Medical Journal of the
Islamic Republic of Iran

Volume 14
Number 4
Winter 1379
February 2001

EVALUATION OF THE CAUSES OF CHOLESTASIS IN INFANTS

F. FARAHMAND, M.D.

From the Department of Pediatric Gastroenterology, Children's Hospital Medical Center, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran.

ABSTRACT

During a period of three years from 1996 to 1998, 124 infants (64 male and 60 female) with an age range of 1-6 months (mean age 1.5 months) with cholestasis were studied. Idiopathic neonatal hepatitis was the most common cause of cholestasis, accounting for 48 cases with a rate of 38.70% in a total of 124 patients, followed by galactosemia in 29 patients (23.38%) and extrahepatic biliary atresia in 20 patients (16.12%).

The prompt identification and diagnostic assessment of these infants are imperative to early surgical intervention (e.g. in biliary atresia) and specific medical therapy (e.g. in galactosemia) and in order to institute effective nutritional and medical support to allow optimal growth and development and prevent progressive liver disease and death.

MJIRI, Vol. 14, No. 4, 333-335, 2001.

Keywords: Cholestasis, Infants, Idiopathic neonatal hepatitis, Extrahepatic biliary atresia (EHBA).

INTRODUCTION

Cholestasis, defined physiologically as a reduction in canalicular bile flow, is primarily manifested as conjugated hyperbilirubinemia. The major clinical consequences however are presumably related to retention of other substances such as bile acids, which are dependent on bile flow for excretion.[1-6] There are multiple causes of cholestasis in early life, in response to various insults. These include structural anomalies of the biliary tract, both intrahepatic and extrahepatic, which result in obstruction of bile flow, and infectious, metabolic, or toxic insults, which cause functional impairment of the hepatic excretory process and bile secretion.[3-8]

Although the causes of cholestasis in infancy are varied, the clinical presentation is similar, reflecting the underlying decrease in bile flow. Specifically, infants with cholestasis present with variable degrees of jaundice, dark urine, light stools, and hepatomegaly with or without splenomegaly and ascites.[1-3,5,7]

Laboratory studies reveal a conjugated hyperbilirubinemia (direct bilirubin >2 mg/dL) and serum transaminase levels are mild to moderately elevated. The result of liver pathology depends on the cause of cholestasis. Early diagnosis of cholestasis in an infant and prompt specific treatment are imperative in order to ameliorate the clinical course and prevent progressive liver disease.

PATIENTS AND METHODS

During a period of three years from 1996 to 1998 in the Children's Hospital Medical Center, 124 patients (64 male and 60 female) with an age range of 1-6 months with cholestasis were studied.

Evaluation of infants with cholestasis in this series was based on family history, physical examination, laboratory and radiographic data, and liver biopsy (Table I).

RESULTS

Age distribution and the causes of infant cholestasis in our series are shown in Tables II and III. The most common age range was 1-2 months (33.8%).

Idiopathic neonatal hepatitis was the most common cause of cholestasis, accounting for 48 cases (38.70%) in a total of 124 patients. Galactosemia and extrahepatic biliary atresia (EHBA) were the second and third following causes of cholestasis with rates of 23.38% and 16.12% in this series.

Table I. Comprehensive list individualized and modified based on clinical judgement.

- Fractionated bilirubin
-*AST, **ALT, PT, PTT, albumin
- Bacterial cultures (blood, urine, stool)
- Viral studies (Hepatitis, TORCH)
- Metabolic screen (urine and serum, aminoacids, thyroid function tests, serum alpha-l antitrypsin)
- Sweat test for cystic fibrosis
- Abdominal ultrasonography
- Hepatobiliary scintigraphy
- Percutaneous liver biopsy
- Open liver biopsy and operative cholangiography

*aspartate aminotransferase
**alanine aminotransferase

DISCUSSION

Evaluation of the cholestatic infant remains a difficult task, owing in part to the diversity of cholestatic syndromes and to the obscure pathogenesis of many of these disorders.

In any infant with suspected conjugated hyperbilirubinemia, it is important to immediately investigate infectious, metabolic and structural causes for which early therapy will alter the outcome of the disease.[1-3,7-9]

Extensive evaluation of the infant with cholestasis leads to a diagnosis of either idiopathic neonatal hepatitis in approximately 30-35% and biliary atresia in 25-30% of infants.[1-3,6,7,12]

Comparison of the results of the present series are nearly similar to other reports.

Term, idiopathic neonatal hepatitis should be restricted to cases of prolonged cholestasis in which more than 50% develop jaundice within the first week of life. Acholic stools are uncommon but may be present if the cholestasis is severe.

Liver biopsy can be helpful in excluding other causes of cholestasis. Several histologic features such as giant cell transformation, hepatocellular swelling and necrosis, represent a stereotypic response of the infant liver to injury.[1-3]

In general, the birth weight of infants with biliary atresia is normal, and jaundice may be present from birth or be inapparent until 3 to 5 weeks of life or later. Acholic stools are common, and consistent absence of stool pigment suggests biliary obstruction.

