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Cholestatic syndrome as a presentation of non-Hodgkin lymphoma. A pediatric case report

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ABSTRACT

Cholestatic jaundice is due to an alteration in conjugated bilirubin secretion; a possible cause is an altered bile flow resulting from an obstruction of the extrahepatic bile duct. A lymphoma is the third most common neoplasm in pediatrics, while pancreatic tumors are rare and mostly benign. The clinical manifestations of retroperitoneal tumors are not very specific and are usually late, so a high level of clinical suspicion is required.

The objective of this study is to describe the case of a 7-year-old boy with cholestatic syndrome with a tumor in the head of the pancreas compressing the extrahepatic bile duct. The tumor diagnosis was non-Hodgkin lymphoma (NHL). It is worth noting that the presence of a tumor in this location in pediatric age is uncommon.

Key words: *cholestatic jaundice; non-Hodgkin lymphoma; retroperitoneal neoplasms; pancreatic neoplasms.*

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INTRODUCTION

Cholestatic syndrome is due to an alteration in conjugated bilirubin secretion caused by hepatocellular disease or an altered bile flow within the bile duct. Outside the neonatal period, the causes of jaundice secondary to bile duct involvement include biliary atresia, congenital biliary dilatation, gallstones, and less frequently, intrinsic biliary tumors or tumors compressing the bile duct, such as lymphomas or pancreatic tumors, among others.[1]

Lymphomas are the third most common type of neoplasm in pediatrics.[2] In most cases, they originate in the lymph nodes; however, they can develop in primary lymphoid tissues (bone marrow, thymus), secondary lymphoid tissues (spleen), or non-lymphoid organs (skin, bones, pancreas, etc.).[2] Pancreatic tumors are rare in pediatrics and are usually benign, such as ampullary tumors or adenomas.[3]

The clinical manifestations of retroperitoneal tumors are not very specific: abdominal pain, nausea, vomiting, dyspepsia, or jaundice. Given their location, manifestations usually occur late,[4] so a high level of clinical suspicion is required for an early diagnosis and timely treatment.

Here we describe the case of a 7-year-old boy with cholestatic syndrome who consulted for anorexia, abdominal pain, and jaundice. During hospitalization, a tumor was found in the head of the pancreas that was compressing the extrahepatic bile duct. The biopsy result confirmed the diagnosis of non-Hodgkin lymphoma (NHL). This form of presentation has only been observed in isolated case reports in the pediatric population.

CASE REPORT

A 7-year-old boy, with no relevant medical history, started with anorexia, weight loss, and intermittent abdominal pain 10 days before the consultation, in addition to jaundice and choluria in the past 48 hours. He was seen at Hospital de Niños Ricardo Gutiérrez, where he was found in a poor general condition, with generalized

Table 1. Blood lab tests upon admission

Lab test	Patient's value	Reference value
Leukocytes	8900/mm^3	4.5–13.5
Hemoglobin	5 mg/dL	11.5–15.5
MCV	78 fl	77–86
MCHC	33.5 g/dL	29.6–35
MCH	26 pg	25.5–28.8
Platelets	461 000/mm^3	150 000–450 000
PT	25%	70–120
aPTT	28 s	26–45
Total bilirubin	6.10 mg/dL	< 1.20
Conjugated bilirubin	5.85 mg/dL	< 0.33
AST	172 U/L	< 40
ALT	209 U/L	< 41
GGT	408 U/L	< 60
AP	1389 U/L	142–335
Amylase	91 U/L	28–100
Urea	13 mg/dL	8–41
Total proteins	6.3 g/dL	6.0–8.0
Albumin	3.8 g/dL	3.8–5.4
Uric acid	4.3 mg/dL	3.4–7.0
Calcium	9.4 mg/dL	8.8–10.8
Phosphorus	4.3 mg/dL	3.1–5.5
Magnesium	2.0 mg/dL	1.7–2.2
Sodium	139.7 mmol/L	135–145
Potassium	3.96 mmol/L	3.50–5.30
Chlorine	106.0 mmol/L	98–106

