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(CASE REPORT)

Primary non-Hodgking lymphoma of Coledoco, which simulates cholangiocarcinoma diagnosed by endoscopic ultrasonography: Case report and literature review

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Abstract

We present the second report in Latin America, and the first case in our country, Colombia, on the presentation of primary Coledoco non-Hodgkin lymphoma, which mimics cholangiocarcinoma diagnosed by endoscopic ultrasonography.

Keywords: Non-Hodgkin lymphoma; Coledoco; Cholangiocarcinoma; Endoscopic

1. Introduction

Non-Hodgkin's lymphoma (NHL) is the term used to refer to a group of different types of cancer that share a single characteristic: they arise from a lesion in the DNA of a parent lymphocyte, which triggers the exaggerated growth of the same, in the lymphoid organs (nodale). The involvement of the gastrointestinal system as a primary form is not frequent and represents between 10% of cases, however, as an extra-nodal secondary form, manifestations are reported in stomach (50-70%) small intestine (20-30) and colon (5-15). (1)

The liver is involved in 40% of cases secondarily; however, primary non-Hodgkin lymphoma of the liver is extremely rare accounting for <1% of all cases of non-Hodgkin lymphoma worldwide. (2) Primary lymphomas usually have a better 5-year prognosis with survival rates between 62-90% when early diagnosis is made, taking into account advances in chemotherapy (mainstay of treatment); In the case of secondary patients, assuming a systemic spread, it has a worse prognosis. (1)

Bile duct involvement is extremely rare and much more as a cause of jaundice in one patient, Bulent¨ Odemis et al (37), conducted retrospective searches of patients with biliary obstruction due to lymphoma between 1999 and 2005, in 1,123 patients, he reported that the incidence of primary non-hodgkin bile duct lymphomas in patients with malignant cholangiocarcinoma was 0.6%, and primary bile duct lymphoma accounted for 0.4% of extranodal non-Hodgkin lymphomas and only 0.016% of all cases of non-Hodgkin's lymphoma. Obstructive jaundice was present mainly due to tumor-related compression in the bile duct, compression of the extrahepatic ducts by periportal, perihepatic, or peripancreatic lymphadenopathy (3, 4).

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Some viruses are involved in the pathogenesis of NHL, probably because of its ability to induce chronic antigenic stimulation and cytokine dysregulation, leading to uncontrolled stimulation of B and T cells, proliferation, and lymphomagenesis. Hepatitis B virus, hepatitis C virus, HIV, Epstein Barr virus, elevated lactate dehydrogenase levels, or low immunity have been associated with the development of primary biliary non-Hodgkin lymphoma (5, 6).

According to a literature review, since Nguyen (7) reported the first case in 1982, 43 cases have been reported, the last case was reported in July 2022(36), so we wanted to collect all the cases reported in the world, to serve as a support study for future reports of similar cases, attaching our case number 44 (Table 1). It is worth noting that it is the second report in Latin America, and the first case in our country, Colombia.

2. Clinical case

A 65-year-old female with a clinical picture of 24 hours of evolution characterized by jaundice associated with body pruritus emphasis on hands and feet. Choluria for 5 days with feeling of fullness, oppressive pain in epigastrium of intensity 4/10 that does not improve despite the use of antacids for which it consults. She reports a history of depression, anxiety, hepatitis c, clostridium difficile colitis, and old HPV infection. Physical examination as the only positive data jaundice, para clinicians reporting leukocytes 5900, N 3200 (54.23%), hemoglobin 13.4, hematocrit 38.5, platelets 150,000, creatinine 0.82, sodium 136, potassium 4.32, chlorine 104, TPT 24.1/26.9, PT 10.2, INR 0.93. TGO 196, TGP 456, alkaline phosphatase 486, total bilirubin 10.51, direct 6.93, indirect 3.58, gamma glutamyl transferase 353, CA antigen 19-9: 2256 U/ml, serum alpha-fetoprotein 4.69, carcinoembryonic antigen 0.85.

