Budd-Chiari Syndrome in Children: Experience With Therapeutic Radiological Intervention

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ABSTRACT

Objectives: Budd-Chiari syndrome (BCS) in children is not uncommon. Published literature on therapy for this condition is scarce. We therefore attempted radiological interventions in these patients to determine their efficacy and safety.

Patients and Methods: Fourteen of 16 children with a median age of 22 months diagnosed as having BCS were subjected to an inferior vena cava/hepatic venogram with the aim to establish a normal antegrade flow in at least 1 hepatic vein (HV).

Results: A normal antegrade flow in at least 1 of the HVs could be established in 11 children. Three patients had angioplasty of the HV (vein size ≤4 mm), 2 underwent HV stent placements (vein size ≥5 mm), and 6 had transjugular intrahepatic porta systemic shunt ([TIPSS] total occlusion of all 3 HVs or veno-occlusive disease). The youngest child undergoing a successful stenting was 7 months of age and the child undergoing TIPSS was 3 years of age. One patient had reversal of fulminant liver failure following a successful TIPSS. Postprocedure, 2 patients developed reversible encephalopathy and 1 had a neck hematoma. There was no procedure-related mortality. The procedure was successful in both patients with stenting (100%), 5 of the 6 patients with TIPSS (80%), and only 1 of the 4 patients (25%) with angioplasty. The median follow-up was 31 months.

Conclusions: Radiological therapeutic intervention is feasible and safe in children with BCS. The overall results of stenting/TIPSS are better than with angioplasty; however, long-term results of these interventions need to be evaluated.

Key Words: hepatic venous outflow obstruction (HVOO), India, liver, pediatric, TIPSS

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Budd-Chiari syndrome (BCS) or hepatic venous outflow obstruction (HVOO) is a disease complex that results from obstruction to the hepatic venous outflow at the level of the hepatic veins (HVs) or the inferior vena cava (IVC). If left untreated, it results in fatal portal hypertension, cirrhosis, and liver failure. Treatment of HVOO involves establishing the patency of the hepatic venous outflow tract. From our anecdotal experience, anticoagulation alone in children with BCS is not effective.

With the introduction of newer radiological interventions, HVOO has been safely treated with good outcome in adults. The published literature on children with BCS is scarce. Furthermore, the literature on radiological therapeutic interventions in pediatric BCS is even more scarce. We report our experience on the efficacy and safety of radiological interventions in children with BCS.

PATIENTS AND METHODS

Sixteen patients (10 boys, 6 girls; age range 4 months–11 years; median age 22 months) presented to the Pediatric Hepatology Clinic, a tertiary center, between 2003 and 2007. The duration of symptoms before visiting the clinic ranged from 1 week to 4 years (median duration 13 weeks).

The chief presenting symptom was abdominal distention secondary to ascites (13/16; 81%). Other presenting features found in this group were fever (8/16; 50%), dehydration because of vomiting and/or diarrhea (6/16; 37.5%), bleeding (hematemesis, malena, and epistaxis) (4/16; 25%), edema of the feet (3/16; 19%), and jaundice (2/16; 12.5%). One child (4 years old) was presented 1 month after diagnosis with acute liver failure, in coma, and severe coagulopathy.

All of the patients had a complete blood count, liver profile, and prothrombin time. Thrombophilia tests included protein C, protein S, antithrombin III, anti-phospholipid antibody, Factor V Leiden mutation, and serum homocysteine. Janus kinase 2 (JAK2) genetic mutation studies could be done in 5 patients because of cost constraints and unavailability in the earlier days of the intervention.

Budd-Chiari syndrome was diagnosed in 10 children by a Doppler sonogram. Of the remaining 6 patients in whom the clinical suspicion of BCS was strong and Doppler was inconclusive, a liver biopsy confirmed 4 patients with BCS. In 2 patients, neither the sonogram nor the liver biopsy could diagnose BCS but the diagnosis was confirmed by hepatic venogram based on strong clinical suspicion.

