Bilio-pancreatic "tumor-like" lesions

1. Fibrous sclerosing (stenosing) cholangitis (cholangiopathies) and hepato-biliary inflammatory pseudo-tumors

2. Autoimmune pancreatitis and pancreatic inflammatory pseudotumors

Only 2 among these 5 patients with biological cholestasis ± icterus have a malignant lesion of the biliary tract and should be operated. Can you identify them?
1a - Sclerosing (fibrous obliterating) cholangitis (cholangiopathies)

- Cholangiocarcinoma (biliary adenocarcinoma) accounts for 15% of hepatobiliary cancer.

- 60% of extrahepatic cholangiocarcinoma involve hilar structures (Klatskin’s tumor); 25% are main bile duct cholangiocarcinoma.

- Recent surgical studies have shown that approximately 10 to 24% of patients operated for biliary obstruction presumed to be hilar or main bile duct malignant lesion are ultimately proved to have idiopathic benign stricture on final histologic review.


Klatskin's tumors; classical presentations

mass forming hilar cholangiocarcinoma

infiltrating hilar and main bile duct cholangiocarcinoma
infiltrating cholangiocarcinoma of the hepatic duct with hilar involvement
infiltrating Klatskin's tumor with liver metastases 3T MRI
Bismuth Cornette I or II: main bile or proximal biliary duct resection + biliary intestinal anastomose (Roux en Y hepatico jejunostomy)
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TYPE III droit et III gauche

Bismuth-Cornette III : extended right or left hepatectomy
(± previous right lobe portal embolisation for extended right hepatectomy)
TYPE III droit et III gauche

Bismuth-Cornette III: extended right or left hepatectomy
(± previous right lobe portal embolisation for extended right hepatectomy)
TYPE III droit ou III gauche

Bismuth-Cornette III : extended right or left hepatectomy
(± previous right lobe portal embolisation for extended right hepatectomy)
Bismuth-Cornette IV: no resection surgery; palliative biliary diversion: endoprosthesis with preferred percutaneously transhepatic approach
33 y.o man, subicterus for ten days, intense asthenia; anorexia.

Mild and fluctuating biological cholestasis (total serum bilirubin between 50 and 80 mg/L)
follow up: 2 months after right portal vein embolisation + external biliary drainage of the left hepatic lobe to maximise its hypertrophy.
enlarged right hepatectomy

right portal vein thrombosis

lymphoplasmocytic infiltration and short (>5mm) circumferential fibrosis of the proximal right biliary duct; fibrous transformation of the adjacent portal vein.
62 yo man, intense jaundice for 2 weeks, asthenia, severe biological cholestasis (bilirubin 252 mg/L)
spontaneous slow regression of the icterus with progressive normalisation of the biological cholestasis, beginning at the end of the first month.
3 years after the beginning

right branch of the hepatic artery crossing the main bile duct posteriorly
78 yo man; left lobe biliary dilatation with intestinal subocclusion; mild elevation of bilirubinemia

segmental dilatation of the left hepatic lobe biliary ducts

indication of MRI!
Left hepatic lobectomy, 4 months after the beginning of the symptomatology: concentric stenosing fibrosis of large as of small bile ducts inflammatory lympho plasmocytic infiltration thrombosis of left lobe portal veins, partially repermeabilised
### Sclerosing cholangitis; associated diseases