As for radiological studies, it began with an ultrasound that showed dilation of the intra- and extrahepatic bile duct without being able to establish obstructive etiology, hepatomegaly and postcholecystectomy stage. Taking into account the findings, cholangio resonance showed irregular focal thickening of the walls of the distal common bile duct, with a solid lesion of 18 millimeters in diameter, neoplastic in appearance, with associated peripancreatic and left retroperitoneal adenomegaly, which conditions biliary obstruction, with significant dilation of the retrograde bile duct (Figure 1).

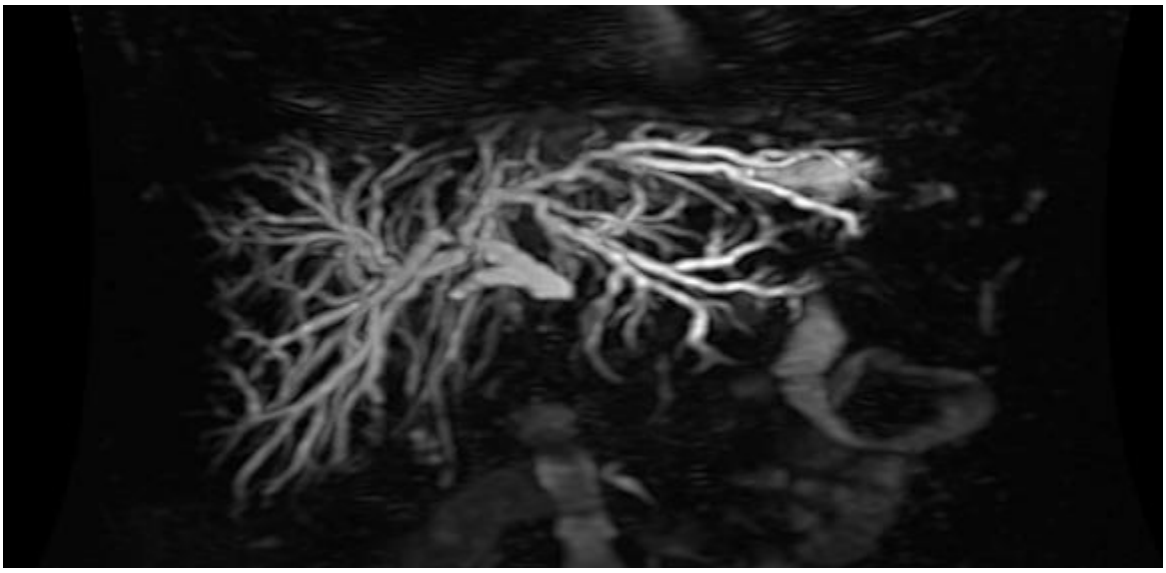

Figure 1 Cholangio Resonance showing obstruction at the middle and distal common bile duct level, secondary to solid bile duct tumor.

Patient with obstructive biliary syndrome where a solid lesion was documented in distal common bile duct associated with pancreatic and retroperitoneal lymphadenopathy. As the first diagnostic possibility cholangiocarcinoma is established, endoscopic ultrasonography is indicated to better characterize the lesion and a biopsy guided by this method and at the same time surgical shunt by endoscopic retrograde cholangiopancreatography (ERCP), abdomen/chest MRI and positron emission tomography (PET SCAN).

High-resolution chest resonance imaging: No signs of involvement from metastatic disease are seen in the chest. Sparse centrilobular emphysema, medium and small caliber inflammatory airway involvement, subsegmental distribution in the pulmonary bases.

Abdominal resonance: Peripancreatic adenomegaly, dilation of the bile duct, at the distal level collapsed with concentric thickening of middle bile duct of high cellularity like the adenomegaly described above, the pancreas has no lesions and the pancreatic duct is not dilated, there are no liver lesions suggesting secondary involvement.

Taking into account the above findings, the hepatobiliary surgery service was consulted, who considered probably endoluminal lesion in middle bile duct, without evidence of lesions suggesting distant metastatic involvement and with local adenomegaly, so it is a surgical candidate, the possibility of performing pancreatoduodenectomy is considered.

