

CASE REPORT

Spleen-Preserving Distal Pancreatectomy after Chemotherapy for Initially Unresectable Pancreatoblastoma in a 3-Year-Old Girl, Paying Attention to Long-Term Change in Spleen Volume and Venous Collaterals

Yasuhiro Murata¹, Shugo Mizuno¹, Kohei Otake², Mikihiro Inoue², Hitoshi Honma³, Hidemi Toyoda³, Kazuo Fukutome⁴, Keiichi Uchida², Yoshihiro Komada³, Shuji Isaji¹

Department of the ¹Hepatobiliary Pancreatic and Transplant surgery, ²Gastrointestinal and Pediatric Surgery, ³Pediatrics and ⁴Pathology Mie University Graduate School of Medicine, 2-174 Edobashi, Tsu, Mie 514-8507, Japan

ABSTRACT

Background The long-term outcomes and validity of the Warshaw operation for childhood pancreatoblastoma remain uncertain. **Case presentation** Here we report a case of an initially unresectable pancreatoblastoma, curatively resected using spleen-preserving distal pancreatectomy with the Warshaw technique after effective chemotherapy in a 3-year-old girl. She was admitted with a large abdominal mass. The tumor arose in the body of pancreas and extended into the pancreatic head and tail, with involvement of the portal vein and splenic vessels and abutment to the common hepatic artery. Because total pancreatectomy and splenectomy with combined resection of the portal vein and common hepatic artery would have been needed to achieve complete resection, the patient initially received combination chemotherapy with cisplatin and 4-O-tetrahydropyranil adriamycin for down-sizing. After completion of chemotherapy, the tumor showed a great reduction in size, allowing for complete resection and splenic preservation using the Warshaw operation for distal pancreatectomy. The postoperative course was uneventful, and the patient received adjuvant chemotherapy successfully. The patient has been disease-free for 39 months postoperatively, without any late complications such as gastric bleeding. Splenomegaly and the formation of perigastric varices and venous periportal collateral circulation was noted. **Conclusion** The Warshaw operation was a feasible and acceptable procedure for pancreatoblastoma in a pediatric patient. Aggressive chemotherapy followed by curative-intent pancreatectomy will be a promising treatment strategy for advanced pancreatoblastoma to preserve remnant pancreatic function and quality of life in children.

INTRODUCTION

The spleen is an essential part of the lymphoid system for the defense against encapsulated bacteria. Patients with functional or anatomic asplenia are at a significantly increased risk of overwhelming infection, particularly involving the encapsulated bacteria *Streptococcus pneumoniae* and *Haemophilus influenzae* [1, 2]. Overwhelming post-splenectomy sepsis (OPSI) is a critical infection that can progress rapidly and has a high mortality if treatment is delayed [3]. Children aged ≤ 2 years are at an especially greater risk of developing the condition [4]. Overwhelming post-splenectomy sepsis occurs more

often after splenectomy for a hematological condition than after trauma [5]. Patients undergoing treatments such as chemotherapy and radiotherapy are at increased risk of OPSI [4]. The most common indications for splenectomy in children are hematologic disease and splenic trauma [6]. Distal pancreatectomy with splenectomy, although an uncommon procedure in children, causes asplenia in children with malignant pancreatic neoplasms or trauma to the pancreatic body and/or tail. Because children with malignant pancreatic neoplasms are at greater risk of developing OPSI, it is necessary to preserve the spleen during distal splenectomy as long as oncological advantages are not lost. Spleen-preserving distal pancreatectomy that preserves the splenic vessels is reported to be a useful procedure for children who have benign or marginally malignant pancreatic neoplasms, such as solid-pseudopapillary tumor (SPT) [7] and pancreatic body and/or tail trauma [8]. However, the splenic artery and vein cannot be preserved if both are involved in the malignant pancreatic neoplasm, as in pancreatoblastoma. In such cases, distal pancreatectomy with splenectomy is often chosen [9]. However, preservation of the spleen should be considered even for children with malignant pancreatic neoplasms, because pre- and postoperative chemotherapy are often

Received October 07th, 2015-Accepted November 18th, 2015

Keywords Pancreatoblastoma; Preoperative care

Abbreviations NEC neuroendocrine carcinoma; PNET Pancreatic neuroendocrine tumors

Correspondence Shugo Mizuno

Department of the Hepatobiliary Pancreatic and Transplant surgery

Mie University Graduate School of Medicine

2-174 Edobashi, Tsu, Mie 514-8507

Japan

Phone +81-59-232-1111

Fax +81-59-232-8095

E-mail mizunos@clin.medic.mie-u.ac.jp

required for such patients. In this situation, the Warshaw technique, a spleen-preserving distal pancreatectomy with combined resection of the splenic artery and vein, is feasible.

Pancreatoblastoma, which is a rare neoplasm mainly occurring in children, has often already advanced to the point of being unresectable at the time of diagnosis. Down-sizing chemotherapy for large or locally advanced tumors is the treatment of choice to help achieve complete resection. Combination chemotherapy with cisplatin and doxorubicin is effective for initially unresectable or marginally resectable pancreatoblastoma [10-15], but there have been only a few reports describing its use in a neoadjuvant setting [10, 11, 13]. This report describes a case of advanced pancreatoblastoma successfully resected with the Warshaw operation after effective chemotherapy in a 3-year-old girl. To our knowledge, ours is the first report of long-term outcomes and the validity of the Warshaw operation for childhood pancreatoblastoma.

