

Cruising through the Clues: Decoding the Mysteries of Liver Function Tests in Healthcare

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ABSTRACT

Background: Liver function tests (LFTs) are vital tools in the realm of healthcare, indispensable for assessing hepatic health and overall liver function. These tests encompass a suite of biochemical markers, including alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), bilirubin (both direct and indirect), and prothrombin time (PT), which collectively furnish valuable insights into liver health.

Methodology: Interpretation of LFT results is a pivotal facet in the early diagnosis and management of liver diseases. An integrated approach, inclusive of clinical data and the analysis of multiple LFT parameters, is of paramount importance to deliver optimal patient care and enhance clinical outcomes.

Results: The evaluation of LFTs is complex, given the diverse etiologies that may underlie abnormal results. Elevated levels of AST and ALT are indicative of hepatocellular damage, while elevated ALP levels signify cholestasis or obstruction of bile flow. Elevated bilirubin levels may be suggestive of liver disease or hemolysis, whereas GGT levels play a pivotal role in identifying alcohol-related liver disease.

Conclusion: The significance of LFTs in diagnosing liver diseases cannot be overstated, particularly in regions with a high prevalence of liver disease, such as the Middle East, where it frequently co-occurs with obesity and type 2 diabetes. LFTs are equally indispensable in diagnosing and tracking the progression of liver diseases in developed nations. In clinical practice, these tests are deployed for a variety of purposes, encompassing the evaluation of suspected liver disease, monitoring the course of liver diseases and malignancies, and screening high-risk individuals for blood-borne viral infections. Additionally, LFTs are crucial when there is a history of alcohol abuse, ascites, chronic hepatic signs, or a familial predisposition to hemochromatosis. It should be noted that minor deviations in LFTs may be encountered in a limited percentage of healthy individuals, approximately 2.5%, and these anomalies do not carry clinical significance.

In summary, LFTs offer a nuanced view of liver function, serving as an invaluable diagnostic and monitoring tool in the realm of healthcare. A comprehensive understanding of the intricate patterns that emerge from LFT results is essential for early disease detection and tailored clinical management.

Keywords: Liver function test; Biochemical markers; Liver health; Hepatic disorders

INTRODUCTION

Liver function tests (LFTs) are a panel of laboratory tests that measure different hepatic enzymes and parameters, including alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), bilirubin (direct and indirect), and prothrombin time (PT). These enzymes and parameters are produced by liver cells and are released into the bloodstream in cases of liver damage or dysfunction^[1,2].

Elevations in LFTs may indicate liver disease; however, interpreting the results can be challenging due to various potential causes. Elevated AST and ALT levels may be caused by muscle damage, heart failure, or pancreatitis, among other conditions. Certain medications, such as statins and antibiotics, may also affect LFT results. Therefore, LFTs should be interpreted alongside other diagnostic tests and the patient's medical history^[1,2].

Diagnosis of liver disease using LFTs depends on the pattern of abnormalities observed in the different tests. Elevated ALT and AST levels suggest hepatocellular damage, while elevated ALP levels suggest cholestasis or bile flow obstruction. Elevated bilirubin levels may indicate liver disease or hemolysis. GGT levels are particularly useful in identifying alcohol-related liver disease^[1,2].

LFTs are valuable tools in diagnosing liver disease, particularly in regions such as the Middle East, where the prevalence of liver disease is high, especially in individuals with obesity and type 2 diabetes. LFTs are also essential in diagnosing and monitoring liver disease progression in developed countries^[1,2].

LFTs are indicated for various purposes in healthcare settings, including suspected liver disease, monitoring the progress of liver disease and malignancy, and screening high-risk individuals for blood-borne viral infections. LFTs may also be ordered when there is a history of alcohol abuse, ascites, chronic liver signs, or a family history of haemochromatosis. It is worth noting that minor abnormalities in LFTs may be present in a small percentage of healthy individuals (approximately 2.5%), but these are not clinically significant^[3,4].

