Biliary atresia

Biliary atresia (also known as Extrahepatic biliary atresia) is a serious but rare disease of the liver that affects newborn infants. In this condition, the common bile duct, a tube that connects the liver and the small intestines, is either blocked or absent. Bile, a digestive substance, builds up in the liver, which then causes cirrhosis, or scarring of the liver. This type of liver damage may require a liver transplant. In the United States and most of the Western world, biliary atresia is the most common reason for liver transplantation in children.

Types

There are several ways to group biliary atresia into types. One way is by looking at whether biliary atresia occurs as an **isolated birth defect**, or alongside others in the same child. About 10% of the time, biliary atresia is syndromic, meaning that the baby is born with multiple birth defects of which the atresia is only one. The other 90% of the time, it is an isolated problem.[1] From a **surgical point of view**, biliary atresia may be classified into several types: type 1, type 2, and type 3. A French classification system uses a type 4. Types 1 and 2 are much less common than type 3 and 4. [1] The classification is based on the ducts involved, whether the bile duct contains bile, and several other conditions.

Signs and Symptoms

The first sign of biliary atresia is **jaundice**, a yellow color to the skin and to the whites of the eyes. Jaundice is caused by the liver not removing bilirubin, a yellow pigment from the blood. Ordinarily, bilirubin is taken up by the liver and released into the bile. However, when the bile ducts are blocked, then bilirubin and other elements of bile build up in the blood. Dangerous jaundice may be difficult to detect. Many healthy newborns have mild jaundice during the first one to two weeks of life due to immaturity of the liver. This normal type of jaundice disappears by the second or third week of life, whereas the jaundice of biliary atresia deepens. Jaundice in newborns after two weeks of life is not healthy. Other signs of jaundice are a **darkening of the urine** and a **lightening in the color of stools**. The urine darkens from the high levels of bilirubin in the blood spilling over into the urine, while stool lightens from a lack of bilirubin reaching the intestines. Pale, grey, or white bowel movements after two weeks of age are probably the most reliable sign of a liver problem.

Causes

The cause of biliary atresia is **not known**. A fetal form and a perinatal form have been described. The former arises in the womb and is present at the time of birth, whereas the latter is more typical and does not become evident until the second to fourth week of life. Some children, particularly those with the fetal form of biliary atresia, often have other birth defects in the heart, spleen, or intestines. Biliary atresia is not an inherited (genetic) disease. Cases of biliary atresia do not run in families; identical twins have been born with only one child having the disease. Biliary atresia is most likely caused by an event occurring during fetal life or around the time of birth. Possible triggers include:

- infection with a virus or bacterium
- a problem with the immune system
- an abnormal bile component
- an error in development of the liver and bile ducts

Diagnosis

Worsening jaundice during the first month of life indicates a liver problem. Diagnosing biliary atresia requires blood and x-ray tests, and sometimes a liver biopsy. If biliary atresia is suspected, the newborn can be referred to several specialists:

- a pediatric gastroenterologist who is an expert in digestive diseases of children
- a pediatric hepatologist who is an expert in liver disease of children
- a pediatric surgeon who specializes in surgery of the liver and bile ducts

Initial tests. The doctor presses on the baby’s abdomen to check for an enlarged liver or spleen and order blood, urine, and stool tests to check for liver problems. Bilirubin levels are assessed and special tests for other causes of liver problems are done. Ultrasound of the abdomen and liver. Ultrasound tests produce an image on a computer screen using sound waves. Ultrasound can show whether the liver or bile ducts are enlarged and whether tumors or cysts are blocking the flow of bile. An ultrasound cannot be used to diagnose biliary atresia, but it does help rule out other common causes of jaundice.

Liver scans. Liver scans are special types of x-rays that use substances that can be detected by cameras to create an image of the liver and bile ducts. One such test is called hepatobiliary iminodiacetic acid (HIDA) scanning. HIDA scans trace the path of bile in the body and can show whether bile flow is blocked.

