electrolyte concentrations. Those with villous atrophy are differentiated based on the immuno-histopathology and electron microscopy findings on the intestinal biopsy.

These findings have been well described in the small and large bowel, but there are few reports in literature on their presence in the gastric mucosa [3]. In our patient, we could establish the diagnosis of MVID by electron microscopy of the gastric mucosa suggesting an alternative to duodenal biopsies that may be technically difficult in neonates. The ultrastructural findings in the gastric mucosa of our patient were very focal, suggesting that a careful and extensive search for microvillous inclusions is essential. The range of changes seen parallels that described in intestinal biopsies, and our findings confirm that these inclusions are probably formed by invagination of the luminal surface and closure of invaginated foci with cytoplasmic flaps rather than by arrested transport towards the luminal surface [4].

The presence of antenatal dilated bowel with increased amniotic fluid volume seen in our patient is commonly seen in ion transport disorders like congenital chloride diarrhea but has also been described in isolated cases of MVID [5]. Other than supportive measures, various drugs like loperamide, somatostatin, corticosteroids and cholestyramine have been tried with no benefit. Small bowel transplantation or small bowel and liver transplantation have been successfully used recently in this condition [6].

We report the first case with MVID from India and highlight the fact that gastric mucosal examination can be used in its diagnosis if a duodenal biopsy is not possible. Any child with a neonatal onset severe diarrhea should undergo early intestinal biopsy after ruling out carbohydrate malabsorption and ion transport disorders by non invasive tests.

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Venovenous Hemodiafiltration and Hypothermia for Treatment of Cerebral Edema Associated With Hyperammonemia

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We report a 50-hour-old newborn with inborn urea cycle disorder and hyperammonia of 2320 µmol/L. The pharmacological treatment of the first metabolic crisis was combined with venovenous hemodiafiltration and therapeutic hypothermia to rescue the patient from a life-threatening cerebral edema.

Key words: *Cerebral edema, Hyperammonia, Inborn urea cycle disorder, Management, Therapeutic hypothermia.*

The accumulation of toxic metabolites leads to the neurological deterioration of newborns with inborn urea cycle disorder and is associated with high morbidity and mortality, when cerebral edema appears. We herein report a neonate where attempts of pharmacological lowering and the extracorporeal removal of plasma ammonia levels [1] were expanded to include therapeutic hypothermia.

CASE REPORT

A 50-hour-old, term, newborn boy (gestation 39 weeks, birthweight 3.2kg) was admitted to a neonatal intensive care unit in an external hospital because of respiratory failure and convulsions. Infection parameters were negative, but arterial lactate was increased (6.3 mmol/L). Initial metabolic workup showed an ammonia concentration of 2320 µmol/L. Because of a suspected urea cycle disorder, protein intake was stopped and intravenous sodium benzoate, arginine-hydrochloride and high glucose were started. The boy was transferred to our institution by helicopter. The newborn had hepatomegaly, and adequate oxygenation and perfusion under moderate catecholamine and ventilator support.

Cardiac ultrasound revealed a small muscular ventricle septal defect without hemodynamic relevance, and the ductus arteriosus had already closed. Transfontanella doppler sonography showed systolic peaks and a markedly elevated pulsatility index of 3.0 (normal values 0.65-0.85) in the anterior cerebral artery [2]. Assuming the presence of cerebral edema, therapeutic hypothermia was started immediately and carried out according to our institutional protocol of neuroprotection, by cooling the boy instantly to a rectal temperature of 33.0°C for 48 hours using CritiCool™ cooling therapy system (MTRE Advanced Technologies, Israel), after obtaining parental informed consent.

