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Case Report

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Botryoid Rhabdomyosarcoma of Common Bile Duct - When Surgery Should Take a Step Back

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Abstract

Biliary rhabdomyosarcoma is a rare malignant tumor of childhood. At presentation, the most frequent symptom is cholestatic jaundice, which also occurs in cholestatic hepatitis, gallbladder and choledochal stones, and choledochal malformation (choledochal cyst). The botryoid variant, with its typical grape-like growth pattern, is the most frequent form of rhabdomyosarcoma affecting the biliary tract. Being a highly chemosensitive tumor, its prognosis has greatly improved in recent years, relegating surgery to a secondary role.

We report a 2 year old girl referred for a choledochal malformation. Suspicion of a neoplastic lesion at the diagnostic imaging, was confirmed at biopsy as a botryoid rhabdomyosarcoma of the common bile duct. Staging imaging did not show metastases, and the child was treated with chemotherapy only and no surgical resection. Ten months after the diagnosis the child is well without tumor recurrence.

This case demonstrates that '*one should step back*' from immediate surgery because chemotherapy can be equally effective.

Keywords: Botroyd rhabdomyosarcoma; Biliary rhabdomyosarcoma; Botryoid rhabdomyosarcoma of common bile duct.

Abbreviations: RMS: Rhabdomyosarcoma; BoRMS: Botryoid Rhabdomyosarcoma; CBD: Common Bile Duct.

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Introduction

Rhabdomyosarcoma (RMS) is a soft tissue malignant neoplasm with skeletal muscle differentiation arising as a consequence of regolatory disruption of skeletal muscle progenitor cell growth and differentiation [1]. It can originate in the head and neck, the limbs, and genitourinary tract [2]. Biliary RMS is extremely uncommon and was first described in 1875 by Wilks and Moxon [3]. Patients with biliary RMS are children with a median age of 3.4 years [4]. Biliary RMS represents 0,5 – 1,5% of all RMS in childhood [5] with the embryonal and alveolar varieties as the most common histological types. There are 2 subvariants of the embryonal type, spindle-cell and botryoid [1], of which the botryoid variant (BoRMS) is the more frequent. This type of tumor is very rare and accounts for 0,04% of childhood primary neoplasms [6]. BoRMS is characterized by large polypoid mass lesions with a grape-like pattern [7], with possible invasion of the liver, pancreas, and duodenum [8]. Because of its rarity, BoRMS is frequently misdiagnosed as a choledochal malformation. However careful examination of a diagnostic cholangio MRI should give rise to a serious suspicion of neoplasia and should lead to biopsy.

60-80% of biliary RMS presents with obstructive jaundice and may also be associated with abdominal pain, abdominal distension, acholic stool, anorexia, nausea, vomiting and fever [4]. More than 95% of these tumors are positive for desmin and myogenin, a gene product that induces skeletal muscle differentiation [5].

In 1956 Farinacci et al [9] and Akes et al [10] in 1971 considered BoRMS as a 'rentless, insidious, infiltrative, incurable growth that usually kills the patient'. A multimodal approach and the high chemosensitive of biliary RMS has lead to a 75% patients 5 year survival rate [11,12]. Indeed Fuchs et al Fuchs in a systematic review and meta-analysis in 2021 [13], reported complete remission and long-term survival without the need for any surgical tumor resection. The high tumor chemosensitivity has forced a *'step-back',* relegating open surgery to confirmatory histological biopsy when other diagnostic tools such us percutaneous or endoscopic biopsy, are not available [1,2].

We report the case of a 2-year-old girl with BoRMS of the Common Bile Duct (CBD) that was successfully treated only with chemotherapy.

Case report

A healthy 2-year-old girl was referred following a three-day history of jaundice, itching, hyperchromic urine, non-acholic stools, and fever (39,5°C). Her previous medical history was unremarkable. Physical examination revealed jaundice, a 2 cm palpable liver below the subcostal margin but no splenomegaly. Laboratory investigations showed total bilirubin 11,59 mg/dL (direct 7,76 mg/dL), ALT 438 U/L, AST 304 U/L, GGT 561 U/L. Abdominal ultrasound showed marked dilation of the extra- and intrahepatic biliary tree and mild dilation of the main pancreatic duct. Abdominal magnetic resonance (MRI) revealed a 10 mm dilatation of the Common Bile Duct (CBD) and sludge in the gallbladder, that lead to consideration of a choledochal malformation.