Liver biopsy. If another medical problem is not found to be the cause of jaundice, a liver biopsy is sometimes performed. For a liver biopsy, the infant is sedated and a needle is passed through the skin and then quickly in and out of the liver. A small piece of liver, about the size of a pencil lead, is obtained for examination under the microscope. Liver biopsies show whether biliary atresia is likely. A biopsy can also help rule out other liver problems, such as hepatitis.

Treatment

Surgery. If biliary atresia appears to be the cause of the jaundice in the newborn, the next step is surgery. At the time of surgery the bile ducts can be examined and the diagnosis confirmed. For this procedure, the infant is put to sleep. While the infant is asleep, the surgeon makes an incision in the abdomen to directly examine the liver and bile ducts. If the surgeon confirms that biliary atresia is the problem, a Kasai procedure is usually performed on the spot.

Kasai procedure (hepato-portoenterostomy). If biliary atresia is the diagnosis, the surgeon generally goes ahead and performs an operation called the Kasai procedure, named after the Japanese surgeon who developed this operation. In the Kasai procedure, the bile ducts are removed and a loop of intestine is brought up to replace the bile ducts and drain the liver. As a result, bile flows from the small bile ducts straight into the intestine, bypassing the need for the larger bile ducts completely.

Liver transplant. If the Kasai procedure is not successful, the infant usually needs a liver transplant within the first one to two years of life. Children with the fetal form of biliary atresia are more likely to need liver transplants—and usually sooner—than infants with the typical perinatal form. The pattern of the bile ducts affected and the extent of damage can also influence how soon a child needs a liver transplant.

The Kasai procedure

The Kasai procedure, also known as the Roux-en-Y or hepatoportojejunostomy, can restore bile flow and correct many of the problems of biliary atresia. This operation is usually not a cure for the condition, although in many children it delays or removes the need for transplants. Without this surgery, a child with biliary atresia is unlikely to live beyond the age of two years. The operation works best if done before the infant is 90 days old and results are usually better in younger children. The improved results of the surgery make the early diagnosis of biliary atresia very important, preferably before the infant is several months old and has suffered permanent liver damage. Some infants with biliary atresia who undergo a successful Kasai operation are restored to good health and can lead a normal life without jaundice or major liver problems.

Outcome of procedure

Both before and after the Kasai procedure, infants receive a specific diet with the right mix of nutrients and vitamins in a form that does not require bile to be absorbed. Poor nutrition can lead to problems with development, so doctors monitor an infant’s nutritional intake closely. Some infants develop fluid in the abdomen after the Kasai procedure, which makes the baby’s belly swell. This condition is called ascites and usually only lasts for a few weeks. If ascites lasts for more than six weeks, cirrhosis is likely present and the infant will probably require a liver transplant. Also common after the Kasai procedure is infection in the remaining bile ducts inside the liver, called cholangitis. Doctors may prescribe antibiotics to prevent cholangitis or prescribe them once the infection occurs. Children with biliary atresia may continue to have liver problems after the Kasai procedure. Even with success of the operation and return of bile flow, some children develop injury and loss of the small bile ducts inside the liver, which can cause scarring and cirrhosis. Unfortunately, the Kasai procedure is not always successful. If bile flow is not restored, liver disease can worsen, cirrhosis develops, and requires liver transplantation within the first one to two years of life. In addition, the Kasai operation, even when initially successful, may not totally restore normal liver development and function. In this case, cirrhosis can still develop and a liver transplant may be necessary. In general, about one-quarter of children who have a Kasai do well enough not to ever need a liver transplant. While the Kasai procedure has been a great advance in the management of biliary atresia, improvements in the operation and clinical management of children who undergo it are needed to improve the outcomes of children with this disease.