Cholestatic liver disease may result from biliary obstruction, pregnancy, hepatotoxic drugs, or malignancy infiltration, whereas hepatocellular damage may be caused by liver infection, alcohol-induced injury, fatty liver disease, drugs, metal overload, hypoxia, or autoimmune diseases. LFT patterns can indicate hepatocellular or cholestatic injury, with raised transaminases indicating hepatocellular injury and increased ALP suggesting cholestasis. Unconjugated hyperbilirubinemia can result from Gilbert syndrome or blood hemolysis. Low albumin levels may be due to severe liver disease, pregnancy, inflammation, malnutrition, or protein loss. Initial

investigations for a hepatotoxic picture include hepatitis profile, ferritin, and transferrin saturation, while an upper abdominal ultrasound is the initial emphasis for cholestatic results^[5,6].

CASE 1: JAUNDICE IN A PREGNANT FEMALE

A 29-year-old pregnant woman at 32 weeks of gestation, presented to outpatient clinic with complaint of intense itching, particularly on her palms and soles, which has been progressively worsening over the last few weeks. She reported that she first noticed mild itching during her previous pregnancy, but it was not bothersome. However, during her current pregnancy, the pruritus had become increasingly severe and had started to interfere with her daily activities, sleep, and overall quality of life. She had also noticed dark urine and pale stools over the past week. There was no history of jaundice or significant weight loss.

She had a history of a previous full-term pregnancy, without complications, and a healthy baby delivered at 40 weeks. She denied any prior history of liver or gallbladder disease, hepatitis, or liver-related disorders. Her medical history was otherwise unremarkable.

There was no family history of liver diseases or significant medical conditions that she was aware of. She was married and worked as a high school teacher. She denied any history of alcohol, tobacco, or recreational drug use. She did not have a history of recent travel or exposure to potential liver toxins. Her diet was balanced, and she took a standard prenatal vitamin.

On physical examination, she appeared well-nourished and in no acute distress. The patient exhibited evident jaundice, characterized by icteric sclera, and yellowing of the skin. She was notably uncomfortable due to the itching. Examination of the abdomen revealed no tenderness or masses. The uterus was consistent with a 32-week gestation. No hepatomegaly or splenomegaly was appreciated. Her skin and sclera showed no signs of jaundice. There were no stigmata of chronic liver disease.

1.1 What are the initial diagnostic workup and evaluation?

Initial laboratory investigations revealed abnormal LFTs, with elevated levels of ALP at 450 U/L (normal reference range: 30-120 U/L) and GGT at 160 U/L (normal reference range: 9-48 U/L). However, ALT and AST levels were mildly elevated than reference range. Total bilirubin levels were significantly raised at 88 µmol/L (normal reference range: 5-21 µmol/L), with a predominant increase in direct (conjugated) bilirubin at 85 µmol/L (normal reference range: 0-7 µmol/L). Serum albumin levels remained within normal limits, while GGT highly elevated than reference range.

This case highlights a complex clinical scenario involving a pregnant patient presenting with jaundice, which may have multifactorial etiologies. While the patient's history excludes common causes of jaundice such as alcohol consumption and travel-related infections, the abnormal LFTs, elevated conjugated bilirubin necessitates further investigation to establish the precise underlying cause. This case underscores the importance of a systematic diagnostic workup in pregnant individuals presenting with jaundice to ensure the well-being of both the mother

and the unborn child. Further evaluation, including imaging and serological studies, is warranted to elucidate the cause of this patient's jaundice.

1.2 What additional diagnostic tests or procedures would you recommend for further evaluation in this case presentation?

Following initial laboratory investigations and physical examination, an abdominal ultrasound was performed which revealed intrahepatic biliary dilation in the absence of gallstones. While all serological tests were negative (hepatitis A,B,C, antimitochondrial antibodies, and anti-smooth muscle antibodies). These findings are suggestive of cholestatic liver disease, due to pregnancy-related cholestasis. The patient has been referred to a hepatologist for further management and monitoring during the remaining weeks of pregnancy^[7,8].