Endoscopic ultrasound was performed evidencing: thickening of the walls of the middle bile duct by a hypoechoic lesion, heterogeneous, with irregular edges, non-vascularized of 13 mm in diameter with exophytic growth, peribiliary adenomegaly, round, well defined, hypoechoic, homogeneous, of secondary neoplastic infiltrative characteristics, dilated common bile duct, 12 mm in diameter larger, biopsy is performed with 22 G acquire (FNB) needle, Two passes are performed using fan technique obtaining adequate material for histology without complications. (Figure 2 and 3)

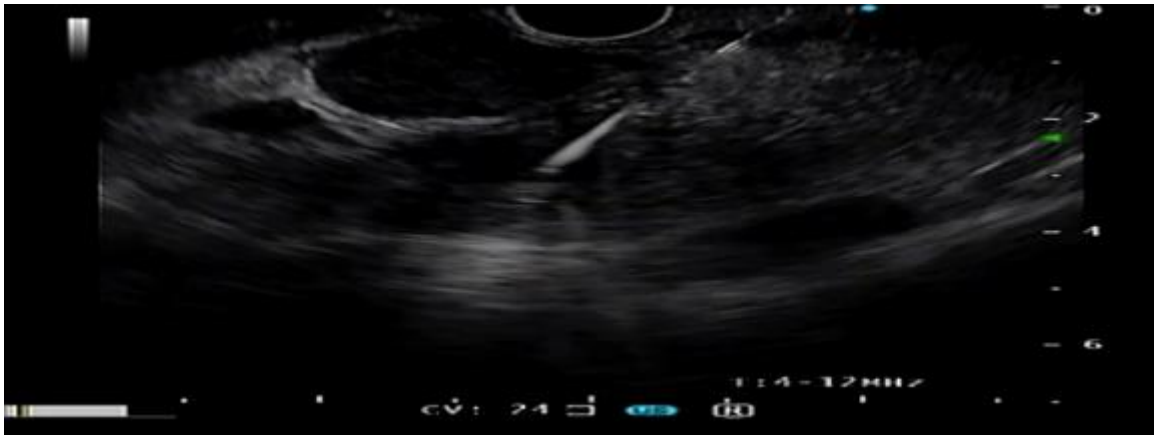

Figure 2 EUS image showing needle biopsy (FNB) of the solid lesion within the common bile duct