With clinical, sonographic, and/or biopsy diagnosis of BCS, IVC gram and hepatic venogram were performed in 14 of the 16 children by the interventional radiologist via a transjugular approach. Inferior vena cava gram was done to look for any extrinsic compression or intrinsic narrowing. Pressure readings were taken above and below the hepatic segments of the IVC. Hepatic venograms were done to look for any stenosis or occlusion. Hepatic venous wedge pressure, free hepatic venous pressure, and pull-back gradient were measured in all of the cases. Selective cannulation of all of the 3 HVs was attempted in all of the cases using 4F multipurpose or headhunter catheters (Cordis Corp).

Eleven (78.5%) of the 14 patients who underwent an IVC or hepatovenogram had radiological interventions to provide normal antegrade flow in at least 1 of the HVs, preferably the right HV (Table 1).

TABLE 1. Children with Budd-Chiari syndrome undergoing radiological intervention (angioplasty/stent/TIPSS)

Patient no./sex	Age, mo	Block (on venogram)	Ostial block	Procedure	Outcome (follow-up in mo)	Etiology
1/F	7	2 HV	Y	Stent (MHV)	Successful (54)	Idiopathic
2/F	11	2 HV	N	Angioplasty (RHV)	Successful (24)	Protein C deficiency
3/F	11	3 HV	Y	Angioplasty (RHV)	Successful lost to follow-up	Idiopathic
4/F	84 (7 y)	VOD	Y	TIPSS	Successful lost to follow-up	Herbal medicine
5/M	108 (9 y)	3 HV	Y	TIPSS	Successful (34)	Idiopathic
6/F	35 (3 y)	3 HV	Y	Stent (RHV)	Successful (30)	Antithrombin III deficiency
7/M	30 (2.6 y)	3 HV	Y	TIPSS at 36 mo (initially, angioplasty [RHV] at 30 mo)	Successful (30)	APLA
8/F	10	2 HV	Y	Angioplasty (RHV)	Expired after 6 mo due to an acute block; before this, irregular follow-up	Idiopathic
9/M	132 (11 y)	3 HV	Y	TIPSS	Successful (22)	Protein C deficiency
10/M	36 (3 y)	3 HV	N	TIPSS	Successful (20)	Idiopathic
11/M	48 (4 y)	3 HV	Y	TIPSS	Successful (12) (presented with grade 4 hepatic encephalopathy)	Idiopathic

APLA = antiphospholipid syndrome; HV = hepatic vein; N = no; MHV = middle hepatic vein; RHV = right hepatic vein; TIPSS = transjugular intrahepatic porta systemic shunt; VOD = veno occlusive disease; Y = yes.

RESULTS

The liver profile revealed serum albumin range 1 g% to 4.3 g% (median 2.7 g%), bilirubin range 0.4 mg% to 28.6 mg%; (median 1 mg%), alanine aminotransferase range 15 to 150 IU/L (median 28 IU/L), and international normalized ratio (INR) range 1 to 3.8 (median 1.3).

In all of those with ascites, the serum-ascitic albumin gradient (SAAG) was >1.1, suggesting portal hypertension as a cause of ascites. The ascitic fluid cell count ranged from 22 to 500/mm^3 (median 50/mm^3), with a lymphocytic predominance (range 65%–90% and median 80%).

Ultrasound detected hepatomegaly in 11 (69%), splenomegaly in 7 (44%), and ascites in 12 (75%) of the 16 patients, respectively. Doppler confirmed HVVO in 10 patients (62.5%), of whom 2 children had all 3 HVs blocked, 7 had 2 HVs blocked, and 1 had 1 HV blocked.

In the 2 of the 16 children in whom a venogram was not performed, (Table 2), 1 had a BCS secondary to a liver abscess and had 2 HVs patent; the other child's family refused the procedure. Of the 14 children who underwent an IVC gram and hepatic venogram, 7 children had all 3 HVs, 4 children had 2 HVs, and 2 children had

1 HV blocked, respectively, with 1 patient having veno-occlusive disease (VOD). There was no intrinsic IVC compression detected in our patient series; however extrinsic compression related to caudate lobe hypertrophy, with no significant pressure gradient across the narrowed segment, was found in 7 of the 14 children. Collaterals between the 3 HVs were visualized in 7 of the 14 patients.

