نحوه اپروچ به ایکتر ناگهانی در خانم ۴۲ ساله در درمانگاه پزشکی خانواده

استاد راهنما سرکارخانم دکتر فنی عضو هیات علمی
ارایه دهنده مبینا جلالوند کارورز پزشکی خانواده

۱۴۰۲/۵/۱۴

Present illness

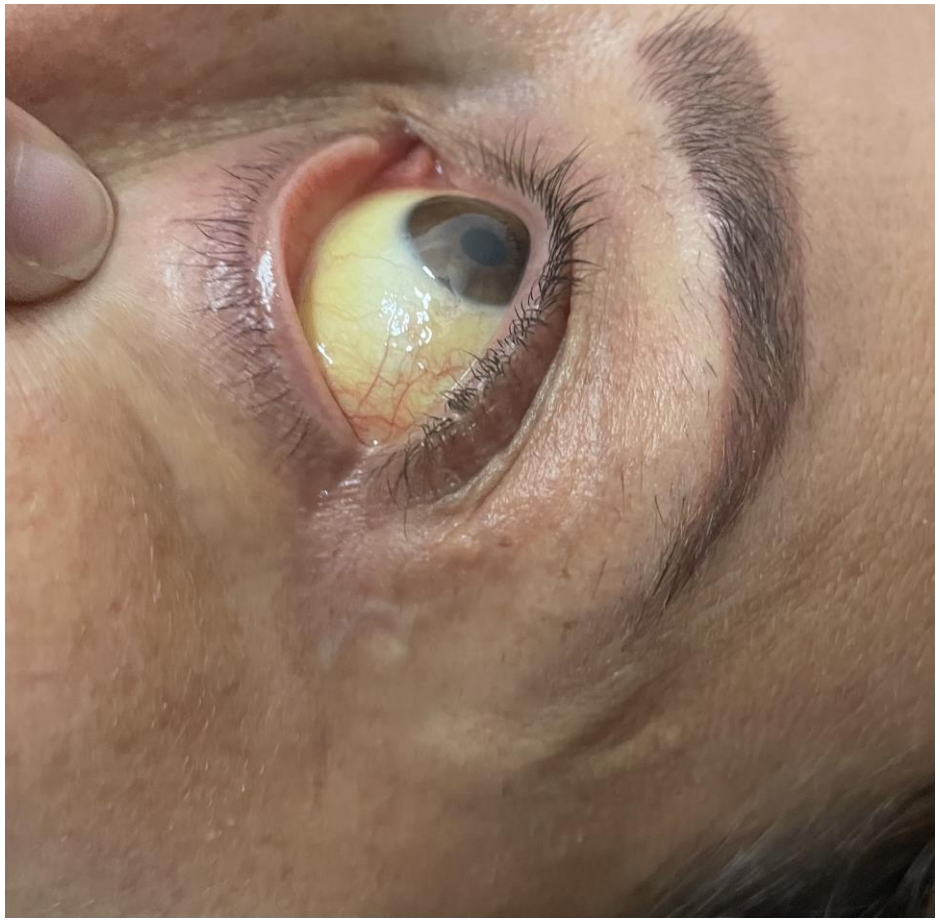
- شکایت اصلی : خارش و زردی پوست
- بیمار خانم ۴۲ ساله با شکایت از زردی بدن و خارش شدید پوست که از چهار روز پیش ایجاد شده به مرکز دیگری مراجعه کرده و سپس با نتایج آزمایشات به این مرکز ارجاع شده است. بیمار از چهار روز پیش دچار زردی پوست و اسکلرا، خارش شدید جنرالیزه، تغییر رنگ ادرار ، دفع مدفوع آکولیک و درد در ناحیه ی RUQ شکم شده است. بیمار از حدود یک هفته ی پیش تهوع و استفراغ داشته است که در حال حاضر بر طرف شده است. علاوه بر این، سابقه ی علائم مشابه سرماخوردگی مانند آبریزش بینی و سرفه ی خفیف حدود دو هفته ی پیش را ذکر می کند. بیمار کاهش وزن اخیر نداشته است. تب ندارد. ضعف و بی حالی ندارد. سابقه ی درد های شکمی در ناحیه ی RUQ را نیز ذکر می کند.

