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Fatal outcome of neonatal group A beta-haemolytic streptococcal infection

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Sir: Endemic episodes of neonatal infections with group A beta-haemolytic streptococci were well known in the early days of neonatal intensive care [2]. Nowadays, neonatal streptococcal septicaemia is mainly caused by beta-haemolytic group B streptococci. Neonatal infections with group C, group D, and group G streptococci are reported sporadically. Neonatal group A streptococcal infections are usually asymptomatic or present as omphalitis. Infection can occur following passage through a colonized vaginal tract or from contact with hospital staff [1]. Maternal pharyngitis has also been described as the source of infection [7].

In the last decade an increasing amount of serious group A streptococcal infections in children as well as in adults has been reported, pointing to a changing epidemiology [3]. Recently we treated a newborn with sepsis due to an infection with group A beta-haemolytic *Streptococcus*. The mother was admitted to a local hospital because of fever and influenza like symptoms. The membranes were intact. Antibiotics were not prescribed, and she delivered spontaneously the next day, at 32 weeks of gestation. The baby, a girl, weighed 1900 g and did well directly after birth. Mild respiratory distress was treated with extra oxygen. At the age of 3 h a fever developed (> 38° C). After an interval of 4 h antibiotic therapy was started (Amoxycillin and Tobramycin). Two hours later she went into severe respiratory and circulatory failure, and was transferred to our neonatal intensive care unit while on mechanical ventilation. During transport severe hypotension was treated with plasma and dobutamin.

Ventilatory failure and shock persisted despite mechanical ventilation and extensive treatment with plasma infusions and inotropic support (Dopamin and Dobutamin). Persistent fetal circulation was treated with Tolazolin and Prostacyclin without success. The baby died 2 h after admission because of massive pulmonary haemorrhage. Autopsy was not obtained.

Cultures of gastric aspirate, tube tip, and blood grew group A beta-haemolytic *Streptococcus*.

After delivery the mother developed puerperal fever. She was treated with antibiotics and recovered. Group A beta-haemolytic *Streptococcus* was cultured from the placenta.

Serious infections with group A beta-haemolytic streptococci are resurging, as demonstrated by an outbreak of acute rheumatic fever [5], and toxic shock syndromes [4, 6]. These clinical entities are caused by exotoxins A and B, produced by group A beta-haemolytic streptococci, especially those belonging to the M-type 1, M-type 3 and M-type 18 strains [5, 6]. The M-protein is type-specific and indicates the agressivity of the *Streptococcus* to leucocytes. An increase in the prevalence of virulent group A beta-haemolytic streptococci may account for the increased incidence of severe infections. In the absence of antibodies against these M-type strains, serious and even fatal disease can occur. The reason for the low incidence in newborns is probably the transplacentally acquired passive immunity. Preterm babies are relatively immunocompromised, particularly as a result of their low immunoglobulin status, which may predispose them to the acquisition of fulminant infectious diseases.

Our case report shows the fatal outcome of perinatally acquired group A beta-haemolytic streptococcal infection. More neonatal infections caused by these bacteria may be expected in the future.

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Growth in patients with phenylketonuria

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Abbreviation *PKU* phenylketonuria

Sir: Patients with phenylketonuria (PKU) are subjected to a diet low in phenylalanine soon after birth. Thus, psychomotor and intellectual retardation are

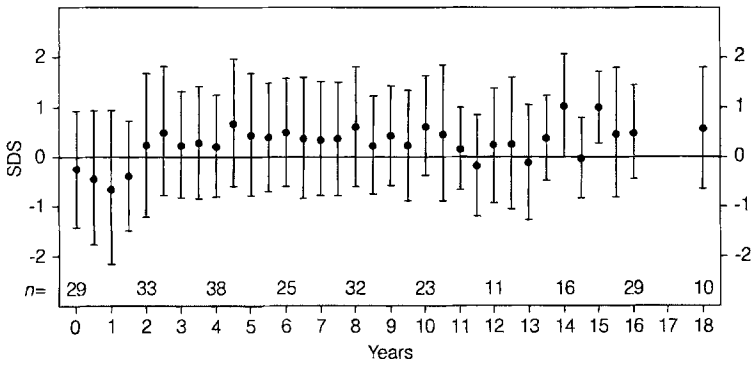

Fig. 1 Height development of patients with PKU: SDS values (mean and SD)

rarely observed today. In addition, height has been reported to be normal [2]. This contrasts to our observation that height is negatively affected during the 1st year of life.

