ARTICLE

GALACTOSEMIA: A CASE STUDY

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ABSTRACT
Inborn errors of metabolism often manifest with varied clinical presentations in the neonatal period. Prevention of morbidity or mortality is frequently contingent on early diagnosis. Midwives have a role to play in recognizing symptoms that may be consistent with such a diagnosis. This paper describes the clinical findings in the case of a newborn in midwifery care who was diagnosed with galactosemia on day 10. This metabolic disorder is described and midwifery implications arising from this case are discussed.

KEY WORDS
galactosemia, midwifery, case study, metabolism, inborn errors

THIS ARTICLE HAS BEEN PEER-REVIEWED.

CASE
Baby boy was a term infant, born at home weighing 4763g (10lb 8oz), and was a second baby for his mother. The day one postpartum visit indicated a healthy newborn who was breastfeeding well, with normal vital signs and no jaundice. He had voided and passed three meconium stools. On day three, the baby was feeding approximately every one and a half to three hours and the birth weight had dropped to 4309g (9lb 8oz). At the day five home visit at 1900 hours, the midwife noted mild jaundice with the sclera slightly yellow, many soaked diapers, and breast stool with every feed. The baby's weight was down to 4281g (9lb 7oz), which was down 10% from his birth weight.

The mother reported that breastfeeding was going well with frequent nursing every one and a half hours. The mother's milk was in, and her breasts were full and leaking. The mother reported that the baby was alert and waking for feeds, but that he had had a large vomit after the last feeding. On further questioning, she reported that the baby had thrown up about a quarter cup of milk. The midwife witnessed the baby spit up a mouthful of milk after a feed during the visit. The vomiting was discussed, as were causes of jaundice and the progression of normal physiologic jaundice was reviewed.

The backup midwife who conducted the day five visit contacted the primary midwife and provided an update regarding the baby's weight loss, the mild jaundice and the vomiting. The primary midwife planned to visit sooner than the usual day 10 to day 14 visit in order to assess for adequate weight gain. Although the drop in weight was surprising, because the newborn appeared well hydrated, the nursing appeared adequate, and there had been plenty of wet and dirty diapers, the midwives were not concerned at this point. The management plan for any further weight loss included a pediatric consultation for a weight loss of greater than10%, in keeping with the College of Midwives of Ontario guidelines.

The following day (day six) at 1500 hours, the mother called to express concern that the baby would not be gaining weight because he had continued to spit up moderate amounts with his feedings. She reported that he continued to be alert, feed well, and was voiding and stooling normally. It was recommended that she document feedings, voids, stools, and vomiting. The midwife planned to visit the next morning to assess weight gain. Etiology of emesis from pyloric stenosis and esophageal atresia were reviewed and ruled out. Warning signs of lethargy, irritability, poor feeding, poor output, and fever were reviewed with the mother, and she was instructed to page with any concerns.

Five hours later, at 21:10 of day six, the mother paged to report that the baby had continued to vomit more and more forcefully in larger and larger amounts, and that he was not feeding well. The midwife directed her to proceed immediately to the hospital for assessment by the pediatrician on call. While the family was en route, the midwife contacted the on call pediatrician and provided the clinical history. The baby was seen in the emergency department where the admission record noted that he was very jaundiced but was in no acute distress, and that he was arousable and active when handled. The admission notes report that his vital signs were normal with temperature of 37^{0}C, pulse 148, respirations 48, and oxygen saturation of 97%. His weight was 4000g (8lb 13oz), which was a weight loss of 16% from birth weight. The anterior fontanel was assessed to be somewhat sunken. His abdomen was soft, with no apparent organomegaly or guarding. The baby was admitted to the pediatric unit for treatment of jaundice and dehydration, with a management plan of intravenous rehydration and phototherapy. outcome of a septic screen. He continued to nurse and vomit about 50cc with each feed. The bilirubin was repeated at 0830 and had dropped to 404 imol/L.→

The following day (day 8) the bilirubin was tested at 0716 hours and had dropped to 355 ìmol/L, but by 1104 hours it was up to 414 ìmol/L. By 1850 hours it had dropped again to 378 ìmol/L. Two days later, on day 10, the pediatrician indicated that the bilirubin seemed to be decreasing with treatment, and that the baby's weight was increasing. There had been no vomiting for 48 hours. At 1700 hours that day, breastfeeding was stopped and the baby was put on a soya-based formula, and a galactosemia screen was ordered. The management plan was for the baby to be discharged once the bilirubin was within normal limits, weight gain was maintained and the galactosemia screen was negative.

The galactosemia screen was returned, positive, on day 13 and mother and baby were discharged home. With soya-based formula feedings, the baby was gaining weight and the jaundice had improved. The family was following up with the clinic for galactosemia at the children's hospital. At a home visit by the midwife on day 20, soya feedings were going well with the baby feeding every two hours, taking two to three ounces. per feed. The baby had regained his birth weight, and urinary and stool output were normal.

GALACTOSEMIA

The sugar found in milk is the disaccharide, lactose. When lactose is digested it is broken into its component monosaccharides: glucose and galactose. Galactosemia is an autosomal-recessive metabolic disorder in which there is a deficiency of the enzyme galactose-1-phosphate uridyl transferase, which is responsible for the normal metabolism of the monosaccharide galactose.

There are over 100 different inheritable mutations that will manifest some degree of galactosemia. Some of these mutations will result in a total inability to process galactose (often referred to as classic galactosemia), while other mutations result in varying degrees of decreased ability to handle galactose in the diet. The Duarte mutation is one of the more common variant types of galactosemia, and individuals with this variant may be asymptomatic. Galactosemia seems to be found in all populations, although the prevalence is variable (for example: 1/62,841 babies screened in Philippines; 1/23,000 in Ireland, 1/700 in the Irish itinerant population).[1] Based on a prevalence study in California, the rate of classic galactosemia is estimated to be 1/47,000 in the white population in the United States of America.