CASE REPORT

A three-year-old girl presented with a large abdominal mass. She had a past history of left hydronephrosis and pervasive developmental disorders. The family history was free of known cancer. Physical examination revealed a well-defined, smooth surfaced and elastic hard mass measuring 10×8 cm² in the mid-epigastrium. Laboratory examination showed elevated serum alpha-fetoprotein (AFP) level (125 ng/mL; normal range: 0–28.5 ng/mL).

Abdominal computed tomography (CT) revealed a heterogeneously enhanced tumor in the upper abdomen measuring 14.0×12.1×6.4 cm³. The superior mesenteric vein and splenic vein were involved in the tumor and were narrowed. The splenic artery and common hepatic artery were tightly adhered to the tumor (**Figure 1**). Magnetic resonance imaging (MRI) demonstrated a large tumor

with heterogeneous high intensity in diffusion-weighted image (DWI) arising from the pancreatic body. There was no evidence of distant metastasis or metastasis to the lymph nodes.

Pathological examination of specimens obtained by core needle biopsy showed solid epithelial cell cords with acinar differentiation and partly squamoid corpuscles separated into distinct lobules by fibrous stroma. Immunohistochemical staining of the tumor cells showed positive AFP, alpha1-anti-trypsin, chymotrypsin, and partly positive CD56 and synaptophysin in the acinar regions, positive beta-catenin in the squamoid corpuscles, and Periodic Acid-Schiff (PAS)-positive granules in the cytoplasm of the acinar-like cells (**Figure 1**). A definitive diagnosis of pancreatoblastoma was made.

Preoperative Treatment Course

First, we considered that a total pancreatectomy and splenectomy with combined resection and reconstruction of the portal vein and common hepatic artery would have been needed for complete resection of the tumor, which would result in an extreme form of pancreatogenic diabetes. Considering the patient’s quality of life and operative risk, we wanted to avoid total pancreatectomy and combined resection of the hepatic artery. Therefore, to shrink the tumor, we initially treated her with three courses of CITA therapy (intravenous injection of CDDP 80 mg/m² on day 1 and 4’-O-tetrahydropyranil Adriamycin (THP-ADM) 30 mg/m² on days 2 and 3). The change of serum AFP level after treatment is shown in **Figure 2**. After completion of three cycles of CITA therapy, serum AFP decreased to within the normal range, and abdominal CT demonstrated that the tumor shrunk markedly from 14.0 cm to 5.6 cm. Tumor contact with the common hepatic artery became unclear at that point, and the patency of the portal vein was drastically improved (**Figure 3**).

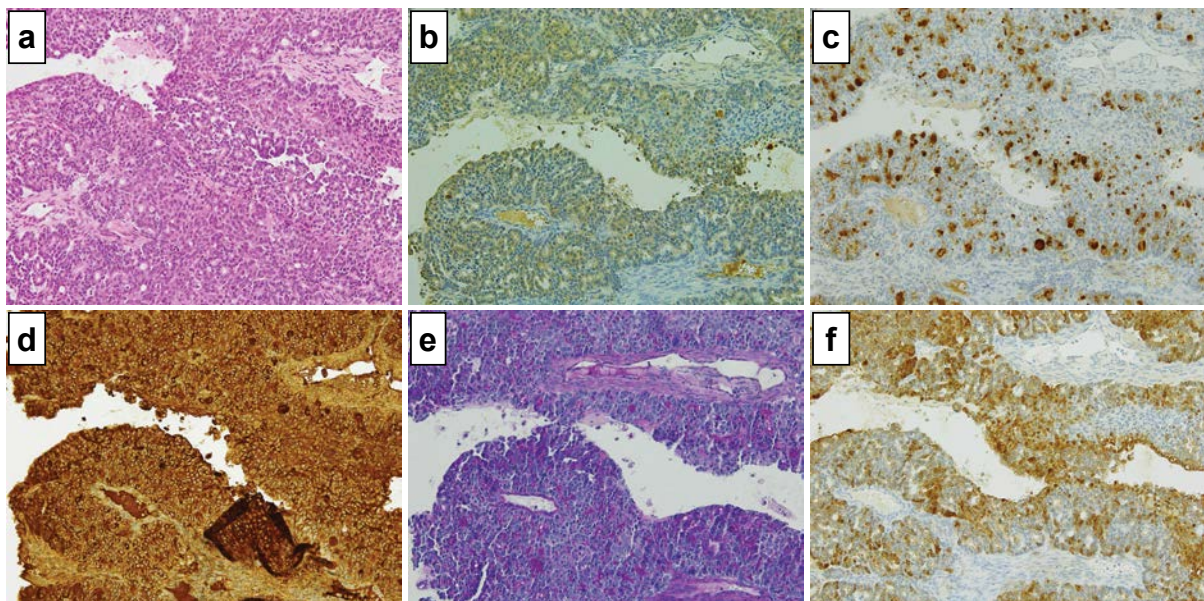


Figure 1. Pathological findings obtained by needle biopsy. Pathological examination of specimens obtained by needle biopsy shows solid epithelial cell cords with acinar differentiation and partly squamoid corpuscles separated into distinct lobules by fibrous (a.), stroma (Hematoxylin and Eosin (HE) staining, (b.)). Immunohistochemical staining of the tumor cells shows positive AFP, (c.), chymotrypsin, (d.), alpha1-anti-trypsin, (e.), Periodic Acid-Schiff (PAS, (f.)) and beta-catenin.

