

Obstructive jaundice due to a chlorinated hydrocarbon in breast milk

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A 6-week-old breast-fed infant had obstructive jaundice and hepatomegaly. When a dry-cleaning solvent, tetrachloroethylene, was detected in the mother's milk and blood, breast-feeding was discontinued. Rapid clinical and biochemical improvement followed. The child grew normally and had normal liver function during 2 years of follow-up.

Un bébé de 6 semaines qui était allaité a présenté un ictère par rétention et une hépatomégalie. L'allaitement a été interrompu quand un solvant pour le nettoyage à sec, le tétrachloroéthylène, a été décelé dans le sang et le lait maternels. Une amélioration clinique et biochimique rapide s'est ensuivie. L'enfant s'est développé normalement et avait une fonction hépatique normale pendant 2 ans d'observation.

Obstructive jaundice (conjugated hyperbilirubinemia) occurring in the first 2 months of life is an uncommon but important clinical problem. It is always associated with pathologic conditions and usually implies disease of the liver or biliary tract.

Approximately 75% to 85% of infants with obstructive jaundice have one of two poorly understood syndromes — extrahepatic biliary atresia or the neonatal hepatitis syndrome.¹ In the latter the infant has obstructive jaundice, patent extrahepatic bile ducts and findings compatible with hepatocellular disease but does not have a specifically identified congenital infection or hereditary metabolic disease. Although extrahepatic biliary atresia is an anatomically distinct disease, many workers suggest that the same basic process produces both biliary atresia and neonatal hepatitis and that the two presentations simply represent single points on the same disease continuum.² Specific congenital infections (rubella, syphilis, cytomegalic inclusion disease, herpes simplex, hepatitis B and toxoplasmosis) as well as one of the metabolic diseases, α_1 -antitrypsin deficiency, have been separated from the neonatal hepatitis syndrome over the past several years, and further

specific disease identification can be anticipated with continuing study of this syndrome.

Other causes of obstructive jaundice occur infrequently. Urinary tract infection, hemolytic disease, intrahepatic biliary atresia, and the metabolic-genetic diseases galactosemia and cystic fibrosis have been identified as causes at our hospital over the past 3 years. In a review of cases of conjugated hyperbilirubinemia in young infants Sass-Kortsak³ cautioned that toxic drugs or chemicals could cause this condition; however, except for his personal observation of a case of phenol poisoning, reports of toxic hepatitis in this age group are unknown to us.

Tetrachloroethylene (perchloroethylene) is a chlorinated hydrocarbon that is widely used as a solvent in the dry-cleaning industry and is a constituent of several household products. While not considered a significant hazard when properly used, it has been reported to cause toxic hepatitis in adults following lengthy industrial exposure.^{4,5} Although Stewart⁶ cited reports of the death of a 16-year-old boy following intoxication from a freshly dry-cleaned, inadequately aired sleeping bag, tetrachloroethylene-associated toxic hepatitis has not been described in children. This presumably reflects the absence of lengthy exposure in childhood.

We report the case of a breast-fed infant who presented at age 6 weeks with obstructive jaundice. Throughout the weeks of nursing, the child's mother had been exposed to tetrachloroethylene and the toxin was present in her milk.

Case report

Dark urine, progressive jaundice and acholic stools appeared over a 1-week period in a previously healthy 6-week-old girl. She had been breast-fed and had not received any medication.

She was irritable and mildly underweight. The edge of her liver was smooth, moderately firm and palpable 3 cm below the right costal margin. She had no evidence of cataracts, cardiovascular disease or splenomegaly. Her hemoglobin value was 12.2 g/dL and, with the exception of occasional target cells, a blood smear was normal. Leukocyte and platelet counts were normal and urinalysis was negative for reducing substances. She was admitted to our hospital for further investigation.

