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Encephalopathy associated with *Yersinia enterocolitica* 0:3

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The central nervous system is often affected by gastrointestinal infections caused by *Shigella* spp, sometimes by *Salmonella* and *Campylobacter* spp.[1] Encephalopathy due to *Yersinia enterocolitica* has not been described.

A previously healthy 10-year-old girl presented with a 3-day history of gastroenteritis and fever up to 38·5°C. A few hours before admission, she became apathetic and disoriented. She did not recognise her mother and was unable to speak. She had not received any drug treatment. On admission, she was stuporous and responded only to pain by withdrawal. She had normal vital signs, a pulse rate of 80 beats per min, and a normal blood pressure. There were no clinical signs of dehydration. Pupils were dilated and had a delayed reaction to light. Reflexes were normal. On admission her haemoglobin was 14·3 g/100 mL, platelets 261×10^9/L, leucocytes $13{\cdot}4\times10^9$/L with 16% bands, 64% polymorphonuclear leucocytes, 7% monocytes, 13% lymphocytes. C-reactive protein was raised (2·3 mg/100 mL), as was her erythrocyte sedimentation rate (35 mm/h). The remainder of her laboratory findings were normal. A urine and serum toxicology screen was negative. Magnetic resonance imaging was done without any abnormal findings. Cerebrospinal fluid (CSF) examination revealed no white blood cells, and a normal protein and glucose concentration. Herpes simplex encephalitis was suspected and treatment with acyclovir was started, but stopped after negative PCR results were obtained. Blood and CSF cultures remained sterile. Stool cultures yielded growth of *Y enterocolitica*, serotype O:3. A positive autoagglutination test suggested presence of the pYV-virulence plasmid. No other bacterial, viral, or parasitic pathogen was identified from the patient's stool samples. Widal serology showed significant antibody titres (1:80) against both *Y enterocolitica* O:3 and OH:3 antigen in her serum, but not in CSF. Antibody titres against neurotropic pathogens including *Borrelia burgdorferi* were not raised. Electroencephalogram (EEG) showed a severe and diffuse slowing of background activity. Neurophysiological examination showed a transitory myasthenic reaction. Nerve-conduction velocity was normal. From the fourth hospital day, the girl's clinical state and EEG abnormalities improved without specific treatment. She was discharged on the seventh hospital day, 3 months later she had no neurological defeat and EEG and neurophysiological tests were normal.

Since no other source was identifiable, enteric infection with *Y enterocolitica* O:3 was the most probable cause of encephalopathy in this patient. In shigellosis, neurotoxicity has been attributed to the shiga toxin, the main toxic product of *Shigella dysenteriae*.[2] However, encephalopathic symptoms are not readily explained by the known properties of the toxin.[3] Brain oedema caused by severe shigellosis has been shown to cause central-nervous-system disease.[4] The neurophysiological abnormalities in our patient in addition to her encephalopathy suggest the action of a toxin. Strains of *Y enterocolitica* secrete a heat-stable enterotoxin (Yst) thought to be involved in the pathogenesis of watery diarrhoea, and a second heat-stable, small enterotoxin has been proposed (Yst II).[5] There is no evidence, however, that either of these toxins are neurotoxic.

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Lyme disease presenting as Tourette's syndrome

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Lyme borreliosis is often misdiagnosed, both in adults and children.[1] Central-nervous-system manifestations of Lyme disease include neurological and psychiatric symptoms.[2] Although abnormal movements have have been observed in Lyme disease,[3] a Tourette's syndrome has not been reported.

A boy at the age of 4 years developed a simple motor tic (blinking) that resolved within a year without treatment. At the age of 9 years, he developed multiple orofacial tics including shaking of the head, and several weeks later a vocal tic occurred. The tics became exacerbated under stress, as typically seen in Tourette's syndrome. Social disabilities such as loss of impulse control, social withdrawal, and worsened performance at school followed. He came to hospital 11 months after onset of symptoms.

Serum IgM antibody titres against *Borrelia burgdorferi* measured by ELISA were not increased; although IgG antibody titres (ELISA) were increased at 58 U/mL (normal ≤10 U/mL) and 100 U/mL at another examination 2 weeks later. Immunofluorescence absorption test (IFT) was also increased (1:128 [normal ≤1:16]). IgG immunoblot[4] was positive. All results indicated an infection with *B burgdorferi*. Examination of the cerebral spinal fluid showed a slight lymphocytic pleocytosis (16 cells per μL), which suggested an inflammatory reaction. The CSF:serum IgG ratio for IgG antibodies was 2·0, indicating intrathecal production of *B burgdorferi*-specific IgG antibodies, as occurs in neuroborreliosis.[3]

The boy was treated with intravenous ceftriaxone 2 g daily for 14 days. The tics improved after the sixth dose, and after the tenth dose the tics resolved completely. His social skills returned to normal. Follow-up examinations showed no reccurrence of tics or other neurological or psychiatric disorder. Serum IgG antibody titres and IFT tests against *B burgdorferi* were 11 U/mL and 1:32 after 1 year.