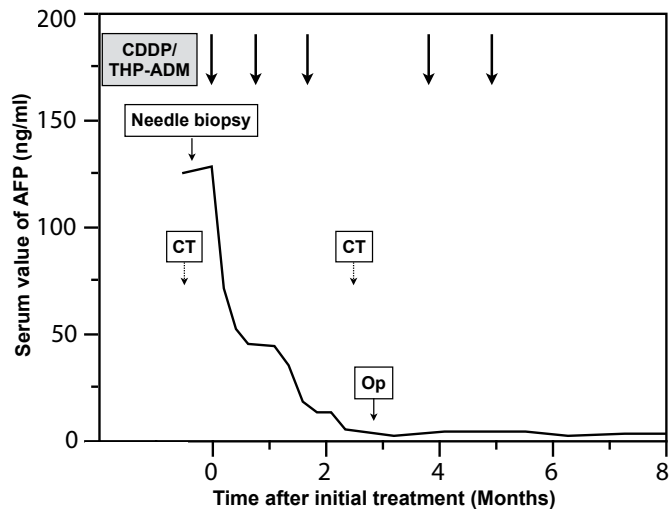


Figure 2. Change of serum AFP level after treatment. For shrinking of the tumor, three courses of CITA therapy (intravenous injection of CDDP 80 mg/m² on day 1 and THP-ADM 30 mg/m² on days 2 and 3) were administered. After completion, the serum level of AFP decreased to within the normal range. Two courses of CITA therapy were added as adjuvant therapy.

Abdominal MRI confirmed the reduction in tumor size, but the tumor's high-intensity heterogeneous enhancement by contrast medium remained. The radiographic response to chemotherapy was partial response (PR) according to the RECIST criteria [16]. As the tumor was considered resectable after completion of chemotherapy, the patient was transferred to the department of pediatric surgery in our hospital.

Operative Finding

The patient was placed in a supine position, and a 7-cm upper abdominal transverse incision was made. The tumor was adhered tightly to the mesocolon of the transverse colon and to the posterior wall of the stomach. Because an invasion of the tumor to the mesocolon was suspected, the root of the middle colic artery and vein, and its right and left branches were divided to remove the affected mesocolon, while preserving the marginal vessels. A part of the seromuscular layer of the stomach invaded by the tumor was dissected and the defect was closed with interrupted sutures. The portal vein was carefully dissected from the pancreas and spared, as the tumor did not invade it directly. After incising the lesser omentum, the common hepatic artery and root of the splenic artery were isolated. The pancreatic parenchyma was transected just above the right edge of the portal vein and the main pancreatic duct was divided. The resected margin at the head of the pancreas was sent for frozen-section pathology, and was determined to be negative for malignancy. Because the inferior mesenteric vein was involved in the tumor, it was divided. The origins of the splenic artery and vein were divided. The common hepatic artery was preserved as there was no invasion by the tumor. The distal pancreas was mobilized and carefully detached from the retroperitoneal membrane. The short gastric vessels and left gastroepiploic vessels were preserved. Finally, several

branches of the splenic artery and vein were ligated and cut at the hilum of the spleen and the resected specimen was removed en bloc. Blood flow inside the spleen was easily detected by intraoperative Doppler ultrasonography after removal of the resected specimen. The duration of surgery was 6 hours, and blood loss totaled 340 mL. A closed drain was placed just below the cut end of the remnant pancreas and removed on postoperative day 3. It was confirmed that glucose tolerance was preserved even after oral intake was started.

Pathological Findings

The tumor was encapsulated and nodular, and measured 5.2×7×3.5 cm³. The tumor tissue showed a lobular structure divided by dense fibrous tissue (**Figure 4a**). Each lobule of the tumor was mainly composed of a solid alveolar structure and partly of an acinar structure (**Figure 4b**). Necrosis with migration of foamy histiocytes and hemosiderin-laden macrophages were seen within the tumor (**Figure 4c**). A pathological diagnosis of pancreatoblastoma was made. Margins were free from tumor cells upon microscopic examination.

Postoperative Course and Adjuvant Chemotherapy

The postoperative course was uneventful, and the patient was transferred to the department of pediatrics on postoperative day 3 for adjuvant chemotherapy. She completed two cycles of CITA therapy. The comparison of CT scans from 1 week, 11 months, and 39 months after surgery is shown in **Figure 5**. The volume of the spleen and platelet count were also monitored. Because it was previously reported that the spleen/liver (S/L) ratio negatively correlates with the platelet count more accurately than does spleen volume [17], we calculated