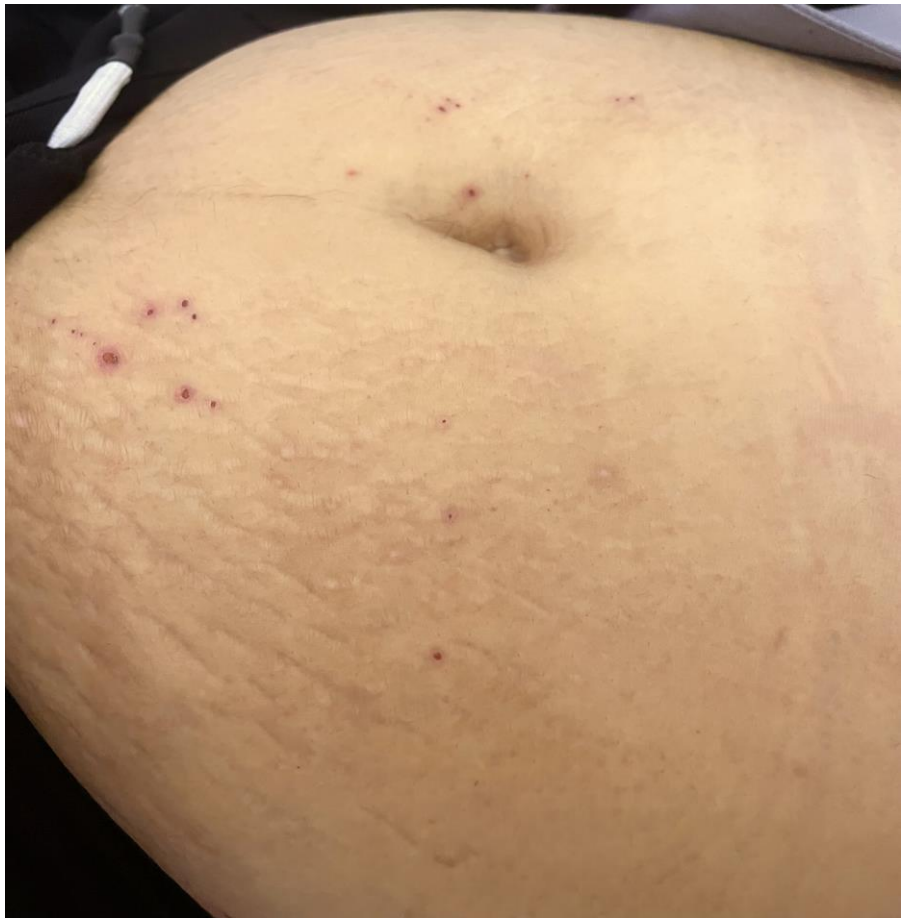
Physical examination

- اسکرا و پوست بیمار واضحا ایکتریک می باشد.
- در سطح پوست اندام ها و شکم شواهد پاپول های excoriated مشاهده می شود.
- سمع قلب و ریه نرمال است.
- درد شکم در ناحیه ی RUQ و LUQ دارد. هپاتومگالی در حد سه سانتی متر در زیر لبه ی تحتانی دنده دارد. کبد در لمس ندولار نمی باشد.
- مورفی ساین منفی می باشد.

- Height:164, Weight:73, BMI:27
- BP:125/81, T:36.3, PR:76, RR:26
- PMH: -
- PSH: Cesarean section
- DH: -
- AH: -
- FH: -

Physical examination





Lab data

WBC	6.9
Hb	13.8
PLT	248
Neut	67.6%
Lymph	21.3%
Ferritin	251
Cr	0.5
Urea	26
Chl	291
HDL	17
LDL	125
FBS	121
CRP	+3
ESR	40
U/A	Normal (SG:1.005)

Bili T	11.5
Bili D	9.8 (85%)
AST	163
ALT	347
ALP	1268
Albumin	4.4
B-hCG	Negative

Sonography

- اکوژنیسیتی پارانشیم کبد به صورت منتشر افزایش یافته است. (کبد چرب گرید یک)
- کیسه ی صفرا با ضخامت جداری افزایش یافته و حاوی سنگهای مجاور هم با دیامتر مجموع ۵۴ م م مشاهده شد.
- مجاری صفراوی داخل و خارج کبدی و ورید پورت دیامتر نرمال دارد.

