Biliary Atresia: Experience with 30 Consecutive Cases in a Single Institute

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Background/Purpose: Biliary atresia is a devastating disease characterized by disruption of the normal anatomy of extrahepatic biliary system with consequent biliary flow obstruction, resulting in secondary inflammation that leads to progressive damage of the extrahepatic and intrahepatic bile ducts occurs. It affects approximately 1 in 9000 – 16000 live births and accounts for more than 50% of pediatric liver transplantation.

Materials & Methods: Participants were thirty patients with confirmed diagnosis of extrahepatic biliary atresia by clinical picture and investigations (20 females, 10 males; mean age 82 days, range 51 – 150 days). All patients in this prospective study had undergone hepatopotojejunostomy. Study cases were recruited from Pediatric Hepatology Unit, Cairo University Children’s Hospital through a period of four years from 2005 to 2009.

Results: Intraoperative: twenty nine cases had type III biliary atresia, while a single case had type II. Three cases of preduodenal portal vein with gut malrotation have been experienced as well as a single case of polysplenia and situs inversus totalis.

Postoperative: response to surgery had been evidenced clinically by bile flow establishment where stool color had changed from acholic to greenish yellow in all cases through the immediate postoperative period (two weeks following Kasai operation), in addition to dramatic improvement in laboratory results, where alkaline phosphatase and bilirubin levels had remarkably decreased in all cases except one.

Repeated attacks of cholangitis had been experienced in fifteen cases (50%) during their first postoperative year with consecutive liver deterioration, making ten patients (33.3%) candidate for liver transplantation. Single mortality had occurred in the postoperative follow up period (three weeks postoperative).

Conclusion: Kasai operation is the established technique for management of biliary atresia; the surgeon has to be professionally acquainted with the technique and its modifications as well as the variations of anatomy in the area of biliary tree and gut. Surgical technique and preservation of total hepatic flow (THF) during and after surgery has a great impact on preventing deterioration of liver functions. Kasai operation success is directly correlated to the age of the patient; however our trend was to operate on the infant even in cases more than three months of age hoping for better outcome regarding immunity even if the patient will be subjected to liver transplantation.

Index Word: Biliary Atresia, technique, Kasai.

INTRODUCTION

Biliary atresia is considered one of the most devastating conditions affecting the Biliary tree and liver in the neonatal period and early infancy. The incidence ranges from 1 in 9000 to 1 in 16000. The nature of the pathology is an obliteratorive fibrosing cholangiopathy of unknown origin that leads to liver cirrhosis and portal hypertension. The etiology of the condition is not known with any degree of certainty. One hypothesis is that the condition had begun from defect in early development and genetic defect in morphogenesis. Infective factors with cytomegalovirus, Rubella, Ebstein-Barr virus, and Human papilloma virus are reported in many series. Associated abnormalities in a
review of ten major series of biliary atresia showed that an average of 21% had additional abnormalities outside the hepato-biliary system as polysplenia syndrome (Biliary Atresia Splenic Malformation-BASM), atrial septum defect, hypoplasia of portal vein, situs inversus, cystic fibrosis, pulmonary artery stenosis, malrotation of bowel, fetal hydrops and annular pancreas.

Physiologic jaundice (unconjugated hyperbilirubinemia) occurs in up to 90% of healthy neonates and is defined as a temporary inefficient hepatic excretion of bilirubin. Conjugated hyperbilirubinemia is always pathological and may be caused by hepatocellular dysfunction secondary to infection, metabolic and endocrine disorders, and some of these causes should be rapidly excluded.

It should be emphasized that most infants with biliary atresia are entirely well during the first 4 to 8 weeks of life apart from moderate jaundice. The diagnosis will only be suspected by demonstration of conjugated hyperbilirubinemia and this must be investigated in an infant with dark urine and pale stools.

In early infancy, the clinical features and biochemical tests of liver function are very similar in hepatocellular disease, hypoplasia of bile ducts and extrahepatic obstruction caused by biliary atresia and choledochal cysts. All four conditions present with jaundice, pale stools and dark urine and may be complicated by bleeding from malabsorption of vitamin K. Biochemical tests of liver function such as the intracellular enzymes Aspartate amino-transferase (AST) and alanine amino-transferase (ALT) give a clue about the severity of liver disease but of little diagnostic help. Intra hepatic bile duct dilatation is not a feature of biliary atresia and this limits the value of sonography. Technetium labeled compounds such as methyl bromoiminodiacetic acid (BrIDA) which are taken by hepatocytes even in presence of jaundice and are excreted into the biliary tract in high concentrations. No excretion of the isotope within 2 hours suggest a differential diagnosis of severe cholestasis or biliary atresia. Percutaneous liver biopsy is mandatory although equivocal histologic findings are present in 13% of cases. Some studies had discussed the issue of histologic findings and assessed obstructive cholestatic changes and hepatic changes. The histopathology criteria for obstructive cholestasis included presence of bile in canaliculi, hepatocytes and ducts, bile duct tortuosity, duct proliferation, ductal plate lesions, portal edema, acute cholangitis, portal fibrosis, septal biliary fibrosis, and biliary cirrhosis. Hepatic changes include giant cell changes, bridging necrosis and confluent necrosis that is either lobular, panlobular or multilobular.