1.3 What is your diagnosis based on the laboratory investigation and clinical findings of the patient?

Based on the clinical presentation, laboratory findings, and exclusion of other causes, she was diagnosed with intrahepatic cholestasis of pregnancy (ICP), a cholestatic liver disease that can occur during pregnancy. (7, 8)

Cholestatic liver disease should be considered in pregnant patients presenting with jaundice, pruritus, and abnormal liver function tests. Early recognition and prompt management can prevent potential complications for both the mother and fetus^[7,8].

1.4 What are the possible etiologies of cholestatic liver disease?

Cholestasis liver disease has various etiologies, including biliary obstruction, pregnancy-related cholestasis, hepatotoxic medications (such as erythromycin and estrogen), and malignancy infiltration^[9]

1.5 what is your management and what is your advice?

She was informed of the benign nature of her diagnosis, and the potential risks of ICP, including preterm birth and fetal distress, were discussed. She was advised to:

- Avoid potential pruritus triggers, such as hot baths.
- Keep her nails short to prevent skin damage from scratching.
- Use moisturizers to soothe the skin.
- Antihistamines was prescribed to help alleviate itching.
- Close fetal monitoring was initiated to assess the well-being of the baby, including non-stress tests and biophysical profiles.
- Ursodeoxycholic acid (UDCA) treatment was discussed as it can reduce pruritus and improve liver function in some cases.
- She was reassured that the obstetric team would closely monitor her and her baby's well-being throughout the remainder of her pregnancy. She was advised to report any significant changes in symptoms or fetal movements promptly.
- Follow-up appointments were scheduled to track her condition and ensure the optimal care and safety of both mother and baby wellbeing.

CASE 2: DARK URINE IN YOUNG MALE

A 30-year-old male patient presented to outpatient clinic with a chief complaint of sudden onset of fatigue, loss of appetite, followed by jaundice and abdominal discomfort for the past one-week duration. He also observed dark-colored urine, pale stool, and experienced right upper quadrant abdominal pain (dull aching). He denied any history of alcohol consumption, drug abuse, or recent travel outside the country. The patient had insignificant past medical and family history (previous episodes of jaundice, hepatitis, or liver-related illnesses). While his social history, married businessman, active lifestyle, not smoke, use recreational drugs, or take any prescription medications. Further history included recent episodes of unprotected sexual intercourse with multiple partners. On general examination, the patient appeared tired, slightly distressed, and displayed clinical signs of jaundice. While abdominal examination revealed mild tenderness in the right upper quadrant, no palpable masses or hepatosplenomegaly were detected, and his vital signs were stable. This case report underscored the critical importance of assessing these concerning symptoms within the context of high-risk behaviors that might have negative implications for the patient's health.

This case presents a complex clinical scenario involving a young adult with a history of high-risk behaviors, including unprotected sexual encounters and intravenous drug use. The combination of clinical symptoms, physical examination findings (jaundice and hepatomegaly), and abnormal liver function tests points to potential liver involvement. The differential diagnosis encompasses a spectrum of possibilities, including viral hepatitis, substance-induced liver injury, or other infectious etiologies^[10,11].

2.1 What are the laboratory investigations that would typically be conducted initially?

Initial laboratory assessments demonstrated derangements in LFTs, with significantly elevated levels of both ALT (344 U/L) and AST (350 U/L), that exceeded the upper limit of normal by more than tenfold. The ALT/AST ratio, approximately 1, was indicative of acute viral hepatitis. Total bilirubin levels were moderately increased at 58 µmol/L, with a predominance of direct (conjugated) bilirubin. Besides, ALP, and GGT were slightly elevated than normal value. Given the clinical context and observed hepatobiliary dysfunction, it was imperative to stress the need for a comprehensive evaluation^[10,11].

2.2 What additional diagnostic tests or procedures would you recommend for further evaluation in this case presentation?

In light of the suspected acute viral hepatitis, further diagnostic investigations were undertaken, encompassing serological assessments for hepatitis A, B, and C. The results unveiled the presence of highly positive markers, notably the detection of hepatitis B virus (HBV) surface antigen (HBsAg), hepatitis B core IgM antibody (HBc-IgM) and presence of positive HBeAG. Concomitantly, coagulation parameters exhibited aberrations, characterized by prolonged prothrombin time (PT), and activated partial thromboplastin time (aPTT), indicative of compromised hepatic function^[10,11].