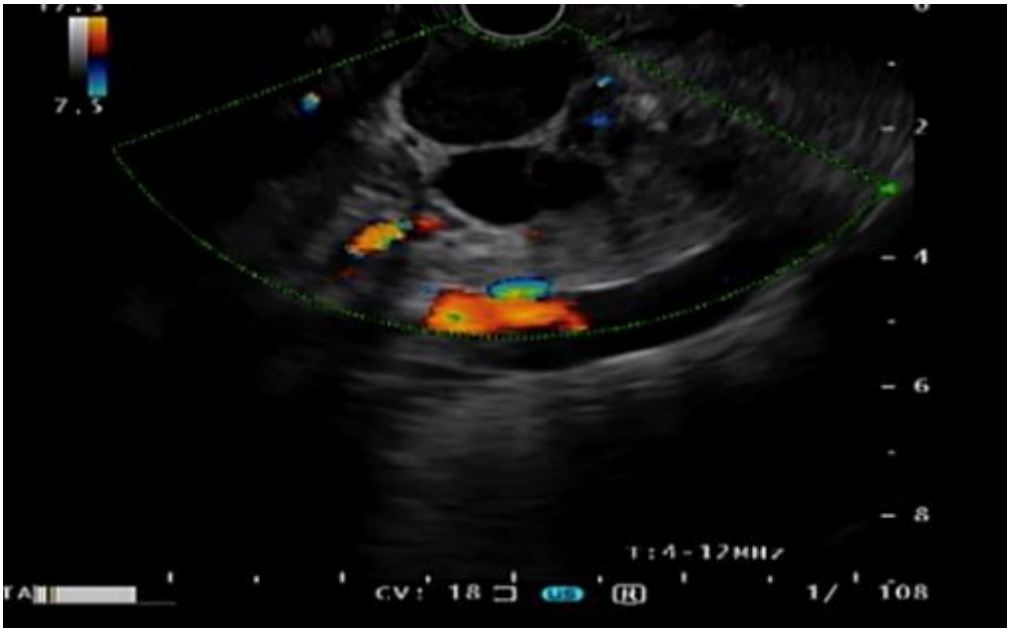

Figure 3 EUS image showing solid middle bile duct lesion with secondary obstruction and peribiliary adenomegaly

ERCP findings: normal-looking toilet papilla in second duodenal portion, dilated intrahepatic bile duct, dilated extrahepatic bile duct with 16 mm diameter common bile duct with obstruction and stenosis at the level of the middle bile duct, fully coated self-expanding metal biliary stent is implanted.

PET SCAN**:** Hypermetabolic nodular thickening of the extrahepatic bile duct in its peripancreatic region, tumor-like. Adjacent peripancreatic (precautionary) hypermetabolic ganglion with a tumor appearance. Study without evidence of other hypermetabolic lesions suspected of tumor involvement. (Figure 4)

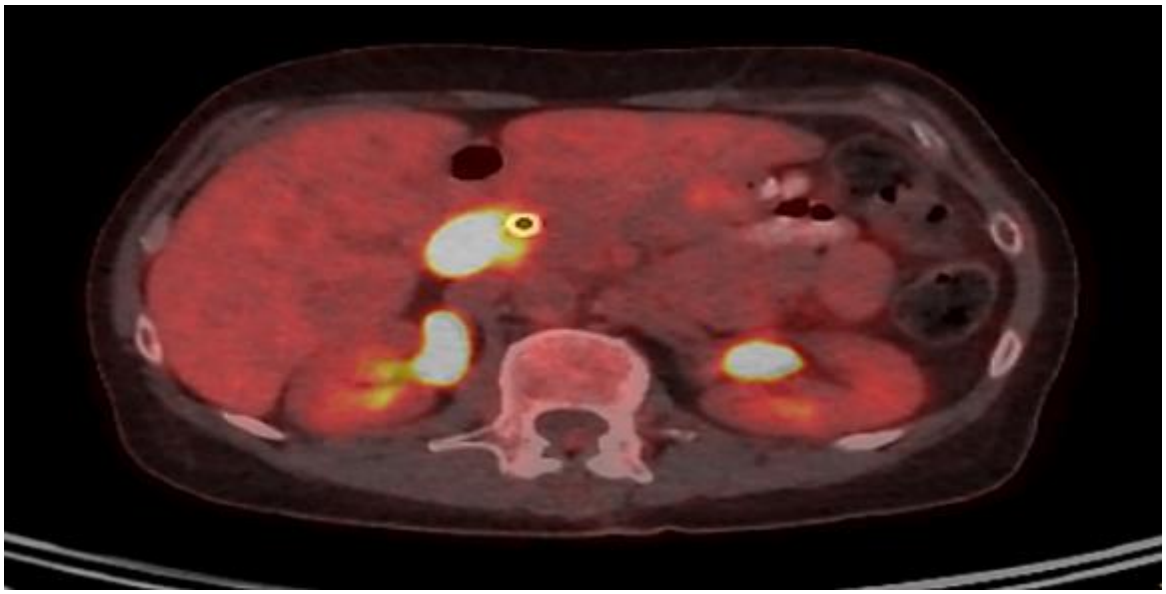

Figure 4 PET-SCAN: there is evidence of significant hyper uptake at the biliary and peribiliary level.