The rate of EHBA in this series was 16.12%, confirmed by an intraoperative cholangiogram performed prior to surgical intervention. Another seven patients suspected of EHBA whose parents disfavored surgical intervention were eliminated from the study, so the frequency of EHBA in this series was less than other reports. Also, in another six patients from a total of 124 cases who presented similar to patients with EHBA but had an intraoperative cholangiography performed, the biliary tree was patent. Later follow up showed that two cases had cystic fibrosis, two cases alpha-l antitrypsin deficiency* and two cases had inspissated bile syndrome without any hemolysis.

Table II. Age distribution of patients.

Age/month	Number of Patients	Percentage
0-1	26	20.4
1-2	42	33.8
2-3	22	17.7
3-4	13	11.2
4-5	12	9.6
5-6	9	7.2
Total number	124	100

Table III. The causes of infant cholestasis in 124 cases.

Cause	Number of patients	Percentage
Idiopathic neonatal hepatitis	48	38.70
Galactosemia	29	23.38
EHBA	20	16.12
Cystic fibrosis	6	4.83
Alpha-1 antitrypsin deficiency	4	3.22
Alagille's syndrome	3	2.41
Tyrosinemia	3	2.41
Choledochal cyst	3	2.41
Inspissated bile syndrome	2	1.61
Hypothyroidism	2	1.61
Bacterial sepsis	2	1.61
Niemann- Pick's disease	1	0.80
Hepatitis B	1	0.80
Total number	124	100

Management in all patients was usually directed towards nutritional support, vitamin supplementation and general medical management of the clinical complications of cholestasis such as pruritus.[1-3,5,11]

In addition, patients with galactosemia were treated with complete elimination of all sources of galactose in their diet, especially milk and milk products that contain lactose.[1-3,11,12]

Surgical treatment in patients with EHBA was de-

*Serum alpha-1 antitrypsin was the basis of diagnosis.

pendent on age of infants and biliary tree anatomy on open cholangiography. Most cases did not have patent extrahepatic bile ducts, so the Kasai hepatoportoenterostomy was performed. Prognosis was dependent on the initial cause of cholestasis and the intensity of hepatic damage.[12-15]

REFERENCES

1. Dellert SF, Balistreri WF: Neonatal cholestasis, In: Walker A, Durie P, Hamilton R, (eds.), Pediatric Gastrointestinal Disease. St Louis: Mosby Year Book, pp. 999-1012, 1996.
2. Balistreri WF: Neonatal cholestasis. J Pediatr 106: 171-184, 1985.
3. Peter F: Chronic cholestasis of infancy. Pediatric Clinics of North America 43(1): 1-27, 1996.
4. Erlinger S: Recent concepts in bile formation and cholestasis. Medicina 81: 387-391, 1990.
5. Suchy FJ: Approach to the infant with cholestasis, In: Suchy FJ, (ed.), Liver Disease in Children. St Louis: Mosby Year Book, pp. 349-355, 1994.
6. Lai MW, Chang MH, et al: Differential diagnosis of extrahepatic biliary atresia from neonatal hepatitis: a prospective study. J Pediatr Gastroenterol Nutri 18: 121-127, 1994.
7. Chang MH, et al: Neonatal hepatitis: a follow-up study. J Pediatr Gastroenterol Nutr 6: 203-207, 1987.
8. Balistreri WF: Liver Disease in Infancy and Childhood, In: Schiff ER, Michael F, (eds.), Schiff's Diseases of the Liver. Philadelphia: Lippincott- Raven, pp. 1369-1445, 1999.
9. Bruguera M: Nonsyndromic paucity of intrahepatic bile ducts in infancy. Hepatology 15: 830-834, 1992.
10. Whitington PF, et al: Clinical and biochemical findings in progressive familial intrahepatic cholestasis. Journal of Pediatric Gastroenterology and Nutrition 18: 134-141, 1994.
11. Bergasa NV, Jones EA: Management of the pruritus of cholestasis. Journal of Gastroenterology 86: 1404-1412, 1991.
12. Mowat AP, Pscharopoulos HT: Extrahepatic biliary atresia versus neonatal hepatitis: a review of 137 prospectively investigated infants. Arch Disease Children 51: 763-770. 1976.
13. Ryckman F, Fisher J, et al: Improved survival in biliary atresia patients in the era of liver transplantation. Journal Pediatric Surgery 28: 382-385, 1993.
14. Deutsch J: Long term prognosis for babies with neonatal liver disease. Arch Disease Children 60: 447-451, 1985.
15. Laurent J, et al: Long-term outcome after surgery for biliary atresia: study of 40 patients surviving for more than 10 years. Gastroenterology 99: 1793-1797, 1990.