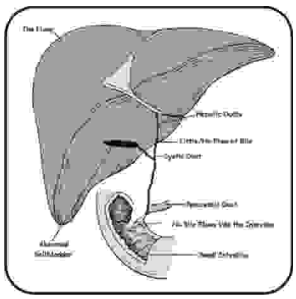
REVIEW PROF-1288

NEONATAL BILIARY ATRESIA



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ABSTRACT... Bilrary atresia continues to emanate controversy & despair among Physicians & patients alike. With the development of liver transplant and new techniques a new insight in NBA surgical care has come forth. This condition is the most common cause of persistently direct (conjugated) hyper bilirubinemia in the first 03 month of life. Kasai portoenterostomy & liver transplantation battle to become todays leading therapy. The main focus of attention however remains that the results after portoenterostomy are decided by the promptness of the initial workup & referral to surgery. More then 80% of babies with NBA have satisfactory bile flow after hepatic portoenterostomy if the procedure is done before 8th week of life.

INTRODUCTION

NBA is characterized by progressive inflamatory obliteration of the extrahepatic bile ducts, with an estimated incidence of one in 15,000 live births & predominance of female patients[1]. The first comprehensive paper was written by J.Thompson of Edinburgh in 1882. J.B.Holmes in 1916 classified cases as correctable (10-15%) and non correctable (85-90%) depending on the pathologic structures identified at the portahepatis area, and Dr William ladd in 1928 ventures into the first successful bile-enteric anastamosis[2]. In 1959 Kasai & Suzuki described a new procedure for biliary atresia that transformed management during the next 30 years[3]. By 1980 most infants with biliary atresia were managed with Kasai operation.

ETIO-PATHOLOGICAL FACTORS

Although much has been written about NBA, its pathogenesis remains speculative. The original theory of an embryogenic accident that settled in occlusion of the extra hepatic biliary tree, was challenged by the absence of jaundice at birth, and histological evidence of patent biliary ducts that progressively disappeared during the initial months of life[4]. Findings in the obstetric history of older patients, high use of drugs, associated illness and fetal loss suggested the possibility of exposure to a noxious agent during the reproductive process[5]. The disease is the result of an acquired inflammatory process with gradual degeneration of the epithelium of the extra hepatic biliary ducts causing luminal obliteration, cholestasis and biliary cirrhosis. The timing of the insult after birth suggests a viral etiology transplacentally. Reovirus type 3 has been implicated[6].

Up to 68% of infants with NBA show antibodies to reovirus type 3 in serum, although no viral particle was isolated. Almost 20% of patients have associated anomalies such as polysplenia, malrotation, preduodenal

portal vein and absent inferior venacva. This raises the possibility of a genetic mutation with defective development of one side of the body[7].

Microscopic biliary structures have been identified in the most proximal aspect of extra hepatic remnant of three types. These are 1. Bile ducts with mean diameter of 500 microns and bile in the lumen 2. Collecting ductules of biliary glands with a mean diameter of 250 microns and 3. Biliary glands without bile and a mean diameter of 100 microns[8]. Postoperative biliary flow after Kasai correlates with the presence and size of bile ducts and collecting ductules exclusively. Electron microscopy can exhibit canalicular biliary membrane filaments whose volume and appearance correlates with adequate bile flow. The degree of hepatic fibrosis associated also relates with post-operative biliary flow. Kasai portoenterostomy relies on the realization that the microscopic structures in the porta hepatis will act as micro-conduits of bile as an internal biliary fistula is created with a segment of bowel. All will eventually merge into one or two ducts.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

Physiologic jaundice of the new born is a common, benign and self limiting condition. Persistent conjugated hyper-bilirubinemia (greater then 20% of total or 1.5 mg%) should be urgently appraised. Initial evaluation should include a well taken history and physical examination, partial and total bilirubin determination, type & blood group, coomb's test, reticulocyte cell count and a peripheral smear[9].

In the NBA the patient develops insidious jaundice by the second week of life. The baby looks active, not acutely ill and progressively develops acholic stools, choluria and hepatomegaly. The diagnostic evaluation of the cholestatic infant should include a series of lab tests that can exclude perinatal infections (TORCH titres, hepatitis profile) systemic & hereditary causes.