The child was born at the Grace Mater-

nity Hospital, Halifax at 36 weeks' gestation to a healthy, type A, Rh(D)-negative, 20-year-old primigravida. Her birth weight was 2480 g. Examinations in the newborn nursery had suggested mild fetal malnutrition but no other abnormalities. Jaundice had not been observed and her liver size was noted to be normal. The baby's blood was type O, Rh-positive and the direct Coombs' test on her cord blood yielded negative results.

At home the child had been well and had not been exposed to infectious illnesses. At 5 weeks of age she had had a routine well-baby examination and had not been noted to have jaundice or hepatomegaly.

The family history was unremarkable. Her parents were healthy, but her father, who worked as a leather and suede cleaner in a dry-cleaning plant, had experienced repeated episodes of personality change, dizziness and confusion following recurrent exposure to solvent vapours at work. Her mother was not taking any medication but had repeatedly been exposed to the same fumes during her regular lunch-hour visits with her husband at the plant. She occasionally experienced mild dizziness after these brief (30- to 60-minute) exposures. The child was never directly exposed to the father's working environment or to freshly dry-cleaned clothes.

Laboratory investigations at the time of admission to hospital revealed direct-reacting hyperbilirubinemia (bilirubin values: total, 8.4 mg/dL; direct, 6.0 mg/dL). The serum glutamic oxaloacetic transaminase value was 85 IU/L (normal, 8 to 26 IU/L) and the serum alkaline phosphatase value, 300 IU/L (normal, 70 to 225 IU/L). No abnormalities were detected by the following: measurement of serum concentrations of total protein, albumin, globulins, immunoglobulins, α_1 -antitrypsin, α -fetoprotein and thyroxine, prothrombin and partial thromboplastin times, sweat chloride concentration, rubella hemagglutination-inhibition titre, and herpes simplex and cytomegalovirus complement-fixation titres; direct Coombs' test; repeated urinalysis; Sabin-Feldman dye test; urine culture for rubella virus and cytomegalovirus; and throat culture for rubella virus.

Hospitalization decreased the frequency of breast-feeding and within 3 days the infant's serum bilirubin values decreased to 4.2 (total) and 3.5 (direct) mg/dL. Breast-feeding was then discontinued and by the 8th hospital day the serum bilirubin values were 1.7 (total) and 1.3 (direct) mg/dL and the serum alkaline phosphatase value was normal.

Investigations of the parents were started immediately after the rapid clinical and biochemical improvement of the child's condition. While investigations of the child and her parents were done with

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the informed consent of both parents, the mother was not aware of our specific concern regarding tetrachloroethylene before her first blood and breast milk specimens were obtained. She had been manually pumping her breasts and bringing the milk to the hospital at regular times throughout each day.

Tetrachloroethylene concentrations were determined in venous blood and breast milk by a gas chromatographic head-space procedure. Standards in the anticipated range of concentrations were prepared in blood and milk. An aliquot of the equilibrated head space was injected on a Teflon-Hallcomid-Carbowax column operated at 80°C in a Carle Model 9000 flame ionization gas chromatograph (Carle Instruments Inc., Fullerton, California) and the concentration of tetrachloroethylene determined by comparison of peak height responses. Halogenated hydrocarbons in urine were checked for by the Fujiwara reaction.

The parents' serum bilirubin, transaminase and alkaline phosphatase values were normal. However, the father's blood contained 3 mg/dL (0.018 mmol/dL) of tetrachloroethylene and his urine contained trace amounts of tetrachloroethylene derivatives. The mother's blood contained 0.3 mg/dL of tetrachloroethylene approximately 2 hours after one of her lunch-hour visits to the plant, and her breast milk, expressed 1 hour after the visit, contained 1.0 mg/dL of tetrachloroethylene. Avoidance of exposure to solvent vapours for the next 24 hours allowed the breast milk concentration to decrease to 0.3 mg/dL. The mother's urine, collected the same afternoon as the breast milk and blood specimens, did not contain chlorinated hydrocarbons.