Upon confirming the diagnosis of acute viral hepatitis, the patient was promptly referred to the hepatologist for further evaluation and management and was initiated on a supportive therapeutic regimen, including intravenous

fluid administration, bed rest, and nutritional support^[10,11]. His liver function and viral load are closely monitored to assess disease progression. Antiviral therapy might be considered based on his clinical course and LFTs.

2.3 what is your advice to the patient^[10,11]?

- The patient was informed of his diagnosis and the importance of diligent monitoring of liver function tests (LFTs) and his overall health.
- He received comprehensive education about the natural course of acute hepatitis B and the critical nature of a structured and regular follow-up plan.
- Counseling was provided to the patient concerning the significance of safe sexual practices and the necessity for his spouse to undergo testing and vaccination for HBV, if required.
- A referral was made to a secondary care specialist to oversee the disease's progression and to ensure the implementation of appropriate therapeutic measures.
- The patient was advised to abstain from alcohol consumption and the use of any medications that could be harmful to the liver.
- He also emphasized the importance of adequate rest and maintaining a well-balanced diet to support his recovery.

CASE 3: BONE PAIN IN GERIATRIC PATIENT

A 65-year-old retired male sought medical attention at the outpatient clinic due to persistent bone pain (right hip and thigh) and generalized weakness over the past several months duration. He observed a change in the shape of his right thigh, which now appeared larger and misshapen compared to the left thigh. The pain had limited his mobility and caused discomfort when walking or sitting for extended periods. He denies any history of trauma, fractures, or previous bone problems in the affected area.

The patient had a history of controlled hypertension and hyperlipidemia, while had no significant prior history of musculoskeletal or orthopedic conditions. Besides, he denied any history of recent surgeries or traumatic incidents. He followed relatively active healthy lifestyle, no history of smoking, occasional alcohol drinking and no history of illicit drug use.

On physical examination, he appeared well-nourished, and he was not in acute distress. Examination of the right thigh reveals hypertrophy, warmth, and tenderness over the affected bone. There is noticeable deformity, and palpation reveals a bony prominence. The range of motion in the right hip is limited, causing discomfort during movement raising concerns regarding an underlying bone pathology, while neurological examination was unremarkable.

3.1 What are the investigations that would typically be conducted initially?

To investigate the cause of his bone pain and deformity, the following diagnostic tests were ordered. X-rays of the right thigh and pelvis revealed characteristic findings of cortical thickening, osteolytic lesions, and areas of increased bone density.

Initial laboratory assessments unveiled an isolated markedly elevated ALP level (400 U/L) (normal range: 30-120 U/L). Importantly, other liver function tests and complete blood counts (CBCs) returned within normal parameters. This isolated ALP elevation warranted further investigation to ascertain its underlying cause.

3.2 What additional diagnostic tests or procedures would you recommend for further evaluation in this case presentation?

A bone scan was conducted to assess the extent of skeletal involvement. It revealed increased radiotracer uptake in the right femur, confirming the diagnosis. Furthermore, laboratory analysis demonstrated low vitamin D levels. Based on the clinical presentation, characteristic X-ray findings, elevated serum ALP levels, and positive bone scintigraphy, he was diagnosed with Paget's disease of bone^[12,13].

Given these findings, the case was referred to secondary care for a more comprehensive evaluation and meticulous clinical assessment was conducted to exclude any concurrent malignancy. Notably, no evidence of metastatic malignancy was detected^[14].

3.3 What is the recommended management approach, and what guidance should be provided to the patient?

A treatment regimen comprising bisphosphonates and vitamin D supplementation was initiated. Over the ensuing months, the patient experienced a gradual amelioration of bone pain, accompanied by the normalization of ALP levels. Timely diagnosis and the implementation of appropriate therapeutic measures are pivotal in preventing further complications and optimizing patient outcomes in cases of Paget's disease of bone^[15].

