Embryonal Rhabdomyosarcoma of the Bile Ducts Causing Obstructive Jaundice in a Child: A Case Report

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ABSTRACT

Jaundice in older children can occur when any obstruction is found within the bile ducts, either from bile stones, parasites, choledochal cysts and rarely, secondary to tumors. We present a previously well, 10-year-old Filipino boy with three-week history of progressive jaundice and tea-colored urine, and was initially assessed to have biliary ascariasis. Ultrasound showed a heterogeneous focus spanning the gallbladder neck and confirmed on endoscopic retrograde cholangiopancreatography as an exophytic mass at the ampulla of Vater. Tumor biopsy and immunohistochemical staining confirmed the diagnosis of Embryonal Rhabdomyosarcoma of the Bile Ducts. Chemotherapy was initiated to reduce the size of the tumor before any surgical intervention could be attempted. Despite chemotherapy, the tumor progressively grew. He acquired a respiratory infection which led to sepsis and his eventual demise. The disease should be considered in the differential diagnosis of a child with obstructive jaundice after exclusion of other more common causes.

Keywords: Endoscopic Retrograde Cholangiopancreatography, biliary tumors, exophytic mass, case report

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INTRODUCTION

Jaundice refers to yellow discoloration of the skin, sclera, mucous membranes, and body fluids. It is a common problem that can be the presenting sign of an isolated disorders of bilirubin metabolism, liver disease or obstruction of bile ducts. Obstructive jaundice commonly occurs when biliary stones or sludge block the common bile duct or when parasites (e.g., ascaris, liver flukes) become trapped in the bile duct lumen. They can also occur secondary to conditions like primary sclerosing cholangitis, choledochal cyst, and very rarely from bile duct tumors.

Bile duct tumors have been reported in children and includes benign lesions such as adenoma and multiple papilloma, while the malignant ones are adenocarcinoma, cholangiocarcinoma, and rhabdomyosarcoma (RMS), the latter being the most common soft tissue malignancy in children but involves the bile ducts in only 25 of 4291 (0.5%) of all cases.[1] A review of literature showed that there are less than 100 reported cases in children with age range from 0.4 to 14 years old.[1-22] Eighty percent of patients presented with jaundice. Locally, using the Philippine Pediatric Society Disease Registry of 4,430,797 entries recorded from the year 2001 to the present, there were only eight recognized cases of malignant neoplasm arising from the biliary tract, but the nature of the neoplasm was not specified. In adults,

there are ten cases of rhabdomyosarcoma of the gall bladder, not the bile ducts.[23-25]

In this report, we present a child with history of an obstructive jaundice and was diagnosed as Embryonal Rhabdomyosarcoma of the Bile Ducts. Both parents were informed and gave verbal consent for the case to be reported. An assent was also obtained from the patient.

CASE REPORT

A 10-year-old boy presented with a 3-week history of gradually progressive jaundice with tea colored urine but no acholic stool or pruritus. He had no other signs and symptoms of abdominal pain, bleeding, weight loss, decreased appetite, bowel changes, fever, or vomiting. Consult was done and a whole abdomen ultrasound was requested which showed the presence of tubular hyperechoic structures in the dilated common bile duct (7 cm). Biliary ascariasis was considered. The patient was conservatively managed with Mebendazole anti-helminthic therapy but his symptoms persisted with deepening of jaundice thus prompting consult and admission at our institution for further evaluation and management.

There was no previous passage of worms, intake of any medication nor tuberculosis exposure. There was no family history of liver disease or malignancy. He is a Grade 5 student, with an average performance.

On physical examination, the child was well nourished (BMI: 15.3, Z score 0) with generalized jaundice. His abdomen was flat, with no visible epigastric vessels. He had normoactive bowel sounds and non-tender abdomen on all quadrants during deep palpation. The liver was firm and sharp with the edge palpable 3 cm below the right costal margin and 5 cm sub-xiphoid. The spleen was not palpable. There was no ascites.

