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SHORT REPORTS

Chloramphenicol-resistant *Salmonella typhimurium* meningitis in an adult

Salmonella typhimurium meningitis is virtually unknown in adults.¹ We report such a case, complicated by chloramphenicol resistance of the organism and a preterminal cerebellar abscess.

Case report

A 65-year-old woman with maturity-onset diabetes and a history of cholecystectomy was admitted to the infection unit with a three-day history of diarrhoea and vomiting. She was feverish (39°C), had a headache, and was confused, dehydrated, and semiconscious with pronounced neckstiffness. There was nystagmus on horizontal and vertical gaze and mild left Horner's syndrome.

Lumbar puncture produced turbid cerebrospinal fluid with distinct polymorph pleocytosis ($4.6 \times 10^9/l$) and a protein concentration of over 10 g/l. Cerebrospinal fluid glucose concentration was 18.8 mmol/l (339 mg/100 ml) and plasma glucose 33.8 mmol/l (609 mg/100 ml). No organisms were seen on microscopy, but bacterial meningitis was diagnosed clinically and antimicrobial treatment started with high-dosage intravenous bolus benzylpenicillin, gentamicin, and metronidazole to cover a range of possibilities.

Peripheral white cell count was $12.3 \times 10^9/l$ with 80% neutrophils. Radiographs of the chest, abdomen, pelvis, skull, and cervical and lumbar spine were normal. Blood cultures were sterile but *S. typhimurium*, subsequently shown to be phage type 204C, was isolated from cerebrospinal fluid and stools two days after admission. Treatment was then changed to chloramphenicol. On the fifth day after admission, however, the organism was shown to be resistant to chloramphenicol with a minimal inhibitory concentration of greater than 32 mg/ml when tested by the plate diffusion method. Chloramphenicol was therefore stopped and definitive treatment with ampicillin and mecillinam, to which the organism was sensitive, was begun. Until this time there had been little clinical improvement. Dexamethasone and mannitol were also given and the hyperglycaemia was controlled with actrapid.

She responded slowly with restoration of consciousness and decreasing cerebrospinal fluid pleocytosis, becoming rational and free from headache, but developed left facial pain, impaired sensation over the left trigeminal nerve dermatome, and a mild right hemiparesis. Radiographs of the internal auditory meati and a computed tomographic scan proved normal. Recurrent bronchopulmonary and urinary infections arose with intragastric feeding and her indwelling catheter, but she was eventually mobilised and became cheerful, lucid, and ambulant. The left facial pain and Horner's syndrome persisted, but the right hemiparesis resolved.

On the 80th hospital day she suddenly became comatose with neck stiffness and a dense right hemiplegia. Subarachnoid haemorrhage from mycotic aneurysm was diagnosed clinically and apparently substantiated by blood-stained cerebrospinal fluid and xanthochromia. Despite recovery after treatment with tranexamic acid, ampicillin, and dexamethasone she relapsed 10 days later and died.

Necropsy disclosed residual basal meningitis and a left cerebellar abscess 4 cm in diameter from which *S. typhimurium* was cultured.

Comment

This patient was admitted with diarrhoea and meningitis due to *S. typhimurium*. The infection had been acquired by drinking unpasteurised milk from a herd infected with this strain. Seventeen other people also developed salmonellosis from this source.

S. typhimurium is usually associated with self-limiting "gastro-enteritis." Septicaemia is uncommon and meningitis exceptional, save in the premature infant.² This patient's age, diabetes, and previous cholecystectomy possibly had a role in her severe illness. Other factors associated with a poor prognosis in bacterial meningitis include raised

cerebrospinal fluid protein concentration and delay in starting correct treatment,³ both of which applied here. Correct treatment with high doses of ampicillin (intravenous and intrathecal) and mecillinam (intravenous) was not started until six days after her admission. Mecillinam has not to our knowledge been used in salmonella meningitis previously, though its use in salmonella endocarditis has been described.⁴

Despite a total of 300 g ampicillin and 50 g mecillinam our patient died with residual basal meningitis and an intracranial abscess, both recognised but rare complications of salmonellosis.¹⁵ Their occurrence in this case highlights the problem in diagnosing salmonella meningitis and in eradicating the organism from the central nervous system.

