Fulminating encephalopathy associated with Shigella flexneri infection

110/60 mmHg and pulse rate 130/min and regular. Results of laboratory investigations were normal. S. flexneri type 2a was later isolated from the stool. Treatment was started with ampicillin 250 mg every 8 hours orally. Six hours after admission she had a grand mal seizure and shortly thereafter became apnoeic and unresponsive to noxious stimulation. The pupils were widely dilated (6 mm) and fixed, and there was no response to caloric or oculovestibular testing. Cerebrospinal fluid analysis was normal. Computerised tomography scan of the brain showed diffuse areas of low density throughout the brain. Five hours later the electroencephalogram was isoelectric. At necropsy the entire bowel was congested and the colonic mucosa was infiltrated by polymorphonuclear cells. Extensive necrosis was present throughout the brain and coning of the cerebellum was noted. The remainder of the organs seemed normal.

Discussion

Neurological complications of Shigella sp. infections are rare and consist of febrile convulsions in children and peripheral neuropathy in adults. Notable in the cases reported here were the lack of severe intestinal involvement and absence of metabolic derangement, and the fulminating nature of the encephalopathy. These facts suggest a toxic aetiology. S. flexneri type 2a may produce an exotoxin similar to that of S. dysenteriae type 1. The toxin produced by the latter is a protein with a molecular weight of 30,000; it is also a potent enterotoxin. It has the properties of a neurotoxin (being paralytic and lethal for rabbit and mouse) and cytotoxic (lethal for cell culture) in addition to causing intestinal fluid secretion. Although the exact role of this substance in the pathogenicity of shigellae remains undefined, we suggest that such a toxin, either elaborated in the gut or ingested preformed, was responsible for the rapidly fatal picture described in these 3 patients. The precise mechanism of action on the nervous system is unknown, since no specific disease was revealed in the brains at necropsy. In all 3 patients, areas of necrosis were present throughout the brains; only in Case 1 were pontine haemorrhages and demyelination seen. Haemorrhages may be explicable on the basis of raised intracranial pressure before death, while the demyelination may reflect an action of the toxin or be an incidental finding. This report supports the evidence of a particular neurotoxic effect in shigellosis.

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Correspondence to Dr R Sandyk, University of the Witwatersrand, Medical School, Hospital Street, Johannesburg 2001, South Africa.

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Influence of breast feeding on the clinical features of salt-losing congenital adrenal hyperplasia

JOSEPH A CURTIS AND JOHN D BAILEY

Division of Endocrinology, Department of Pediatrics, Hospital for Sick Children, Toronto, Canada

SUMMARY Feeding habits before diagnosis were reviewed in 32 infants with salt-losing congenital adrenal hyperplasia who were admitted to hospital in adrenal crisis. Most breast-fed babies failed to thrive, seldom vomited, and despite severe salt wasting, presented at a later age than their formula-fed counterparts.

Salt-losing congenital adrenal hyperplasia (SL-CAH) is a genetically inherited enzyme deficiency, the most commonly affected enzyme being 21-hydroxylase. Clinically, SL-CAH is characterised by a non-specific failure to thrive in the first few days of life that progresses to acute addisonian crisis with anorexia, vomiting, dehydration, dystrophy, diarrhoea, and circulatory insufficiency in the 2nd week.

Although the initial crisis occurs in most infants with SL-CAH in the 2nd or 3rd weeks of life, it can occur as early as the first week or as late as several months. Kowarski suggests that the age at which the infant presents depends on the severity of the case, which in turn is related to the degree of sodium
depletion. Salt loss would thus be fairly mild in infants who present after the 3rd week of life.

The diagnosis of SL-CAH in a 39-day-old, breast-fed infant who presented with failure to thrive without vomiting and had a plasma sodium concentration of 108 mmol/l led us to examine whether the method of feeding newborn infants with SL-CAH influenced the age and characteristics of the clinical presentation.

Patients and methods

The medical records of all patients with SL-CAH seen at our hospital from 1953 to 1980 were studied for details of feeding before diagnosis, age at presentation, and presenting symptoms. If the history was incomplete, the data were checked with the infant's mother, family practitioner, and paediatrician. Altogether 50 cases were identified, the diagnosis in each being confirmed by measurement of urinary ketosteroids and pregnanetriol, and, more recently, of plasma 17-hydroxyprogesterone.

Thirty-two of these infants (23 boys, 9 girls) were discharged from hospital shortly after birth, undiagnosed and apparently healthy, and were readmitted only when they were in adrenal crisis. Eight had been breast fed, 5 were fed breast milk and formula consecutively, and 19 were fed with formula alone. The remaining 18 infants (1 boy, 17 girls) had been noted at birth to have features suggestive of CAH, but were omitted from the study because they had been detained in hospital for observation and further investigations.

Results

The clinical features of the breast-fed and formula-fed infants are given in the Table.

Although 4 of the babies reverted to breast feeding without further incident, the condition of the other 2 deteriorated rapidly and they became shocked within 48 hours, because of repeated vomiting in one infant and refusal of breast milk in the other.

