

MATTERS ARISING

Acute necrotising encephalopathy of childhood presenting with multifocal, symmetric brain lesions occurring outside Japan

I was interested in the article by Mizuguchi *et al* on acute necrotising encephalopathy of childhood as a new syndrome presenting with multifocal, symmetric brain lesions.¹ The article admirably describes the pathogenesis of this special childhood encephalopathy.

I must point out however, that the authors said that they failed to find any reports of similar cases occurring outside Japan. My instructor and I previously reported three infants with acute encephalopathy with a striking ultrasonographic finding—"bright thalamus"—suggesting panthalamic infarction.² Afterwards, five more children with similar problems were treated. Their clinical and neuroimaging manifestations have been reported at the 7th Congress of the International Child Neurology Association in 1994.³ In the same report 17 children, including 14 Japanese, were reviewed from the English literature.⁴⁻¹⁰ Of the three not from Japan; two were from the United Kingdom⁹ and one was from the United States.⁴ At least eight other cases were presented at a local conference without publication in Taiwan.

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Mizuguchi replies:

I am grateful to Wang for his comments on our paper.¹ Until the submission of our paper, we had been unaware of the occurrence of acute necrotising encephalopathy of childhood (ANE) outside Japan. Now Wang has made it clear that ANE is as prevalent in Taiwan as it is in Japan. Many of the Taiwanese patients described by Wang *et al* have typical features of ANE.² The high prevalence of ANE in the far east implies the involvement of genetic or environmental factors pertinent to that region. Wang also reviewed patients with probable ANE reported from the United States and from England. These patients seem to have a mild form of ANE, judging from their clinical course and laboratory findings.

It is our view that the patients having CSF pleocytosis and other evidence of encephalitis, such as the one reported by Okuno *et al*,³ should be excluded from ANE. Many of these patients show a prolonged course, prominent focal signs, and asymmetric or atypical distribution of brain lesions, features that are incompatible with ANE.

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Suspected triphenyltin poisoning

In 1990 Wu *et al* reported a patient with suspected acute triphenyltin intoxication.¹ Extensive studies on this class of compounds in animals²⁻³ and the comprehensive review by Bock⁴ did not produce any firm evidence that these organic aryltin compounds had any serious adverse effects on the nervous system. Indeed, such compounds are currently widely used as agricultural pesticides and although very occasionally toxic effects are reported by field workers, there has never been any suggestion that the nervous system is significantly involved.⁵ The reported case of Wu *et al* developed severe ataxia, dysmetria, nystagmus, and blurred vision from which he eventually recovered to a large degree. Even if the compound taken in this suicide attempt had been contaminated in some manner by an alkyltin compound, these are not the signs or symptoms expected.

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Wu *et al* reply:

Cavanagh expresses his concern about the case of acute triphenyltin intoxication reported by us.¹ He claims a lack of evidence for the adverse effects of aryl organotin compounds on the nervous system in animal studies and clinical reports. Finally, he concludes that it certainly was not a case of triphenyltin intoxication.

Firstly, the formulation of the pesticide taken by our patient in a suicide attempt was carefully analysed by gas liquid chromatography coupled with a mass detector. According to the mass spectra obtained, this agent was either triphenyltin acetate or triphenyltin hydroxide. The mass spectra of these two compounds are identical in our analysis. Triphenyltin compounds are widely used as fungicidal and molluscicidal agents in Taiwan agriculture. The patient's girlfriend had hidden the crucial history from both doctor and the patient's family for some reason for the first two months after the incident. As the patient did not recover from his coma, his girlfriend finally told us the truth and provided the pesticide to doctors.

According to the comprehensive review of Bock,² when a high dose of triphenyltin acetate was fed to rats (>20 mg/kg), guinea pigs (5-20 ppm), and rabbits (140 mg/kg), they developed muscle weakness, unsteady gait, paralysis in the hind limbs, tremor, and convulsion, and eventually died in coma. Although increased water content of the brain and spinal cord was the only abnormal finding on pathological examination, inhibition of adenosine triphosphatase, protease, and amylase in brain microsomes have been reported in other studies.³⁻⁴ Uncoupling of oxidative phosphorylation in the mitochondria has also been suggested as a contributor to the cellular mechanism of triphenyltin toxicity.⁵

Although triphenyltin compounds have been regarded as less neurotoxic than alkyltin compounds, neurological manifestations in human cases with triphenyltin intoxication have been reported in isolated instances. Headache, vomiting, nausea, and impaired vision were noted in cases poisoned by triphenyltin acetate.² Moreover, two cases with triphenyltin acetate poisoning had severe headache, dizziness, vertigo, transient loss of consciousness and, paraesthesia in the legs.⁶ Thus it is likely that more severe neurological deficits may develop in our case who had taken a possible lethal dose of triphenyltin compound with the intention of committing suicide. He developed abdominal pain, diarrhoea, and vomiting on the first day of poisoning. Headache, blurred vision, unsteady gait, consciousness disturbance, and polyneuropathy occurred subsequently. Also, systemic problems with abnormal liver function and leukopenia coincided with the neurological manifestations. These clinical features are consistent with the previous studies on animals and clinical reports.

We are grateful to Cavanagh for giving us the opportunity to reiterate the unusual case with acute triphenyltin intoxication in a suicide attempt.

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