When admitted to our department, the child was generally unwell with worsening jaundice (total bilirubin: 12,33 mg/dL). Abdominal ultrasound showed a right hepatic duct at 4mm diameter, a left hepatic duct at 5 mm and a common hepatic at 11 mm with an enlarged galbladder. A percutaneous drain (8 Fr 40 cm) was placed in the gallbladder. A Magnetic Resonance Cholangiopancreatography (MRCP) showed dilation of the intra and particularly the extrahepatic bile ducts and showed a large filling defect in the lumen of the Common Bile Duct (CBD) that was not consistent with sludge or calculi (Figure 2) A percutaneous transhepatic cholecystocholangiography, performed through the biliary drain, confirmed a 3 cm filling defect in the CBD. There were no pancreatic abnormalities (Figure 3). On suspicion of a biliary tumor a percutaneous biopsy (Biopince 18G 10 cm) was undertaken. The specimens were sent for histological examination that revealed 'atypical cellularity composed of small round cells with eosinophilic cytoplasmic extensions and small round nuclei with dense chromatin'. The cells were embedded in a myxoid matrix with a hypercellular zone (cambium layer) immediately beneath the epithelium (Figure 4). Immunohistochemical staining was positive for myogenin and desmmin and negative for keratin, S100, MyoD1 and smooth muscle actin (Figure 5). The Ki67 was 40%. The phenotypic profile indicated an embryonic rhabdomyosarcoma with neoplastic cellularity bordering an epithelial flap pathognomonic of the botryoid variant. A total-body PET/TC for staging showed FDG uptake only at the level of the CBD [Figure 7]. There were no thoracic metastases and the bone marrow was normal.

Treatment followed the protocol of the European Paediatric Soft Tissue Sarcoma Study Group (EpSSG) 2005 for nonmetastatic rhabdomyosarcoma and consisted of cyclophosphamide, vincristine and dactinomycin. Prior to chemotherapy, the gallbladder drain was removed and replaced with an internal biliary stent (Wallflex 8 cm length and 8 mm diameter) at Endoscopic Retrograde Cholangiopancreatography (ERCP) (Figure 6). At this procedure, neoplastic tissue of pseudonodular morphology was found to have extended up to the division of hepatic ducts.

Following 2 months of chemotherapy, the cholestasis was relieved and a second ERCP was undertaken to remove the biliary stent and for further biopsies that were negative for neoplasia.

Abdominal MRI and chest CT scans 6 months after commencing showed complete tumor regression and no adenopathies or focal lesions. Following completion of chemotherapy the child is doing well with no evidence of relapse (Figure 8).

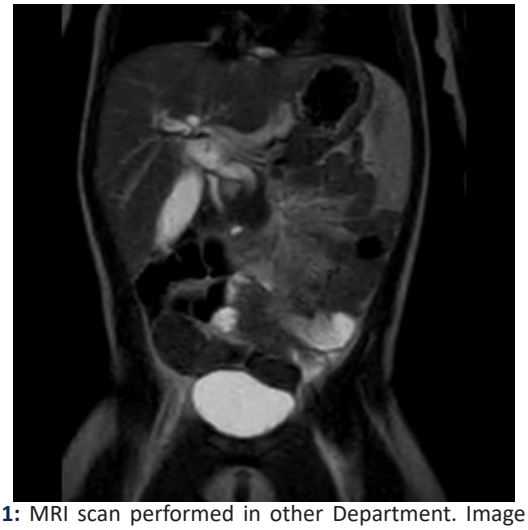

Figure 1: MRI scan performed in other Department. Image shows dilatation of common bile duct with heterogeneous intensity suggestive of choledochal cyst.

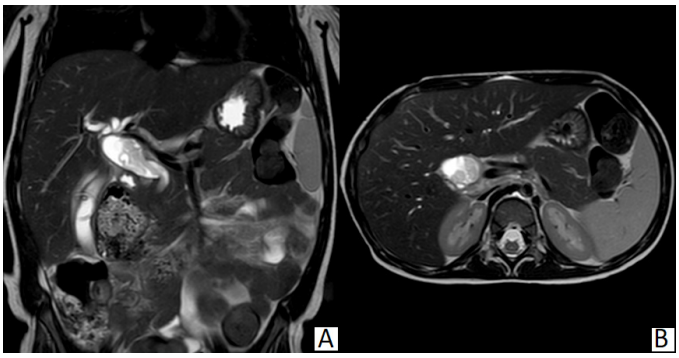

Figure 2: Coronal (A) and axial (B) MRI scans performed in our Department show dilation of the biliary tree and heterogeneous fillining defect in the lumen of the choledochus (arrow) characterized by solid component.

