tube compresses the site of injection and effectively maintains the sclerosant at the injection site and controls bleeding.

The insertion of a rigid oesophagoscope is occasionally difficult or even impossible, but this difficulty does not arise with the flexible gastroscope. We and others³ have also found that the rigid oesophagoscope perforates the oesophagus of an appreciable number of patients. In our series of 150 patients there have been no oesophageal perforations using the flexible gastroscope. The minor complications associated with oesophageal injection sclerotherapy are substernal pain, tachycardia, and an occasional small pleural effusion.

Our experience with both the rigid and the flexible instruments has shown that the flexible gastroscope with the outer tube provides an easier and safer method of injecting

oesophageal varices. An endoscopist will find little difficulty in mastering the technique.

The oesophageal tube was provided by KeyMed.

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(Accepted 31 July 1979)

SHORT REPORTS

Pseudomonas meningitis treated with azlocillin

Infection of the brain or meninges by *Pseudomonas* species is rare, difficult to treat, and usually associated with neurosurgical procedures. We report a case with a remarkably long latent period of seven years between surgery and evidence of infection, which was successfully treated with a new antibiotic, azlocillin.

Case report

In 1971 a man aged 20 presented with headache of one month's duration and signs of a mass in the posterior fossa. A ventricular catheter and Rickham reservoir were placed through a frontal burr hole, and a ventriculogram showed a left cerebellar mass. A cystic cerebellar astrocytoma was completely excised. After a two-week course of ampicillin and cloxacillin he made an excellent recovery. In 1978 he was admitted with a three-week history of headache and of fever and photophobia for two days. His temperature was 39°C and he had a stiff neck. The lumbar cerebrospinal fluid (CSF) contained $195 \times 10^6/l$ ($195/mm^3$) white cells (half neutrophils and half lymphocytes). The CSF concentration of protein was 3 g/l and of sugar 3.9 mmol/l (70 mg/100 ml). Culture was sterile. The next day he felt better apart from persisting headache and was afebrile with no signs of meningitis. Fifteen days after admission his temperature rose to 39°C, his headache worsened, and he was given penicillin, cloxacillin, and chloramphenicol. Two days later *Pseudomonas aeruginosa* was cultured from lumbar CSF after 24 hours. On this occasion the CSF contained $250 \times 10^6/l$ ($250/mm^3$) white cells (65% neutrophils, 35% lymphocytes) and glucose concentration was 1.8 mmol/l (32 mg/100 ml) with a simultaneous plasma glucose concentration of 7.4 mmol/l (131 mg/100 ml). The Rickham reservoir was aspirated and large numbers of Gram-negative rods were seen on direct microscopy. The reservoir was removed and grew *Ps aeruginosa*. The fever settled over five days. The patient felt better until 12 days after removal of the reservoir, when he suddenly developed headache, vomiting, and a temperature of 37.5°C. This time the CSF contained $525 \times 10^6/l$ leucocytes ($525/mm^3$), mostly neutrophils. He was given azlocillin 5 g intravenously every six hours for 10 days. His symptoms abated. At the end of the 10 days he went home. He was back at work within a month. On the seventh day of treatment the CSF concentration of azlocillin was 5 µg/ml. The minimum inhibitory concentration (MIC) of the *Ps aeruginosa* was 1 µg/ml. This CSF contained only $30 \times 10^6/l$ ($30/mm^3$) lymphocytes, and sugar concentration was normal.

Comment

Pseudomonas species are rare primary pathogens in previously fit people. Nosocomial infections have often been associated with isolation of the organism from sinks, antiseptic solutions, or ward equipment.¹ The upper respiratory and urinary tracts are often colonised when selective pressure is exerted by giving broad-spectrum antibiotics to which the organism is resistant.^{2,3} The organism may be conveyed to the scalp and thence to the CSF via communicating wounds or drains.

