Hassab’s operation for Joubert syndrome with congenital hepatic fibrosis: A case report

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ABSTRACT

INTRODUCTION: Joubert syndrome is characterized by psychomotor developmental delay, hypotonia, oculomotor abnormalities, occasional retinal dystrophy and cystic kidneys, and frequent and often, striking breathing abnormalities, especially in the neonatal period, with panting tachypnea followed by apnea. We report a case of Joubert syndrome with hepatic fibrosis, portal hypertension, and pancytopenia treated by Hassab’s operation.

PRESENTATION OF CASE: Our patient was a 27-year-old woman with a history of tachypnea, muscle hypotonia, and psychomotor retardation shortly after birth and a diagnosis of Joubert syndrome at 2 years of age. At 19 years of age, she was diagnosed with progressive pancytopenia. At 27 years of age, she visited her local doctor for sudden-onset hematemesis. Endoscopy revealed esophageal varices exhibiting the red color sign and no evidence of recent bleeding. Splenomegaly and development of portal collateral circulation were observed on computed tomography scans. The patient was referred to our hospital, where she was diagnosed with Joubert syndrome and hepatic fibrosis, portal hypertension, and hypersplenism. After performing Hassab’s operation, the pancytopenia improved, but anticoagulant therapy was required for splenic vein thrombosis. The patient was discharged on postoperative day 25. Two years following surgery, the gastroesophageal varices were controlled, and no progression of the splenic vein thrombosis or hepatic failure was evident.

CONCLUSION: This is the first case report of Hassab’s operation for congenital hepatic fibrosis in a patient with Joubert syndrome, a rare congenital condition. We achieved a favorable clinical outcome.

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1. Introduction

Joubert syndrome is an autosomal recessive disorder that first reported in 1969 [1]. It is characterized by psychomotor developmental delay, hypotonia, oculomotor abnormalities, occasional retinal dystrophy and cystic kidneys, and frequent and often, striking breathing abnormalities, especially in the neonatal period, with panting tachypnea followed by apnea. Joubert syndrome and related disorders (JSRD) are used to describe individuals with Joubert syndrome accompanied by additional findings including retinal dystrophy, renal disease, ocular colobomas, occipital encephalocoele, polydactyly, oral hamartomas, endocrine abnormalities and hepatic fibrosis [2]. We report a case of Joubert syndrome with hepatic fibrosis, portal hypertension (PH), and pancytopenia treated by Hassab’s operation. To the best of our knowledge, our patient is the first such case to be reported.

2. Presentation of case

Patient: 27-year-old woman
Family history: Older sister with Dandy–Walker syndrome
History of present illness: On postnatal day 2, the patient was treated by her local doctor for tachypnea. At 1 year of age, she was noted to have muscle hypotonia and psychomotor retardation, and she was diagnosed with Joubert syndrome. At 19 years of age, she suffered from increasingly severe anemia, with pancytopenia progressing despite the prescription of iron formulations. At 25 years of age, a bone marrow biopsy ruled out hematological disease. At 27 years of age, following the sudden onset of hematemesis, an upper gastrointestinal endoscopy revealed esophageal varices that were positive for the red color (RC) sign without any evidence of active

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bleeding. She was kept nil per mouth and started on proton pump inhibitors with no recurrence of hematemesis. Because the computed tomography (CT) scans and abdominal ultrasound revealed splenomegaly, the patient was referred to our department for further treatment of the splenomegaly, pancytopenia, and esophageal varices.

On initial examination, body height was 156.3 cm, body weight was 33.8 kg, body mass index was 13.8 kg/m², body temperature was 37.2 °C, blood pressure was 99/65 mmHg, and pulse was 85 beats/min. An enlarged spleen was palpable as a mass on the left abdominal region. Laboratory findings were a white blood cell count of 1000/µL [reference value (RV): 3300–9000/µL], her hemoglobin was 9.5 g/dL (RV: 11.5–15 g/dL), and her platelet count was $20 \times 10^3$/mm³ (RV: 150–400 $\times 103$/mm³). She had a Child–Pugh score of A (6 points). The indocyanine green retention rate at 15 min was 13%. The blood urea nitrogen level was 33 mg/dL (RV: 8–20 mg/dL), serum creatinine level was 2.13 mg/dL (RV: 0.4–0.8 mg/dL).

