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GALACTOSAEMIA IN AN INFANT: CASE REPORT

F.V. Murila, MBChB, MMed, Lecturer, Department of Paediatrics and Child Health College of Health Sciences, University of Nairobi, P.O. Box 19676, Nairobi

## GALACTOSAEMIA IN AN INFANT: CASE REPORT

F.V. MURILA

### SUMMARY

**Galactosaemia is a disorder of galactose metabolism in which raised levels of galactose and galactose-1-phosphate damage various organs. It is a very rare disease (incidence 1 in 60,000) and the diagnosis is often missed, leading to poor prognosis. A case of clinical galactosaemia that was diagnosed at the age of 11 months is reported. It is important to be aware of this condition as early treatment may prevent some of the complications.**

### INTRODUCTION

Galactosaemia is a very rare disorder of galactose metabolism whose mode of inheritance is autosomal recessive(1). It is characterised by a deficiency of any of three enzymes. These are galactokinase, galactose-1-phosphate uridyl transferase (GALT) and uridyl diphosphogalactose-4-epimerase. A deficiency of galactokinase leads to an increase in serum galactose with subsequent galactosuria. The excess galactose is converted to galactitol which leads to cataract formation. Intelligence is spared. Deficiency of GALT (classical galactosaemia) and the epimerase lead to an increase in galactose-1-phosphate which results into damage to the cells of the kidney, liver, brain and ovaries. This is coupled with an increased susceptibility to infections. As in galactokinase deficiency there is excess galactose which is converted to galactitol that is responsible for cataract formation.

Ovarian dysfunction and cataract formation may begin prenatally due to transplacental galactose derived from the diet of a heterozygous mother. The neonatal period is characterised by jaundice, hepatomegaly, hypoglycaemia, severe sepsis and convulsions(2). Later in life the child develops cirrhosis and neurological manifestations which include cerebellar dysfunction, as evidenced by tremor and ataxia(3). Mental retardation and personality disorder, speech disorder and convulsions also occur. Ovarian dysfunction manifests as primary or secondary amenorrhoea and premature ovarian failure.

Renal damage manifests as Fanconi's syndrome. Inhibition, by the excess galactose-1-phosphate, of the enzymes involved in glucose metabolism, the main ones being glucose-6-phosphate and glycogen phosphorylase causes hypoglycaemia.

In the diagnosis of galactosaemia urine tests are positive for a reducing substance (clintest) and yet negative for glucose (clinstix test). Galactose is identified by urine chromatography(2).

Assay of the respective enzyme in the red blood cell, white blood cell and fibroblasts shows a deficiency of the enzyme(4). Red blood cells (RBC) lactose-1-phosphate levels are high(2).

Treatment consists of dietary restriction of lactose. In spite of strict lactose restriction, however, neurological and gonadal damage are relentlessly progressive(2,5).

### CASE REPORT

J.M. was well until the age of three months when he was hospitalised for malaria and pneumonia at a peripheral hospital. He was readmitted with the same condition at the age of four months.

At the age of nine months, he developed unilateral left-sided focal seizures which would last minutes to hours and would occur twice a week. The child was referred to a paediatrician in Nairobi.

On examination the child was found to be in good general condition and of good nutritional status, did not have pallor, oedema or dehydration. The head was of normal size, fontanelles were closed and the child was awake but irritable. The muscle tone and reflexes were normal and the neck was soft. The other systems were essentially normal. Full haemogram, VDRL, EEG, CT scan were all found to be normal. An impression of complex convulsions most likely temporal lobe epilepsy was made and the child was put on carbamazepine 7.5 mg two times a day. Twitching recurred two days later and random blood sugar was found to be 0.7 mmol/l. The child was admitted into hospital where he was found to have recurrent hypoglycaemia. A diagnosis of insulinoma was made and a freeze sample of insulin was obtained during one of the episodes of hypoglycaemia. Insulin levels were found to be normal 8.2 uIU/ml (normal=5-30 uIU/ml).

During the first 24 hours of admission, despite a drip of 10% dextrose with boluses of 50% dextrose, the blood sugar remained persistently low ranging between 0.3 to 1.2 mmol/l. Despite the persistent hypoglycaemia, the urine tested positive for a reducing substance using the non-specific clintest.