Discussion

In infants with SL-CAH the clinical features typically reflect the severity of salt depletion, which is governed by the level of aldosterone in the body. Since aldosterone clearance is slow in newborn infants, an adequate concentration of the hormone is maintained even if the secretion rate is low. However, in the 2nd week of life aldosterone clearance increases, due to maturation of hepatic enzyme pathways, and increased secretion is necessary. In SL-CAH, aldosterone secretion occurs in inverse proportion to the severity of the 21-hydroxylase defect. Thus, presentation tends to be early in severe salt-losers, and is later in milder cases in whom the aldosterone level remains adequate for a longer time. However, as this study has shown, the severity of salt depletion does not always dictate the age at presentation, most of the breast-fed babies presenting late despite severe salt wasting. This may be surprising since most of the formula used during the period of the study contained a far higher sodium content than either modern formula feeds or breast milk.

While breast-fed infants with SL-CAH have all the biochemical features of adrenal insufficiency at an early age, they do not show the clinical picture of the classical adrenal crisis because the salt depletion is not complicated by the severe water loss that results from vomiting. Thus, they are not recognised as having a serious metabolic disorder, their weight loss being ascribed to insufficiency of breast milk. Weaning, which is known to precipitate vomiting

### Table

<table>
<thead>
<tr>
<th>Method of feeding</th>
<th>Number of patients</th>
<th>Age at presentation (days)</th>
<th>Failure to thrive</th>
<th>Vomiting</th>
<th>Daily weight loss (%)</th>
<th>Plasma sodium (mmol/l)</th>
<th>Number with severe salt depletion*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>8</td>
<td>31 (14-44)</td>
<td>7</td>
<td>1</td>
<td>0.34</td>
<td>110 (93-125)</td>
<td>4</td>
</tr>
<tr>
<td>Breast and formula</td>
<td>5</td>
<td>33 (10-77)</td>
<td>3</td>
<td>2</td>
<td>0.46</td>
<td>118 (97-126)</td>
<td>1</td>
</tr>
<tr>
<td>Formula</td>
<td>19</td>
<td>17* (5-56)</td>
<td>5</td>
<td>14</td>
<td>0.95</td>
<td>119 (97-132)</td>
<td>3</td>
</tr>
</tbody>
</table>

*P value <0.05, Duncan’s analysis of variance. †Calculated as a percentage of birthweight lost per day. ‡Plasma sodium <110 mmol/l.
even in healthy infants,\textsuperscript{5} unmasks the true nature of
the underlying disorder in many such infants who,
already profoundly salt-depleted and unable to
tolerate further fluid loss, sink rapidly into severe
dehydration and shock. The aldosterone content of
breast milk is unknown, but it may, as in the case of
progesterone, reflect blood concentration.\textsuperscript{6} The
possibility that this or other breast milk steroids might
exert a therapeutic effect on breast-fed infants with
SL-CAH cannot be excluded, but given the profound
salt wasting present in these infants, the plasma
concentration of such hormones after absorption
from the gastrointestinal tract would seem to be
insufficient to influence renal sodium conservation.

SL-CAH should be included in the differential
diagnosis of failure to thrive at the breast, and
plasma electrolytes determined before the introduc-
tion of formula which may precipitate vomiting.
For this reason, although breast feeding should always be encouraged, it is particularly desirable in
babies with suspected SL-CAH while the results of
confirmatory diagnostic tests are awaited and treat-
ment is begun.

We thank Dr M M Wood, HSC, for statistical
analysis, and Miss C Conway for typing the
manuscript.

The radioimmunoassay method for plasma 17-
hydroxyprogesterone was developed at HSC by Dr
Graham Ellis, using an antibody (type M 156)
which was obtained from Professor W R Butt,
Birmingham and Midland Hospital for Women.

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Correspondence to Dr A Curtis, Department of Paediatrics,
The Regional Hospital, Wilton, Cork, Ireland.

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Supplementary water for breast-fed babies in a hot and dry climate---not
really a necessity

N M GOLDBERG AND E ADAMS

Department of Paediatrics, Josefat Medical Centre, Eilat, Israel

SUMMARY Urine osmolarity under hot and dry
climatic conditions remains within the expected
physiological ranges and thus shows that supple-
mental water for breast-fed infants is not necessary.

It is generally agreed that infants in a hot and dry
climate need extra water. This assumption was
based more on caution than on knowledge.\textsuperscript{1} Recently
breast-fed infants in a hot and humid climate were
found to do well without supplementary water.\textsuperscript{2,3}

A field study was undertaken in two bedouin
villages on the coastal side of the Sinai desert during
the summer to find out the fluid requirement of
totally breast-fed infants in a hot and dry climate.

Materials and methods

Fifteen healthy exclusively breast-fed infants (9
boys, 6 girls) were studied. They were aged between
40 and 150 days.

Urine was collected using adhesive collector bags.
The samples were taken either after 1000 hours or
before 1600 hours. Urine was then frozen and
analysed within 24 hours using the Fiske osmometer
(Fiske Associates, Burlington, Mass. 01803).

Temperature and humidity readings for the
duration of the study were provided by the Israeli
Meteorological Service.

Results

Urine osmolarity measurements are shown in the