Initial complete blood count showed anemia [hemoglobin 86g/L (N: 119 – 150g/L)], leukocytosis [WBC: 15.2 (N: 4.5 to 13 x10^9/L)] and thrombocytosis [platelet count: 623 10^9/L (N: 150 to 450 x10^9/L)] but without eosinophilia. The transaminases were slightly increased [Aspartate aminotransferase (AST) 127 IU/L (N: 17 – 59 IU/L); Alanine aminotransferase (ALT) 65 IU/L (N: <50 IU/L)] but with a markedly elevated alkaline phosphatase 745 IU/L (N: 3 – 126 IU/L) and gamma glutamyl transferase (GGT) 496 U/L (N: 15 – 73 U/L). The total bilirubin was elevated [11.58 mg/dL (NV: 0.2 – 1.3 mg/dL)] which was predominantly direct [10.15 mg/dL (0.0 – 0.4 mg/dL)]. The liver synthetic function indicated an elevated INR of 2.34 but with normal Albumin [44g/L (N: 35 -50g/L)]. Serological markers for HBsAg, Anti-HAV IgM and IgG were non-reactive.

A repeat abdominal ultrasound was done on our institution which showed unenlarged liver but with a heterogeneous parenchymal echo-pattern. A fairly-defined heterogeneous focus that measures approximately 8.3 x 2.1 cm was seen spanning the gallbladder neck up to the dilated common bile duct (1.3 cm). The right main intrahepatic duct (4.4 cm) and left main intrahepatic duct (1.3 cm) were also dilated as well as their 1st order radicles. Portal, intrahepatic veins, and the inferior vena cava were unremarkable. The previously noted tubular hyperechoic structures were no longer seen, therefore the possibility of a neoplastic lesion was considered.

An endoscopic retrograde pancreatography (ERCP) was performed to further visualize the lesions in the bile ducts. ERCP displayed an ampulla of Vater that had a bulbous, nodular, friable, and exophytic mass (Figure 1). Cholangiogram

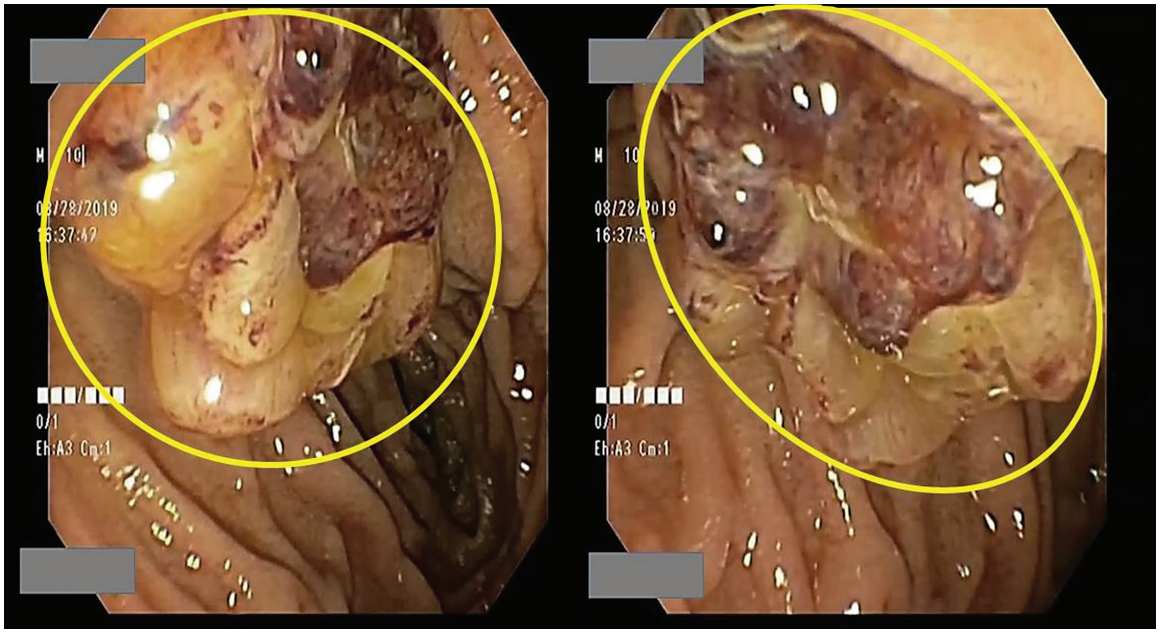

Figure 1. A bulbous, nodular, friable and exophytic mass *(yellow circles)* at the Ampulla of Vater seen during ERCP.