<table>
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<th>Idiopathic</th>
<th>Secondary etiology</th>
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<td>Crohn’s disease</td>
<td>Infection</td>
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<td>Ulcerative colitis</td>
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<td>Idiopathic fibrosis</td>
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<td>Retroperitoneal fibrosis</td>
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<td>Mediastinal fibrosis</td>
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<td>Peyronie’s disease</td>
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<td>Idiopathic lobular panniculitis</td>
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<td>Reidel’s thyroiditis</td>
<td>Angioimmunoblastic lymphadenopathy</td>
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<td>Pseudotumour of the orbit</td>
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<td>Autoimmune &amp; connective tissue disorders</td>
<td>Caroli’s disease</td>
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<td>Systemic lupus erythematosus</td>
<td>Cystic fibrosis</td>
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<td>Rheumatoid arthritis</td>
<td>Pancreatic disorder</td>
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<td>Systemic sclerosis</td>
<td>Autoimmune pancreatitis</td>
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<td>Sjögren’s syndrome</td>
<td>Chronic pancreatitis</td>
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<td>Celiac disease</td>
<td>Toxic</td>
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<td>Type 1 diabetes mellitus</td>
<td>Intraductal formaldehyde or hypertonic saline</td>
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<td>Autoimmune hemolytic anemia</td>
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<td>Immune thrombocytopenic purpura</td>
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<td>Lupus nephritis</td>
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<td>Membranous nephropathy</td>
<td>Hepatic allograft arterial occlusion</td>
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<td>Rapidly progressive</td>
<td>Paroxysmal nocturnal hemoglobinuria</td>
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<tr>
<td>Glomerulonephritis</td>
<td>Posttraumatic sclerosing cholangitis</td>
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<tr>
<td>Chronic sclerosing salivadenitis</td>
<td>Others</td>
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<tr>
<td>Primary biliary cirrhosis</td>
<td>Hepatic inflammatory pseudotumor</td>
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<tr>
<td>Alloimmune disorders</td>
<td>Neoplastic/Metastatic disease</td>
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<tr>
<td>Hepatic allograft rejection</td>
<td>Eosinophilic cholangitis</td>
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<tr>
<td>Graft-versus-host disease</td>
<td>Portal biliopathy</td>
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<tr>
<td>Infiltrative disorders</td>
<td>Langerhans cell histiocytosis</td>
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<td>Amyloidosis</td>
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<td>Sarcoidosis</td>
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<td>Systemic mastocytosis</td>
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<td>Hypereosinophilic syndrome</td>
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<td>Hodgkin’s disease</td>
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<td>Cholangitis glandularis proliferans</td>
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Sclerosing cholangitis may mimic hilar or main bile duct cholangiocarcinoma

It is always difficult to get precise histologic data with biopsies or endoluminal biliary brushing and surgical resection is often decided mainly on MDCT and MR images.

Of course precise knowledge of clinico-biological evolution is fundamental to avoid unnecessary mutilating surgery and we have to be very careful in radiology reports and to take in account clinical, biological atypies in multidisciplinary concertations.

In atypical cases, one can decide
- to complete biological data; IgG4, auto antibodies, CA 19-9 … etc
- a supplementary follow-up of one to three months
- a trial of corticotherapy (?)
- repeated endobiliary brushings or better: endoluminal biliary duct biopsy by transhepatic US guided approach
1b. hepato biliary inflammatory pseudotumors

48 yo woman, jaundice, cholestasis


Guided biopsies of the juxta hilar mass confirm the diagnosis of inflammatory pseudotumor.

MDCT 45''

MDCT 70''

MDCT delayed

MRCP

interventionnal ERCP
42 yo woman, mild biological cholestasis without clinical icterus, probabilistic diagnosis of Klatskin’s tumor.


Right hepatectomy (after neo-adjuvant chemotherapy) confirms the histological diagnosis of biliary inflammatory pseudotumor.
48 yo woman, right upper quadrant pain with mild fever, moderate cholestasis (bilirubin 53 mg/L), elevated AST and ALT (15/20*N) CRP 20 mg/L.
One month later, the whole anomalies spontaneously disappeared, clinico-biologic as radiologic ones.
Hepatobiliary inflammatory pseudotumor is the main differential diagnosis of mass-forming hilar (Klatskin's) tumor.

Inflammatory pseudotumors are histologically characterized by a proliferation of fibroblasts or myofibroblasts and inflammatory cell infiltration (mainly polyclonal lymphocytes and plasma cells).

Two types are described: fibrohistiocytic predominantly peripheral and lymphoplasmocytic, central (juxta hilar) and mass forming (with IgG4 elevation).

Delayed enhancement in contrasted MDCT and MRI is a strong argument for the diagnosis; unfortunately it is also seen in cholangiocarcinoma.

Zen Y et coll. Pathological classification of hepatic inflammatory pseudotumor with respect to IIgG4-related diseases Modern pathology 2007,20:884-894
1c. differential diagnosis of main bile duct “tumor-like” lesions

73 yo woman, increasing jaundice, palpable mass of the right upper quadrant

calculo-cancer of the gallbladder with infrahilar pedicular extension
Grawitz tumor of the right kidney
73 yo woman, biliary pain and biological cholestasis; cholecystectomy 3 years, no weight loss.