Clinical failure following Kasai operation correlates significantly with the presence of syncitial giant cells, focal necrosis, bridging necrosis, lobular inflammation and cholangitis and success is associated with the presence of bile in zone I (Periportal canaliculi).

Prognosis of cases of biliary atresia has many aspects, some of which has been documented and proved by many authors as the timing of the procedure: where the Kasai operation has 30% to 90% short term success rate if the patient is under 10 weeks of age. Despite a few cases of successful Kasai operation in older babies, it is thought that the progressive inflammatory nature of the disease leads to irreversible liver damage despite a portoenterostomy after 14 weeks.

The long term success is rare and one third of patients will require urgent liver transplantation within 12 months because of failure of Kasai procedure.

**PATIENTS AND METHODS**

From 2005-2009 the work was conducted on 30 patients, 20 females (66.7%) and 10 males (33.3). Cases were referred from the hepatology unit in pediatric hospital of Cairo university and were done in the pediatric surgical department in the same hospital.

Data collected from the patients’ files were: 1-age, gender, 2-perinatal parameters (birth course, birth weight), 3-clinical data as associated anomalies, symptoms (jaundice, acholic stools, dark urine), examination (weight, height, head circumference, reflexes, hepatomegaly), 4-laboratory values preoperatively and postoperatively (bilirubin levels, transaminases and alkaline phosphatase), 5-results of preoperative ultrasonography, histologic picture of percutaneous preoperative liver biopsy (obstructive cholestatic and hepatic changes).

Intraoperative cholangiography was done and findings from the intraoperative biopsy taken from...
portahepatis and biliary remnants with gall bladder were documented.

The patient was declared unfit for surgery if he is feverish due to an attack of cholangitis or having some respiratory infection till the attack subsides. Patients with major cardiac anomalies were excluded from the study.

In the 30 cases, hepatportojejunostomy (Kasai operation) was done, the incision was chevron incision with the long limb on the right side and short limb on left side about 4 cm from midline aiming to deliver the whole liver after separation of ligamental attachment (The right and left triangular ligaments)

The ligamentum teres with the umbilical vein was divided and then transfixed to avoid inadvertent bleeding in cases of portal hypertension.

The portoduodenal ligament and structures like hepatic artery with its divisions and any aberrant artery as left hepatic artery arising from left gastric artery were inspected (micro Doppler is very useful tool in that aspect), microsurgical instruments are very useful with magnification. If any of the arterial supply of the liver is transected, microvascular anastomosis could be performed using 8/0 interrupted prolene sutures. The cystic artery is usually well developed in cases of biliary atresia and could be used directly to revascularize any of hepatic branches or as transposition graft. Keeping good blood flow to the liver is important especially after delivering the liver out of the incision where tension on the Inferior Vena Cava may affect venous return to the heart and hence cardiac output. It’s a valuable trend to cooperate with the anesthetist in that regard to keep total hepatic flow constant all over the procedure. It is preferable to use invasive arterial blood pressure monitoring. Excision of the gall bladder with fundus first technique is used aiming at porta hepatis using bipolar diathermy at gall bladder fossa.

The cystic artery has to be seen and ligated which is usually sizable with near caliber to right hepatic artery.

At the porta hepatis, all fibrous remnants has to be removed cautiously and any structure with lumen has to be carefully dissected seeking for hepatic ducts. Injection of saline : adrenaline 1 : 200,000 will aid in diminishing bleeding instead of excessive coagulation that might sacrifice patent duct. Great care must be taken while retracting the portal vein and its tributaries and avoid any inadvertent coagulation which may cause catastrophic bleeding, also undue traction can provoke intraluminal coagulation in the portal vein itself or any of its tributaries. Small tributaries from the liver to the portal vein that may hinder the anastomosis had to be ligated and separated avoiding diathermy coagulation especially towards the portal vein side. Coring of porta hepatitis is done avoiding excessive coring in the depth to avoid provoking excessive fibrous tissue but extending to the periaterial territories where the biliary radicals are abundant. At this point bleeding usually occurs, for which compression with gauze soaked with saline adrenaline is sought and the jejunum is prepared for anastomosis. The distal limb is dissected and the proximal end is closed using 2 rows of 6/0 PDS sutures; to avoid leaking, the first row is running simple through and through, and the second row is interrupted Lambert sutures. The closed end is usually sutured to the stomach to avoid intussusception and obstruction of the anastomosis.

