Case reports

Case 1—A 22-year-old Kenyan Asian man presented with pain in the right hip for one month, weight loss of 9 kg, and lassitude. He was pale and thin, with a fixed flexion deformity of 15° in the right hip and little movement because of intense pain. Temperature was 38.5°C, chest expansion 4 cm, haemoglobin concentration 10.1 g/dl, ESR 96 mm in the first hour. The results of all serological tests were negative. Histological and bacteriological examination of inguinal node and hip synovial biopsy specimens failed to confirm tuberculosis. X-ray films showed loss of joint space in the right hip with obliteration of the right sacroiliac joint. The patient remained very ill and a trial of antituberculosis treatment was ineffective. He developed polyarthritis, and further x-ray films showed bilateral sacroiliitis. Phenylbutazone produced considerable improvement.

Case 2—A 26-year-old Pakistani man presented with malaise, fever (39°C), night sweats, and severe left hip pain for four months. He was thin, with his left hip fixed in a flexed and adducted position. Chest expansion was 4.5 cm, ESR 87 mm in the first hour, the results of serological tests negative, and chest x-ray film normal. All cultures of an open synovial biopsy specimen failed to confirm tuberculosis. A trial of antituberculous treatment failed. Repeat x-ray films two months later showed bilateral sacroiliitis, and his lumbar spine was stiff. Phenylbutazone produced rapid improvement.

Case 3—A 35-year-old British woman presented with left hip joint pain, early morning stiffness, fever (38.6°C), anorexia, and weight loss for six weeks. She was toxic and ill with pallor and painful restriction of all hip movements. The haemoglobin concentration was 8.9 g/dl, ESR 70 mm in the first hour, and the results of serological and antinuclear factor tests were negative. Cultures were sterile apart from klebsiella isolated from the faeces. She then developed polyarthritis, and x-ray films showed bilateral sacroiliitis. Phenylbutazone produced a considerable improvement.

Case 4—A 36-year-old British man presented with lassitude, weight loss (9 kg), fever (38.5°C), night sweats, and right hip pain for four months. There was painful limitation of movement of the hip, and effusion of the right knee. The ESR was 113 mm in the first hour and the haemoglobin concentration 13.1 g/dl. The results of serological tests and cultures were negative and x-ray films were normal. High-dose salicylates were ineffective and the patient continued losing weight, with a falling haemoglobin concentration and fever. Despite exhaustive investigations, no firm diagnosis was made. Trials of antituberculous and antituberculous treatment failed. He gradually developed stiffness of the lumbar spine and early kyphosis. When reviewed seven months after the onset of symptoms he had early morning stiffness, chest expansion 5 cm, and reduced lumbar spine movements. The clinical picture now suggested ankylosing spondylitis, and phenylbutazone produced dramatic improvement. Recent x-ray films, apart from showing bilateral calcaneal spurs, have still shown normal appearances.

Discussion

Unilateral sacroiliitis has been observed in early ankylosing spondylitis, and symptoms may precede sacroiliitis by some years.¹ Chest expansion of under 5 cm is an important physical sign in ankylosing spondylitis.² Cases No 1 and 2 may represent spondylitic forms of juvenile chronic arthritis in view of histories of "arthritis" at the ages of 12 and 15, respectively. Alternatively, they could represent incomplete forms of Reiter's syndrome progressing to sacroiliitis and spondylitis.³ Ebringer⁴ has reported an association between klebsiella infection, ankylosing spondylitis, and the possession of HLA-B27 antigen. This organism was isolated in patients 3 and 4.

Ankylosing spondylitis may present with severe systemic upset and pyrexia of undetermined origin, but these manifestations are poorly recognised. Sacroiliitis should be looked for in undiagnosed fever.

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Neural tube defects and immunoreactive β -melanocyte-stimulating hormone in amniotic fluid

Our recent findings of large amounts of β -melanocyte-stimulating hormone (β -MSH) in the human brain¹ and cerebrospinal fluid (CSF)² suggested that neural tube defects might be detected by finding MSH peptides in amniotic fluid.

Patients, methods, and results

Amniotic fluid was obtained at diagnostic amniocentesis (2nd trimester) or at artificial rupture of the membranes (3rd trimester) from 66 patients. There was a neural tube defect in 10 (anencephaly seven, meningocele three) and there were three stillbirths. A modification of the method of Thody and Plummer³ was used to measure immunoreactive β -MSH in blood and amniotic fluid and in three placentas and the attached umbilical cords from full-term normal deliveries. The tissues were homogenised in 1M HCl, the extracted β -MSH separated by centrifugation, and the supernatant lyophilised for immunoassay. In each case curves parallel to the standard were obtained.

β -MSH concentrations were significantly higher in amniotic fluid than in normal plasma (mean = 66.3 $\pm$ SE 5.9 ng/l compared with 16.2 $\pm$ 1.2 ng/l for plasma) and fell (figure) with increasing length of gestation. In the seven with neural tube defects the β -MSH concentration in the second trimester was 80.9 $\pm$ 19.6 ng/l, compared with 83.1 $\pm$ 7.3 ng/l for the normal pregnancies. The amniotic fluid β -MSH concentration from the three stillbirths was higher than normal (118.3 $\pm$ 32.0 compared with 83.1 $\pm$ 7.3), but the difference was not significant. The β -MSH content of the three placentas and corresponding cords were 553 and 582; 526 and 120; and 674 and 0 μ g/g.