Ultrasound study of the abdomen should be the first diagnostic imaging study done to cholestatic infants to evaluate the presence of a gall bladder, identify intra or extra hepatic bile ducts dilatation, and liver parenchyma echogenecity. NBA songraphic characteristics are: absent or small gall bladder that does not contract upon hormonal stimuli, and increased liver echognecity. The postprandial contraction of the gallbladder eliminates the possibility of NBA even when nuclear studies are positive.

Nuclear studies of bilioenteric excretion after pre-stimulation of the microsomal hepatic system with phenobarbitone for 3-5 days is the diagnostic imaging of choice. NBA patients will show an increased hepatic uptake during early injection without significant bilioenteric excretion in delayed films (24 hrs). The presence of radioisotope in GI tract excludes the diagnosis of NBA. Hepato-cellular causes of jaundice will show poor concentration of isotope in the liver associated to delayed or absent excretion.

Percutaneous liver biopsy should be the next diagnostic step if previous studies suggest NBA and the infant has no associated coagulopathy. Findings of NBA are: bile duct proliferation and fibrosis. Unfortunately these changes are nonspecific of NBA and can be found in neonatal hepatitis. The mini laparotomy is the final diagnostic alternative. Through a small right subcostal incision a gallbladder cholangiogram and liver biopsy is done. Infants with radiographic evidence of patent extra hepatic biliary tract have no NBA. Small hypoplastic ducts are associated to Alagilles syndrome. In the NBA the gall bladder can be a fibrous remnant, present but filled with white bile (hydrops), with no communication with the biliary tree, or with distal extra-hepatic communication. Once the diagnosis of NBA is established intra operatively a Kasai portoenterostomy is constructed. Recently diagnostic laparoscopy has been found useful in the evaluation of cholestatic infant.

MANAGEMENT

Medical management of NBA is uniformly fatal. Kasai portoenterostomy has decreased the mortality of NBA during the last 30 years. This procedure if done before the first 6-8 weeks of life will yield biliary flow in 75-80% of infants. It consists of removing the obliterated extra hepatic biliary system, and anastomosing the most proximal part to bowel segment. The initial mini-laparotomy incision is extended once the diagnosis is

confirmed. The gallbladder, cystic duct and extra hepatic remnant is mobilized, the distal common bile duct is ligated proximally & dissection proceeds towards the portahepatis. At the portahepatis the remnant looks like a fibrous cord with the shops of a cone. At this point the cord is transected perpendicularly to the liver level. The raw surface left over is anastomosed to a limb of jejunum in roux-en-y fashion. It is estimated that in 10-15% cases distal patency of the extra hepatic bile ducts and gall bladder can be used as conduit instead of bowel. This variation in the procedure eliminates the possibility of developing cholangitis, but increases the risk of anastomotic leak from ischemia[2].

In Pursuit of reducing the episodes of cholangitis Kasai procedure was modified providing an external conduit to diminish the intra luminal pressure and secretory liver gradient. Almost three fourths of patients will develop portal hypertension inspite of adequate postoperative bile flow. They will manifest esophageal varices, hypersplenism and ascites. Esophageal varices usually develop 2-8 years after portoenterostomy and are managed with endoscopic sclero-therapy effectively. Ascites will need salt restriction & diuretics. Secondary hypersplenism can be managed with partial embolization of splenic artery. Essential fatty acids malabsorption leading to caloric & nutritional deficiencies should be managed with high concentration medium chain triglyceride formulas. Pruritis is difficult to manage. Antihistamines are first line of treatment due to their tranquilizing effect. Other drugs used are cholestyramine to reduce enterohepatic circulation, phenobarbitone to increase biliary flow and rifampin[10].

The new era of liver transplantation, small donar accessibility, newer immunosuppressor agents along with social and cultural bindings has yet to evolve in a developed system in our country.

CONCLUSION

Persistent jaundice in the newborn must be managed urgently. A diagnosis should be established early in life of child and Kasai portoenterostomy offered to infants before their 8th week of life. This will allow more then one-third of NBA children to survive. Without surgical management survival of infants with NBA is 8-12 months due to irreversible liver failure.

The greatest mortality in NBA occurs during the first two years after portoenterostomy. Long term followup of children living for more then 10 years after Kasai portoenterostomy shows moderate hepatic dysfunction, controlled portal-hypertension, a normal intellectual coefficient, and good quality of life[11].

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