Problem list

Bili T	11.5
Bili D	9.8 (85%)
AST	163
ALT	347
ALP	1268

- خانم ۴۲ ساله (سابقه ی بیماری قبلی ندارد)
- اسکلرا و پوست ایکتریک
- خارش پوست
- تغییر رنگ ادرار
- مدفوع آکولیک
- درد در ناحیه ی RUQ شکم
- هپاتومگالی
- افزایش ضخامت جداری کیسه ی صفرا و حاوی سنگهای مجاور هم با دیامتر مجموع ۵۴ م م

Initial evaluation of abnormal liver tests

- **History**
- The history should determine if the patient has had exposure to any potential hepatotoxins, is at risk for viral hepatitis, has other disorders that are associated with liver disease.
- Alcohol consumption
- Drug use (the amounts ingested, and the durations of use)(prescription medications, over-the-counter medications, herbal and dietary supplements, illicit drug use)
- Risk factors for viral hepatitis (potential parenteral exposures, intravenous drug use, blood transfusion prior to 1992, travel to areas endemic for hepatitis, and exposure to patients with jaundice)
- Occupational exposure to hepatotoxins (industrial chemicals such as vinyl chloride and the mushrooms *Amanita phalloides* and *Amanita verna*, which contain a potent hepatotoxin, amatoxin)

History

- Past medical history: Patients should be asked about conditions that are associated with hepatobiliary disease, such as right-sided heart failure (congestive hepatopathy), diabetes mellitus, skin pigmentation, arthritis, hypogonadism and dilated cardiomyopathy (hemochromatosis), and obesity (nonalcoholic fatty liver disease), pregnancy (gallstones), inflammatory bowel disease (primary sclerosing cholangitis, gallstones), early onset emphysema (alpha-1 antitrypsin deficiency), celiac disease, and thyroid disease.

Physical examination

Temporal and proximal muscle wasting suggest longstanding disease.

Stigmata of liver disease include spider nevi, palmar erythema, gynecomastia, and caput medusae.

Ascites or hepatic encephalopathy may be seen in patients with decompensated cirrhosis.

Dupuytren's contractures, parotid gland enlargement, and testicular atrophy are commonly seen in advanced alcoholic cirrhosis and occasionally in other types of cirrhosis.

An enlarged left supraclavicular node (Virchow's node) or periumbilical nodule (Sister Mary Joseph's nodule) suggest an abdominal malignancy.

Increased jugular venous pressure, a sign of right-sided heart failure, suggests hepatic congestion.

A right pleural effusion, in the absence of clinically apparent ascites, may be seen in advanced cirrhosis.

Neurologic and psychiatric signs and symptoms may be seen in patients with Wilson disease.

The abdominal examination should focus on the size and consistency of the liver, the size of the spleen and an assessment for ascites.

Abnormal laboratory tests

- **Hepatocellular pattern:**

Disproportionate elevation in the serum aminotransferases compared with the alkaline phosphatase.

Serum bilirubin may be elevated.

Tests of synthetic function may be abnormal.

- **Cholestatic pattern:**

Disproportionate elevation in the alkaline phosphatase compared with the serum aminotransferases.

Serum bilirubin may be elevated.
Tests of synthetic function may be abnormal.

- **Isolated hyperbilirubinemia**

An elevated bilirubin level with normal serum aminotransferases and alkaline phosphatase levels.

R Value

- The R value (also known as the R factor) can be used to help determine the likely type of liver injury in patients with elevated aminotransferases and alkaline phosphatase.
- R value = (ALT ÷ ULN ALT) / (ALP÷ ULN ALP)

≥5: Hepatocellular injury

>2 to <5: Mixed pattern

≤2: Cholestatic injury

Reference ranges

Albumin: 3.3 to 5.0 g/dL

Alkaline phosphatase:

- Male: 45 to 115 units/L
- Female: 30 to 100 units/L

Alanine aminotransferase (ALT):

- Male: 29 to 33 units/L
- Female: 19 to 25 units/L

Aspartate aminotransferase (AST):