The etiology of BCS was identified in 5 of the 16 patients. Two patients had protein C deficiency, 1 had anti-phospholipid antibody syndrome, 1 had antithrombin III deficiency, and 1 had BCS secondary to a hepatic abscess. One patient with VOD had taken herbal medicine for vitiligo. JAK2 mutation was not detected in any of the 5 patients who were tested.

Three of the 14 children did not have any radiological interventions in spite of demonstrated blocks (Table 2). In 2 of these 3 children the catheter failed to negotiate through the veins, the infants being 4 and 5 months of age. One of these 2 infants expired after 1 month because of massive variceal bleeding, whereas the other infant, aged 5 months, is being maintained on anticoagulants with a close follow-up. He is doing well with resolution of ascites and normalization of liver function. In the remaining child, there was a long segment block and 2 HVs were

TABLE 2. Children with Budd-Chiari syndrome in whom radiological intervention was not possible or was not done

Patient no./sex	Age, mo	Block (on venogram)	Ostial block	Intervention	Outcome (follow-up)	Etiology
1/M	4	2 HV	N	Not possible	Died after 1 mo	Idiopathic
2/M	5.5	1 HV	N	Nil	Doing well (36 mo)	Idiopathic
3/M	5	1 HV	Y	Not possible	Currently on anticoagulation (15 mo)	Idiopathic
4/M	14	2 HV (on Doppler)	No venogram	Nil (refused)	Lost to follow-up	Idiopathic
5/M	42 (3.6 y)	1 HV (on Doppler)	No venogram	Nil	Recovered	Liver abscess

HV = hepatic vein; N = no; Y = yes.
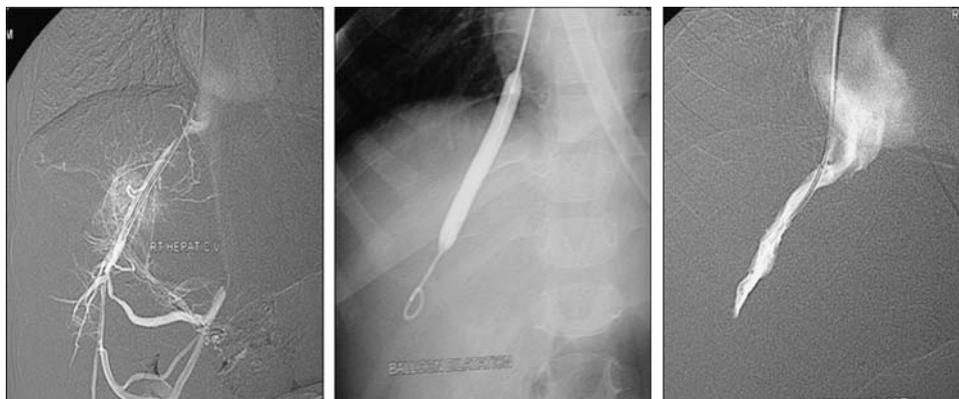
FIGURE 1. Right hepatic vein ostial stenosis in a 2-year-old boy. Dilatation with a 5-mm balloon.

patent; hence further radiological therapeutic intervention was deferred. The child is well with no ascites.

Radiological Intervention

The interventional procedures were done under full general anesthesia considering the pediatric age group and the technically difficult nature of the interventions. Intravenous heparin (100 mg/kg body weight) was given at the start of the procedure. None of the patients in the study were taking anticoagulants before the procedure.

In the 11 children who had an intervention (Table 1), the decision about the type of radiological intervention—angioplasty or stenting of the HV or transjugular intrahepatic porta systemic shunt (TIPSS)—depended on the degree and type of HV block.