Histopathological findings are those of a neoplasm consisting of uniform, large lymphoid cells. With the immunohistochemical study, these tumor cells show expression of CD20, CD10, BCL6 and BCL2; negative for C-MYC and MUM 1. The cell proliferation rate measured with KI67 is 90%. (Figure 5)

Theimmunological analysis by fjorus cytometry, euroflow platform, immunophenotype study polyclonal b lymphocytes, cellularity 1%, T57.1% lymphocytes, CD4 positive 20%, CD8 positive 37.1%, mature B lymphocytes 42.9% of these kappa positive 29.2%, lambda positive 13.7%. (Figure 5)

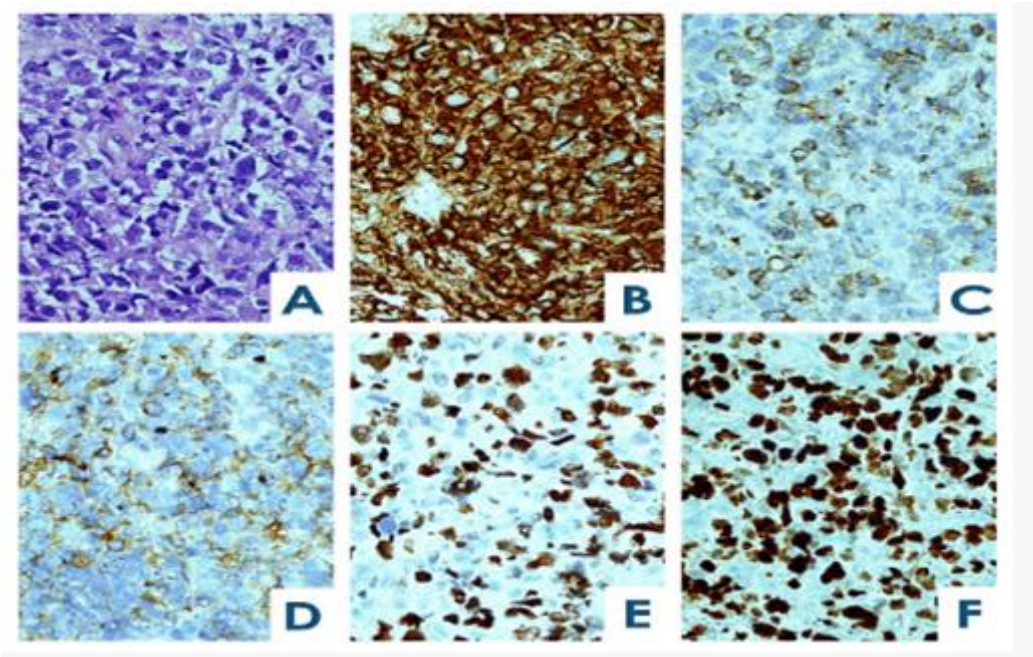

Figure 5 A. Hematoxylin-Eosin 40X. Large lymphoid tumor cells, B. CD20 positive in the cytoplasmic membrane of tumor cells, C. BCL2 positive in the membrane of tumor cells, D. CD10 positive in the membrane of tumor cells, E. BCL6 positive in the nuclei of tumor cells, F. KI67 90% cell proliferation rate

In situ hybridization studies were performed, which showed absence of translocation for BCL2 (18q21), BCL6 (3q27) and C-MYC (8q24)

The immunophenotypic findings are those of diffuse large cell B lymphoma, compatible with germinal center origin.

Taking into account the pathological findings, the possibility of surgery is aborted, it is evaluated by hemato oncology those who initiate immunochemotherapy with doxorubicin, rituximab plus cyclophosphamide, vincristine and prednisone (R-CHOP).

3. Discussion

The worldwide review of case reports (Table 1), allow us to conclude that the average age of presentation is more of young patients with an average of 46.22 years (4-81 years) with the presence of 3 pediatric patients under 18 years (4, 10 and 11 years), contrasting markedly with what has been reported so far by the association of European-American lymphoma which was at 70 years the average (38) . This leaves an alarming signal to suspect it from younger ages. The distribution by gender is comparable 54.4% (24) male and 45.4 % (20) female, the mean follow-up was 22.6 months of which 59.09% alive, 22.7 deceased, 18.1% who do not report outcomes. Regarding the histological findings and taking into account that we are collecting cases from 1982 (7) to date there are variations in terms of nomenclature, but we can group them as follows 45.4% (20) diffuse B-cell lymphoma, 34% (15) large B-cell lymphoma, 6.8% MALT lymphoma, 4.5% (2) T-cell lymphoma, 2.2% (1) follicular lymphoma, and 6.8% (3) did not report histologic type.