MCV: mean corpuscular volume. MCHC: mean corpuscular hemoglobin concentration.
MCH: mean corpuscular hemoglobin. PT: prothrombin time. aPTT: activated partial thromboplastin time.
AST: aspartate aminotransferase. ALT: alanine aminotransferase. GGT: gamma-glutamyltransferase. AP: alkaline phosphatase.

jaundice. His abdomen was soft, depressible, and non-tender. A tumor with ill-defined margins and soft consistency was found in the right upper quadrant. The patient had normal colored stools and choluria.

The patient was admitted to the hospital for diagnosis and management. A full blood panel was ordered (*Table 1*), and the following altered values were reported: total bilirubin: 6.10 mg/dL; conjugated bilirubin: 5.85 mg/dL; aspartate aminotransferase (AST): 172 U/L; alanine aminotransferase (ALT): 209 U/L; gamma-glutamyltransferase (GGT): 408 U/L; alkaline phosphatase (AP): 1389 U/L; leukocytes: 8900/mm^3; hemoglobin: 5 mg/dL; prothrombin time (PT): 25%; activated partial thromboplastin time (aPTT): 28 seconds.

In order to identify the etiology of the cholestatic syndrome, the following serologies were ordered: hepatitis B, C, and A, HIV, cytomegalovirus, Epstein Barr virus, toxoplasmosis, and nontreponemal tests; all results were negative. An abdominal Doppler ultrasound showed a heterogeneous retroperitoneal mass with defined margins and irregular peripheral and central vascularization. A computed tomography (CT) with oral and intravenous contrast was performed to establish the characteristics of the image mentioned above (*Figure 1*). It showed that the liver's shape and size were preserved; the gallbladder was greatly distended, but did not contain gallstones. It also showed dilatation of the intrahepatic and extrahepatic bile duct in its proximal portions, but it was not possible to see the distal portions at the level of the pancreatic head. There, a soft mass with ill-defined margins was identified, which showed homogeneous enhancement with intravenous contrast. It measured approximately 47 × 35 mm in diameter. The pancreatic duct was dilated and measured 3 mm.

A diagnosis was made of obstructive jaundice as a consequence of extrinsic biliary compression caused by a tumor. The initial presumptive diagnosis was a malignancy due to the patient's general status. Other possible causes included benign neoplasms. At first, endocrine neoplasms were not considered.

In order to establish an etiological diagnosis, an exploratory laparotomy to obtain a biopsy specimen of the lesion and an intraoperative cholangiography were performed (*Figures 2* and *3*). A tumor was found in the head of the pancreas, causing compression at the level of the common bile duct. The cholangiography showed dilatation of the intrahepatic and extrahepatic bile duct and pancreatic duct, without intraluminal involvement. A biopsy of the pancreatic tumor was performed at the level of the unaffected portion of the pancreas and a regional lymph node. A drainage was left in the bile duct. After the procedure, the patient showed an improvement in his general status and in relation to cholestasis.

The pathological study of the tumor reported diffuse large B-cell lymphoma. The specimen corresponding to the unaffected portion of the pancreatic parenchyma was also analyzed and it showed that the tissue architectural structure was preserved; the biopsy of the lymph node showed reactive alterations.

Figure 1. Double-contrast computed tomography. A: Axial section. B: Coronal section. (Right arrow: distended gallbladder. Left arrow: tumor in the head of the pancreas)