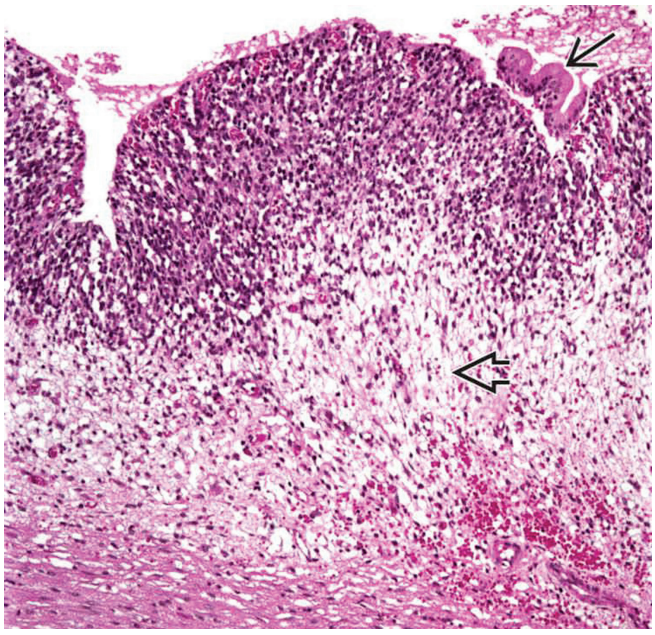

Figure 2. Cambium Layer: characteristic cambium layer consists of densely packed tumor cells beneath biliary epithelium which is largely denuded *(top arrow)*. Deeper portion of tumor is hypocellular with loose myxoid stroma *(middle arrow)*.

showed dilated common bile duct (16 mm), common hepatic duct (17.2 mm), right intrahepatic duct (8.4 mm), left intrahepatic duct (8.2 mm) with multiple ovoid filling defects seen spanning from the proximal to distal common bile duct. The tissue biopsy (Figure 2) for both the duodenal ampullary mass and common bile duct mass revealed chronic inflammation and foci of stromal expansion along with identification of a Cambium layer. On histochemical staining, both tissues tested positive for Vimentin, smooth muscle actin (SMA), Myogenin and MYOD1 which confirms the diagnosis of embryonal rhabdomyosarcoma of the bile ducts.

Based on the findings of the ERCP, a chest and abdominal computer tomography (CT) scan was then performed to document the extent of the lesion, the possibility of metastasis, and then formulate a plan for possible surgical resection. The chest CT scan was unremarkable. The abdominal CT scan confirmed the presence of the mass in the porta hepatis (6.3 x 3.2 x 4.2 cm) extending to the neck and proximal body of the gallbladder and also to the body and uncinated process of the pancreas (Figure 3). The liver was enlarged with no focal lesions seen.

On exploratory laparotomy, the multi-lobulated mass was noted starting at the Hartmann's pouch extending to the common hepatic duct and distally to the common bile duct up to the duodenum (Figure 4). Detailed inspection of the whole pancreas was done and no tumor extension was documented. Due to the lesion's configuration and extent, only a biopsy of the mass was performed as resection was not yet an option. Neo-adjuvant chemotherapy was initiated to reduce the size of the tumor before any surgical intervention could be attempted.

The final diagnosis was Biliary Rhabdomyosarcoma, embryonal type, stage I group 3 according to the Tumor, Node, and Metastases pre-treatment staging system[26] (Tables 1 and 2).