End to side portojejunostomy is then done with 6/0 PDS sutures with 2 needles where the posterior wall of both the jejunum and porta hepatitis are taken using parachute technique with 4 to 6 stitches taking the jejunum short of mucosa to guarantee contact between serosa and Glisson capsule of the liver. The jejunual loop is passed through the gastro colic ligament to guarantee retrocolic position (a step which is not followed in cases of malrotation and preduodenal portal vein). Then the anterior row of sutures is taken. Sometimes if abundant omentum is found and is used to cover anastomotic site to lessen the leaking bile and to give blood supply to anastomotic liver and facilitate dissection if second operation is to be undertaken.

End to side jejunostomy is carried using interrupted submucosal 6/0 PDS sutures and patency of the anastomosis is watched. Closure of rents in the gastro colic ligament and between mesenteries of both jejunal loops is then done.

Tube drainage in closed system without suction is then done. Closure of abdominal muscles using delayed absorbable suture as 3/0 PDS is used as delayed healing and ascites due to liver condition could lead to dehiscence.
RESULTS

There were 20 females and 10 males. Their ages at operation ranged from 51 to 150 (mean age was 82 days). Associated anomalies were noted in 6 patients (20%). Three of them had preduodenal portal vein with gut malrotation, one case had situs inversus totalis, one with polysplenia (Biliary Atresia Splenic Malformation (BASM) and the last had penoscrotal hypospadias with bifid scrotum.

Twenty nine patients (96.3%) had type III atresia at the porta hepatis, and one patient (3.33%) had type II atresia of hepatic ducts and non had type I.

Fig 1. Delivering the liver outside
Fig 2. Gall bladder is dissected
Fig 3. Situs inversus
Fig 4. Type II Biliary atresia
Table 1. Associated anomalies:

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>No.</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preduodenal portal vein with malrotation</td>
<td>3</td>
<td>(10%)</td>
</tr>
<tr>
<td>Poysplenia</td>
<td>1</td>
<td>(3.3%)</td>
</tr>
<tr>
<td>Situs Inversus Totalis</td>
<td>1</td>
<td>(3.3%)</td>
</tr>
<tr>
<td>Bifid scrotum and penoscrotal hypospadias</td>
<td>1</td>
<td>(3.3%)</td>
</tr>
</tbody>
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Mean operative time was 3 hours ranging from (2.5 hours to 4.5 hours).

Table 2. Results after portoenterostomy:

<table>
<thead>
<tr>
<th>Result</th>
<th>No.</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful portoenterostomy</td>
<td>15</td>
<td>(50%)</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>(3.3%)</td>
</tr>
<tr>
<td>Lost to follow up</td>
<td>4</td>
<td>(13.5%)</td>
</tr>
<tr>
<td>Liver transplantation</td>
<td>2</td>
<td>(6.7%)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Candidates for transplantation</td>
<td>8</td>
<td>(26.5%)</td>
</tr>
</tbody>
</table>

Bile drainage was good in the first week in 29 cases, and one case had deteriorated liver functions from fulminate hepatic necrosis that progressed to multiorgan failure and died 3 weeks after surgery in the pediatric intensive care unit.

Period of follow up was about one year for all cases. The earliest indicator of success of portoenterostomy was restoration of bile flow and disappearance of jaundice (below 2 mg/dl).

Cholangitis was detected by recurrent attacks of fever and cholestatic jaundice in nearly half of the cases. (15 cases, 50%)

DISCUSSION

Before the introduction of the portoenterostomy operation the mortality rate of biliary atresia was virtually 100%. Death from cirrhotic liver failure occurs within 2 years in untreated cases. Hays and Synder reported in 1963 that less than 5% of children with biliary atresia survived beyond early childhood, the majority of cases died from complications of spontaneous hemorrhage as described early by Thomson. From these early reports it is shown that these children had no remedy other than intervention. Successful drainage of bile was observed after resection of all residual biliary tissue in the porta hepatitis and anastomosis of the resected area to a Roux Loop of bowel allowing satisfactory transit of bile into the gut (The portoenterostomy operation).

It is undoubtful issue that age at presentation and operation is the first prognostic factor in success of the procedure to save the liver from the catastrophic outcome. Most infants presenting within 80 days will not show clinical features of cirrhosis or irretrievable liver damage, such as ascites, splenomegaly or heterogeneity on the liver ultrasound.

The role of the surgeon and surgical circumstances cannot be over emphasized in providing a chance for these miserable children to live with their native liver or at least providing better circumstances regarding better immunity and body weight to ease the process of liver transplantation. The King’s college study states that the age of the infant has an effect on outcome although this is not as clear-cut as was once thought. It is not a linear effect and it is difficult to determine real variation in outcome at anywhere up to 80 days of age. Beyond that fibrosis does begin to be detrimental although even beyond 100 days, Kasai operation has advantages and even long-term jaundice free survival.