At this point an impression of galactosaemia was entertained and the decision was made to stop all milk feeds

including breast milk and to put the infant on a soya preparation. Urine was obtained for purposes of determining the nature of the reducing substance therein but subsequently the urine was found to test negative for clintest. Twenty four hours later, the blood sugar was 3.5 mmol/l and the twitching had not recurred. The chemical diagnosis was not established due to the fact that the enzyme assays could not be done locally and the parents did not have the means to have them done abroad. A lactose challenge test was deemed unwise in view of the preceding persistent hypoglycaemia with repeated convulsions. After the blood sugar had remained normal for another 24 hour, the child was discharged on soya formula. Breastfeeding was completely withdrawn. He has been followed up since discharge and on no occasion have the twitches recurred. The random blood sugar has varied between 3.5-7.5 mmol/l.

Early 1998 the child was put back on cow's milk by the mother. No convulsions occurred but the random blood sugar dropped to 2.8 mmol/l. Milk was withdrawn and a month later the random blood sugar was normal again (3.5 mmol/l). He is the first child of a 43-year old para 0 + 1 who had been married for 10 years.

She attended antenatal clinic and the pregnancy was free of illnesses and use of medications. The infant was delivered at term by caesarean section due to breach presentation. He had a normal Apgar score and a birthweight of 3.5 kilograms. The infant breastfed well and had an uneventful postnatal period. The milestones were essentially within normal limits. Speech development and weight gain have also been normal. There are no reports of unexplained childhood deaths, mental retardation, mental illness, blindness or similar illness reported in the family. Currently he is in good condition and his height (106 cm), weight (16.5 kg), and head circumference (52.5 cm) are normal for age. He does not have cataract, but has a hepatomegaly of 3 cm. In the central nervous system, he is well oriented in time space and person and has normal speech. There were no cranial nerve palsies. Muscle bulk tone, reflexes and gait were all normal. No tremors or abnormal movements were noted.

## DISCUSSION

This report describes a child whose neonatal period was free of symptoms and he continued to thrive normally despite the presence of galactosaemia. In galactosaemia the severity of the disease varies depending on the residual enzyme levels(2). This patient probably had intermediate disease since he did not manifest any symptoms as a neonate. His growth and development were also satisfactory for his age. It is noted, however, that he did develop recurrent infections during the first half of his infancy and later hypoglycaemia with convulsions. His diagnosis was based on the finding of a reducing sugar in the urine coupled with persistent hypoglycaemia both of which resolved on withdrawal of lactose from his diet.

Although galactosuria was not demonstrated or enzyme analysis carried out to confirm the diagnosis of galactosaemia, the prompt cessation of the fits together with the normalisation of the blood sugar with concomitant absence of sugar in urine after lactose restriction points definitely to a diagnosis of

galactosaemia. Fructosaemia presents in a similar manner (hypoglycaemia and sugar in urine) but recovery occurs only after withdrawal of sucrose from diet. The patient continued to take sucrose in his diet without any untoward effects. So far he is growing normally, has normal speech and does not have cataracts or neurological dysfunction. However, he has over the last year developed a hepatomegaly of three centimetres which may be due to lapses in dietary restriction. In one series 50% of patients over six years developed neurological dysfunction and in another series 13% over three years of age had impaired motor function. In general, among galactosaemics, 60% develop speech disorder, 20% have growth retardation and 80% of the females have ovarian dysfunction(6). It is not possible, at this point, to say what his prognosis will be as the damage progresses despite dietary restriction.

The reason for the progressive neurological damage is not known but it may be due to other sources of galactose like vegetable, fruits and liver which are usually not restricted because they are over-looked as sources of galactose(7,8). On the other hand is the abnormal glycosylation of neural tissue due to the fact that galactose is not metabolised to UDP glucose which normally serves as the donor of galactose to neural tissue(9,10).

The infertility of the mother coupled with a spontaneous abortion may suggest ovarian dysfunction although there is controversy whether or not this does occur in the heterozygous female(11).

There are, to my knowledge, no reports of galactosaemia in this country. This could be due to the fact that the diagnosis is often missed due to the low index of suspicion and the unavailability of routine neonatal screening

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