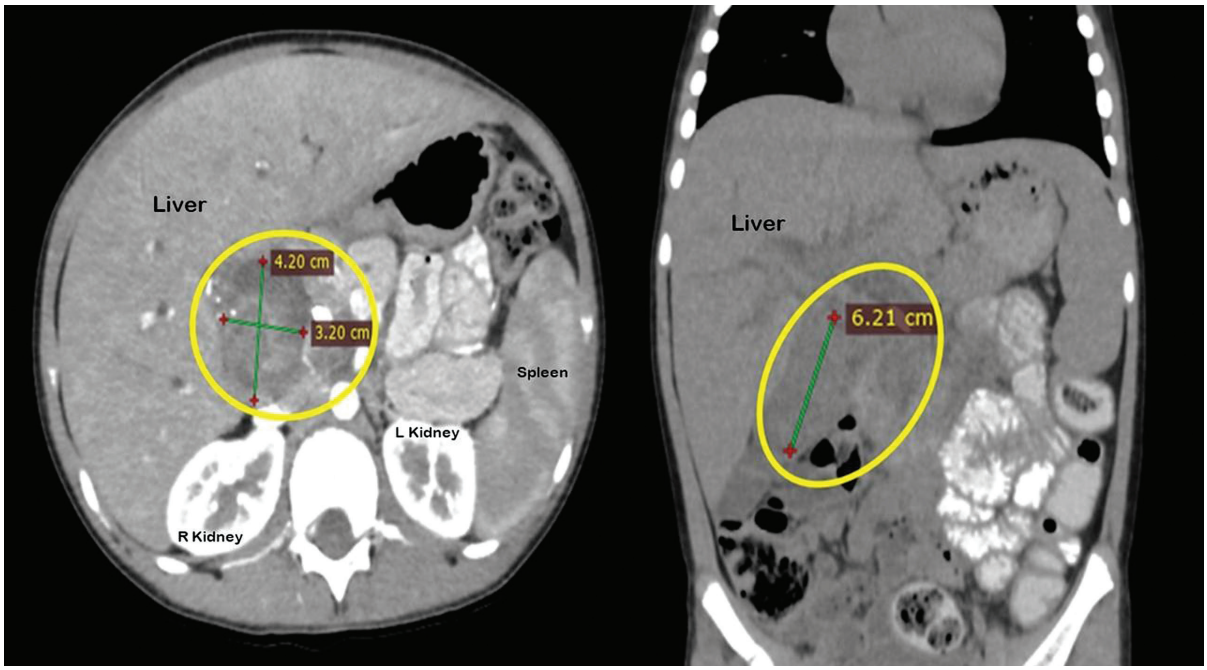

Figure 3. Porta hepatis mass *(yellow circles)* extending to the neck and proximal body of the gallbladder and pancreas.

Table 1. IRSG Surgical-pathologic Grouping system[26]

Group	Definition
I	Localized tumor, completely removed with pathologically clear margins and no regional lymph node involvement
II	Localized tumor, grossly removed with (a) microscopically involved margins, (b) involved, grossly resected regional lymph nodes, or (c) both
III	Localized tumor, with gross residual disease after grossly incomplete removal, or biopsy only
IV	Distant metastases present at diagnosis

Table 2. IRSG Staging System[26]

Stage	Sites of primary tumor	Tumor size (cm)	Regional lymph nodes	Distant metastases
1	Orbit, non-PM head/ neck; GU non-bladder/ prostate; Biliary tract	Any size	N0, N1	M0
2	All other sites	≤5 cm	N0	M0
3	All other sites	≤5 cm >5 cm	N1 N0 or N1	M0
4	Any site	Any size	N0 or N1	M1

PM – Parameningeal; GU – genito-urinary; N0 – regional nodes not clinically involved; N1 – regional lymph nodes clinically involved by tumor, M0 – no distant metastases; M1 – distant metastasis at diagnosis