Newborns with classic galactosemia present very soon after birth with symptoms, which include jaundice, vomiting, enlarged liver, cataracts and failure to thrive. Left untreated, classic galactosemia can result in mental and motor skill delays, blindness, liver impairment and death. The treatment involves a galactose-restricted diet and counselling. It is necessary for these babies to be weaned immediately from breast milk or any formula containing lactose or galactose and to be put on a soya-based product.

Even with early diagnosis and treatment, long-term manifestations of the condition seem to be present in most individuals with galactosemia, including some mental delays, learning disorders, fine and gross motor skill complications, and (amongst females) ovarian failure. In families in which galactosemia has been diagnosed, subsequent newborns can be diagnosed quickly using cord blood samples.[1]

Badawi et al reported findings when 32 children with galactosemia in Ireland were followed between 1977-1992. They found survival was enhanced with aggressive neonatal management. Symptoms improved with a galactose-restricted diet but complications did not correlate with the day of starting the diet.[2] In evaluating the cognitive outcome in a British cohort of 45 children, Shield and colleagues found that variability in cognitive outcome appeared to be determined by the genotype rather than the degree of metabolic control.

In some jurisdictions galactosemia is part of newborn screening programs. In an Irish centre where this approach is used, the mean time to diagnosis is 6.9 days.[2] There is debate, however, about the efficacy of this approach, in part because neonates may present based on symptoms alone before the results of testing are available. It has been suggested that any newborn who presents in the first two weeks of life with symptoms consistent with galactosemia should be screened. This latter approach is used in Ontario, the jurisdiction in which our case presented.

Infants with galactosemia are likely to present at the end of the first or during the second week of life with progressive jaundice resulting from an elevated direct serum bilirubin. The hyperbilirubinemia may initially be indirect, as a result of hemolysing action on red blood cells from the galactose-1-phosphate. The jaundice is thought to result from a direct toxic effect on the liver of galactose-1-phosphate that builds up due to the deficiency of the enzyme galactose-1-phosphate uridyl transferase.[7] The jaundice may be accompanied with vomiting, diarrhea, poor weight gain, and, sometimes hypoglycaemia. Occasionally central nervous system symptoms may be prominent in situations where toxicity of galactose-1-phosphate is directed to the brain. A later symptom is cataract formation.[7]

DIFFERENTIAL DIAGNOSIS

There are more than 300 known inborn errors of metabolism, which manifest with varied clinical presentations. These metabolic disorders may be broadly classified into macromolecular and micromolecular groups. Those in the micromolecular group of metabolic disorders often present with acute onset of symptoms in the neonatal period. Prevention of serious long-term sequelae or death is often contingent on early diagnosis.[7,] Galactosemia is one of the inborn errors that present very early in the neonatal period, with presenting symptoms that are often consistent with sepsis. However, with full term infants where there is no particular septic risk, and the presenting symptoms include lethargy, poor feeding, apnea or tachypnea, or recurrent vomiting, inborn errors of metabolism should be considered as part of the differential diagnosis. Sepsis may co-exist with inborn errors of metabolism and it is, therefore, important that they not be excluded from the differential diagnosis even when sepsis is present. When jaundice is part of the presentation, galactosemia should be considered along with hereditary tyrosinemia, alpha$_1$-antitrypsin deficiency, neonatal hemochromatosis, Zellweger syndrome, Niemann-Pick disease, and glycogen storage disease type IV.[7] →

When inborn errors of metabolism are considered as part of a differential diagnosis, the screening laboratory studies should include: complete blood count with differential, urinalysis, blood gases, serum electrolytes, blood glucose, plasma ammonia, urine reducing substances, plasma and urine amino acids (quantitative), urine organic acids, and plasma lactate. The two specific tests that will be useful in diagnosing of galactosemia are the presence of reducing substances in urine and RBC galactose-1-phosphate uridyl transferase.[7]

MIDWIFERY IMPLICATIONS

The onset of symptoms of galactosemia at the end of the first week in this case was consistent with the expected time frame for the condition. The newborn visits for this baby were made according to the usual schedule of midwifery visits on day one, three and five. On day five, early symptoms were present, but went unrecognized, although good midwife to midwife communication allowed for a plan to be put into place to follow this baby more closely than usual. The parents were instructed to watch for signs of any problems associated with either hyperbilirubinemia or the vomiting including: lethargy, irritability, poor feeding, poor output, fever, increasing jaundice, or vomiting. The parents did identify persistence in the vomiting, and, later, continued vomiting and poor feeding. This identification resulted in rapid follow-up with pediatrics, on day six, when the vomiting had intensified. The weight loss noted on day five continued, and the formerly mild jaundice was severe. Excellent communication between the back-up and primary midwife, and between the midwives and the pediatrician ensured that the rapid onset and progression of the baby's condition was understood and managed.

The midwives provided supportive care while the diagnosis was being made. Help was provided during the transition to bottle-feeding, including assistance with rapid cessation of breastfeeding. It is imperative for midwives to have a good understanding of rapid weaning, as well as bottle and formula feeding, in order to assist women in circumstances such as this one. This mother breastfed her first infant, and appreciated assistance with new strategies to soothe her second baby without breastfeeding.

Providing accurate information to the family was complemented by a useful website that the family could access.[4] Spending time with the family following the diagnosis, and re-visiting the birth experience with them, may have assisted to normalize mothering and parenting and to re-focus the family on their new baby, and away from the diagnosis.

AUTHORS' BIOGRAPHIES

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