- Male: 10 to 40 units/L
- Female: 9 to 32 units/L

- Bilirubin, total: 0.0 to 1.0 mg/dL
- Bilirubin, direct: 0.0 to 0.4 mg/dL
- Gamma-glutamyl transpeptidase (GGT):
  - Male: 8 to 61 units/L
  - Female: 5 to 36 units/L
- Prothrombin time (PT): 11.0 to 13.7 seconds

R value

- Patient’s ALT: 347
- ULN ALT: 25
- Patient’s ALP: 1268
- ULN ALP: 100
- R-value: 1.09

When to refer to a specialist

- Referral to a gastroenterologist or hepatologist should be considered for patients with unexplained, persistent liver biochemical test elevations (≥2 times the upper limit of normal for aminotransferases or 1.5 times the upper limit of normal for alkaline phosphatase) and for patients who are being considered for liver biopsy.
- Upper limit of normal for aminotransferases: approximately 30 units/L for men and 20 units/L for women
- If the liver tests normalize or remain mildly elevated (<2 times the upper limit of normal for aminotransferases or less than 1.5 times the upper limit of normal for alkaline phosphatase), expectant management is reasonable in most cases. In such patients, we would follow their liver biochemical and function tests every six months.

Cholestatic liver injury

- In patients with cholestasis, the alkaline phosphatase is typically elevated to at least four times the upper limit of normal.
- The magnitude of the serum alkaline phosphatase elevation does not distinguish extrahepatic cholestasis from intrahepatic cholestasis.
- Alkaline phosphatase can come from other sources, such as bone and placenta.
- The gamma-glutamyl transpeptidase (GGT) may also be elevated in the setting of cholestasis.
- To confirm that an isolated elevation in the alkaline phosphatase is coming from the liver, a GGT level or serum 5'-nucleotidase level should be obtained.
- If, however, there are abnormalities in other liver chemistries or markers of hepatic function, particularly an elevated bilirubin, confirmation is typically not required.

Cholestatic liver injury

- The most common causes:

1. partial bile duct obstruction
2. primary biliary cholangitis (PBC)
3. primary sclerosing cholangitis (PSC)
4. Drugs: androgenic steroids and phenytoin

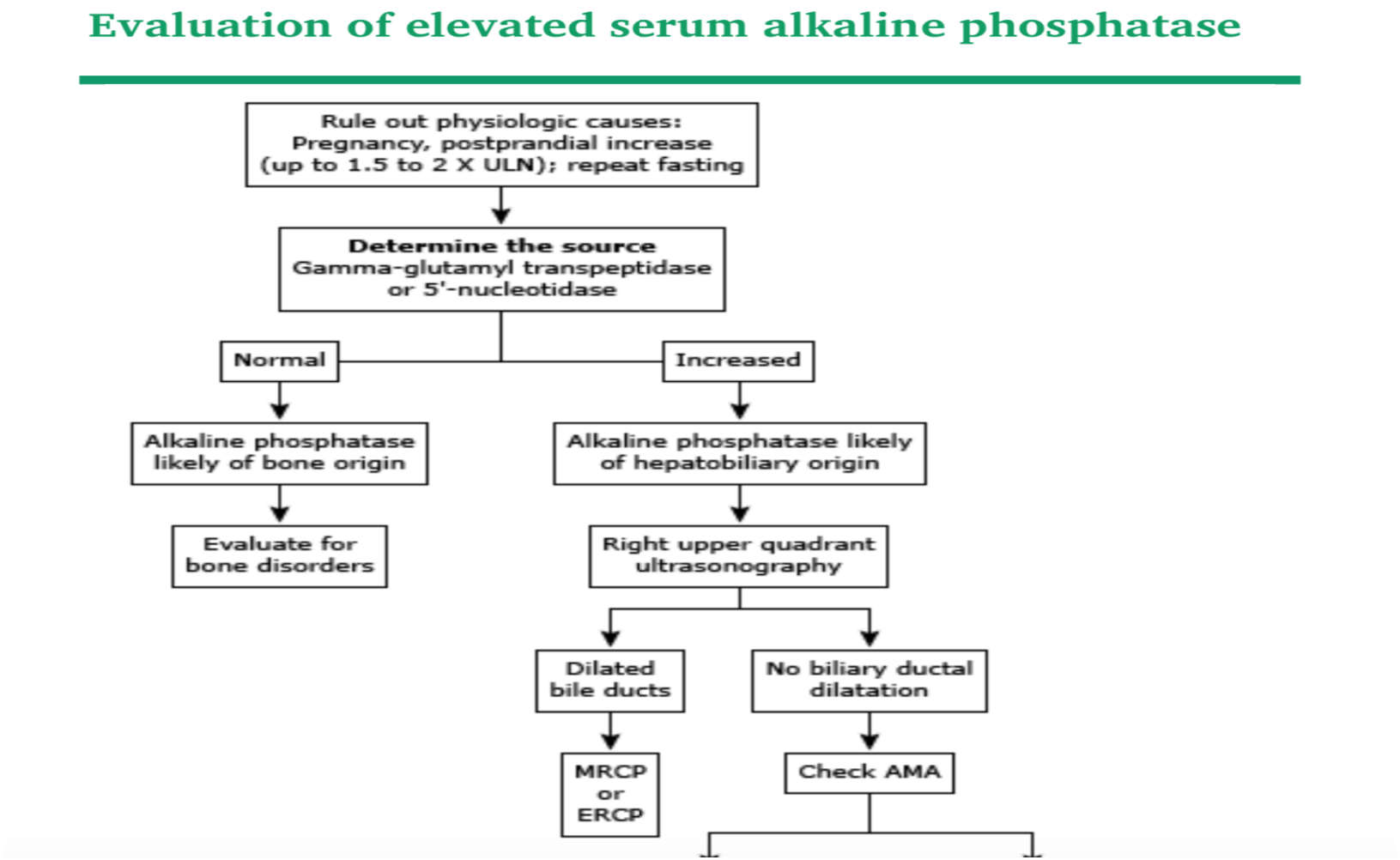
Causes of an elevated alkaline phosphatase