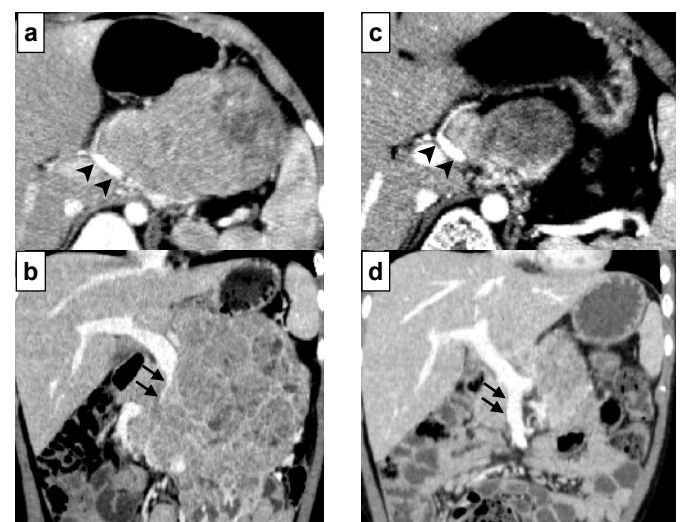


Figure 3. Comparison of CT scans before and after chemotherapy. (a, b.) Before chemotherapy, showing a heterogeneously enhanced tumor in the upper abdomen, measuring 14.0 x 12.1 x 6.4 cm³. The common hepatic artery ((a.) black arrowheads) is adhered to the tumor. The superior mesenteric vein and splenic vein are involved in the tumor with narrowing of the veins ((b.) black arrows). (c, d.) After chemotherapy, showing that the tumor maximum size decreased from 14.0 cm to 5.6 cm. The tumor contact with the common hepatic artery became unclear ((c.) black arrowheads), and the patency of the portal vein improved ((d.) black arrows).

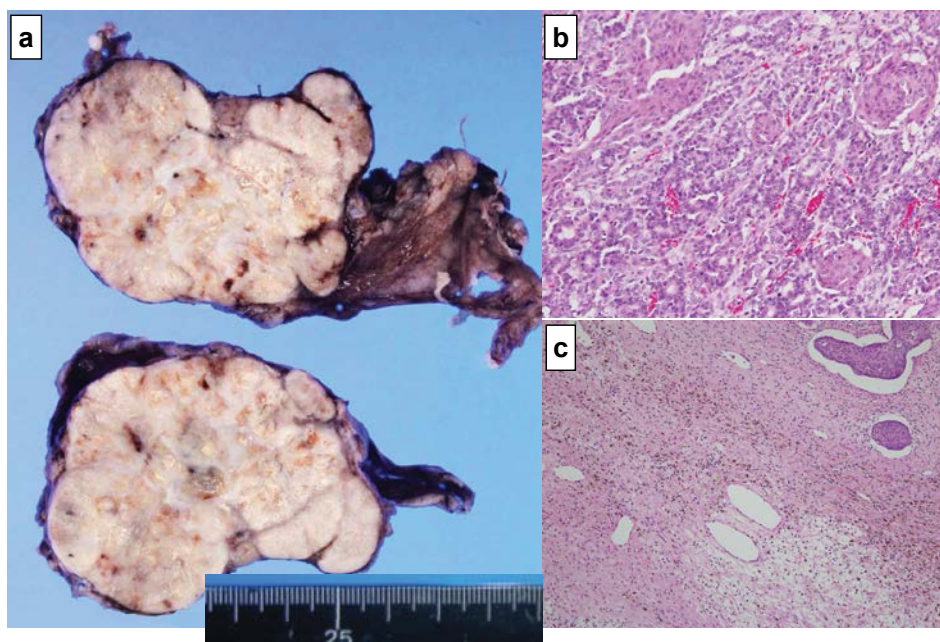


Figure 4. Pathological Findings. **(a).** The tumor tissue shows lobular structure divided by dense fibrous tissue. **(b).** Each lobule of the tumor is mainly composed of solid alveolar structure and partly of acinar structure. **(c).** Necrosis with migration of foamy histiocytes and hemosiderin-laden macrophages.

the S/L ratio to monitor hemodynamic change of the portal venous system and platelet count. Volume measurements were derived from CT images of the spleen and liver at several time points after surgery. Prior to surgery, the S/L ratio was 0.25 (**Figure 5a**).

There was no hypoperfusion indicating splenic infarction, and the preservation of the short gastric and left gastroepiploic vessels was confirmed by CT scan 1 week after surgery, although the spleen was slightly enlarged and venous periportal collateral circulation was detected, reflecting the hemodynamic change immediately caused by the Warshaw operation (**Figure 5b**). On CT imaging performed 11 months after surgery, perigastric varices along the lesser curvature of the stomach were detected and venous collaterals along the portal vein were further developed (**Figure 5c**). Splenic volume increased to 166 ml, and the S/L ratio also increased to 0.346. On CT scan performed 39 months after surgery, the perigastric varices and venous collaterals along the portal vein did not change remarkably (**Figure 5d**). Splenic volume increased to 265 mL, and the S/L ratio gradually increased to 0.518, reflecting the progression of sinistral portal hypertension. Chemotherapy-induced thrombocytopenia was seen 3 months after surgery by 6 months postoperatively, the platelet count recovered and reached approximately only half the level of the immediate postoperative count (**Figure 5a**). There was no recurrence in the remnant pancreas. The patient has been disease-free for 39 months and has not suffered any late complications such as gastric bleeding. Her serum AFP remains within normal limits.