Immunoreactive β -MSH concentrations in amniotic fluid at various weeks of gestation. The decrease with gestation is significant ($r = 0.64$, $P < 0.001$).

Comment

We have confirmed the presence of immunoreactive β -MSH in the amniotic fluid⁴; furthermore, our finding that its concentration in amniotic fluid is higher than in plasma suggests a concentrating mechanism or a source of β -MSH other than maternal plasma. The fetal pituitary contains β -MSH, corticotrophin-like intermediate lobe peptide (CLIP), and β - and γ -lipotrophin⁵ which cross-reacts with β -MSH in most immunoassays. Nevertheless, the higher concentrations of β -MSH found after fetal death make this source unlikely. The detection of immunoreactive β -MSH in full-term placentas suggests that the placenta may be the source of amniotic fluid β -MSH. If this surmise is correct the differential is unlike that for placental lactogen, which occurs in lower concentrations in amniotic fluid than in maternal plasma and increases in the latter with the increasing size of the placenta: by contrast, β -MSH in amniotic fluid decreases with length of gestation.

Increased amniotic fluid β -MSH concentrations were not found in association with neural tube defects, although human nervous tissue¹ and CSF² contain large amounts of MSH peptides. Presumably,

therefore, β -MSH produced by sources such as the placenta masks any contribution from fetal nervous tissue. Possibly, however, the concentration of related peptides produced by the nervous tissue, such as α -MSH or enkephalin and endorphin, may be raised in the amniotic fluid associated with a fetal neural tube defect, and we are now examining this possibility.

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Abuse of pentazocine

Pentazocine (Fortral) was first marketed in the United States in 1967 as a powerful non-narcotic, non-addictive analgesic. Despite increasing evidence of abuse, official¹ and commercial opinion has remained largely unchanged. In the data sheet for pentazocine this statement appears, "... abrupt discontinuation in patients receiving large doses has occasionally resulted in mild withdrawal symptoms. Withdrawal has raised few problems."

True addiction to pentazocine has been reported.² In common with other drugs it is widely used by those who abuse drugs and is available on the black market. We report here six cases that have been under our care (table), and an illustrative case report.

Case report

A 20-year-old pharmacy technician, previously not a drug user, began

injecting herself intravenously with pentazocine two years ago during a period of personal crisis. She tried several times to withdraw from the drug but failed because of the severity of withdrawal effects. When admitted to Queen Elizabeth Hospital in June 1977 she was taking 300-400 mg pentazocine daily. She had dermal tracking and thrombophlebitis of both arms, and widely dilated pupils. Abrupt discontinuation of the drug was followed by a withdrawal syndrome which lasted for two weeks and included severe cramps; severe abdominal pain; backache, nausea, and vomiting; anorexia; sweating; agitation; and a severe depression of several weeks' duration which did not respond to tricyclic antidepressants. Most symptoms were alleviated by a combination of chlordiazepoxide, aspirin, and metoclopramide. She was not abusing any other drug.

She has now been rehabilitated and has remained free from further drug abuse. She is the only pentazocine addict known to us to have been successfully withdrawn and to be no longer using drugs. Her withdrawal symptoms were similar to those of our other patients who withdrew from pentazocine.

Comment

Our six patients represent the tip of a much wider problem, and we know from them of others in Birmingham who regularly abuse pentazocine but have not sought medical help. The drug is obtained by theft, forgery, and overprescribing, as reported.⁴ Withdrawal from pentazocine is difficult and relapse is frequent. The withdrawal symptoms are severe and in many ways resemble those of diamorphine. Many initially take the drug for "kicks" rather than for medical reasons, but the number of abusers among the medical and para-medical professions is disturbing. Most abusers develop tolerance, tending to increase the dosage. Euphoria is a major reason for repeated administrations (though the main reason for continuing abuse is to avoid withdrawal effects).

Those who use pentazocine by injection suffer the same medical complications as other parenteral drug abusers—abscesses, induration, and cellulitis if used intramuscularly, and dermal tracking and thrombophlebitis if used intravenously. We believe that careful prescribing of the drug will not prevent abuse. As with narcotic abuse, only statutory controls are likely to be effective and consideration should be given to reclassifying pentazocine as a controlled drug.

¹ World Health Organisation's Expert Committee on Drugs and Drug Dependence, *Technical Report Series*, p 437. Geneva, WHO, 1970.
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Details of six known pentazocine abusers

Patient	1	2	3	4	5	6
Sex	F	F	M	M	F	F
Age (years)	23	23	38	26	20	21
Occupation	Nurse	Nil	Train driver	Nurse	Pharmacist	Nurse
Source of drug	Black market, theft	Prescription	Prescription	Theft, forgery, black market	Theft	Theft
Daily dose (mg)	180	240	180	600	400	180
Route	Intramuscular	Intramuscular	Intramuscular	Intravenous	Intravenous	Intramuscular
Initial reason for taking	'Kicks'	Medical	Medical	'Kicks'	'Kicks'	Medical
Withdrawal symptoms	Yes	Yes	Yes	Yes	No	Yes
Relapsed	Yes	Yes	Yes	Yes	No	Yes
Other drugs abused	Yes	No	Yes	No	No	No