Mirizzi’s syndrome (pedicular infrahilar compression due to cystic stone) can be seen even after cholecystectomy, in a long cystic duct remnant!
54 yo man, chronic diarrhea, weight loss, cholestasis

primary sclerosing cholangitis
How can we recognize a primary sclerosing cholangitis?


Obliterating fibrous cholangitis involve large intrahepatic bile ducts (≠primary biliary cirrhosis)

Young men S/R 2/1, average age of diagnosis: 40 yo

Frequently (75%) associated to IBD (specially mild or infraclinic ulcerative pancolitis)

IgG4 are elevated in only 9% of the cases

Annual incidence of cholangiocarcinoma: 1.5% (elevation of CA 19.9)

Short stenosis with upstream dilatations, predominantly peripheral; beading.
72 yo man, follow up of primary sclerosing cholangitis
69 yo woman; cholecystectomy 12 years ago; biliary pain, fever, cholestasis

Cholesterol stones incrusted in the wall of proximal hilar bile ducts (confirmed at surgery)
18yo teenager; cystic fibrosis with liver insufficiency

Pedicular and porta hepatis portal varices due to portal hypertension (secondary biliary cirrhosis and portal thrombosis, often misnamed “portal cavernoma”)
2a. autoimmune pancreatitis

-autoimmune pancreatitis (AIP) is a **chronic inflammation** of the pancreas due to a **postulated autoimmune mechanism**.

-occasionally, AIP is **associated with other autoimmune disorders** such as chronic IBD, autoimmune cholangitis, Sjögren’s disease, retroperitoneal fibrosis, diabetes mellitus, SLE, vasculitis, thyroiditis.

-histologic hallmark is **inflammatory lymphoplasmocytic periductal inflammation with massive fibrosis**

-AIP is the main differential diagnosis of pancreatic adenocarcinoma and is important to avoid unnecessary surgery.

-remarkable response to steroid therapy because of its autoimmune pathogenesis must be used to confirm the diagnosis.
MDCT imaging of autoimmune pancreatitis

- focal (head) or diffuse hypertrophy (sausage shaped) of the pancreas
- loss of lobularity
- no peripancreatic fat stranding
- peripheral rim of a hypoattenuation "halo"

- associated distant lesions (autoimmune cholangitis, retroperitoneal fibrosis ..)
Ductal pancreatobiliary lesions in autoimmune pancreatitis (MRCP or retrograde endoscopic wirsungography)

Diffuse pancreatic ductal narrowing without or with minimal upstream dilatation; stenosis of intrapancreatic main bile duct is frequently observed.
42 yo woman, autoimmune pancreatitis
quick response to corticosteroid (40 mg /day for 1 week followed by a taper of the daily dose by 5 mg per week ) is essential to know and to use for the diagnosis

Morana G et al. Autoimmune pancreatitis: Instrumental diagnosis JOP. J Pancreas (Online) 2005; 6(1 Suppl.):102-107
55yo man, AIP, diffuse homogeneous hypermetabolism with 18 FDG PET/CT can help for differential diagnosis with pancreatic adenocarcinoma

Utility of $^{18}$F-FDG PET/CT for differentiation of autoimmune pancreatitis with atypical pancreatic imaging findings from pancreatic cancer
Lee TY¹, Kim MH², Park DH et al.² AJR Am J Roentgenol 2009;193:343-348
36 yo woman, pain of the right upper quadrant with cholestasis and anorexia.

AIP localised to pancreatic head; homogeneous mass of the pancreatic head; dilatation of supra pancreatic main bile duct; no dilatation of the upstream main pancreatic duct.
- are AIP one of the 'IgG4 related diseases'?

63 yo woman, abdominal pain, cholestasis, renal insufficiency

CT

diffuse hypertrophy of the pancreas with loss of lobularity

no dilatation of the main pancreatic duct

intrahepatic bile duct dilatation (autoimmune cholangitis)

retroperitoneal fibrosis with ureterohydronephrosis
after one month of corticosteroids

three months later
40 yo man, intense epigastric pain with weight loss and increasing cholestasis; low back pain.

AIP, iliac retroperitoneal fibrosis, portal vein thrombosis with cavernoma.
How can we recognize/identify autoimmune corticosensitive cholangitis?
Are serologic data useful for the diagnosis of PAI?


