straightening product, Alberto Culver, for about 48 hours, noting an initial burning sensation in the treated area. Within 48 hours she had developed shortness of breath, generalised swelling of the joints and legs, and a pruritic maculopapular rash that spread from the neck area over most of the body.

On admission she was feverish and had a symmetrical polyarthropathy affecting particularly the wrists, metacarpal and interphalangeal joints, and both knee joints, which had moderate effusions. Shallow mucosal mouth ulcers and palpable, tender left supraclavicular and axillary nodes were present. Liver and spleen were not palpable, and neurological examination was unremarkable.

Laboratory results showed haemoglobin concentration 11.4 g/dl; white cell count $6.8 \times 10^9/l$ with normal differential and picture; and erythrocyte sedimentation rate 77 mm in first hour. Repeat blood cultures, viral screening, antistreptolysin-O titre, liver function tests, protein electrophoresis, Paul Bunnell test, serum hepatitis antigen, screening for brucella, serum Wassermann reaction, urine microscopy, sickle-cell screening, and malaria studies were all negative or yielded no useful information. Rheumatoid and anti-nuclear factor tests were negative and IgM concentration was normal at 198 IU/ml (normal 55-230 IU/ml), but IgG was raised at 260 IU/ml (normal 75-200 IU/ml) and IgA raised at 246 IU/ml (normal 45-200 IU/ml).

Treatment was started with Benoral Suspension 10 ml twice daily, and steroid treatment was begun two days later at a dose of 30 mg of enteric-coated prednisolone daily. Good clinical control of the polyarthropathy enabled the steroid dosage to be reduced to 5 mg twice daily after 10 days, by which time erythrocyte sedimentation rate was 21 mm in the first hour and the rash had largely cleared. She was discharged taking enteric-coated prednisolone 5 mg twice daily and naproxen 500 mg in the morning with food. Steroids were reduced over the next three months and all medication then stopped; tests for rheumatoid factor remained negative and both the rash and joint symptoms resolved completely.

Comment

We considered that this was a serum sickness type 3 reaction, probably due to the hair straightener. The straightener was later found to contain a total of 14 compounds, of which either hydrolysed animal protein or protamine nucleic acid complex may have been the precipitating factor in this case. Serum sickness due to hair straightener has not previously been reported, and the consumer safety unit at the Department of Trade, the Health and Safety Commission, and the manufacturers of the product are not aware of any similar cases.

I thank Dr M F Grayson for allowing me to report on one of his patients.

¹ Dickson FJ. The role of antigen-antibody complexes in disease. *Harvey Lect* 1963;58:21.

² Ruddy S, Gigli I, Austen KF. The complement system of man. *N Engl J Med* 1972;287:489-95.

(Accepted 21 October 1981)

Department of Rheumatology and Rehabilitation, North Middlesex Hospital, Edmonton, London N18 1QX

K E KOTOWSKI, MA, MRCP, senior registrar

Mumps virus isolated from a fetus

A prospective study¹ confirmed an association between gestational mumps and spontaneous abortion and showed a fetal mortality of 27% in 33 women who developed mumps in the first trimester of pregnancy, compared with a mortality of 13% in uninfected mothers. We report the isolation of mumps virus from a fetus spontaneously aborted four days after the mother developed clinical mumps.

Case report

A 28-year-old woman, gravida 4 para 1, had started her last menstrual period before her fifth pregnancy on 2 May 1981. On 1 August she developed clinical mumps and four days later spontaneously aborted a 10-week fetus. Serum samples taken at an earlier antenatal visit and four weeks later confirmed the clinical diagnosis, the mumps virus complement fixation titres having risen from <8 to 256.

The fetus was examined in the laboratory. Specimens of lung, liver, and brain were pooled and the homogenised suspension inoculated on to tissue cultures for virus isolation. A haemadsorbing virus was detected in primary baboon kidney-cell cultures on the 10th day, and this was shown to be mumps virus by a direct fluorescence antibody technique using a rabbit antimumps serum conjugated with fluorescein. To determine any chromosome abnormalities fibroblast cultures were set up from the fetal material using standard techniques and cultured in Eagles's medium with 20% fetal calf serum. After 19 days chromosome preparations were made and stained with toluidine blue. Of 50 cells examined, only three showed aberrations: one a chromosome break, one a chromatid break, and one an extra fragment. G-banded preparations showed a normal female karyotype.