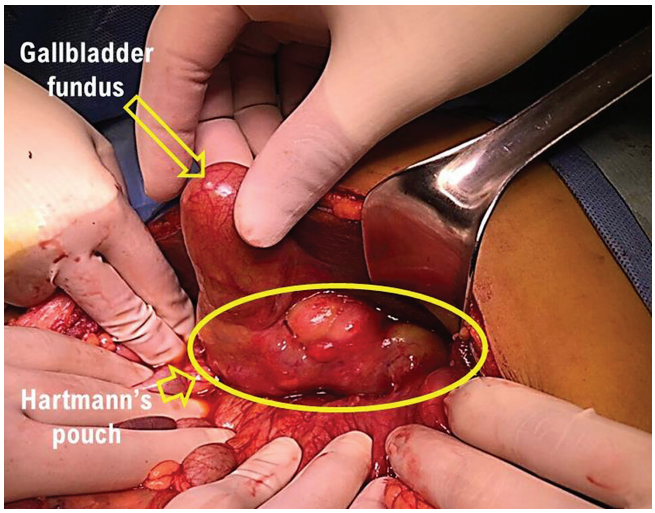

Figure 4. Intraoperative images of a multi-lobulated mass at Hartmann's pouch *(yellow circle)*.

Patient was subsequently referred to Pediatric Hematology Oncology service and underwent chemotherapy with standard doses of Vincristine, Actinomycin D, and Cyclophosphamide (VAC therapy). After completing 15 courses of VAC therapy, repeat abdominal CT scan showed progression of size (7.8 x 5.2 x 5.3 cm) of previously identified mass. Chemotherapy was re-started and shifted to Vincristine, Doxorubicin, Cyclophosphamide, Ifosfamide, and Etoposide regimen. However, after two courses of chemotherapy, the patient's clinical status deteriorated when he acquired a respiratory infection which led to sepsis and his eventual demise.

DISCUSSION

We present a rare case of embryonal rhabdomyosarcoma of the bile ducts in a 10-year-old Filipino boy who exhibited progressive jaundice that was initially believed to be from biliary ascariasis but on detailed evaluation eventually proven to be secondary to malignant neoplasm. Obstructive jaundice was considered on the basis of jaundice, direct hyperbilirubinemia, and a markedly elevated gamma glutamyl transpeptidase, an enzyme assay specific for bile ducts. This was further supported by imaging studies, which included an ultrasound of the hepatobiliary tree and a CT scan of the abdomen, that demonstrated a mass compressing on the biliary tree. The character of the tumor was confirmed by the biopsy done during ERCP and exploratory laparotomy.

Rhabdomyosarcoma is the most common form of soft tissue sarcoma and is the third most common extracranial solid tumor of childhood after Wilms tumor and neuroblastoma. It is a malignant mesenchymal tumor that is included in a group of small blue round cell tumors like neuroblastoma, lymphoma, and primitive neuroectodermal tumors (PNET). The pathogenesis of RMS remains unclear; however, it is thought that it arises due to the disruption of skeletal muscle progenitor cell growth and differentiation.[27]

RMS of the bile ducts is a very rare childhood disease and according to the Intergroup Rhabdomyosarcoma Studies I-IV report conducted between 1972 and 1998, only 0.5% of cases (25 of 4291) involved the intrahepatic or extrahepatic biliary tree.[1] In a more recent survey by the European Pediatric Soft-Tissue Sarcoma Group, 30 out of the 1752 (1.7%) patients were diagnosed to have the disease during an 11 year period.[2] Overall, there are only 97 reported cases of childhood rhabdomyosarcoma of the bile ducts, 82 from case series and 15 case reports, with the youngest at 5 months[3] and the oldest at 14 years old[8]. There is no local publication on the disease. In 79 cases that reported the initial presentation of the patient, 80% were jaundiced.[1-22] Other associated symptoms included abdominal pain (25%) and fever (20%), and only a few cases had abdominal distension (8%) and vomiting (8%). Since the presence of jaundice is alarming, patients with biliary rhabdomyosarcoma usually seek medical consult early and a prompt diagnosis can be made. Our patient was diagnosed after four weeks from the onset of symptoms. In a study of 10 cases from Italy, the average range of time to arrive at a diagnosis was 0 to 16 weeks (mean of 0.9 weeks).[22] The initial assessment of our case was a biliary ascariasis on the basis of an ultrasound finding of a tubular hyperechoic structure in the common bile duct. Although ascariasis is endemic in our country, the patient has no previous history of passage

of worms and does not have the characteristic description of one infected with ascariasis who is stunted, malnourished, and with cognitive dysfunction.[28] He is a well-nourished boy with no stunting and with average school performance. In the 15 published case reports on biliary rhabdomyosarcoma, choledochal cyst was the initial assessment in seven[1,9-11,15-17], as it is one of the typical differential diagnosis for obstructive jaundice in children, while one case of each was initially diagnosed as gall bladder hydrops[16] and hepatic hydatid cyst[18]. The diagnosis of the other six reports were not indicated.