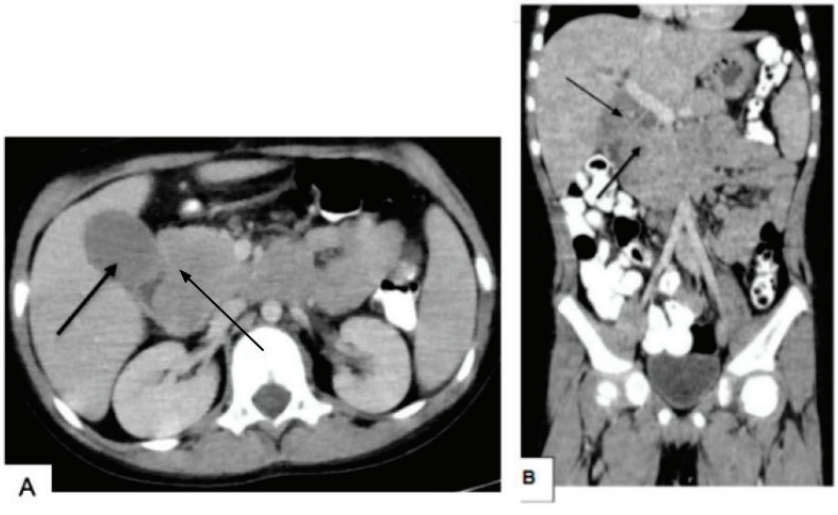


Figure 2. The tumor is very close to the duodenal section

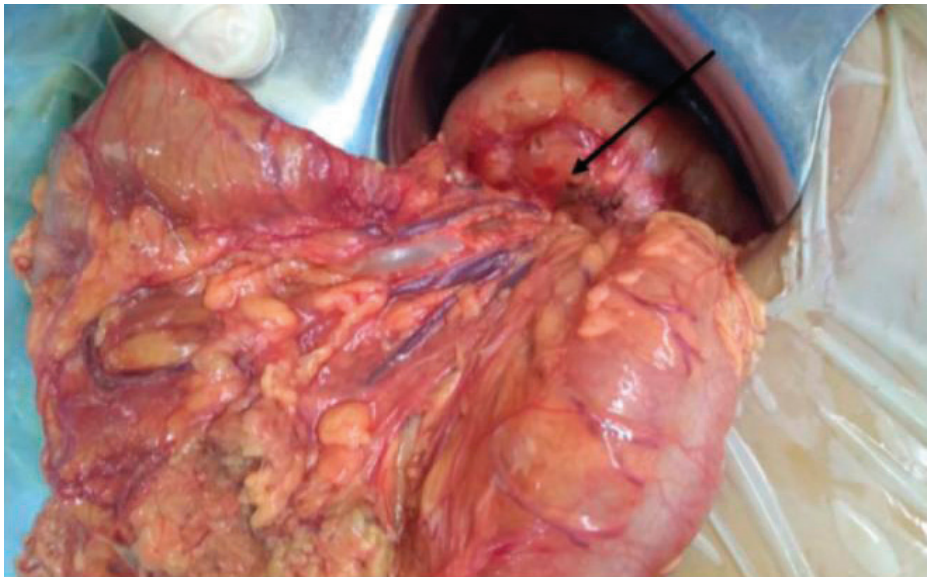
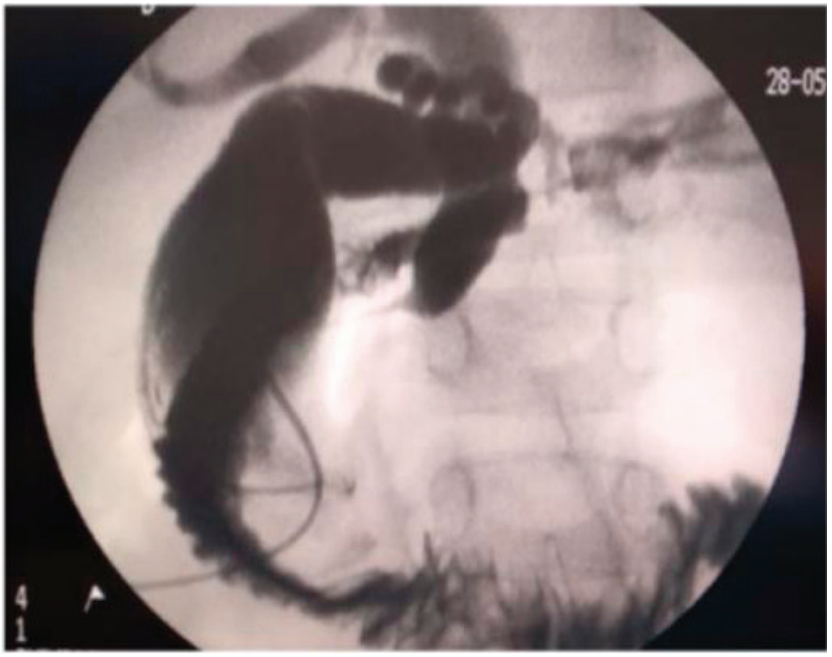