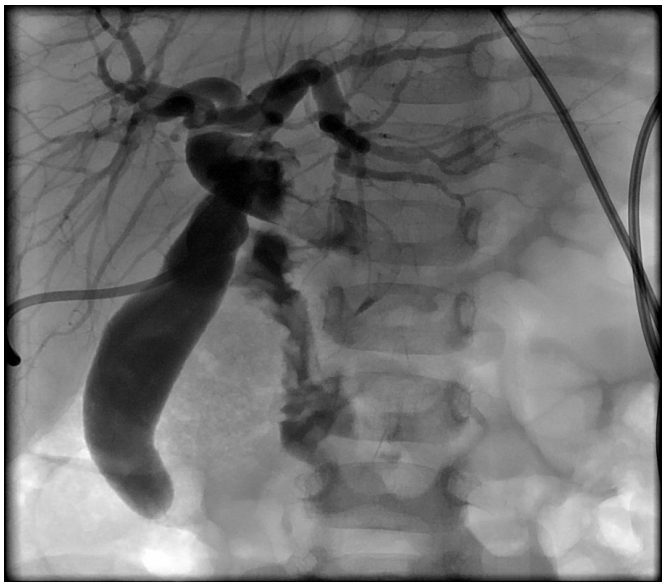

Figure 3: Image acquired during percutaneous transhepatic cholangiography. The biliary tract is dilated and a filling defect in the choledochus with irregular material is visible.

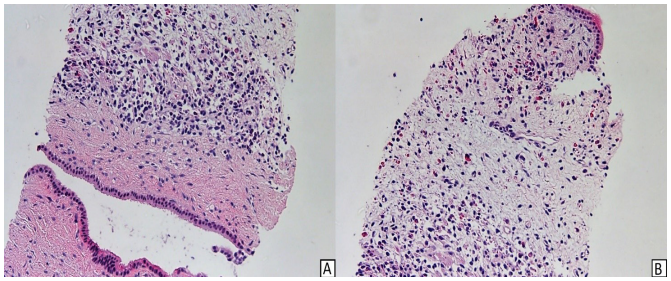

Figure 4: (H&E, 10x) Histopathological appearance of the tumor shows small round cells, eosinophilic cytoplasmic projections and round in a myxoid stroma suggestive of skeletal muscle differentiation. Hypercellular area just beneath the epithelium with a tumor-free zone is a typical botryoid rhabdomyosarcoma's pattern, called "cambium-layer".

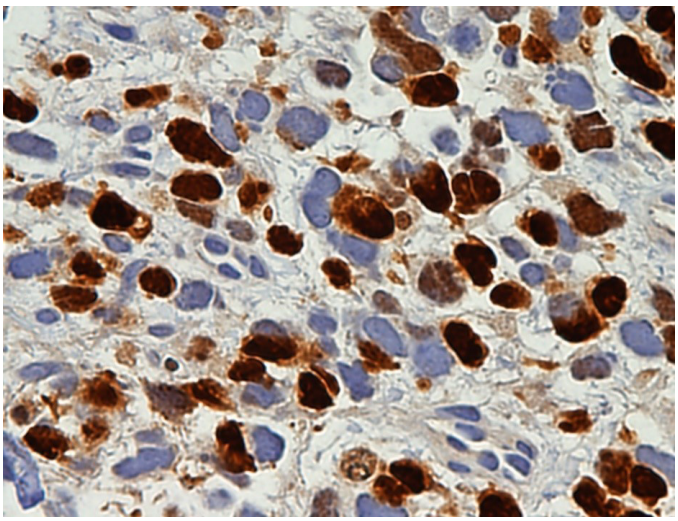

Figure 5: Tumor cells show positive immunostains for myogenin. The expression of myogenin has been demonstrated to be extremely specific for rhabdomyoblastic differentiation.

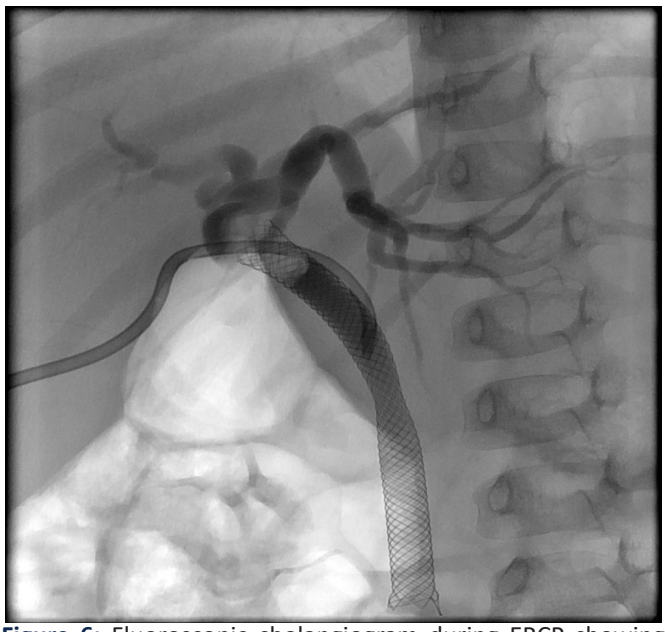

Figure 6: Fluoroscopic cholangiogram during ERCP showing a dilatation of biliary tree and the presence of internal stent (Wallflex 8 cm in length and 8 mm in diameter).