Angioplasty alone of the veins was done (n = 3) if the vein size was small (≤4 mm). OptaPro (Cordis Corp, Miami Lakes, FL) or Optiplast (Bard Peripheral Vascular Inc, Tempe, AZ) angioplasty balloons were used over either 0.035 or 0.014 wires (Fig. 1).

Stenting of the HV ostium was done (n = 2) when the caliber of the vein was more than or equal to 5 mm, with a significant gradient (>7 mmHg) across ostial stenosis with veno-venous collaterals to the patent vein. Balloon-mounted bare metal stents were used (8 mm × 18 mm [Biotronic Peiron] or 6 mm × 18 mm [Cordis Palmaz] blue balloon-mounted stents) to stent the HV ostia through a 6F arterial sheath (Fig. 2) in the right internal jugular vein. Balloon-mounted stents were preferred over self-expanding stents because of the need for precise placement at the ostium and possibility of future intervention and redilatation with a larger size balloon, if needed. Covered stents were not used because of their higher thrombogenicity, chances of occlusion of side branches of
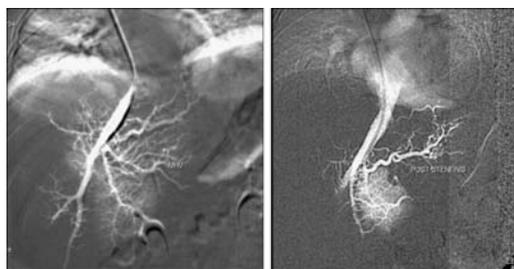
FIGURE 2. Occluded right and left hepatic veins, dilated middle hepatic vein with ostial stenosis middle hepatic venous stenting with an 8 mm ballon mounted stent.

the HVs, higher cost, and inability to dilate further if needed in the future.

Transjugular intrahepatic porta systemic shunt procedure was done (n = 6) for total occlusion of all 3 HVs or VOD. Dedicated Gore Viatorr stents (Gore Viatorr Assoc, Flagstaff, AZ) were used in all of the cases. This stent has a covered portion in the liver parenchyma and a 2-cm bare portion that allows free flow of blood into the branches of the portal vein. In 5 patients, using a RTPS puncture set (Cook, Bloomington, IN) and long chiba needle, the right posterior branch of the portal vein was punctured from the IVC and the Gore Viatorr stent graft was placed in the liver parenchyma from the portal vein to the IVC (Fig. 3). The stent was dilated by 7- to 8-mm balloons. In 1 patient with VOD, TIPSS was done by puncturing the right posterior branch of the portal vein from the patent right HV (Fig. 4). In 1 patient, a large collateral was embolized with coils after a TIPSS procedure (Fig. 5). In the 4-year-old child presenting with grade IV hepatic encephalopathy and coagulopathy, a TIPSS was successfully performed after anti-coma measures reversed the encephalopathy. This child had a presenting serum bilirubin of 28.6 mg/dL and an INR of 3.8, which at 3 months post-TIPSS declined to a serum bilirubin of 1.3 and an INR of 1.4.

Of the 11 patients who underwent intervention, 5 have been continued on warfarin. The remaining 6 have been started on aspirin or clopidogrel. The clinicians were not comfortable with starting warfarin in these children because they were from remote areas where regular monitoring of INR would be difficult. In addition, a 5-month-old patient has been put on warfarin alone when an attempt to intervene was unsuccessful because of a small-caliber HV. The median HV wedge pressure preprocedure was 24 mmHg (22–38 mmHg) and median value of 0 mmHg postprocedure (0–9 mmHg).

Postprocedure complications included hepatic encephalopathy in 2 patients and a neck hematoma in 1 patient at the site of jugular puncture. Both patients with hepatic encephalopathy recovered within 2 days of anticoma measures. There was no procedure-related mortality. The median postprocedure stay was 4.5 days (range 2–13 days). In patients with ascites, the effect of a successful establishment of a patent HV was associated with complete resolution of ascites within 48 to 72 hours.