The child was loaded with a combination of arginine–HCL 4 mmol/kg/h and sodium benzoate 250 mg/kg/h, simultaneously. L-carnitine was added with 75 mg/kg/d. Parenteral nutrition was continued with glucose 8.5 mg/kg/min and fat (Intralipid) with 0.1 g/kg/d. Insulin was necessary to keep blood glucose under 180 mg/dL. A reassessment of ammonia after one hour showed an increase to 2391 µmol/L and venovenous hemodiafiltration (VVHDF) was started urgently. The loading of arginine-HCl and sodium benzoate was continued during the first hour of VVHDF, before the dosages were reduced to 0.25 mmol/kg/h and 8 mg/kg/h, respectively. Hemosol B0 bicarbonate solution (Gambro, Sondalo, Italy) served as a replacement and dialysis fluid. Serum ammonia concentrations decreased continuously under this treatment and showed a concentration of 830.4 µmol/L after three hours of dialysis. At this point, transfontanella doppler showed improved cerebral perfusion with a PI of 0.9. VVHDF was stopped after six hours at a serum ammonia concentration of 224.3 µmol/L. There was no rebound of ammonia or nor a recurrence of cerebral edema. The metabolic investigation revealed an argininosuccinate lyase deficiency, confirmed by enzymatic analysis in erythrocytes. Extubation was possible on day 10, and the boy was then transferred to an intermediate care unit. MRI showed cystic and ischemic lesions in the parieto–occipital white matter and wide ventricles, characteristic of metabolic stroke. During an eight months follow-up, the boy showed an improved cerebral MRI and promising neuromotor development.

DISCUSSION

This report concerns a term newborn who suffered from severe cerebral edema caused by an inborn urea cycle disorder. Similar to acute liver failure in adults, toxic metabolites such as ammonia, glutamate and glutamine are significantly increased in such cases [3]. Although the pathogenesis of cerebral edema is still not completely understood, accumulation of these metabolites has been shown to cause astrocyte swelling [4] and, in addition, cellular mitochondrial dysfunction. This, in turn, can induce cerebral oxidative stress, leading to cerebrovascular dilation and hyperemia. However, there is evidence that induction of hypothermia can reverse many pathophysiologic abnormalities leading to cerebral edema [5].

Jalan, *et al*. [6, 7] reported about a decline of the markers of oxidative stress and the restoring of cerebrovascular autoregulation, when moderate hypothermia was used for uncontrolled intracranial hypertension in instances of acute liver failure in adults. Whitelaw, *et al*. [8] hypothesized that mild systemic cooling through the removal of an overhead heat source could have reduced the enzymatic production of ammonia in a comatose newborn with hyperammonia, who had not responded to hemofiltration. We used therapeutic hypothermia on the basis of these reports. However, it was carried out actively by a cooling-system and already initiated before the start of hemodiafiltration, one hour after admission. A considerable reduction of cerebral edema was already experienced just four hours after admission, because PI decreased and remained at normal ranges.

The monitoring of cerebral edema by the PI remains debatable. On the one hand, PI has been shown to correlate strongly to intracranial pressure [9], but conversely, absolute values of PI were not reliable to guide clinical

decisions in a group of traumatic brain injury patients, according to a recent study [10]. However, PI has been frequently used as a non-invasive estimate of ICP and CPP and has enabled continuous assessment of the cerebral dynamics of the anti-coagulated newborn during CVVHDF.

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Infantile Systemic Hyalinosis

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Infantile systemic hyalinosis is a rare disorder characterized by widespread deposition of hyaline. They usually present with skin lesions, joint contractures, and intractable diarrhea. We report a 2 year 4 month old boy with growth retardation, typical facial appearance, gingival enlargement, generalized stiff skin, joint contractures, and intermittent diarrhea. Skin biopsy revealed deposition of hyaline.

Key words: *Hyalinosis, Skin involvement.*

Infantile systemic hyalinosis (ISH) is a rare, progressive, fatal autosomal recessive condition [1]**.** Till 2009, fewer than 20 patients with ISH were reported and all of them died in early childhood, mainly due to severe diarrhea, pulmonary infections, or septicemia. It is characterized by widespread deposition of hyaline material in many tissues such as skin, gastrointestinal tract, adrenals, skeletal muscles, gingiva and other loci [2-4]. We report a case of infantile systemic hyalinosis.

CASE REPORT

A 2 year 4 months old boy presented with history of skin lesions on the face, ear, neck and the perianal regions since the age of 6 months. The skin lesions were progressively increasing in size and number. His parents noticed that he experienced discomfort on being handled and had difficulty in moving his limbs. Over the last one year, he gradually developed severe joint contractures in most of the large and small joints. He also started having recurrent episodes of diarrhea. There was no history of similar illness in any family member; elder sister aged 6 year was normal.

On examination, the child had normal developmental milestones, coarse facies , anteverted nose, and low set ears. He was short for age (height 75 cm, -2SD). His