To manage the patient's condition, he was informed about his diagnosis and the nature of Paget's disease. He was advised to^[15]:

- Receive regular follow-up with an orthopedic specialist for disease monitoring.
- Pain management, which may include analgesics and anti-inflammatory medications.
- Physical therapy to maintain mobility and function.
- Calcium and vitamin D supplements to support bone health.
- Surgical intervention, if necessary, for correcting deformities and managing complications like fractures.
- He was reassured that with appropriate management, his symptoms could be alleviated, and his quality of life improved.
- Regular monitoring would help in tracking disease progression and ensuring timely intervention when required.
- Follow-up appointments were scheduled to ensure his treatment plan was effective and modified as needed to address his specific condition.

CASE 4: EVALUATION OF ELEVATED ALP

A 33-year-old office manager female patient presented with a constellation of symptoms, including fatigue, generalized bone pain particularly in her arms and legs, which has become progressively more uncomfortable.

Also, she complained genderized weakness and persistent sense of tiredness which had gradually worsened over the past six months. She also expressed concern about her overall health. She had no known chronic medical conditions and was not currently taking any medications. She did not have a history of trauma, surgeries, or significant past illnesses. She did not smoke or use illicit drugs or consuming alcohol and maintained a balanced diet.

During the physical examination, she appeared fatigued but was well-nourished. There were no signs of jaundice, lymphadenopathy, or hepatosplenomegaly. Musculoskeletal examination revealed tenderness in multiple areas of the body, particularly at the long bones.

Notably, a routine blood test revealed an isolated elevation in alkaline phosphatase (ALP) levels, with ALP measuring 350 U/L, well beyond the normal reference range (30-120 U/L). Importantly, all other liver function tests were found to be within normal limits.

4.1 What additional investigations are typically recommended to evaluate the underlying cause of an elevated ALP level?

The diagnostic approach in this scenario encompassed additional investigations to elucidate the underlying cause of the elevated ALP. Initial assessments revealed that serum levels of calcium and phosphate were within normal ranges. However, a striking deficiency of serum 25-hydroxyvitamin D (25(OH)D) was detected, measuring at 15 nmol/L (with the normal reference range being 50 nmol/L)^[16]. Further, imaging in the form of X-rays was pursued to explore potential bone lesions, fractures, or metastatic processes. Notably, the bone scan yielded no evidence of Paget's disease or other substantial bone abnormalities.

Ultimately, based on her clinical presentation and laboratory findings, Sarah Miller is diagnosed with severe vitamin D deficiency and commenced treatment with vitamin D supplementation in tandem with calcium supplementation. Over the course of several months, the patient reported a gradual amelioration in her symptoms, including the resolution of bone pain and weakness, accompanied by a subsequent decline in ALP levels to within normal limits^[17]. This case underscores the importance of considering vitamin D deficiency as a possible etiology in cases of isolated elevated ALP levels, particularly in patients presenting with bone pain and weakness. Early recognition and the initiation of vitamin D supplementation play a pivotal role in preventing the progression of vitamin D deficiency-induced osteomalacia, ultimately leading to enhanced patient outcomes.

4.2 Can you provide information on the recommended treatment and prophylactic doses for individuals with vitamin D deficiency?

The management of vitamin D deficiency hinges on factors such as the severity of the deficiency, the patient's age, and their overall health status. Here are some general management recommendations:

- In cases of vitamin D deficiency in adults, a common approach involves administering vitamin D3 at a treatment dose of approximately 50,000 IU per week for a duration of 6 to 8 weeks. Following this initial treatment phase, a maintenance dose ranging from 1,000 to 2,000 IU per day is typically recommended. Severe cases may necessitate higher doses^[18].
- For individuals with severe vitamin D deficiency who cannot tolerate oral supplements or require expedited symptom relief, vitamin D injections are considered. The typical dose for such injection's ranges from 300,000 to 600,000 IU of vitamin D2 or D3, administered intramuscularly or intravenously. This is often followed by a regimen of maintenance therapy involving oral supplements^[18].
- Prophylactic dose for individuals at risk of vitamin D deficiency due to limited sun exposure or dietary intake, a prophylactic dose of vitamin D3 is typically recommended. This dose generally ranges from 800 to 1,000 IU per day, with the potential for higher doses in certain cases^[19].
- Sunlight exposure is an effective means to boost vitamin D levels. However, the amount of sunlight required varies based on factors such as skin type, time of day, and geographic location^[20].
- Dietary adjustments with vitamin D-rich foods such as fatty fish, egg yolks, and fortified cereals into one's diet can contribute to increasing vitamin D levels^[19].
- She was encouraged to spend more time outdoors, getting moderate sunlight exposure, and engage in regular physical activity.
- Regular follow-up appointments were scheduled to monitor her vitamin D levels and overall progress.