Regarding the therapy used, 86.3% underwent hepatic pancreatoduodenectomy and hepaticojejunal anastomosis surgery in "Y de Roux", some accompanied by chemotherapy 69%, and only 9% received chemotherapy as an exclusive treatment.

It should be noted that of the 86.3% of patients who underwent surgery, the diagnosis of primary tumor of the bile duct was made in the pathology specimen; an unnecessary procedure, if endoscopic ultrasonography with biopsy plus needle aspiration (FNB) had been used as in our case.

The International Prognostic Index (IPI) groups a series of prognostic factors that allow predicting the probable clinical evolution of NHL, in our case it was developed and validated before adding rituximab to curative chemotherapy based on anthracyclines (40), the IPI of our patient is 1 point which indicates 77% progression-free survival and 90% overall survival. Clinical trials (41-44) have confirmed that rituximab can improve the survival of patients with diffuse large B-cell lymphoma, and therefore the relevant management for it is immunochemotherapy with doxorubicin, rituximab plus cyclophosphamide, vincristine and prednisone (R-CHOP), as in our case.

Table 1 Review of cases of bile duct lymphoma in the world

No case.	Author	Age (years)	Gender	Lymphoma subtype	Treatment	Follow-up (months)	Denouement
1	Nguyen7	59	M	Diffuse lymphohistiocytic	Surgery and chemotherapy	8	Died
2	Takehara et al.8	60	M	Diffuse , median cell	Surgery and chemotherapy	Unknown	Unknown
3	Kaplan et al.9	42	M	Small uncleft	Surgery and chemotherapy	10	Died
4	Tartar and Balfe10	48	M	Unknown	Surgery and chemotherapy	14	Hurrah
5	Tzanakakis et al.11	70	M	Small mixed diffuse and large B cells	Surgery and chemotherapy	4	Died
6	Kosuge et al.12	68	F	Diffuse small cleft cell	Surgery, chemotherapy, and radiation therapy	16	Died
7	Brouland et al.13	34	F	T cell - large B cell	Surgery and chemotherapy	48	Hurrah
8	Machado et al.14	43	F	mixed small nodular and large B cells	Surgery and radiation therapy	6	Hurrah
9	Chiu et al.15	25	F	Diffuse mixed small and long T cell origin	Surgery	12	Died
10	André et al.16	44	F	Follicular centrocytic-centroblastic	Surgery and chemotherapy	48	Hurrah
11	Maymind et al.17	39	F	Large diffuse B-cell	Surgery, chemotherapy, and radiation therapy	13	Hurrah
12	Podbielski et al.18	66	M	Large B cells	Surgery	Unknown	Unknown
13	Oda et al.19	58	M	Small mixed diffuse and large B-cells	Surgery	32 days	Died
14	Corbinais et al.20	29	M	High-grade T cell	Chemotherapy	12	Hurrah
15	Eliason and Grosso21	41	M	Large diffuse B-cell	Surgery	Unknown	Unknown
16	Gravel et al.22	4	M	lymphoblastic lymphoma pre-B type	Surgery and chemotherapy	18	Hurrah