An abdominal CT scan found that the hepatic margin appeared blunted. Spleen enlargement was observed, and development of portal collateral circulation and gastroesophageal varices were noted. A small volume of ascities was present, and bilateral renal atrophy and renal cysts were observed (Fig. 1). Upper gastrointestinal endoscopy found esophageal (in the upper third of the esophagus, F2–3, Cb, and RC2) and gastric (F1, RC0) varices near the cardiac orifice (Fig. 2). Gastroesophageal varices were classified on the basis of the criteria used to describe endoscopic findings in Japan. In brief, the severity of gastroesophageal varices was classified as follows: F1, straight and small-caliber varices; F2, beady varices; F3, tumor-shaped varices; Cw, white varices; Cb, blue varices; RC0, absence of red color (RC) sign; RC1, a few RC signs; RC2, several RC signs; and RC2, many RC signs. The patient was diagnosed with Joubert syndrome with congenital hepatic fibrosis (CHF), which was deemed to be consistent with the observation of...
hepatic cirrhosis and PH, esophageal varices, hypersplenism, and pancytopenia.

In the present case, endoscopic variceal ligation (EVL) was not performed as the bleeding point of gastroesophageal varices could not be determined on upper gastrointestinal endoscopy. Furthermore, endoscopic injection sclerotherapy (EIS) was unsuitable due to an extremely low platelet count ($20 \times 10^3/mm^3$). Because preoperative CT showed collateral circulation around the portal vein, we determined that splenic enlargement was present with the increased likelihood of hemorrhage during surgery. Therefore, we considered performing partial splenic artery embolization (PSE). However, because relatively severe renal dysfunction thought to be a symptom of JSRD was present, we hesitated in performing PSE from the viewpoint of preserving the renal function. It has previously been reported that variceal blood flow is reduced following Hassab's operation because this procedure cuts off the blood supply, thereby enabling effective endoscopic injection [3]. Therefore, we selected modified Hassab's operation because it can be simultaneously performed with devascularization.

Surgical findings included hepatic fibrosis with blunting of the hepatic margins. The spleen was enlarged, and there was a small volume of ascites. We devascularized of the lower esophagus and upper portion of the stomach in the region of the left gastric and left gastric artery were dissected. To preserve vascular nutrition, three branches of the left gastric artery were not dissected. We dissected the splenic artery and vein near the splenic hilum and excised the spleen. We performed a pyloroplasty by making an incision along the long axis of the seromuscular layer of the pylorus. We then performed a liver biopsy. The duration of surgery was 471 min. The volume of blood lost was 3538 ml; 1680 ml of packed red blood cells, 1200 ml of fresh frozen plasma, and 200 ml of platelet concentrate were transfused.

Histopathological findings: Extensive fibrous expansion in the hepatic portal region was observed. An irregular pattern was observed because the fibrosis of the liver parenchyma spared the islets; this was consistent with the findings of CHF [3].

Postoperative course: The platelet count also gradually increased postoperatively; it had increased to $63.1 \times 10^3/mm^3$ by day 13. A CT scan on day 7 revealed the devascularization of the upper stomach was accomplished, and the reduction of the esophageal varices was confirmed. A thrombus in the splenic vein persisted; no thrombus was observed in the portal vein trunk (Fig. 4). Direct oral anticoagulant (DOAC) (edoxaban tosylate hydrate, 30 mg/day) was provided as anticoagulant therapy. The patient was discharged on day 25. Upper gastrointestinal endoscopy at postoperative month 3 showed the varices Lm, F2, Cb, and RCO in the middle to lower third of the esophagus and Lg-cCf, F1, Cb, and RCO in the gastric cardia. Improvement was noted when compared with the preoperative state. Contrast-enhanced CT scan at postoperative month 3 showed persistent splenic vein thrombosis, which had not extended to the portal vein trunk. Two years following surgery, there has been no progression of hepatic failure and the clinical course has been favorable.