CASE 5: ELEVATED GGT

A 55-year-old male patient presented with a constellation of symptoms, including persistent fatigue, loss of appetite, and abdominal discomfort over four months duration. Also, he observed changing in his urine to dark color for the past two weeks. He noticed the yellowing of his skin and eyes, which prompted him to seek medical attention. He mentioned a long history of heavy alcohol consumption for over two decades but had never sought treatment for his alcohol dependence. He had not been diagnosed with liver disease in the past and had no history of viral hepatitis. He was not on any regular medications and has no known drug allergies. He denied any history of trauma, recent surgeries, or hepatotoxic medication use.

Upon examination, he appeared visibly jaundiced, with yellowing of the skin and sclera. He experienced tenderness in the right upper quadrant of the abdomen, and the liver is palpable approximately 3 cm below the costal margin. There was no evidence of ascites, spider nevi, or encephalopathy.

5.1 What are the laboratory investigations that would typically be conducted initially?

To elucidate the cause of these symptoms, a series of initial investigations were pursued. Notably, LFT was conducted, alongside an abdominal ultrasound. The LFT disclosed elevated levels of ALT and AST, indicating liver cell damage. Elevated bilirubin levels, particularly direct bilirubin, indicative of impaired bilirubin excretion.

Also, LFTs showed a highly elevated level of GGT, while mild elevated ALP above normal limits. Prothrombin time (PT) and international normalized ratio (INR) were prolonged, suggesting impaired liver synthesis.

The abdominal ultrasound demonstrated mild hepatomegaly, coupled with fatty infiltration of the liver, but no evidence of ascites or hepatic masses.

Critical to the diagnostic process, it was ascertained that the patient had a history of heavy alcohol consumption, equating to approximately 6-8 alcoholic drinks per day over the course of a decade. Further inquiry uncovered sporadic episodes of binge drinking.

Given the elevation in GGT, in conjunction with the patient's history of alcohol misuse, the leading diagnostic consideration was alcoholic liver disease^[21]. However, to confirm the diagnosis and assess the extent of liver damage, additional investigations, including a liver biopsy, were deemed necessary.

The patient was counseled to abstain from alcohol and was directed towards a substance abuse treatment program. Simultaneously, he was initiated on suitable medications and advised on lifestyle modifications to address his liver disease.

5.2 What are the possible causes or differential diagnoses for an isolated elevation of GGT when other liver function tests are within normal limits?

Isolated elevation in GGT while other liver function tests remain within normal parameters presents a diagnostic challenge, as it can emanate from a variety of causes unrelated to liver function. Potential differential diagnoses for this scenario encompass drug-induced elevation, attributable to medications such as phenobarbital, phenytoin, carbamazepine, and rifampicin, metabolic factors such as obesity and metabolic syndrome, diabetes mellitus, cardiovascular disease, chronic obstructive pulmonary disease (COPD), pancreatic etiologies such as acute pancreatitis or pancreatic cancer, renal disease, alcohol consumption, and smoking. The comprehensive exploration of a patient's medical history, alongside thorough physical examination and further investigative studies is indispensable in determining the root cause of GGT elevation^[22].

5.3 What are the potential etiologies of coexisting elevation in GGT and certain liver enzymes?

Elevated GGT levels may stem from a broad spectrum of conditions that can impair liver function and bile flow. These encompass alcohol use disorder and alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), viral hepatitis (hepatitis B and C), biliary tract obstruction or cholestasis, drug-induced liver injury, primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), Wilson's disease, and hemochromatosis^[23]. The coexistence of elevated GGT and irregular liver enzyme levels warrants comprehensive evaluation to pinpoint the specific etiology, guiding the appropriate management and therapeutic strategies.