Requests for reprints should be sent to Dr M Ellis.

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Vitamin D deficiency and deafness

In metabolic and connective tissue disorders that cause secondary skeletal abnormalities temporal bone disease and deafness may be included in the clinical picture. These disorders include osteitis deformans, osteogenesis imperfecta, osteitis fibrosa cystica, osteoporosis, and osteopetrosis.¹ We report on two patients in whom vitamin D deficiency resulted in biochemical osteomalacia and was associated with bilateral cochlear deafness.

Case reports

CASE 1

A 35-year-old Asian man, who had been a vegan for four years, was referred to the ear, nose, and throat department with a two-year history of progressive bilateral deafness and tinnitus. Before outpatient consultation a severe headache had necessitated emergency medical admission for investigation. There was no vertigo or family history of deafness. The only physical sign was localised tenderness over the left frontotemporal region. The tympanic membranes were normal.

Audiological assessment showed bilateral subtotal trough-shaped fully recruiting cochlear deafness, with a mean pure-tone threshold of 85 db. Bithermal caloric tests were normal. Tomography showed bilateral cochlear demineralisation. Preliminary biochemical evaluation (table) indicated a

probable diagnosis of osteomalacia. The extremely low plasma 25-hydroxy vitamin D (25-OHD) concentration confirmed the diagnosis. Calciferol replacement treatment 3000 units daily was started. Two months later a mean unilateral hearing improvement of 12 db was apparent.

CASE 2

A 49-year-old vagrant Irish ex-labourer was admitted in a state of confusion, dishevelment, and dehydration. One year previously he reported the onset of muscular weakness, progressive bilateral deafness, tinnitus, and episodic vertigo. Neurological examination showed gross wasting and weakness of the small hand, calf, and deltoid muscles. The tympanic membranes were normal; there was no spontaneous nystagmus. Audiometry showed a trough-shaped 55 db bilateral recruiting deafness, and caloric testing bilateral canal hypofunction.

Biochemical evaluation (table) showed a reduced 25-OHD concentration, which was consistent with osteomalacia, probably due to inadequate dietary vitamin D intake. Results of cochlear tomography were normal, but skull radiography showed pronounced basilar impression. The temporal relation of the auditory and muscular symptoms suggested a direct correlation. He discharged himself from hospital before treatment could be started.

Results of preliminary biochemical evaluation and radiology in two patients

	Case 1	Case 2
<i>Plasma variables</i>		
Venereal disease research laboratory test	Negative	Negative
Treponemal haemagglutination test		
Fluorescent treponemal antibody absorption test		
Calcium (corrected) (mmol/l)	2.16	2.56
Inorganic phosphate (mmol/l)	0.68	0.90
Alkaline phosphatase (U/l)	193	482
Urea (mmol/l)	4.0	2.7
Creatinine (μ mol/l)	66	55
25-OHD (nmol/l)*	<5.3	15.3
<i>Radiology</i>		
Skull	Normal	Pronounced vertebrobasilar impression
Cochlear tomography	Demineralisation	Normal
Skeletal survey	Normal	Normal

*Measured by competitive protein-binding assay.

Conversion: SI to traditional units—calcium, inorganic phosphate: 1 mmol/l = 2 mEq/l. Urea: 1 mmol/l $\approx$ 6 mg/100 ml. Creatinine: 1 μ mol/l $\approx$ 11.3 μ g/100 ml. 25-OHD: 1 nmol/l = 0.4 ng/ml.

Comment

It is generally accepted that serum abnormalities of calcium, inorganic phosphate, alkaline phosphatase, and 25-hydroxycholecalciferol or 25-OHD may enable early osteomalacia to be diagnosed in the absence of radiological features of demineralisation. In the series of Dunnigan *et al* only 29% of children with biochemical evidence of rickets showed radiological abnormalities.² Localised bone pain and muscle wasting are recognised symptoms of osteomalacia, but deafness has not been reported as a presenting feature.