Ten of these patients (8 of whom underwent therapeutic intervention and a remaining 2 who did not have intervention) are being followed up. One patient who had undergone an angioplasty was apparently well for 1 year (irregular follow-up) and then presented with hematemesis, to which she succumbed. The patient could not be shifted to our center because she lived in a rural area. The 8 children with intervention on follow-up are completely
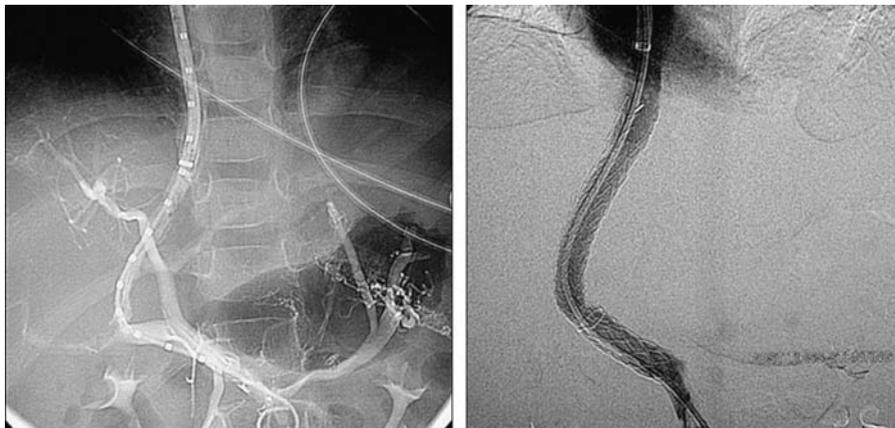
FIGURE 3. Transjugular intrahepatic porta systemic shunt from inferior vena cava to portal vein in a 9-year-old boy. All hepatic veins were occluded.
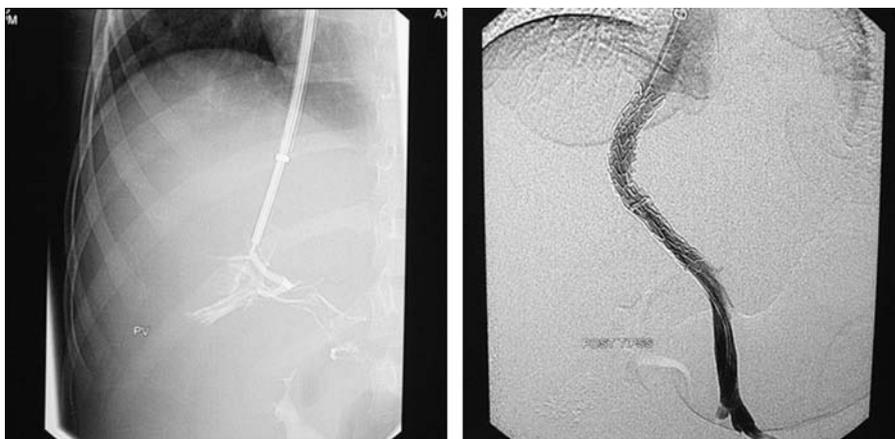
FIGURE 4. Transjugular intrahepatic porta systemic shunt from right hepatic vein to portal vein in a 7-year-old girl with normal hepatic venograms and histopathological diagnosis of veno-occlusive disease.

asymptomatic with remission of all symptoms and normal liver profile and are receiving anticoagulation or antiplatelet treatment. There has also been a notable improvement in their growth and their milestones. Patients placed on warfarin maintain INR between 2 to

2.5 times the normal. The median follow-up period has been 31 months (range 12–54 months).

Patients with TIPSS and HV stents had a better outcome than with angioplasty. Of the 2 children who underwent stent placement,

FIGURE 5. Inferior vena cava to portal vein transjugular intrahepatic porta systemic shunt in a 3-year-old boy. All of the hepatic veins were occluded. The large collateral was embolized with coils.

both are currently asymptomatic and doing well. Of the 5 patients in whom TIPSS was inserted as a procedure of first choice, 4 are asymptomatic, whereas 1 was lost to follow-up. The sixth patient with TIPSS followed a failed angioplasty and is doing well (Fig. 5). Angioplasty was attempted as the first procedure of choice in 4 patients. Two patients had failed angioplasties, 1 underwent a TIPSS (as mentioned above), and the other child succumbed to a massive gastrointestinal bleed mostly because of rethrombosed HV, the third patient was lost to follow-up, and only 1 patient in this group continues to be stable.