The aim of the surgery is to excise all extra hepatic biliary remnants to allow for a portoenterostomy reconstruction onto a portal plate denuded of all fibrous tissue. This should be the objective not only in type III biliary atresia but also in those who have a visible bile-containing proximal communication.

The King’s college technique is adopting the original technique of hepatic portoenterostomy of Kasai with stressing on elements described as crucial. The liver should be fully mobilized by dividing its ligaments so that the organ can be everted outside the abdominal cavity.
This maneuver does impair venous return by kinking on the cava and may need a concomitant increase in intravenous volume support\textsuperscript{29,30}. This issue is important and needs in intravenous volume support\textsuperscript{29,30}, collaboration between anaesthetist and working surgeon is vital, as it is sometimes mandatory to reposition the liver for a while till restoration of volume and improvement in mean arterial pressure. In this study\textsuperscript{27}, it was experienced that hypothermia can increase the impact of the condition so active and passive re-warming should be promptly taken.

It is recommended by King's college study\textsuperscript{27} to avoid excessive coring as it impairs bile drainage because any divided ductules become obliterated by subsequent scar tissue. This is a nice technical point and bleeding from this cored liver necessitates coagulation which will occlude some of communicating bile ducts. Some studies recommend giving post operative corticosteroids\textsuperscript{31,32}. The need for this therapy can affect decreasing fibrous tissue occluding this biliary channels in the early postoperative period.

Davenport et al recommend wide dissection at the porta hepatis\textsuperscript{30}. In this study trial to wide dissection at porta hepatis was carried and also at gall bladder fossa. This was by achieved by bipolar diathermy and saline adrenaline injection without using extensive coagulation.

There are three key portal landmarks with exposure of the origin of the umbilical vein from the left portal vein in the fossa of Rex and exposure of the usual extrahepatic bifurcation of the right portal pedicle and division of small veins to the plate directly from the portal vein to expose the caudate lobe posteriorly.

In large centers with experienced surgeons, about 50 to 60 % of all infants will clear their jaundice and achieve a normal (< 20 µ mol/L) bilirubin\textsuperscript{27,30}.

Several modifications were made to the original Kasai operation, aiming at allowing more free bile flow and prevent reflux and cholangitis.

Ohi\textsuperscript{33} illustrated and evaluated the results of various modified procedures performed throughout Japan between 1981 and 1985. He found that 43 % had suffered attacks of cholangitis and that first attack commonly occurred from one to three months after porteentestomy. Only 10% developed infection for the first time more than 6 months after surgery. Importantly, 45% of 153 patients who had the originally modified type of porteenterostomy had at least one attack of cholangitis compared with 41% of those who had modified procedures which included Roux on Y loops with tube enterostomies, complete diversion of bile via cutaneous stomas, interposition biliary conduits and gastric tube reconstructions.

Patency of the gall bladder and distal common bile duct was observed in 28 % of boys and 18% of girls in 904 cases collected by the Biliary Atresia Registry of N. America\textsuperscript{34}. There's less incidence of cholangitis, 35% compared with 55% for other types of reconstruction. Complications as bile leaks, gall bladder obstruction and kinking of the common bile duct are more frequent than after the standard porteenterostomy.

Attempts to replace the Roux Loop with a conduit fashioned from the appendix (Porto-appendiceal-duodenostomy) have proved less effective than the standard operation and comparative study between the results of 2 operations revealed effective bile drainage in 31 % of cases with appendiceal conduit versus 82% in those with standard Roux loop of jejunum\textsuperscript{35}.

Bacterial cholangitis decrease with age and is less frequent after 2 years and occasionally may be precipitated by mechanical obstruction within the Roux loop caused either by stenosis of an anastomosis or by an intra-abdominal adhesion\textsuperscript{36}.

Other reported complications as portal hypertension, intrahepatic cystic changes, metabolic problems, hepatopulmonary syndrome, pulmonary hypertension and malignant change in liver have great impact on course of the disease\textsuperscript{37}.

## CONCLUSION

Improvement of outcome of biliary atresia patients has to be directed towards improving the prognostic factors. Some of these factor, however, are outside the province of the surgeon as age at operation, associated anomalies, and histologic pattern of liver at time of surgery.

The surgeon who operate should not be an occasional in that field or working in a frustrated attitude
regarding the outcome of these miserable infants, but has to pay attention to all surgical factors and anatomical variants of these cases with their associated anomalies.

Modifications of Kasai operation, if used, should be targeted into special cases. Adopting the original technique with meticulous surgery gives the best results if special care is given to avoid clumsy dissection at porta hepatis to benefit from the most possible draining area of bile with keeping total hepatic blood flow during and after surgery.

REFERENCES