**Table 1. Diagnostic Criteria for Autoimmune Pancreatitis.**

<table>
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<tr>
<th>Findings on Imaging Radiography (One Required)</th>
<th>Cross-Sectional Imaging</th>
<th>ERCP or MRCP</th>
<th>Serologic Analysis</th>
<th>Pancreatic–Biliary Histologic Analysis</th>
<th>Nongastrointestinal Histologic Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffusely enlarged pancreas</td>
<td>Segmental pancreatic ductal narrowing</td>
<td>Elevated serum IgG4 level</td>
<td>Periductal lymphoplasmacytic infiltration or fibrosis</td>
<td>Tubulointerstitial nephritis with immune deposits within tubular basement membranes</td>
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</tr>
<tr>
<td>Enhanced peripheral rim of hypotension “halo”</td>
<td>Focal pancreatic ductal narrowing</td>
<td>Elevated serum IgG or gamma globulin level</td>
<td>Obliterative phlebitis</td>
<td>Pulmonary interstitial lymphoplasmacytic infiltration with IgG4-positive plasma cells†</td>
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<tr>
<td>Low-attenuation mass in head of pancreas</td>
<td>Diffuse pancreatic ductal narrowing</td>
<td>Presence of ALA, ACA II, ASMA, or ANA</td>
<td>IgG4-positive plasma cells in tissue†</td>
<td>Chronic sialadenitis with IgG4-positive plasma cells†</td>
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</tbody>
</table>

* Criteria were modified from those of the Japan Pancreas Society. ERCP denotes endoscopic retrograde cholangiopancreatography, MRCP magnetic resonance cholangiopancreatography, ALA antilactoferrin antibody, ACA II anti–carbonic anhydrase II antibody, ASMA anti–smooth-muscle antibody, and ANA antinuclear antibody.

† The presence of tissue IgG4-positive cells is not necessarily abnormal, but an increased number of infiltrating IgG4-positive plasma cells is abnormal.
Is there an interest of 18FDG PET/CT for he diagnosis of PAI ?

66 yo woman AIP, metabolic hyperactivity in caudal pancreas, thyroid and salivary glands. These extrapancreatic sites of 18 FDG are not seen in pancreatic adenocarcinoma.

Utility of $^{18}$F-FDG PET/CT for differentiation of autoimmune pancreatitis with atypical pancreatic imaging findings from pancreatic cancer.

Lee TY$^1$, Kim MH$^2$, Park DH et al.$^2$ AJR Am J Roentgenol 2009;193:343-348
Utility of $^{18}$F-FDG PET/CT for differentiation of autoimmune pancreatitis with atypical pancreatic imaging findings from pancreatic cancer
One exemple of differential diagnosis of AIP

80 yo man, weight loss, cholestasis; it’s not an AIP nor an adenocarcinoma. What is it???

High grade NHL with pancreatic localisation
2b. Inflammatory pseudotumor of the pancreas

56 yo man, alcoholic and smoker, clinical presentation of mild pancreatitis

Obs Pr. B Dupas Nantes
Surgery is decided: Whipple intervention.

2 échoendoscopic guided biopsies with cytologic analysis: no suspect cell;

New imaging investigations after 3 months.

CA 19-9 136.8 U/ml
immunological staining: smooth muscle actine specific +++

inflammatory pseudotumor or inflammatory myofibroblastic tumor

cellular fusiform proliferation with variable degrees of atypia

lymphoplasmocytic infiltration

myxoid stroma
71 yo woman, icterus, seric bilirubin: 180 mg/L.
Fluctuating evolution of cholestasis and clinical jaundice

Follow up 3 months

Follow up 6 months

intervention (Whipple)

inflammatory pancreato-cholangitis (fibro-hyaline transformation and lymphoplasmocytic infiltration)
Au total

Inflammatory pancreatobiliary “tumor-like” lesions are a challenge for radiologist and surgeons

It is often impossible to get histological data despite progress of endoscopic and radiologic guided biopsies and decisions must be based on MDCT and MR images

Biology can contribute to diagnosis when Ig G4 are elevated but this is quite rare in west europa

Clinicians have to be very attentive to atypies in clinical or biological evolution

It is often wise to wait some weeks before surgery (3 months for example) in equivocal cases and a corticosteroid test can be useful to avoid unnecessary mutilating surgery.