DISCUSSION

Children aged ≤ 2 years are at greater risk of OPSI, and preoperative chemotherapy contributes to an increased risk of OPSI [4]. In the present case, the patient was a 3-year-old girl and had received preoperative chemotherapy. If

distal pancreatectomy with splenectomy was performed for the present case, there was a possibility that serious post-splenectomy sepsis would occur and adjuvant chemotherapy could not be continued. Autologous splenic transplantation is a treatment option to preserve splenic function, performed mainly for patients with severe splenic trauma. It is usually done by transplanting part of the splenic tissue into pouches created in the omentum [19, 20]. The extent of possible immunoprotection provided by autologous splenic transplantation is unknown, and whether the regenerating tissues are able to prevent severe infection and reduce the morbidity and mortality rates from OPSI remains unclear [21]. Therefore, we considered that a spleen-preserving distal pancreatectomy was necessary in the present case. Currently, two procedures are established to preserve the spleen during distal pancreatectomy: one meticulously separates the splenic artery and vein from the pancreas by dividing each of the many small branches between the pancreas and vessels [22]; the other dissects and resects the splenic artery and vein but carefully preserves the collateral blood supply of the spleen from the short gastric and gastroepiploic vessels, often referred as the Warshaw operation [23, 24]. For some cases of pancreatoblastoma with involvement of the splenic artery and vein (e.g., the present case), preservation of the splenic vessels is not possible because it would increase surgery time and blood loss to divide and spare the splenic artery and vein from the tumor. For such cases, the Warshaw operation for distal pancreatectomy is an acceptable procedure (especially in children), with the oncological advantages of removing lymphatics along the splenic artery and vein, as well as preserving the spleen. The Warshaw operation was based on the conservation of the short gastric and gastroepiploic vessels. The original 1988 paper describing the Warshaw operation describes the main collateral supply as the short gastric vessels,

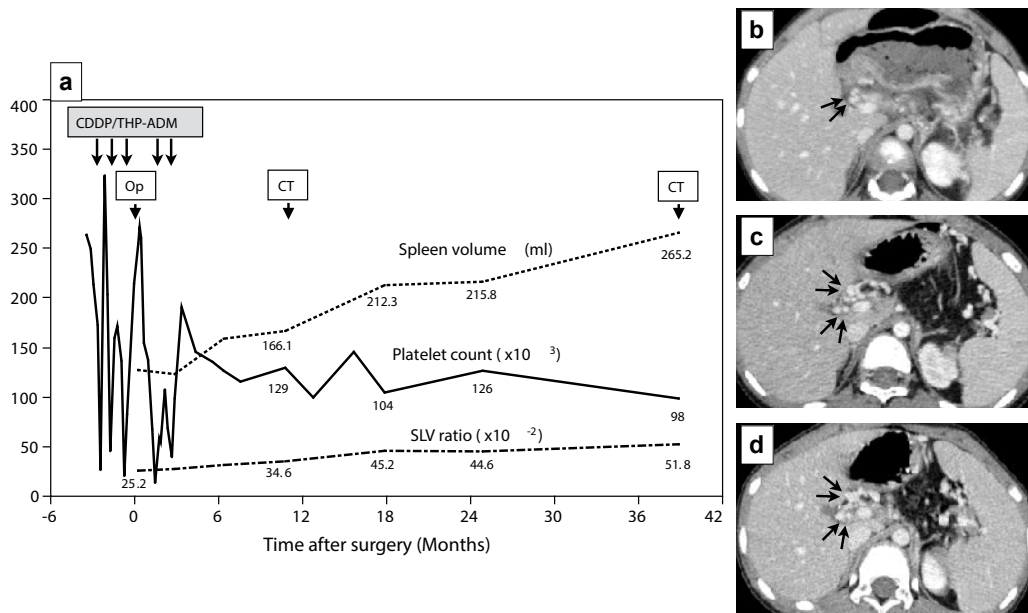


Figure 5. Comparison of CT scans performed before and 1 week, 1, and 3 years after surgery. Chemotherapy-induced thrombocytopenia was observed by 3 months after surgery. Platelet count then recovered and reached approximately half the level of the postoperative count by 6 months, and thereafter did not vary. **(a.)** The splenic volume and spleen/liver volume ratio (S/L ratio) increased gradually. Venous collaterals along the portal vein were identified on CT scan performed on postoperative day 7 **(b.)**, black arrows). **(c.)** Eleven months after surgery, they were further developed ((**c.**) black arrows). **(d.)** Thirty-nine months after surgery, they had not changed remarkably.

although it also describes that the left gastroepiploic vessels should be identified and preserved [23, 24]. However, the most recent experimental and clinical investigations demonstrated that the left gastroepiploic artery was the main collateral vessel to the spleen after a spleen-preserving distal pancreatectomy with resection of the splenic vessels [25]. Therefore, it is very important to incise the retroperitoneum along the pancreatic margin and mobilize the spleen carefully, so both the short gastric vessels and left gastroepiploic vessels are preserved. The color and size of the spleen should be assessed and blood flow confirmed at the splenic hilum by intraoperative Doppler ultrasonography.

Since the initial Warshaw paper, several studies have verified that distal pancreatectomy with preservation of the spleen using the Warshaw operation is associated with shorter surgical time, decreased blood loss, and shorter hospital stay compared with distal pancreatectomy with splenectomy. The risk of postoperative failure due to splenic infarction is relatively low with the Warshaw operation [26, 27]. In terms of the long-term outcome after the Warshaw operation, the studies describe that while perigastric varices were identified in 25–30% of patients by abdominal CT, the varices were asymptomatic and did not cause bleeding [26, 28]. The study retrospectively describing the hemodynamic changes in splenogastric circulation reported that abdominal CT revealed perigastric varices in 70% of patients and submucosal varices in 20%. Gastrointestinal bleeding from gastric varices only occurred in one patient [29]. These studies suggest that the development of perigastric varices frequently occur after the Warshaw operation.