17	Kang et al.23	73	F	Low-grade B cell MALT-type lymphoma	Surgery	23	Hurrah
18	Young-Eun Joo et al 24	21	F	Large diffuse B-cell	Surgery, chemotherapy,	17	Hurrah
19	Yong Keun Park et al 25	81	F	MALT lymphoma	surgery	12	hurrah
20	Carolina De La Rosa et al 26	50	M	large B cells	surgery, chemotherapy	unknown	unknown
21	Min A Yoon et al 27	62	M	MALT	surgery	unknown	unknown
22	Jiamei Wu et al 28	59	F	Diffuse Large Cell	surgery	2	dead
23	KV Ravindra et al 29	11	M	Low-grade B cells	Surgery and chemotherapy	62	alive
24	KV Ravindra et al 29	30	F	Diffuse B-cell	surgery	3 days	dead
25	KV Ravindra et al 29	3	F	Diffuse B-cell	Surgery and chemotherapy	48	alive
26	KV Ravindra et al 29	80	M	High-grade B cells	Chemotherapy and bone marrow transplant	72	alive
27	KV Ravindra et al 29	60	M	Low-grade B cells	Chemotherapy	18	alive
28	KV Ravindra et al 29	55	F	Diffuse B-cells grades	Surgery and chemotherapy	38	alive
29	KV Ravindra et al 29	41	M	large B cells	Surgery, chemotherapy,	unknown	Died
30	KV Ravindra et al 29	10	F	Large B cells	Surgery and chemotherapy	4	alive
31	KV Ravindra et al 29	32	M	Large B cells	Surgery and chemotherapy	unknown	unknown
32	Kasturi Das et al 30	36	M	Diffuse Large B cells	Surgery and chemotherapy	68	alive

33	Kasturi Das et al 30	51	M	Diffuse Large B cells	chemotherapy	18	alive
34	F Yoneyama et al 31	55	F	Diffuse Large B cells	Surgery and chemotherapy	53	alive
35	Baron et al 32	41	M	Diffuse B cells	Surgery and Immunosorbers	12	alive
36	Baron et al 32	59	F	Diffuse B cells	Surgery and immunosuppressants	24	alive
37	Luigiano et al 33	30	M	Large B cells	Surgery and chemotherapy	6	alive
38	Gen Sugawara et al 34	33	M	Follicular lymphoma	surgery	12	alive
39	Hideaki Dote et al 35	66	M	Diffuse Large B cells	Surgery and chemotherapy	8	alive
40	Nicolás Pararás et al 36	61	F	Diffuse Large B cells	Surgery, chemotherapy	8	alive
41	Bulent¨ Odemis et al 37	57	F	large B cells	Surgery, chemotherapy, radiation therapy	10	alive
42	Bulent¨ Odemis et al 37	18	M	Large B cells	Surgery	Unknown	dead
43	Bulent¨ Odemis et al 37	64	F	large B cells	Surgery and chemotherapy	Unknown	Unknown
44	Our Firm	65	F	Diffuse large B-cell lymphoma	Chemotherapy	tracking	Hurrah

4. Conclusion

The manifestations of primary bile duct lymphoma are jaundice, fever, abdominal pain, weight loss and presence of an abdominal mass, in our case it was only pain and jaundice. Primarily, its diagnosis is practically anecdotal in 0.4% and 0.016% of all cases of non-Hodgkin lymphoma (3,4). Diagnosis of primary extrahepatic duct lymphoma is difficult by computed tomography, MRI, or MRI cholangiopancreatography, because in most cases, the associated clinical and radiological features closely resemble those of cholangiocarcinoma and there is no objective way to differentiate them. Therefore, a tissue biopsy is required to have the histological diagnosis, which must become the gold standard when considering bile duct surgery, for which we have different methods such as biopsy of the tumor mass guided by an ultrasound or CT, endoscopic brushing in ERCP, percutaneous transluminal cholangiography or cholangioscopy (37), which can vary in success rates from 20-80% depending on the expertise available in the institution (39). Taking into account the access route, we consider that endoscopic ultrasonography with needle aspiration biopsy (FNB) should be, as in our case, the method of choice for the preoperative evaluation of bile duct tumors, saving many unnecessary surgeries and especially of great morbidity and mortality, such as those reported so far as hepatic pancreatoduodenectomy and hepaticojejunal anastomosis in "Y de Roux.

Immunochemotherapy with doxorubicin, rituximab plus cyclophosphamide, vincristine and prednisone (R-CHOP) (25,33) make up the gold standard for this disease.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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