A solitary elevation in GGT (gamma-glutamyl transferase) with concurrent normal liver function tests poses a diagnostic challenge, as it can arise from numerous etiologies that are unrelated to liver function. Some plausible

causes of GGT elevation with normal liver function tests include drug administration, such as phenobarbital, phenytoin, carbamazepine, and rifampicin, obesity and metabolic syndrome, diabetes mellitus, cardiovascular disease, chronic obstructive pulmonary disease (COPD), pancreatic disease, such as acute pancreatitis or pancreatic cancer, renal disease, alcohol consumption, and smoking. A comprehensive medical history and physical examination, in addition to further investigations, are imperative in determining the underlying cause of GGT elevation^[22].

Elevated GGT levels can be attributed to a wide range of conditions that can impair liver function and bile flow. These include alcohol use disorder and alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), viral hepatitis (hepatitis B and C), biliary tract obstruction or cholestasis, drug-induced liver injury, primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), Wilson's disease, and hemochromatosis^[23].

5.4 Could you offer insights into the recommended management plan for this case?^[22,23]

- He was informed of his diagnosis and the need for close monitoring of LFTs and overall health.
- He was counseled on the importance of completely avoiding alcohol to prevent further liver damage.
- He started on appropriate medications to manage the complications of alcoholic hepatitis, including corticosteroids, to reduce liver inflammation.
- A dietician provided guidance on a balanced diet with an emphasis on protein intake and vitamin supplementation.
- He was scheduled for regular follow-up appointments to monitor the progression of the disease and to assess the response to treatment.
- He received counseling regarding the natural history of alcoholic hepatitis.
- He was educated about the importance of rest, maintaining a balanced diet, and the need to involve his family in his recovery process.
- Continued patient's support and rehabilitation are essential to address his alcohol dependence and prevent relapse.

CASE 6: NASH OR NAFLD

A 45-year-old obese schoolteacher female attended local health center with complained of persistent fatigue, mild right upper abdominal discomfort, and a sense of fullness and early satiety after meals after meals. She has not experienced jaundice but is worried about her overall well-being. She was previously diagnosed with type 2 diabetes and dyslipidemia, which was well-controlled with oral medication and lifestyle modifications. Also, she was suffering from moderate obesity with a body mass index (BMI) of 35. She had no known history of liver disease or history of viral hepatitis. She did not smoke or use illicit drugs or consuming alcohol. She was currently married and had two children.

Upon physical examination, she appeared well-nourished, not in distress. Her abdominal examination was soft with mild tenderness in the right upper quadrant. There were no signs of jaundice, ascites, or hepatic

encephalopathy. While the neurological examination was unremarkable. The presence of hepatomegaly and mild tenderness in the right upper quadrant was noted, prompting the need for further investigation.

6.1 What further diagnostic tests or procedures would you advise for a more comprehensive evaluation in this case presentation?

In light of the clinical presentation, laboratory investigations were initiated, encompassing LFTs. The results revealed elevated levels of ALT and AST, suggestive of liver cell damage, while ALP and bilirubin levels remained within normal limits.

For a comprehensive evaluation of the patient's condition, it was imperative to pursue additional diagnostic tests. Imaging studies, such as an abdominal ultrasound or CT scan, were conducted, which showed evidence of hepatic steatosis, with a bright liver and no signs of focal liver lesions. leading to the identification of evidence consistent with non-alcoholic fatty liver disease (NAFLD). Fibro Scan (Transient Elastography) Showed evidence of liver fibrosis, indicating the presence of liver scarring. The imaging displayed diffuse hepatic steatosis, accompanied by mild fibrosis^[24]. Based on her clinical presentation, laboratory findings, and imaging studies, she was diagnosed with nonalcoholic steatohepatitis (NASH) with evidence of liver fibrosis.

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6.2 What laboratory tests could you provide indications of nonalcoholic steatohepatitis (NASH) or liver cirrhosis within the realm of LFTs?