In the present case, follow-up contrast-enhanced CT did not show any hypoperfusion in the spleen. The preservation of the short gastric vessels, gastroepiploic

vessels and remnant splenic vessels of the splenic hilum were confirmed. However, the development of perigastric varices and periportal collateral formation was detected and gradually progressed over the first year postoperatively, reflecting progression of sinistral portal hypertension caused by hemodynamic change. As previously reported, the S/L ratio negatively correlates with platelet count after orthotopic liver transplantation. Patients with a postoperative S/L ratio >0.35 tend to have lower platelet counts [17]. In the current case, as the splenic volume increased, the S/L ratio gradually increased up to 0.518, resulting in thrombocytopenia. Although no complications have been detected at 39 months postoperatively, further periodical follow-up with CT will be needed to continue to observe outcomes. The Warshaw operation was considered acceptable for the present case because splenic preservation was beneficial to prevent fatal postoperative infections, enabling the completion of adjuvant chemotherapy. To our knowledge, this is the first paper showing that the Warshaw operation is a safe and acceptable procedure for pancreatoblastoma, even in a 3-year-old child. Further evaluation of late outcome and accumulation of cases will be warranted to elucidate the feasibility of the Warshaw operation for children.

Pancreatoblastoma is an extremely rare malignant pancreatic tumor, mainly presenting in childhood, but it is the most common malignant pancreatic tumor occurring in children younger than 10 years [30]. The most important prognostic factor is complete resection of the tumor. The prognosis for unresected cases and incompletely resected cases is extremely poor. A previous report described that the 5-year survival rate for resected cases was 65%, whereas for patients with unresectable pancreatoblastoma, there were no survivors at 5 years [15]. Adjuvant chemotherapy

is also recommended for resected cases, because these lesions have a high recurrence rate and patients must be followed closely [30]. At the time of diagnosis, many patients are evaluated as initially having unresectable tumors due to local extension or distant metastasis [30, 31]. Chemotherapy or radiotherapy is required to shrink tumors and good responses to chemotherapy are noted in the pediatric group [32]. Cisplatin, Adriamycin, 4'-O-tetrahydropyranyl Adriamycin (THP-ADM), etoposide, cyclophosphamide, and vincristine have been reported to be effective chemotherapeutic agents [10].

To our knowledge, there have been nine pediatric patients with initially unresectable or marginally resectable pancreaticoblastoma who underwent successful pancreatectomy after preoperative chemotherapy [10, 13, 33-37]. These cases comprised six boys and three girls with an average age of 6.3 years. Preoperative chemotherapy was performed because of locally advanced tumors in five cases, liver metastasis in two cases, lymph node involvement in two cases, lung metastasis in one case, and a tumor thrombus in the portal vein in one case. The regimen included cisplatin and Adriamycin for five cases, cyclophosphamide, etoposide and THP-ADM for two cases, ifosfamide, vindesine and carboplatin for one case and an unclear protocol for one case. Operative procedures involved pylorus-preserving pancreaticoduodenectomy (PPPD) with resection of the upper jejunum and right hemicolectomy and combined resection of the portal vein for one case, pancreaticoduodenectomy (PD) for one case, distal pancreatectomy for one case, regional pancreatectomy for one case, central pancreatectomy for one case, and unclear procedures for three cases. Most of the resected cases received postoperative chemotherapy with good outcomes. All patients were alive at the time of publication, and mean survival time after surgery was 60 months (range: 5–120 months for seven cases, unclear for two cases).

In the present case, the portal vein was occluded by the tumor and the tumor contacted the splenic artery and common hepatic artery. Resectability was initially impossible according to the National Comprehensive Cancer Network (NCCN) guidelines of pancreatic adenocarcinoma [38]. Moreover, the tumor extended through the entire pancreas so that a total pancreatectomy and splenectomy with combined resection of the portal vein and common hepatic artery were needed to achieve curative resection without tumor spillage. Considering the quality of life and surgical risk, a total pancreatectomy with combined resection of major vessels should be avoided for a child, if possible. Therefore, we decided to choose chemotherapy as an initial treatment to reduce tumor volume. Consequently, aggressive chemotherapy with cisplatin and THP-ADM was effective and enabled us to perform complete resection with no residual tumor cells. Importantly, our preoperative treatment was feasible and safe without serious adverse events and consequently allowed us to avoid total pancreatectomy with combined resection of

the portal vein. Furthermore, adjuvant chemotherapy with cisplatin and THP-ADM was smoothly achieved postoperatively. 4'-O-tetrahydropyranyl Adriamycin was discovered by Umezawa *et al.* in 1979 during a search for new anthracycline antibiotics among 4'-O-substituted compounds with less toxicity than other anthracycline anticancer drugs. In its preclinical studies, this compound possessed similar antitumor efficacy as Adriamycin [39]. CITA therapy, a combination therapy with THP-ADM and cisplatin, is well known as an effective protocol for hepatoblastoma based on the result of cooperative treatment studies conducted by the Japanese Study Group for Pediatric Liver Tumor (JPLT-2) [40], but its effect on pancreaticoblastoma has remained unclear. The current report demonstrated that preoperative CITA therapy can be a safe and efficient regimen for initially unresectable pancreaticoblastoma, even in a neoadjuvant setting. More trials of preoperative chemotherapy will be warranted to establish a standard treatment protocol in the management of advanced pancreaticoblastoma.

CONCLUSIONS

In conclusion, we treated a case of advanced pancreaticoblastoma, resected curatively after effective chemotherapy with a good outcome after a spleen-preserving Warshaw operation for distal pancreatectomy in a 3-year-old girl.