Liver transplantation

Liver transplantation is a highly successful treatment for biliary atresia and the survival rate after surgery has increased dramatically in recent years. Children with biliary atresia are now living into adulthood, even having children of their own. Because biliary atresia is not an inherited disease, the children of survivors of biliary atresia do not have an increased risk of having it themselves. Improvements in transplant surgery have also led to a greater availability of livers for transplantation in children with biliary atresia. In the past, only livers from small children could be used because the size of the liver had to match. Recently, advanced methods have been developed to use part of an adult’s liver, called “reduced size” or “split liver” transplants, for transplant in a child with biliary atresia. In addition, surgery has been developed that allows taking part of a living adult donor’s liver to use for transplantation. Thus, parents or relatives of children with biliary atresia can donate a part of their liver for transplantation. Because healthy liver tissue grows quickly, if a child receives part of a liver from a living donor, both the donor and the child can grow complete livers over time. Use of reduced size livers from deceased donors and left lobe livers, which are the smaller part of the liver, from living donors have greatly increased the availability of transplantation for children with liver disease. At present, almost all children with biliary atresia requiring a liver transplant will be able to receive “the gift of life,” in the form of a liver from a deceased or living donor. After liver transplantation, an important regimen of medicines is used to prevent the immune system from rejecting the new liver. Doctors may also continue to prescribe special diets, vitamins, blood pressure medications, and antibiotics.

Related Problems

Cirrhosis and the need for a liver transplant is caused by injury and loss of the bile ducts that drain bile from the liver. Bile is made by the liver, passes through the bile ducts and into the intestines where it helps digest food, fats, and cholesterol. The loss of bile ducts causes bile to remain in the liver. When bile builds up it can damage the liver, cause scarring and loss of liver tissue, and eventually cirrhosis. A liver transplant is necessary after liver failure, usually within the first or second year of life.

Complications

The following complications are possible:

- Infection
- Irreversible cirrhosis, with portal hypertension
- Liver failure
- Hepatocellular carcinoma (liver cancer)

The liver affected by cirrhosis does not work well and is more rigid and stiff than a normal liver. As a result, the blood flow through the liver is slowed and under higher pressure. This condition is called portal hypertension. Portal hypertension can also cause flow of blood around, rather than through, the liver. This complication can cause intestinal bleeding that may require surgery and may eventually lead to a recommendation for liver transplantation. Cirrhosis of the liver can also lead to problems with nutrition, bruising and bleeding, and itching skin. Itching, called pruritis, is caused by the build up of bile in the blood and irritation of nerve endings in the skin. Doctors may prescribe medications for itching including resins that bind bile in the intestines or antihistamines that decrease the skin's sensation of itching.

Research

Researchers are studying the possible causes, diagnoses, and treatments of biliary atresia. One of the largest research initiatives is the Biliary Atresia Research Consortium (BARC), a network of centers funded by the National Institute of Diabetes and Digestive and Kidney Diseases. The BARC network comprises ten liver disease and transplant centers and one data-coordinating center. The centers work together to coordinate research and share ideas and resources. The network will enroll infants with biliary atresia in a large study to evaluate the best ways of managing the disease and to carry out clinical trials of new and promising treatments or approaches for diagnosis and monitoring the disease. Because biliary atresia is a rare disease, only a network of centers can identify enough infants with this disease to carry out studies of new therapies. Centers will collect blood, tissue, and other samples from infants with biliary atresia so researchers can learn more about the condition and find better treatments. An important goal of BARC is to help find the causes of biliary atresia and recommend ways for its early detection and proper management. Continued research has expanded our understanding of the cause of biliary atresia.[2] While biliary atresia is not considered a genetic disease, genes do probably contribute in some way to its development. Mutations in genes that control the development of the liver, especially the bile ducts, as well as genes involved in the inflammatory process may contribute to the conditions. Indeed, an improper immune response directed at the biliary system may play a role, being prompted by a viral infection or as part of an autoimmune process similar to that seen in arthritis.

Expected Outcome

Survival rates for biliary atresia are measured by the percentage of children who live for four years after treatment. In the U.K. and France, this ranges from roughly half the children who have a Kasai but no transplant, to about 90% of children who have a liver transplant.[1]

Epidemiology

The worldwide incidence of biliary atresia ranges from about 5/100,000 to 32/100,000 live births. In Western Europe, it occurs in about 1/18,000 live births. Worldwide rates are highest in Asia and the Pacific region. It is more common in girls than in boys.[1]

References

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