In a retrospective study height was evaluated in 87 patients with PKU (41 boys, 46 girls). Seventy-two patients had classical PKU type I and 17 patients mild PKU type II according to Blascovics et al. [1]. PKU specific diet was started at less than 4 weeks of age in 80 patients and before the end of 8 weeks in 7 patients. Chronological age was 12.2 ± 4.8 years (mean ± SD) at the time of the last follow up. Height data are presented as standard deviation score (SDS) and compared with reference data published by Tanner et al. [3]. There was a significant loss of height-SDS during the 1st year of life with a maximum SDS deviation of –0.69 at the age of 1 year (*t*-test: $P<0.05$). During the 2nd year catch-up growth was noted. All patients reached a normal height without any additional therapeutic intervention (Fig. 1). There was no significant correlation between the loss of height SDS, the mean annual serum phenylalanine or tyrosine levels or the amount of protein intake (2 g/kg/day during the 1st year, 2.5 g/kg/day during the years 2 to 5).

Though no sufficient explanation was found for the loss of height SDS during the 1st year of life, further studies are needed to investigate this phenomenon particularly in view of the data reported by Verkerk et al. [4].

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Detection of increased urinary N-acetylaspartylglutamate in Canavan disease

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Abbreviations *NAA* N-acetylaspartate *NAAG* N-acetylaspartylglutamate

Sir: Canavan disease is an autosomal recessive leukodystrophy. Clinical features are hypotonia, later progressing to hypertonia and spasticity, megalencephaly, mental retardation, and optic atrophy. The estimation of N-acetylaspartic acid (NAA) levels by gas chromatography/mass spectrometry in the urine is the preferred method for the diagnosis of Canavan disease [4].

NAA is found almost exclusively in the nervous system and constitutes one of the most abundant low molecular weight cellular metabolites in cerebral tissue; nevertheless its biochemical function is still uncertain [1]. One of the potential roles ascribed to NAA is its involvement as a precursor for the synthesis of N-acetylaspartylglutamate (NAAG) [3], a dipeptide which is present in millimolar levels in the neural tissues of mammals [2]. Here, we report the detection of high levels of NAAG in the urine of three patients with Canavan disease.

We have analysed urine obtained from three patients with clinical and neuroradiological signs of Canavan disease, including severe optic atrophy, and deficiency of aspartoacylase activity in skin fibroblasts. Elevated levels of NAA in urine were found in all three patients. Further evaluation of the urine specimens was carried out by high resolution proton magnetic resonance spectroscopy at 300 MHz (Bruker MSL spectrometer). Apart from the many common metabolites and the dominant NAA, resonances of the closely related NAAG could be identified in the urine of the three patients. In order to establish a quantitative relationship between NAA and NAAG, all urine samples were analysed by capillary zone electrophoresis with UV detection (Fig. 1). Table 1 depicts the concentrations of NAA and NAAG with reference to creatinine. Our results show a marked increase of NAAG in the urine of individuals with Canavan disease as compared to normal subjects. The high levels of NAAG in urine may be due, like in the case of NAA, to a rapid and efficient excretion by glomerular filtration. Furthermore, these data suggest that urinary NAAG parallels the NAA excretion in Canavan disease. To our knowledge, the presence of NAAG has not previously been reported in urine of patients with Canavan disease.

In rat brain, NAAG has been shown to exhibit a high affinity for cerebral glutamate receptors indicating its potential function as a neurotransmitter for glutamatergic synapses [8]. More recently, this concept of NAAG being involved in neurotransmission has been invigorated. NAAG was identified in the ganglion cells of the human retina [5] and in neurons of the primate visual pathway [6], indicating an important role of NAAG in the visual system. Furthermore, the release of NAAG