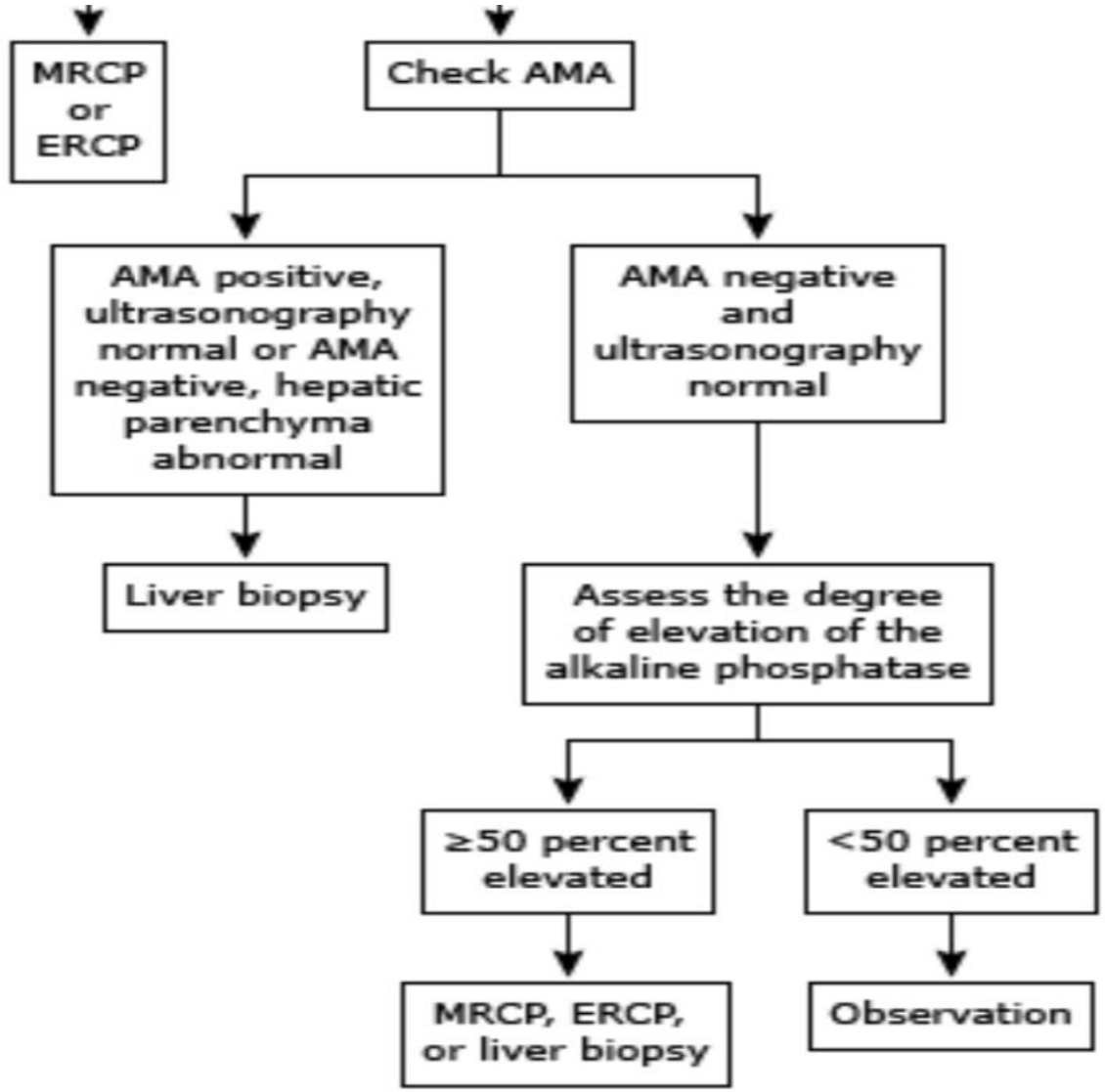
Marked elevation (≥4 times the upper limit of normal)*	**Extrahepatic biliary obstruction¶**
	Choledocholithiasis (most common) ■ Uncomplicated ■ Complicated (biliary pancreatitis, acute cholangitis)
	Malignant obstruction ■ Pancreas ■ Gallbladder ■ Ampulla of Vater ■ Bile duct ■ Metastasis to perihilar lymph nodes
	Biliary strictures ■ Primary sclerosing cholangitis with extrahepatic bile duct stricture ■ Complications after invasive procedures ■ Chronic pancreatitis with stricturing of distal bile duct ■ Biliary anastomotic stricture following liver transplantation
	Infections ■ AIDS cholangiopathy ■ *Ascaris lumbricoides* ■ Liver flukes