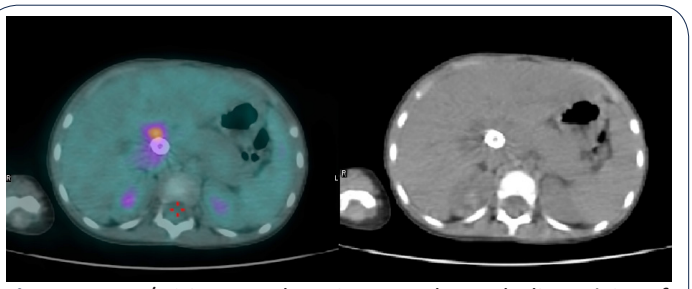

Figure 7: PET/TC images show increased metabolic activity of the common bile duct at the level of the internal stent.

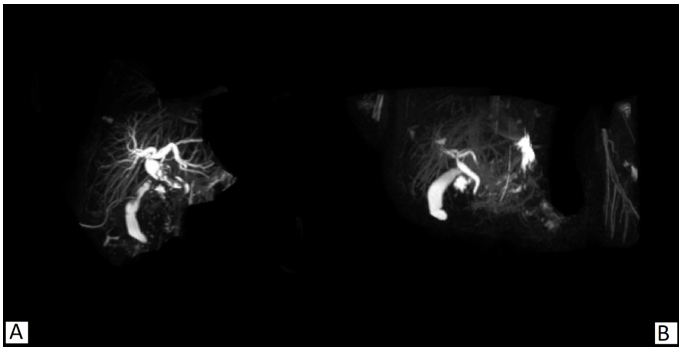

Figure 8: Magnetic resonance cholangiopancreatography (MRCP) pre- (A) and post-(B) chemotherapy. The dilation of the biliary tree and the heterogeneous filling defect in choledochus are no longer present after treatment. In image B no residual tumor is visible.

Discussion

Biliary RMS is a malignant tumor of young children. It typically arises in the CBD but can originate anywhere in the biliary tree. Typical symptoms are jaundice, abdominal pain and distention, acholic stools, nausea, vomiting and fever [4] that can mimic other conditions, such as cholestatic hepatitis, stones in the extrahepatic biliary tree, and choledocal malformations. The recent literature reports several patients who have undergone surgery because of such misdiagnoses, particularly choledochal malformations [6,11,14-23].

The goal of surgery was a complete resection of the primary tumor [2,14] that could be difficult to achieve, particularly at the the biliary-pancreatic junction where a duodeno-cephalopancreatectomy was often required with significant incidence of complications [24]. In 1997, Sanz et al reported the first case of a complete response to a combination of chemotherapy and radiotherapy for an unresectable biliary RMS [25]. Since then the prognosis for children with RMS has markedly improved as a result of such multi-modal treatment [24] that is now the recommended management for patients with biliary RMS [1]. In particular BoRMS [1] carries a more favorable prognosis such that primary surgery and radiotherapy are avoidable [24]. In the event of surgery for a misdiagnosis, a biopsy for histological examination rather than resection of the lesion is recommended [24].

As a general principle a suspicion of a biliary tumors on imaging or ERCP, should lead to a biopsy [24] for confirmation of diagnosis and should be followed by chemotherapy as the recommended form of management [24]. In the event of obstructive jaundice, an internal biliary stent placed at ERCP, rather than a percutaneous biliary drain, carries has a lesser risk of infection during chemotherapy [27]. Surgery should be reserved for the small subset of patients with persistent tumor after chemotherapy. Most children with biliary RMS without distant metastasis, can expect long-term survival [8] with 100% survival for the botryoid subtype [24].

Conclusion

Biliary rhabdomyosarcoma is a rare tumor, but must be considered in the differential diagnosis of a child with obstructive jaundice. Radiological evidence of grape-like intraluminal masses favour BoRMS. Following diagnostic biopsy (percutaneous, endoscopic, surgical), multimodal management with chemotherapy and radiotherapy is now the recommended form of management, with chemotherapy alone for the botryoid variety. We emphasize that surgery now takes “a step back” and is only recommended for persistent tumor following chemotherapy.

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