3. Discussion

Liver dysfunction and PH related to JSRD are thought to be due to congenital hepatic fibrosis. PH in CHF is caused by an increase in blood flow resistance in the liver itself and is considered to be due to congenital vascular abnormalities and progressive fibrosis [4].

There is no radical cure for CHF, and then symptomatic treatments are given mainly. CHF complications, including variceal bleeding, hypersplenism, cholangitis, and to a lesser extent, biliary stones, cholangiocarcinoma, and hepatocellular carcinoma, are treated in a routine manner [4]. When liver failure progresses, a liver transplantation may be necessary [5].

Hassab's operation is effective for treating complex medical conditions such a gastroesophageal varices, pancytopenia, and PH. It has been reported that Hassab's operation for patients with liver cirrhosis has a potential to improve protein catabolism and impair liver function possible, and restoration of nutrition state [6]. It is believed to be due to an increase in effective hepatic blood flow by controlling inflow and steal of PV blood flow.

We investigated the prognosis of 16 patients with previous modified Hassab's operations at our hospital. The five patients who had preoperative RC signs were treated for gastric varices, and the RC sign postoperatively disappeared in all of these cases. Five of the ten patients (50%) treated for esophageal varices remained
positive for the RC sign. Of these, at least half underwent additional procedures, such as EIS or EVL (Table 1). Fukasawa et al. also reported on the effectiveness of treating varices with Hassab's operation and reported resolution in 49.5% of cases, alleviation in 19.6%, and persistence in 30.9% [7]. For this reason, cases need to be periodically followed up after surgery by upper gastrointestinal endoscopy, particularly for patients presenting with esophageal varices. Additional internal medical treatment should be administered as required.

In general, following splenectomy, portal vein or splenic vein thrombosis (PSVT) is observed in 0–85.7% of cases [8–14]. It has been reported that early prophylactic anticoagulation was associated with a reduced incidence of PSVT, although it was not associated with the incidence of anticoagulation-associated complications [15].

There are no guidelines regarding the management of PSVT in cirrhosis. Anticoagulation treatment is frequently used, but there are limited data concerning its safety and benefits. Francoz et al. administered anticoagulant therapy with low-molecular-weight heparin or vitamin K antagonists (VKAs) to patients with PSVT accompanying liver cirrhosis and reported recanalization in 42% of cases compared with 0% among controls [16]. DOACs, a new type of anticoagulant therapy, offer the same anticoagulant effects as VKAs but without dietary restrictions or individual variation in effects; therefore, the coagulation time does not need to be measured. It has been reported that the use of DOACs for liver cirrhosis patients seems to be as safe as traditional anticoagulants [17, 18]. As shown in the present case, a further advantage of DOACs is that they can be simply used in patients with mental retardation. Therefore, we used DOAC, and although complete recanalization of PSVT was not achieved, there has been no thrombus progression.

Hassab's operation is not the primary treatment for progressive hepatic fibrosis but might be considered as an interim treatment to prolong the amount of time until the patient requires hepatic transplantation.

4. Conclusion

We treated a patient with Joubert syndrome, a rare disease, with Hassab's operation successfully. Although Hassab's operation is relatively invasive, it is highly reliable for treating hypersplenism and gastroesophageal varices with a high risk of hemorrhage, and is reported to be effective to improve liver function in patients with liver cirrhosis. This surgery also appears to be effective for complex conditions such as Joubert syndrome with CHF. This work has been reported in line with the SCARE criteria [19].

Conflicts of interest

The authors declare that they have no conflicts of interest.

Sources of funding

The authors declare that they have no supportive funding.

Ethical approval

This work was approved by the Tohoku University ethics committee.

Consent for publication

Written informed consent was obtained from the patients for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.
Authors’ contributions

Miyazawa K is a major contributor in writing the manuscript. Hara Y, Shimizu K, Nakaniishi N, Tokodai K, Nakaniishi C, Miyagi S, Kawagishi N, and Ohuchi N were attending doctors and performed clinical treatment including surgical operation.

All authors have read and approved the final manuscript.

Registration of research studies

This work does not require a registration of research studies because it is a case report.

Guarantor

Miyazawa K and Ohuchi N are accept full responsibility for the work and had controlled the decision to publish.

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