Intrahepatic cholestasis
Drug and toxins associated with cholestasis[Δ]
Primary biliary cholangitis[Δ]
Primary sclerosing cholangitis[Δ]
Intrahepatic cholestasis of pregnancy
Benign postoperative cholestasis
Total parenteral nutrition
Infiltrative diseases[Δ] ▪ Amyloidosis ▪ Lymphoma ▪ Sarcoidosis ▪ Tuberculosis ▪ Hepatic abscess
Metastatic carcinoma to the liver[Δ]
Liver allograft rejection
Other cholangiopathies (eg, IgG4 cholangiopathy, ischemic cholangiopathy, COVID-19)
Alcohol-associated hepatitis
Sickle cell disease (hepatic crisis)

Nonhepatic causes[◇]
Transient hyperphosphatemia of infancy and childhood

Approach to cholestatic liver injury




MRCP or ERCP
Check AMA
AMA positive, ultrasonography normal or AMA negative, hepatic parenchyma abnormal
AMA negative and ultrasonography normal
Liver biopsy
Assess the degree of elevation of the alkaline phosphatase
≥50 percent elevated
<50 percent elevated
MRCP, ERCP, or liver biopsy
Observation

Diagnostic tests

- If ultrasonography suggests obstruction due to a stone or malignancy, or if the onset of the cholestasis was acute, endoscopic retrograde cholangiopancreatography (ERCP) should be carried out.
- If the cholestasis is chronic or ultrasonography shows biliary dilatation without an apparent cause or in patients who are at high risk for ERCP, magnetic resonance cholangiopancreatography (MRCP) or computed tomography (CT) should be obtained.
- In some cases, endoscopic ultrasonography may help identify an obstruction.
- If the results of ERCP or MRCP are negative for biliary tract disease, liver biopsy should be considered.