The down-sizing chemotherapy followed by curative-intent pancreatectomy is a promising strategy for marginally resectable or unresectable pancreaticoblastoma. The Warshaw operation is a safe and acceptable procedure for pancreaticoblastoma invading the splenic artery and vein to preserve the spleen, even in pediatric patients.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Author's Contributions

HT and HH and YK were involved in diagnosis, preoperative chemotherapy, and adjuvant therapy and follow-up after surgery. KF was involved in pathological diagnosis. KO and MI and KU were involved in the surgery and postoperative care of the patient. YM was involved in the surgery and wrote the case report, made literature review and drafted the manuscript. SM and SI were involved in the surgery and both revised the paper. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare that they have no competing interests.

References

1. Aavitsland P, Froholm LO, Hoiby EA, Lystad A. Risk of pneumococcal disease in individuals without a spleen. *Lancet* 1994; 344:1504. [PMID: 7968138]
2. Davidson RN, Wall RA. Prevention and management of infections in patients without a spleen. *Clin Microbiol Infect* 2001; 7:657-660. [PMID: 11843905]
3. Holdsworth RJ, Irving AD, Cuschieri A. Postsplenectomy sepsis and its mortality rate: actual versus perceived risks. *Br J Surg* 1991; 78:1031-1038. [PMID: 1933181]
4. Okabayashi T, Hanazaki K. Overwhelming postsplenectomy infection syndrome in adults - a clinically preventable disease. *World J Gastroenterol* 2008; 14:176-179. [PMID: 18186551]
5. Meekes I, van der Staak F, van Oostrom C. Results of splenectomy performed on a group of 91 children. *Eur J Pediatr Surg* 1995; 5:19-22. [PMID: 7756228]
6. Coignard-Biehler H, Lanternier F, Hot A, Salmon D, Berger A, de Montalembert M, et al. Adherence to preventive measures after splenectomy in the hospital setting and in the community. *J Infect Public Health* 2011; 4:187-194. [PMID: 22000846]
7. Uchida H, Goto C, Kishimoto H, Kawashima H, Sato K, Yoshida M, Takazawa S. Laparoscopic spleen-preserving distal pancreatectomy for solid pseudopapillary tumor with conservation of splenic vessels in a child. *J Pediatr Surg* 2010; 45:1525-1529. [PMID: 20638537]
8. Rutkoski JD, Segura BJ, Kane TD. Experience with totally laparoscopic distal pancreatectomy with splenic preservation for pediatric trauma-2 techniques. *J Pediatr Surg* 2011; 46:588-593. [PMID: 21376217]
9. Benoist S, Penna C, Julie C, Malafosse R, Rougier P, Nordlinger B. Prolonged survival after resection of pancreaticoblastoma and synchronous liver metastases in an adult. *Hepatogastroenterology* 2001; 48:1340-1342. [PMID: 11677959]
10. Defachelles AS, Martin De Lassalle E, Boutard P, Nelken B, Schneider P, Patte C. Pancreatoblastoma in childhood: clinical course and therapeutic management of seven patients. *Med Pediatr Oncol* 2001; 37:47-52. [PMID: 11466723]
11. Inomata Y, Nishizawa T, Takasan H, Hayakawa T, Tanaka K. Pancreatoblastoma resected by delayed primary operation after effective chemotherapy. *J Pediatr Surg* 1992; 27:1570-1572. [PMID: 1469578]
12. Murakami T, Ueki K, Kawakami H, Gondo T, Kuga T, Esato K, Furukawa S. Pancreatoblastoma: case report and review of treatment in the literature. *Med Pediatr Oncol* 1996; 27:193-197. [PMID: 8699999]
13. Meneses CF, Osorio CD, de Castro Junior CG, Brunetto AL. Autologous stem cell transplantation as first line treatment after incomplete excision of pancreaticoblastoma. *Rev Bras Hematol Hemoter* 2013; 35:148-149. [PMID: 23741195]
14. Caracciolo G, Vicedomini D, Di Blasi A, Indolfi P, Casale F, De Dominicis G, Saggiomo G, Greco N. Adenocarcinoma of the pancreas in childhood (pancreatoblastoma): report of a case with good response to chemotherapy. *Tumori* 1995; 81:391-394. [PMID: 8804461]
15. Dhebri AR, Connor S, Campbell F, Ghaneh P, Sutton R, Neoptolemos JP. Diagnosis, treatment and outcome of pancreaticoblastoma. *Pancreatology* 2004; 4:441-451. [PMID: 15256806]
16. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer* 2009; 45:228-247. [PMID: 19097774]
17. Chikamori F, Nishida S, Selvaggi G, Tryphonopoulos P, Moon JJ, Levi DM, Kato T, Island ER, et al. Effect of liver transplantation on spleen size, collateral veins, and platelet counts. *World J Surg* 2010; 34:320-326. [PMID: 20012612]
18. Melles DC, de Marie S. Prevention of infections in hyposplenic and asplenic patients: an update. *Neth J Med* 2004; 62:45-52. [PMID: 15127830]