Deficiency of vitamin D or its metabolic derivatives 25-hydroxycholecalciferol and 1,25-hydroxycholecalciferol may result directly in auditory dysfunction, or exert a secondary effect by disturbances of calcium metabolism. Calcium ions play an important part in membrane permeability. Active transport mechanisms that include ATPase activity, which maintain the differential biochemical integrity of the inner ear fluids vital for normal cochlear function, may be calcium dependent. In addition, ionised calcium is necessary for normal nerve function and deficiency may adversely affect transmission of the nerve action potentials generated by the cochlea. Retrocochlear deafness in hereditary vitamin-D-resistant rickets, due to secondary hyperparathyroidism causing osteosclerotic narrowing of the internal auditory canals, has been described.³

Basilar impression is a bony, vascular, and neural malformation in the craniocervical region that may be associated with deafness and episodic vertigo.⁴ The acquired type is rare but may occur secondary to osteomalacia.⁵ In case 2 we are not certain whether a direct relation between the two conditions existed as no other skeletal radiological abnormalities were present. Finally, demineralisation of the otic capsule may lead to secondary degenerative changes in the spiral ligament, stria vascularis, and cochlear hair cells. Whatever the mechanism, the threshold improvement in case 1 after treatment suggests a previously unrecognised causal correlation between vitamin D deficiency and cochlear deafness.

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Valproic acid in Sydenham's chorea

Valproic acid is an effective anticonvulsant that may act by facilitating the gamma-aminobutyric acid (GABA) neurotransmitter system.¹ Patients with Huntington's chorea who have low brain concentrations of GABA do not respond to treatment with valproic acid,^{2,3} but one patient with familial paroxysmal choreoathetosis improved when taking the drug.⁴ I present the first report of a patient with Sydenham's chorea treated with valproic acid.

Case report

A 19-year-old previously healthy woman developed twitching of the right hand that progressed to all parts of the body over the next two months. Stress or fatigue exacerbated the movements, which disappeared during sleep. She came to hospital when she began to have slurred speech and difficulty in walking. She had no neurological symptoms apart from emotional lability noted by her mother. Although she had experienced frequent upper respiratory infections, she could not recall any specific illness before the onset of her movement disorder. A non-pruritic, evanescent, red rash had been present on her trunk and proximal limbs for two months, and during the first month of her illness her right shoulder and right thumb ached. At no time did she have fever, joint swelling, chest pain, or shortness of breath. There was no family history of chorea.

On examination the most prominent finding was pronounced choreoathetosis of the arms, legs, trunk, face, eyes, and tongue. Muscle tone was reduced. She had a macular, erythematous, irregular rash on the trunk and upper arms during the first day in hospital. There was a moderate aortic systolic ejection murmur and softer mitral systolic murmur at the apex. She did not have fever, arthritis, or skin nodules. Antistreptolysin titre was 166 Todd units. The following investigations were normal: erythrocyte sedimentation rate; C-reactive protein concentration; titres of antihyaluronidase, antinuclear antibody, and anti-DNA; lupus erythematosus test; serum protein electrophoresis; throat swab; concentrations of triiodothyronine, thyroxine, and electrolytes; cerebrospinal fluid; electroencephalography; computed tomography; electrocardiography; echocardiography; and chest x-ray examination.

The oral contraceptive pill that she had been taking for one year was stopped and she was given diazepam and penicillin. Her chorea continued to worsen until her speech was unintelligible and she had difficulty in swallowing and could not walk unassisted. Valproic acid 250 mg twice daily was started; within six hours the chorea had begun to lessen and after 48 hours she could walk and swallow normally. Speech also improved but mild chorea persisted. After four days the valproic acid was stopped. By the next day her chorea and dysarthria had worsened. When the drug was restarted again at the same dose three days later speech returned to normal and the chorea lessened to affect only the arms and abdominal muscles. Chorea gradually disappeared over the next month and the drug was stopped.

Comment

When the presenting symptom is chorea, as in this patient, laboratory tests often do not confirm the diagnosis of rheumatic fever. Other symptoms and signs and the absence of other causes support the diagnosis of Sydenham's chorea, although the oral contraceptive pill used by this patient may have influenced the severity of the disease.

The rapid response to low-dose valproic acid and the subsequent deterioration when the drug was stopped support the effectiveness of the treatment. Valproic acid increases GABA throughout the body,⁵ but its effectiveness in chorea is probably centrally mediated. Although