A study from North America considered early life factors like gender, high birth weight of term births, all births adjusted for gestational age, history of prenatal care, and paternal age at birth with suspected RMS etiology. However, the only finding with positive association for all RMS types was the male gender of patients which was similar with our case.[29]

Different imaging studies were done on our patient as well as in the different case reports which include ultrasound of the hepatobiliary tree, CT scan of the abdomen and magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography (MRCP). Ultrasound is the imaging of choice in the initial evaluation of the jaundiced child as it is non-invasive and readily available, but it is operator dependent.[30] Contrasting reports were seen in the two ultrasounds done on the patient. The initial one showed dilatation of the common bile ducts (1.2 and 1.3 mm, normal value: <7 mm) and hepatic ducts with tubular hyperechoic structures which lead to a diagnosis of biliary ascariasis. The second ultrasound demonstrated an 8 cm mass from the gall bladder neck up to the dilated common bile ducts and hepatic ducts with a neoplastic lesion considered. Given these findings, an ERCP was done to ascertain the exact nature of the bile duct obstruction thru a tissue biopsy and if needed, stenting of the common bile duct.[15] The obstruction was identified as a tumor and based on the histology of chronic inflammation, foci of stromal expansion, and presence of Cambium layer; it was considered as malignant. Immunochemical staining showed positivity for vimentin, an antibody common in progenitor cells; for myogenin and MYOD1 which documented myogenic differentiation; and the smooth muscle actin which stains the more differentiated cells.[31] Further CT scan was performed to better evaluate local extent and facilitate staging.

The patient was classified as Stage 1 based on the site of the primary tumor (biliary), tumor size (any), and the absence of tumor-involved regional lymph nodes and distant metastases (Table 2). Patient was also classified as low risk, subgroup B based on the age (<21 years old), favorable site (non-orbit), histologic type (embryonal), and absence of nodal and distant metastases.[32] Since the tumor could not be excised on exploratory laparotomy, it is classified as Grade III based on the surgical pathologic grading system, with only localized tumor.[32] (Table 1)

Patients with rhabdomyosarcoma has been treated with a combination of surgery, chemotherapy, and irradiation. The initial exploratory laparotomy of our patient could have been avoided as a complete primary resection of the tumor can only be achieved in 20% of cases.[3] The plan for our patient is chemotherapy with Vincristine, Actinomycin D, and Cyclophosphamide (VAC) for shrinkage of the tumor followed by delayed excision of initially unresected mass. The mass however progressively grew in size even after 15 courses of VAC therapy. In some cases, if the mass remains unresectable even after chemotherapy, liver transplantation has been done with favorable outcome.[14] There is no evidence to show that our patient will benefit from radiotherapy as the lesion is localized. The estimated cancer-free survival of patients with and without irradiation are similar (49% vs 47%).

Prognosis of our patient would have been favorable if resection of the tumor was possible. In a study of 17 children with rhabdomyosarcoma of the biliary tree with a median age of four years, the five-year overall and estimated free survival were 58% (45–71) and 47% (34–50), respectively[3]. Age and histology type were important predictive factors with better outcome for those ≤10 years of age and in those with embryonal rather than alveolar rhabdomyosarcoma, both of which are present in our patient. However, even with chemotherapy, tumor progression was noted with involvement of the para-aortic and aortocaval lymph nodes on imaging. This may be due to the patient's large tumor size (>5 cm) which is associated with poorer outcomes as compared to smaller (<5 cm) ones.[33]

CONCLUSION

In summary, we have reported a rare case of a 10-year-old Filipino boy with embryonal rhabdomyosarcoma of the biliary duct who presented initially with progressive jaundice and was initially diagnosed as biliary ascariasis. The disease should be considered in the differential diagnosis of a child with obstructive jaundice after exclusion of other more common causes.

Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

Both authors declared no conflicts of interest.

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