Case report

Adult Reye's syndrome after dengue

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SUMMARY An adult (21 year old) male is described who developed Reye's syndrome in association with dengue type 1 infection.

Reye's syndrome of encephalopathy and fatty degeneration of the viscera is considered to be a disease of young children.¹ The first adult case was described in an American 25 year old male.² The reason for the apparent sparing of adults may be either that adults are not susceptible to this type of biochemical derangement or, alternatively, that adult cases of Reye's syndrome are escaping diagnosis.³ This is an additional example of an adult with the clinical, biochemical, and histopathological changes typical of Reye's syndrome. In this case the illness followed dengue.

Case report

In the third month of an epidemic of type 1 dengue a 21 year old Jamaican man developed a febrile illness accompanied by marked headache, severe limb pains, and vomiting. Ten days from the onset of fever, as the initial symptoms subsided, he became increasingly drowsy. He had last consumed ackee two weeks previously. There was no history of drug or toxin ingestion and he had had no other recent febrile illness.

On admission to the University Hospital of the West Indies, on the 13th day of his illness, the two abnormal physical signs were a heart rate of 112 beats per minute and disturbance of consciousness: he was drowsy, being only able to answer direct questions slowly and with difficulty. In addition, the liver size and consistency were normal. Investigations on admission revealed a blood glucose of 1.0 mmol/l, plasma ammonia 32 μ mol/l, and blood free fatty acids 1.4 mmol/l, serum albumin 27 g/l, globulin 29 g/l, peak total bilirubin 26 μ mol/l, serum aspartate aminotransferase (SGOT) 42 IU/l (normal less than 24 IU/l); with normal serum

alanine aminotransferase (SGPT), alkaline phosphatase, prothrombin time, haemoglobin, white blood count total and differential. Cerebrospinal fluid (CSF) was clear, colourless, and no cells were seen, the CSF glucose was 3.4 mmol/l and protein 121 mg/l (after intravenous glucose had been given).

Liver biopsy was performed the next day. Light microscopy revealed panlobular microvesicular fatty change and glycogen depletion of hepatocytes as the only histological changes (Fig. 1). By electron microscopy hepatocytes were seen to contain excessive quantities of fat but total glycogen depletion was not observed. Most outstanding of the changes were those affecting the mitochondria (Fig. 2); these included swelling with rarefaction of the matrix, reduction in the number of orientation of the cristae and diminution in the number of matrical dense granules. Peroxisomes appeared to be normal in number and morphology.

The patient recovered fully. Dengue antibodies initially positive 1:1280 were unchanged eight days later. Attempts to culture the virus from CSF were unsuccessful.

Discussion

Reye's syndrome occurs in various degrees of severity. According to Partin,³ our patient would be classified as moderately affected. The alerting factors were a neurological syndrome appearing with the resolution of an acute viral infection together with a low blood glucose (in the absence of ingestion of toxin) and a raised blood ammonia. These, together with a normal CSF and the typical light and electron microscopic changes in the liver biopsy,^{1 4 5} confirm the diagnosis. That our patient was 21 years old emphasises that adults, too, may develop Reye's syndrome.

In Jamaica, the commonest cause for hypoglycaemia and disturbed consciousness is from

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Fig. 1 Light photomicrograph of liver biopsy. Pericentral area (portion of terminal hepatic vein at right) showing microvesicular fatty change with central nuclei. Eccentric displacement of nuclei is visible when solitary macrovacuoles are found. Haematoxylin and eosin, $\times 540$ (original magnification).

Fig. 2 Electron micrograph. Enlarged mitochondria with expanded, flocculated matrix and fragmentation of cristae $\times 22\,400$ (original magnification).

poisoning by unripe fruit of the ackee tree.⁶ The liver biopsy may serve to separate the two conditions, as the fatty change is microvesicular in Reye's syndrome and macrovesicular in ackee poisoning.^{1 7} We have not found that the electron microscopic appearances are particularly helpful as an aid in the differential diagnosis. In both conditions the major damage is borne by the mitochondria, where the changes are identical. Ackee poisoning, however,

produces acute changes, our patient had last consumed ackee two weeks before.

An epidemic of type 1 dengue appeared in Jamaica in March 1977 (E Rose, personal communication). At least 210 000 individuals in a population of 2 million are considered to have been affected (A Dyer, personal communication). The complications of dengue in Jamaica have been described.⁸ Reye's syndrome is not included. Our patient

developed Reye's syndrome while recovering from a typical attack of dengue. The previous outbreak of dengue in Jamaica was in 1968, which would be too long ago to give a persistent dengue antibody titre of 1:1280. The patient also categorically denied having had any other similar illness within the time span of the 1977 dengue epidemic in Jamaica. The high antibody titre is consistent with his developing dengue two weeks previously.

Reye's syndrome has been observed to occur sporadically with a wide variety of viral infections including adenovirus type 3, coxsackie A, A 9, B, B₄, ECHO 8, 11, Epstein Barr, Herpes simplex, influenza A and B, measles, parainfluenza, polio type 1, reovirus, rubella and varicella.⁹ It seems likely, therefore, that Reye's syndrome is a non-specific reaction to many viral infections. We are not aware, however, of Reye's syndrome having been previously reported in association with dengue.

However, as dengue occurs in many parts of the world: southern North America, South America, the West Indies, the Mediterranean seaboard, the Middle East, Africa, southern Russia, India, China, South-East Asia, many Pacific islands and northern Australia, it may prove worthy of further attention. For example, in South-East Asia, where both dengue and Reye's syndrome are common, there is a seasonal variation in the prevalence of Reye's syndrome, the peak occurrence being during the monsoon season,¹⁰ which is also the time of the peak prevalence of dengue, as then the *Aedes* mosquitoes' breeding and biting activity is maximal. In this regard, dengue differs from all the other viral illness so far associated with Reye's syndrome in requiring an intermediary insect vector for transmission. From our study of this case we may draw the following conclusions: (1) that Reye's syndrome does occur in adults; (2) that Reye's syndrome in adults has the same pathophysiology

as described in children; and (3) that dengue virus is another predisposing cause of Reye's syndrome.

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