Discussion

Approximately 1% of breast-fed infants may have prolonged jaundice,⁷ however, as with physiologic jaundice, "breast-milk jaundice" is always an unconjugated hyperbilirubinemia.^{1,7} Therefore, the obstructive nature of our patient's jaundice suggested it was unrelated to breast-feeding. The clinical presentation was most compatible with either extrahepatic biliary atresia or the neonatal hepatitis syndrome, and the early results of investigations, with no evidence of hemolytic disease, urinary tract infection, sepsis, metabolic disease or a specific congenital infection, supported this differential diagnosis.

Although we have seen fluctuations in the bilirubin values of infants with both extrahepatic biliary atresia and the neonatal hepatitis syndrome the clinical and biochemical improvement in our case was unusually good and rapid. In fact, it suggested a specific change of therapy rather than spontaneous resolution of a disease process. This led to investigation of the two major factors changed by the infant's hospitalization — environment and feeding. The his-

tory of recurrent parental exposure to tetrachloroethylene suggested the potential for maternal transfer of this simple chlorinated hydrocarbon to the infant, as numerous centres, including ours, have reported the presence of chlorinated hydrocarbon insecticides in breast milk.⁸

Although tetrachloroethylene could be detected in the mother's breast milk for 24 hours after one brief exposure, its concentration decreased from 1.0 to 0.3 mg/dL over this interval. The mother's blood tetrachloroethylene concentration was 0.3 mg/dL when the breast milk concentration was 1.0 mg/dL, which suggests selective concentration of the chlorinated hydrocarbon in milk. Again, this observation is in keeping with data on chlorinated hydrocarbon insecticides, which also have been found in higher concentrations in breast milk than in blood.⁹ As there was a 1-week interval between the discontinuing of the breast milk feedings and the sampling of the infant's blood, we were unable to document the presence of tetrachloroethylene in the infant. Nevertheless, the infant's only food, breast milk, had been shown to contain tetrachloroethylene, which provided credible documentation of significant exposure to a chemical known to be well absorbed from the gastrointestinal tract.⁶

It is difficult to explain this infant's hepatotoxicity in the presence of normal liver function in her parents, and it appears that it is the infant's abnormal rather than the parents' normal findings that require explanation. Considered alone, the parents' normal findings are in keeping with industry's experience with tetrachloroethylene. It has been considered a relatively safe chlorinated hydrocarbon: with severe brief exposures in adults only mild transient increases in serum transaminase values have been reported,⁵ while lengthy exposures have produced evidence of hepatic dysfunction only after months of exposure.⁴ The magnitude of this infant's exposure is impossible to assess because of the numerous maternal and infant factors involved over an interval of approximately 4 weeks. Neonatal and adult livers respond differently to many toxic and infectious agents,¹ and it is possible that the neonatal liver is more sensitive to tetrachloroethylene than the adult liver, for which it is only mildly toxic. The brief clinical course and rapid return of liver function to normal in this infant make it unlikely that her response resulted from a viral illness with hepatitis; however, we cannot exclude the possibility of a toxic insult being superimposed on mild hepatitis. Indeed, the work of Crocker and associates¹⁰ has established the enhanced

hepatotoxic effects of such virus-chemical interactions in nursing mice.

With greater numbers of women working outside the home, there is an increasing potential for exposure of pregnant and nursing women to environmental toxins. While studies in animals have not demonstrated evidence of adverse effects on the fetus following exposure of pregnant animals to chlorinated hydrocarbons,¹¹ little consideration has been given to the possible effects of transmission of these agents in breast milk. Our experience with this family shows the potential for such transmission of at least one of the chlorinated hydrocarbons. Furthermore, our experience with liver function studies in the parents lends support to Gehring's¹² observation that liver cell dysfunction is an inadequate criterion for defining safe environmental concentrations of the less hepatotoxic of the chlorinated hydrocarbons. In view of the potential hazard for infants this observation is particularly relevant for nursing women.

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