Comment

We believe this to be the first report of isolation of mumps virus from a human fetus. Little direct evidence has previously existed of fetal infection early in pregnancy. No firm evidence associating maternal mumps with prematurity or congenital malformations appears to exist, and the postulated association with endocardial fibroelastosis is still debatable.² Garcia *et al*,³ however, claimed to have found morphological evidence of mumps infection in three placentas and the adrenal cortex of one fetus obtained from mothers whose

pregnancies were terminated because they had had mumps in the second or fifth month.

Experimental infection of rhesus monkeys⁴ has shown that mumps virus can cross the placenta. The virus was isolated from fetal tissue for only one week after mothers were infected in the first trimester of pregnancy. The brevity of this period of virus replication in the fetus was thought to be responsible for the lack of mumps antibody in the progeny, who nevertheless showed a delayed hypersensitivity response to intradermal mumps antigen. This "split immunological recognition" has also been observed in man. That mumps virus can cross the placenta late in pregnancy was also suggested by Jones *et al*,⁵ who isolated the virus at birth from the pharynx of two out of three infants whose mothers had had clinical mumps four to seven days before delivery.

Studies of the chromosomes of the infected fetus reported on above failed to show any abnormalities suggestive of an underlying genetic cause for the fetal death. Although mumps virus may cause changes in lymphocyte chromosomes similar to those caused by measles—that is, chromosome and chromatid breaks and multiple fragmentation—the few cells (three out of 50) showing this type of damage were within normal limits for cells grown in tissue culture and do not suggest widespread virally induced chromosome damage. Given the presence of the virus, however, some more localised chromosome damage might possibly have been caused in organs not examined.

This case shows conclusively that transplacental mumps infection occurs.

We thank Mr A Williams for referring this patient.

¹ Siegal M, Fuerst HT, Peress NG. Comparative fetal mortality in maternal virus diseases. *N Engl J Med* 1966;274:768-71.

² Hanshaw JB, Dudgeon JA. *Virus diseases of the fetus and newborn*. Philadelphia: W B Saunders, 1978.

³ Garcia AG, Pereira JM, Vidigal N, Lobato YY, Pegado CS, Branco JP. Intrauterine infection with mumps virus. *Obstet Gynecol* 1980;56:756-9.

⁴ St Geme JW Jr, Peralta H, Van Pelt LF. Intrauterine infection of the rhesus monkey with mumps virus: abbreviated viral replication in the immature fetus as an explanation for split immunologic recognition after birth. *J Infect Dis* 1972;126:249-56.

⁵ Jones JF, Ray CG, Fulginiti VA. Perinatal mumps infection. *J Pediatr* 1980;96:912-4.

(Accepted 28 October 1981)

John Radcliffe Hospital, Headington, Oxford OX3 9DU

J B KURTZ, MRCP, MRCPATH, consultant virologist, department of virology
A H TOMLINSON, DPHIL, FRCPATH, top-grade microbiologist, Public Health Laboratories

J PEARSON, BA, scientific officer, department of medical genetics

Chest infection caused by *Lactobacillus casei* ss *rhamnosus*

Association of lactobacilli with human infection has rarely been documented,¹ although some cases of septicaemia or endocarditis caused by lactobacilli have been reported.²⁻⁴ Organisms of this genus are generally reported from routine laboratory investigations as "contaminants" or "normal flora" when grown from specimens other than blood. I report a case in which the organism was responsible for chest infection and was isolated from sputum.

Case report

A 61-year-old woman with chronic myeloid leukaemia was admitted complaining of cough with yellow sputum and difficulty in breathing. On examination chest infection was suspected. She was afebrile and there was no evidence of generalised infection. White cell count on admission was $39 \times 10^9/l$ (neutrophils $32 \times 10^9/l$). Oral cephalixin 500 mg six-hourly was prescribed and specimens of sputum and blood taken for culture. Sputum was thick and purulent. Microscopy showed many pus cells and large Gram-positive bacilli. No acid-fast bacilli were present. Culture of sputum produced pure and heavy growth of a diphtheroid organism, which was reported as normal flora. Two days later a second specimen of sputum showed similar microscopic features and produced pure and heavy growth of a diphtheroid as before.

As there was no clinical improvement three days after cephalixin treat-