19. Katsura S, Kawamura D, Harada E, Enoki T, Hamano K. Single-incision laparoscopic splenectomy and splenic autotransplantation for an enlarged wandering spleen with torsion. *European J Pediatr Surg Rep* 2014; 2:23-25. [PMID: 25755963]
20. Takayasu H, Ishimaru Y, Tahara K, Otani Y, Yamagishi J, Ikeda H. Splenic autotransplantation for a congested and enlarged wandering spleen with torsion: report of a case. *Surgery today*. 2006; 36:1094-1097. [PMID: 17123138]
21. Pisters PW, Pachter HL. Autologous splenic transplantation for splenic trauma. *Ann Surg* 1994; 219:225-235. [PMID: 8147604]
22. Kimura W, Inoue T, Futakawa N, Shinkai H, Han I, Muto T. Spleen-preserving distal pancreatectomy with conservation of the splenic artery and vein. *Surgery* 1996; 120:885-890. [PMID: 8909526]
23. Warshaw AL. Conservation of the spleen with distal pancreatectomy. *Arch Surg* 1988; 123:550-553. [PMID: 3358679]
24. Warshaw AL. Distal pancreatectomy with preservation of the spleen. *J Hepatobiliary Pancreat Sci* 2010; 17:808-812. [PMID: 19882099]
25. Egorov VI, Yashina NI, Zhurenkova TV, Petukhova MV, Starostina NS, Zarinskaya SA, Dmitriyeva KA, Shevchenko TV, et al. Spleen-preserving distal pancreatectomy with resection of the splenic vessels. Should one rely on the short gastric arteries? *Jop* 2011; 12:445-457. [PMID: 21904069]
26. Ferrone CR, Konstantinidis IT, Sahani DV, Wargo JA, Fernandez-del Castillo C, Warshaw AL. Twenty-three years of the Warshaw operation for distal pancreatectomy with preservation of the spleen. *Ann Surg* 2011; 253:1136-1139. [PMID: 21394008]
27. Carrere N, Abid S, Julio CH, Bloom E, Pradere B. Spleen-preserving distal pancreatectomy with excision of splenic artery and vein: a case-matched comparison with conventional distal pancreatectomy with splenectomy. *World J Surg* 2007; 31:375-382. [PMID: 17171488]
28. Tien YW, Liu KL, Hu RH, Wang HP, Chang KJ, Lee PH. Risk of varices bleeding after spleen-preserving distal pancreatectomy with excision of splenic artery and vein. *Ann Surg Oncol* 2010; 17:2193-2198. [PMID: 20309639]
29. Miura F, Takada T, Asano T, Kenmochi T, Ochiai T, Amano H, Yoshida M. Hemodynamic changes of splenogastric circulation after spleen-preserving pancreatectomy with excision of splenic artery and vein. *Surgery* 2005; 138:518-522. [PMID: 16213907]
30. Shorter NA, Glick RD, Klimstra DS, Brennan MF, Laquaglia MP. Malignant pancreatic tumors in childhood and adolescence: The Memorial Sloan-Kettering experience, 1967 to present. *J Pediatr Surg* 2002; 37:887-892. [PMID: 12037756]
31. Glick RD, Pashankar FD, Pappo A, Laquaglia MP. Management of pancreaticoblastoma in children and young adults. *J Pediatr Hematol Oncol* 2012; 34 Suppl 2:S47-50. [PMID: 22525406]
32. Klimstra DS, Wenig BM, Adair CF, Heffess CS. Pancreatoblastoma. A clinicopathologic study and review of the literature. *Am J Surg Pathol* 1995; 19:1371-1389. [PMID: 7503360]
33. Yonekura T, Kosumi T, Hokim M, Hirooka S, Kitayama H, Kubota A. Aggressive surgical and chemotherapeutic treatment of advanced pancreaticoblastoma associated with tumor thrombus in portal vein. *J Pediatr Surg* 2006; 41:596-598. [PMID: 16516645]
34. Ogawa T, Okinaga K, Obana K, Nakamura K, Hattori T, Ito T, Yanagawa Y, Tanaka F, et al. Pancreatoblastoma treated by delayed operation after effective chemotherapy. *J Pediatr Surg* 2000; 35:1663-1665. [PMID: 11083448]
35. Ohata R, Okazaki T, Ishizaki Y, Fujimura J, Shimizu T, Lane GJ, Yamataka A, Kawasaki S. Pancreaticoduodenectomy for pancreaticoblastoma: a case report and literature review. *Pediatr Surg Int* 2010; 26:447-450. [PMID: 20165952]
36. Shorter NA, Glick RD, Klimstra DS, Brennan MF, LaQuaglia MP. Malignant pancreatic tumors in childhood and adolescence: The Memorial Sloan-Kettering experience, 1967 to present. *J Pediatr Surg* 2002; 37:887-892. [PMID: 12037756]
37. Gu WZ, Zou CC, Zhao ZY, Liang L, Tang HF. Childhood pancreaticoblastoma: clinical features and immunohistochemistry analysis. *Cancer Lett* 2008; 264:119-126. [PMID: 18308466]
38. National Comprehensive Cancer Network (NCCN) Practice Guidelines for pancreatic cancer. [Available at :[http://www.nccn.org/clinical asp](http://www.nccn.org/clinical_asp)(free registration is required for login)]
39. Majima H, Ohta K. Clinical studies of (2''R)-4'-O-tetrahydropyranil adriamycin (THP). *Biomed Pharmacother* 1987; 41:237-243. [PMID: 3311190]
40. Hiyama E, Ueda Y, Onitake Y, Kurihara S, Watanabe K, Hishiki T, et al. A cisplatin plus pirarubicin-based JPLT2 chemotherapy for hepatoblastoma: experience and future of the Japanese Study Group for Pediatric Liver Tumor (JPLT). *Pediatr Surg Int* 2013; 29:1071-1075. [PMID: 24026876]