Azlocillin, one of the ureido-penicillins,⁴ a recently developed group of antibiotics, has a wide spectrum of antibacterial activity. It is notably potent against *Pseudomonas* spp, the mode MIC being only 4 µg/ml. Like other penicillins its penetration into the CSF is related to

the degree of meningeal inflammation, but interestingly in our case of low-grade meningitis the concentration achieved, without recourse to intrathecal therapy, was five times the MIC of the organism. The most widely used anti-pseudomonal agent is gentamicin, but this penetrates poorly into the CSF and possibly bactericidal concentrations might be achieved only at the cost of damage to the eighth cranial nerve. Carbenicillin is only moderately active and penetrates CSF poorly, so that daily intrathecal therapy is essential. Azlocillin appears to be the agent of choice in this uncommon but serious infection.

We thank the staff of the department of medical microbiology, the London Hospital, for the bacteriology and antibiotic assays; Dr A M Geddes, East Birmingham Hospital, for advice; Dr John Mason, of Bayer (UK) Ltd; and Mr T T King, consultant neurosurgeon, the London Hospital, for permission to report his case.

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(Accepted 6 July 1979)

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Prediction of fetal sex: a cautionary tale

Amniocentesis, which is being performed increasingly, allows determination of the genotype of the fetus. A problem arises whether or not the mother should be told the sex of her fetus. This case shows that things are not always what they seem, and provides support for not telling the mother the sex of her fetus.

Case report

Amniocentesis was performed, because of maternal age, at 14 weeks on a 39-year-old woman in her fourth pregnancy. The amniotic fluid α -fetoprotein was normal, and the fetal genotype was 46XY. The mother did not want to know the sex of the infant and so was not told. She then gave birth at term to a phenotypically normal girl (weight 4.2 kg (9lb 4 oz)): the external genitalia were entirely normal and there were no hernias. Chromosome analysis confirmed the 46XY genotype and a buccal smear was chromatin negative. When the girl was 1 year old a human chorionic gonadotrophin (HCG) stimulation test raised the plasma testosterone concentration from a basal value of 0.2 nmol/l (0.06 ng/ml) to 6.4 nmol/l (1.85 ng/ml).

The chromosomes of two older sisters (both phenotypically normal girls) were analysed and the oldest one (13 years) was also found to be genotypically

46XY. Her basal serum concentration of testosterone was 15 nmol/l (4.33 ng/ml) and rose to 18 nmol/l (5.19 ng/ml) after HCG stimulation.

Comment

In both these girls who were genotypically male and phenotypically female the likely diagnosis is androgen insensitivity (testicular feminisation syndrome). The rise in plasma testosterone concentration after HCG stimulation excluded gonadal agenesis and any enzyme defect of testosterone biosynthesis. Androgen insensitivity, which is probably an X-linked disorder,¹ results from a failure of end-organs to respond to testosterone.² The uterus is absent, but normal breast development occurs in puberty if the testes are not removed: the testes should eventually be removed because of the risk of neoplasia.³ The diagnosis is normally made during investigation for amenorrhoea or following the appearance of testes (usually as a hernia) but may not be made at all. This is the first time, so far as I know, that the diagnosis has been made in part through amniocentesis.

This case shows that the future sex of an infant cannot be predicted with certainty by amniocentesis, and this is one reason why the mother should probably not be told the sex of her child.

I am grateful to Dr Stanley Walker, department of cytogenetics at the University of Liverpool, for expert help and to Mr E Parry-Jones, consultant obstetrician at HM Stanley Hospital, for allowing me to publish details of his patient.

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(Accepted 25 July 1979)

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Life-threatening arrhythmias and intravenous cimetidine

Animal studies have shown histamine (H₂) receptors in the heart and coronary circulation, and cardiovascular complications in man have been associated with cimetidine.^{1,2} We describe two cases in which life-threatening arrhythmias occurred during treatment with intravenous (IV) cimetidine.

