

## Letters

### Post-influenzal encephalitis and Reye's syndrome

SIR,—Sulkava, Rissanen and Phylala describe their recent experience of post-influenzal encephalitis caused by influenza A virus with a favourable outcome in all patients.<sup>1</sup> Our recent experience with this virus was distinctly unpleasant with the death of our patient from Reye's syndrome.

AK (No 840663), a 14-year-old schoolboy, developed a mild sore throat on 9 November 1980. On 17 November 1980 he was sent home from school generally unwell, photophobic with a headache. He was treated with aspirin and an antibiotic and his symptoms resolved over two days. On 21 November 1980 he became squeamish and vomited. He was given metaclopramide to no avail and on 22 November 1980 his behaviour was altered with some aggression and by the next day, this was more extreme with progressive disorientation. He was taken to hospital where his conscious level quickly deteriorated, encephalitis was diagnosed and cerebrospinal fluid obtained at lumbar puncture contained only one cell, with normal protein and glucose. He was transferred to the Institute of Neurological Sciences and on examination he was lying limply occasionally moving his upper limbs. There was no response on either side to supraorbital pressure. Both upper limbs extended to pain, with flexion of his lower limbs. His breathing was rapid, between 24 and 46 per minute. Pupils were large and symmetrical with sluggish reaction to light. Optic discs were normal. Doll's-eye movements were impaired bilaterally. Upper limbs were flaccid with diminished reflexes, while in the lower limbs, tone was increased and reflexes were brisk, more so on the right side. Both plantar responses were extensor. There was no neck stiffness and he was afebrile. Pulse was 140 per minute, regular and blood pressure 150/70 mmHg. Examination of heart, lungs and abdomen was normal, there was no icterus and no lymphadenopathy.

EEG showed high voltage semi-rhythmic delta waves, highest amplitude being in frontal areas. Computed

tomography of the brain was normal. Urinalysis yielded no cells or protein. Serum urea and electrolytes, glucose, chest radiograph and sedimentation rate were all normal. Full blood count only revealed a mild polymorph leukocytosis with a total white blood count of  $13.2 \times 10^9/l$ . He was considered to have post-infectious encephalopathy and was given dexamethasone and cimetidine (the latter for mild gastrointestinal bleeding). He had two respiratory arrests in the first 24 hours requiring ventilation and three hours after the second episode a period of hypotension (systolic pressure 90 mmHg) and relative drop in pulse rate (to 100 per minute) occurred. Plasma protein substitute was infused, but loss of brain stem reflexes occurred from this time. Liver function tests then revealed bilirubin of  $56 \mu\text{mol/l}$  (normal 5-17) alkaline phosphatase 124 Iu/l (normal for age) aspartate transaminase of 858 Iu/l (normal 13-42), alanine transaminase 1104 Iu/l (normal 10-55), and lactate dehydrogenase of 732 Iu/l (normal 240-525). Blood culture and monospot were negative. Lumbar puncture was repeated on 25 November 1980 with normal pressure and dynamics, cloudy fluid with no xanthochromia, 1600 red cells per ml, no white cells and no organisms. CSF protein was 0.75 g/l (normal less than 0.5 g/l) with normal glucose and IgG. No oligoclonal banding was detected and culture was sterile. He was supported fully, diabetes insipidus for 36 hours was treated, until he died on 27 November 1980.

Later serological viral studies from 25 and 27 November 1980 confirmed influenza A titres of 1:32 and 1:1024 respectively. (No subtyping was performed, but the prevalent laboratory studies showed  $H_1N_1$  to be circulating at this time.) Necropsy yielded on frozen section of liver, fat globules in all hepatocytes except in periportal areas, and the liver, which was pale, weighed 1400 g with histology showing hepatocyte atrophy and binucleate hepatocytes. The brain showed "brain swelling" without any reactive changes and the brain stem was particularly haemorrhagic and necrotic. No virus was cultured from brain, liver, lung, heart or jejunal contents.

In Flewett and Houl's study,<sup>2</sup> group 1 cases were fatal. These cases were

similar in that there was an encephalopathy as in our patient rather than encephalitis, but the patients differed by having the virus cultured from the respiratory tract and, in one case from the brain, in all cases except one where the lung pathology was typical for influenza.<sup>2</sup> Liver histology was not reported. Comparison of the infecting virus between mild and fatal cases revealed no difference. The Communicable Diseases (Scotland) Unit have records of 3394 cases with laboratory evidence of influenza A virus infection in the period January 1976 to December 1980. There were 27 deaths and of these, our patient was the only case reported with neurological involvement.

The pathophysiology of Reye's syndrome is unclear, but many viruses have been associated: varicella zoster and influenza B are the most frequent, but influenza A has been reported.<sup>3</sup> Mortality in this syndrome, even with full supportive treatment, is very high. Venes *et al* report good results in deeply comatose patients with the addition of careful treatment of raised intracranial pressure detected by continuous intracranial pressure monitoring.<sup>4</sup> This study was not a controlled trial, but if we believe their treatment is helpful, then acute awareness of this diagnostic possibility is mandatory in such a rapidly progressive condition, albeit a rare complication of a common virus infection.

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### References

- 1 Sulkava P, Rissanen A, Pyhala R. Post-influenzal encephalitis during the influenza A outbreak in 1979/1980. *J Neurol Neurosurg Psychiatr* 1981; 44:161-3.
- 2 Flewett TH, Houl JG. Influenzal encephalopathy and postinfluenzal encephalitis. *Lancet* 1958; 2:11-15.
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- 4 Venes JL, Shaywitz BA, Spencer DD. Management of severe cerebral edema in the metabolic encephalopathy of Reye-Johnson syndrome. *J Neurosurg* 1978; 48:903-15.