Intrahepatic cholestasis

- In patients with intrahepatic cholestasis, antimitochondrial antibodies (AMA), antinuclear antibodies, and anti-smooth muscle antibodies should be checked.
- If positive, AMA are highly suggestive of PBC, and a liver biopsy may be considered.
- If AMA are absent, additional testing includes

1. MRCP to look for evidence of primary sclerosing cholangitis
2. Testing for hepatitis A, B, C, and E
3. Testing for Epstein-Barr virus and cytomegalovirus
4. Pregnancy testing

Intrahepatic cholestasis

- If the above tests are negative and the alkaline phosphatase is persistently more than two times the upper limit of normal for more than six months, we obtain a liver biopsy.
- If the alkaline phosphatase is less than two times the upper limit of normal, all of the other liver biochemical tests are normal, and the patient is asymptomatic, we suggest observation alone, since further testing is unlikely to influence management

Bilirubin & jaundice

- The normal serum bilirubin concentration in adults is less than 1 mg/dL, less than 5 percent of which is present in conjugated form.
- Clinical examination cannot detect jaundice until the serum bilirubin is greater than 2 mg/dL.
- The yellow discoloration is best seen in the periphery of the ocular conjunctivae and in the oral mucous membranes (under the tongue, hard palate).

Classification of hyperbilirubinemia

Unconjugated hyperbilirubinemia

- overproduction of bilirubin,
- impaired bilirubin uptake by the liver
- abnormalities of bilirubin conjugation

Conjugated hyperbilirubinemia

- hepatocellular diseases
- impaired canalicular excretion
- defective reuptake of conjugated bilirubin
- biliary obstruction (extrahepatic or intrahepatic cholestasis)

Conjugated hyperbilirubinemia

- Both conjugated and unconjugated bilirubin are elevated.
- There is a disproportionate elevation in the alkaline phosphatase compared with the serum aminotransferases.
- Tests of synthetic function (eg, albumin, prothrombin time) may be abnormal.

Extrahepatic cholestasis (biliary obstruction)
Choledocholithiasis
Intrinsic and extrinsic tumors (eg, cholangiocarcinoma, pancreatic cancer)
Primary sclerosing cholangitis
AIDS cholangiopathy
Acute and chronic pancreatitis
Strictures after invasive procedures
Certain parasitic infections (eg, *Ascaris lumbricoides*, liver flukes)

Intrahepatic cholestasis
Viral hepatitis
Alcohol-associated hepatitis
Non-alcohol-associated steatohepatitis
Chronic hepatitis
Primary biliary cholangitis
Drugs and toxins (eg, alkylated steroids, chlorpromazine, herbal medications [eg, Jamaican bush tea], arsenic)
Sepsis and hypoperfusion states
Infiltrative diseases (eg, amyloidosis, lymphoma, sarcoidosis, tuberculosis)
Total parenteral nutrition
Postoperative cholestasis
Following organ transplantation
Hepatic crisis in sickle cell disease
Pregnancy
End-stage liver disease

Result of EUS

Pancreas: There was no mass lesion seen in the pancreatic head, neck, body, tail, or uncinate process

Biliary System: BD was measured up to 5 mm in diameter at distal part and contained no stone or sludge. Microlithiasis were observed in gallbladder.

سطوح پیشگیری

Primordial Prevention

Primary Prevention

Secondary Prevention

Tertiary Prevention

Quaternary Prevention

Primordial Prevention

آموزش به پزشکان و کارکنان سلامت در ارتباط با تشخیص و درمان سنگ های صفراوی

آموزش سبک تغذیه ی سالم

Primary Prevention

انجام معاینات دوره ای و پرسش های مناسب در مورد ریسک فاکتورهای بیماری های کبدی و صفراوی بر اساس شرایط هر بیمار

Secondary Prevention

غربالگری ریسک فاکتورهای بیماری های کبدی و صفراوی در ویزیت های پزشک خانواده

Tertiary Prevention

درمان به موقع و با روش مناسب برای بیمار انجام شود
ارجاع بیمار به سطوح بالاتر در مواقع لازم انجام شود
درمان سرپایی یا ارجاع بیمار و درمان به صورت بستری بر اساس شرایط بیمار

Quaternary Prevention

عدم استفاده از پروسیجر ها و درمان های غیر ضروری
عدم استفاده از روش های تشخیصی نا مناسب با شرایط بیمار