Case reports

(1) A previously fit 48-year-old man was found on gastroscopy to have a benign antral ulcer. He had developed late-onset asthma six months previously for which he had taken 5 mg prednisolone daily. An ECG was normal. He was started on cimetidine 1 g/day by mouth but, because his pain persisted, after 48 hours cimetidine 400 mg 6-hourly was given intravenously (IV). Twenty-four hours later, five minutes after the third dose of cimetidine IV, his blood pressure fell abruptly from 120/80 to 80/60 mm Hg without evidence of haemorrhage or perforation. It gradually rose to 100/60 mm Hg over the next six hours. After the fourth dose of cimetidine he became asystolic but responded to IV isoprenaline. Over the next eight hours he had six similar episodes, the final one proving fatal. All occurred either immediately after cimetidine (one injection) or on withdrawal of isoprenaline. Plasma electrolytes and arterial blood gases were normal throughout. Frusemide, dexamethasone, flucloxacillin, and gentamicin had also been given. Necropsy showed polyarteritis nodosa, slightly atypical in that it was confined to the heart, spleen, stomach, and duodenum.

(2) A 56-year-old man with no previous history of heart disease was transferred from another hospital with anuria after the fashioning of an ileal conduit six days earlier. On admission he was clinically septicæmic and pus was obtained on abdominal paracentesis. ECG showed sinus tachycardia but was otherwise normal. Four hours later he became hypotensive and had a cardiorespiratory arrest in asystole, from which he was rapidly resuscitated. He was given cimetidine 400 mg IV to prevent gastrointestinal bleeding. Ten minutes later sinus arrest occurred. After resuscitation he remained stable for three hours, when a further dose of cimetidine IV was associated with atrial extrasystoles and then cardiorespiratory arrest. He was again resuscitated. No more cimetidine was given and there were no further arrhythmias. The patient died 14 days after admission from renal failure and pseudomonas septicæmia. There was no necropsy. Serial measurements

of plasma electrolytes and arterial blood gases showed no significant abnormalities. Ampicillin, gentamicin, and frusemide were given in addition to the drugs required for resuscitation.

Comment

Both patients had other conditions that might have caused their arrhythmias, but each showed a striking temporal association with the administration of cimetidine. We can only speculate whether it played a causal role. In the isolated guinea-pig heart histamine-induced prolongation of the PR interval is probably mediated by H₁ receptors located at the atrioventricular node, while H₂ receptors in the myocardium are responsible for the positive inotropic and chronotropic effects of histamine.³ The highest plasma histamine concentrations have been in patients with sepsis or after major surgery. Thus the bradycardia and atrioventricular dissociation previously described could well have resulted from cimetidine-induced H₂ blockade in ill patients with high plasma concentrations of histamine.

An alternative hypothesis implicates prolactin. Cimetidine blocks dopamine as well as histamine receptors, and therefore causes prolactin release. In healthy human volunteers there was a rapid rise in serum prolactin a few minutes after an intravenous bolus of 400 mg cimetidine.⁴ Interestingly, there was no such rise after an oral dose. In rats pharmacological doses of prolactin may induce arrhythmias.⁵ Indeed, we have seen two patients with prolactinomas and otherwise unexplained arrhythmia. Since patients under stress already have high serum prolactin, IV cimetidine may further increase this hormone and thus may precipitate arrhythmia. Disorders of cardiac rhythm in seriously ill patients are often ascribed to rapidly changing metabolic or haemodynamic factors. IV cimetidine may complicate their management.

We thank Drs P B Cotton and L M Selby for referring the first case and Professor D K Peters for permission to report the clinical details of the second. Fuller details of the case histories are available on request from JC, to whom requests for reprints should be addressed.

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(Accepted 9 July 1979)

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Determination of subfractions of amniotic fluid alpha-fetoprotein in diagnosing spina bifida and congenital nephrosis

The alpha-fetoprotein (AFP) test is well established as a diagnostic tool for the early antenatal detection of neural-tube defects and congenital nephrosis. Nevertheless, this and other diagnostic measures currently available do not permit a completely accurate distinction between normal fetuses and fetuses with these malformations. We recently found that human AFP can be separated into subfractions by chromatography on concanavallin A (con A).¹ About 2-5% of fetal serum AFP does not bind to con A, and this is a constant feature throughout gestation. In contrast, 15-40% of AFP in amniotic fluid during the second trimester is non-reactive with con A. It seemed to us that the increased leakage of AFP from the fetus to the amniotic fluid associated with neural-tube defects and congenital nephrosis should not only lead to a higher concentration of AFP in amniotic fluid but could also change the relative proportions of the con A