Rapid efficacy of antibiotic treatment followed by a decrease in Borrelia-specific antibody titres suggests that the multiple motor and vocal tics were at least partially caused by the tertiary stage of borreliosis.[5] Persistence of the tics

and increasing severity of the social disabilities over several months suggest that the first signs of a Tourette-like syndrome 11 months previously were an expression of an early Lyme infection. Infection with *B burgdorferi* should be considered in cases of Tourette's syndrome in endemic areas.

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Protective prion protein polymorphisms against sporadic Creutzfeldt-Jakob disease

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Familial Creutzfeldt-Jakob disease (CJD) and Gerstmann-Sträussler-Scheinker syndrome (GSS) are linked to point and insertional mutations of *PrP* gene. More than 80% of people with CJD do not have mutations of the *PrP* gene and lack a family history, and these CJD cases are known as sporadic. The *PrP* gene has been shown to harbour methionine (Met)/valine (Val) polymorphism at codon 129 in the general population as well as in familial and sporadic CJD. We have reported that a new polymorphism of the *PrP* gene exists in healthy Japanese people in which guanine is replaced by adenine in the first position of codon 219 with substitution from glutamic acid (Glu) to lysine (Lys).[1]

20 definite and 65 probable Japanese cases of sporadic CJD were analysed for codon 219 polymorphism. No cases were found to have the codon $219^{Glu\,Lys}$ heterozygous polymorphism (table). This absence of codon 219 polymorphism contrasts with that in the Japanese general population. Comparison between sporadic CJD and controls showed a significant difference (χ^2 9·02, p=0·0027, χ^2 test for independence).

In a study of codon 129 polymorphism in the UK, there were differences in the frequency of the Met/Met homozygote (37% *vs* 83%) as well as in that of Val/Met heterozygote (51% *vs* 9%) between the general population and people with sporadic CJD.[2] The dominant prevalence of the Met/Met homozygote in sporadic CJD might suggest that patients with this genotype are more prone to CJD than those with other genotypes. However, 9% of people with sporadic CJD have the Val/Met heterozygote at the codon 129; codon $129^{Val\,Met}$ heterozygous polymorphism cannot entirely prevent the development of sporadic CJD. Codon $219^{Glu\,Lys}$ heterozygous polymorphism has not been detected in Europeans.[1] We subsequently reported that Japanese patients who have GSS with codon $219^{Glu\,Lys}$ heterozygous polymorphism differ in the clinicopathological features from the GSS patients with the codon $219^{Glu\,Glu}$. In GSS, the aminoacid substitution to Lys at codon 219 is likely to alter the disease processes.[3] Our results indicate that the codon $219^{Glu\,Lys}$ heterozygous polymorphism of the *PrP* gene is likely to serve as a protecting factor against sporadic CJD.

	Glu/Glu	Glu/Lys	Lys/Lys	Case frequency (%)
Control	88	12	0	12
Sporadic CJD	85	0	0	0
Definite	20	0	0	
Probable	65	0	0	

Codon 219 zygosity

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Triggering of delayed-onset postherpetic neuralgia

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Postherpetic neuralgia usually merges with the pain of acute shingles.[1] Occasionally, however, neuralgia develops after a lengthy pain-free interval.[2] This report of four patients seen over 2 years suggests a possible trigger.

An 80-year-old woman developed shingles affecting the first and second divisions of the right trigeminal nerve which resolved within 3 weeks. 10 years later she underwent an uneventful right cataract extraction. Within 24 h she developed persistent and intractable burning pain in the distribution of her previous shingles rash. Examination showed mild hypoalgesia in this area.

A 75-year-old woman developed shingles affecting the first division of the left trigeminal nerve coinciding with a left-sided brainstem stroke. The skin lesions and nearly all the brainstem features resolved over a few weeks. 6 months later, she developed pain and blurring of vision in her left eye. A dendritic corneal ulcer was found which, although unproven virologically, was judged clinically typical of herpes simplex infection. She received topical aciclovir and recovered within 3 months. With the onset of the dentritic ulcer she developed severe burning pain affecting the first division of the left trigeminal nerve, where there was hyperpathia, allodynia, and impaired temperature appreciation.

A 71-year-old man developed shingles affecting the first division of the right trigeminal nerve, with eyelid oedema and punctate epithelial erosions which were treated with aciclovir and steroids. He recovered within 6 weeks. 18 months later, he developed a small, painful venous cavernous haemangioma of his right upper lip. Simultaneously he also developed persistent discomfort with numbness and tingling affecting the first and second divisions of the right trigeminal nerve, where hypoalgesia, dysaesthesiae, and allodynia were detectable.

A 45-year-old woman developed shingles affecting the right nasociliary nerve accompanied by acute iritis. She received topical aciclovir and steroid eye drops, and recovered within a month. 2 years later, she developed burning pain affecting the right eye and side of the nose, coinciding with a dull pain in the right upper jaw. A chronic abscess of the right upper lateral incisor was found and the tooth was extracted. Whilst the jaw pain resolved, the ocular and nasal pains persisted. Examination showed three tiny