Figure 3. Intraoperative cholangiography showing dilated intrahepatic and extrahepatic bile duct and distended gallbladder



A CT of the central nervous system and chest and a bone marrow aspiration were performed to stage the NHL; results were normal. A lumbar puncture showed tumor cells corresponding to stage IV. Chemotherapy was started according to the GATLA NHL-BFM protocol.

The patient responded favorably to the treatment. A control abdominal CT was performed 2 months later and showed absence of lesions and no dilatation of the bile duct.

DISCUSSION

NHL accounts for 60% of pediatric lymphomas and 7% of malignancies in the pediatric population.[5] Pediatric lymphomas comprise a heterogeneous group of diseases, such as Burkitt lymphoma, lymphoblastic lymphoma, and large cell lymphomas, whose incidence increases with age.[6] The mean age at presentation is 10 years, and there is a higher male prevalence (2 to 3:1).[5] In most cases, lymphomas are primary;[5] however, they can be secondary to other pathologies, such as primary immunodeficiency (ataxia-telangiectasis) or secondary immunodeficiency (HIV). Other associations are being studied, such as interleukin-10 receptor deficiency.[7]

The forms of presentation of NHL are variable: they depend on the histologic subtype and affected regions. Primary, secondary, and non-lymphoid organs may be involved, and symptoms depend on tumor location.[2] NHL is characterized by a high proliferation rate, so it can be diagnosed at early stages, unlike other lymphomas with silent behavior. For this reason, bone marrow involvement at diagnosis is less frequent. B symptoms (fever, night sweats, weight loss) are present in only 30% of cases.[8]

Peripancreatic involvement has been scarcely described in pediatrics. In adults, pancreatic lymphomas typically appear as a large homogeneous mass in the head of the pancreas with extrapancreatic extension. It is not usually associated with significant dilatation of the pancreatic duct. However, it was dilated in our patient. This is consistent with another clinical case described in the bibliography.[9]

An established diagnosis may be achieved based on a pathological study of the organs involved. A biopsy of the most accessible tissue is recommended, because it allows assessing the complete tissue architectural structure.[2] Non-surgical procedures, such as image-guided puncture, are less invasive, less expensive, and associated with fewer complications, but the current evidence is insufficient in this regard.[10]

A histopathological diagnosis of NHL depends on the identification of specific morphological features and immunophenotype that can be determined by immunohistochemical staining or flow cytometry of tumor cells, which allow the assignment of a specific lymphoid lineage and state of cell differentiation.[11]

The survival rate of patients with mature B-cell neoplasms is 80–90%.[5] Prognosis has improved significantly with the introduction of chemotherapeutic agents developed during the last years of the 20th century. NHL survivors are at increased risk for second malignancies, recurrence, or progression of disease, as well as chronic diseases secondary to treatment and impaired neurocognitive functions.[12] However, these complications are rare, and NHL survivors usually have a good quality of life.

CONCLUSION

Whenever a child is seen due to cholestatic jaundice, it is important to determine the cause. An exhaustive history taking and complete physical and laboratory examination are essential to assess the patient's condition. If compression of the bile duct is suspected, imaging tests should be performed to guide the diagnosis. Malignancies, such as NHL, should be considered in the differential diagnosis because a timely consultation to a referral center is critical to improve survival. ■

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