DISCUSSION

The pattern of BCS in children at our center resembles that of adult populations with BCS in India (1,2) and worldwide (3,4). Unlike previous reports from India, where IVC was the major site of block in adults (5), recent reports have shown a shift in the trend from IVC blocks to HV or combined (HV+IVC) block (1). None of our 16 pediatric patients presented with intrinsic IVC blocks; all had only HV blocks.

In our series of 16 children, HVOO most commonly presented with ascites with a high SAAG of >1.1, a low cell count, and a relatively preserved liver function. The ascitic fluid showed a low count with a lymphocytic predominance; this should not be confused with abdominal tuberculosis, in which ascitic fluid has lymphocytic predominance but with high cell counts and a SAAG <1.1. This is important in the Asian context, where children with ascites are often started on antituberculous therapy, which not only is not beneficial but also may actually worsen the hepatic function. In our experience, any infant presenting with ascites has BCS unless it is proved otherwise. Timely diagnosis and ability to intervene radiologically is important in countries like India, where a liver transplant option is not easily available.

Radiological therapeutic interventions have been described in adults (2,6,7). We describe the successful use of therapeutic interventions like angioplasty, HV stenting, or TIPSS in 11 of our children with BCS. There is scarce information on the use of such modalities as the only mode of definitive treatment of BCS, especially in children (8). A recent Indian study of radiological intervention in the adult population (2) described 49 patients with BCS undergoing radiological intervention who were evaluated prospectively for 7 years. The results showed that, unlike other Indian studies in adults (5), HVOO was more common (59.1%) than IVC obstruction (16.3%). This has also been noted in our pediatric series. Eighty percent of the adult cases were diagnosed on Doppler as compared with 62.5% of our cases. In our series, Doppler seemed to underestimate the number of blocked veins and also missed the diagnosis completely in 6 of our patients. Although the adult patients study quoted an inherited hypercoaguable state in 85.7% of patients, only 25% of our children had a documented hypercoagulable state. However, fever or diarrhea leading to dehydration and preceding the symptoms of BCS was documented in 45% of our patients. Technical success in the adult study was more than 80% in medium term. In our study, medium-term success with TIPSS was

100%, but the overall success rate of all of the interventions was 73%, with higher success rates with HV stent placement and TIPSS than angioplasty.

Radiological intervention is an attractive alternative to surgery like a portacaval shunt surgery that is associated with significant morbidity and mortality (9). Besides, shunt surgery requires a good caliber of the portal vein, and given the median age of 22 months in our patients, this would not have been technically feasible.

Radiological intervention ameliorated symptoms like ascites, hematemesis, and hepatomegaly in the postoperative follow-up period of the patients. However, radiological interventions like HV stenting were possible only in those patients who had short-segment ostial blocks and an HV diameter greater than or equal to 5 mm, whereas angioplasty was performed in those patients who had an HV diameter less than or equal to 4 mm. TIPSS was performed in those patients in whom HV stenting was not possible. The youngest child subjected to a TIPSS procedure was 3 years old after a failed balloon dilatation.

The overall results of HV stenting/TIPSS seem to be better than with angioplasty. Angioplasty may be used as a bridge to stenting/TIPSS that may be performed once the child grows and has a larger caliber of the vein. This would need to be carried out under the watchful eye of a multidisciplinary team consisting of a hepatologist, a pediatrician, and an interventional radiologist at a tertiary center. Close clinical, imaging, and laboratory follow-up will ensure HV patency and long-term survival. Data pooled in from other centers would be needed to reconstruct guidelines for the management of children with HVOO.

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