Diagnosing NASH and liver cirrhosis via laboratory investigations involves the assessment of various parameters. In NASH, as liver inflammation intensifies, ALT and AST levels may exhibit an increase. Moreover, GGT and ALP levels may rise, denoting liver cell damage and bile duct obstruction, respectively^[25].

In the context of cirrhosis, several laboratory findings can be indicative of the condition. These include a reduction in serum albumin levels, an elevation in bilirubin levels, and an extension of prothrombin time (PT), reflecting impaired synthetic function of the liver. Furthermore, elevations in ALP and GGT levels may be observed, signaling bile duct obstruction and liver cell injury, respectively^[26].

It is important to acknowledge that these laboratory changes are not exclusive to NASH or cirrhosis and can be associated with a range of liver disorders. Consequently, confirmation of the diagnosis may necessitate further assessments, such as imaging studies and liver biopsy^[27]. An accurate diagnosis is essential to inform the appropriate management and treatment of these conditions.

The patient received counsel on implementing lifestyle modifications, including weight loss, and increased physical activity. Additionally, a treatment plan was initiated to address his concurrent conditions, namely, diabetes and dyslipidemia. Subsequent follow-up LFTs demonstrated an improvement in ALT and AST levels, indicative of the successful management of the patient's NAFLD.

6.3 What criteria do physicians use to differentiate between nonalcoholic steatohepatitis (NASH) and nonalcoholic fatty liver disease (NAFLD)?

Physicians differentiate between NASH and NAFLD through a combination of clinical assessment, laboratory tests, and imaging studies. Here are some key factors that help in distinguishing between the two^[28,29]:

Liver Biopsy: A liver biopsy is considered the gold standard for distinguishing NASH from NAFLD. It involves the microscopic examination of liver tissue to assess inflammation and fibrosis. NASH is characterized by the presence of inflammation and hepatocyte injury, which are typically absent in simple NAFLD.

Liver Enzyme Levels: In NAFLD, liver enzymes (ALT and AST) are often elevated, indicating liver inflammation and injury. However, in NASH, these enzyme levels tend to be even higher, reflecting more significant liver damage.

Imaging Studies: Imaging studies like ultrasound, CT scans, or MRI can help identify signs of fatty liver in both NAFLD and NASH. However, these tests cannot distinguish between the two conditions or provide information on the degree of inflammation and fibrosis.

Fibrosis Assessment: Non-invasive tests, such as FibroScan or elastography, can assess liver fibrosis without the need for a biopsy. These tests can help identify the extent of fibrosis, which is typically more severe in NASH than in NAFLD.

Clinical Assessment: Physicians also consider the patient's clinical history, risk factors, and the presence of metabolic syndrome. NASH is often associated with more significant metabolic abnormalities, such as obesity, type 2 diabetes, and dyslipidemia.

Serum Biomarkers: There is ongoing research into the development of serum biomarkers that can aid in differentiating NASH from NAFLD. These biomarkers may include markers of liver inflammation and fibrosis. It's important to note that the diagnosis and differentiation of NASH and NAFLD may involve a combination of these methods. In many cases, a liver biopsy may be reserved for situations where the diagnosis remains uncertain or when the degree of fibrosis needs to be precisely assessed.

6.4 What is your proposed management approach for the patient with NASH in this case?^[28,29]

She was advised to continue her efforts to manage her weight through a balanced diet and regular exercise to improve insulin sensitivity and reduce liver fat.

- Her diabetes and hyperlipidemia medications were reviewed, and she was encouraged to maintain tight glycemic control.
- She was scheduled for regular follow-up appointments to monitor her liver function and assess the progression of liver fibrosis.
- She was encouraged to continue abstain from alcohol entirely, as it can exacerbate liver damage in NASH.
- She received education on NASH, its potential progression, and the importance of adhering to her management plan to prevent liver complications.

CASE 7: ELEVATED INDIRECT (UNCONJUGATED) BILIRUBIN

A 25-year-old male presented to the outpatient clinic with a history of intermittent jaundice and fatigue that he had been noticing for several years. He described episodes of yellowing of the skin and eyes, often triggered by

factors such as fasting, stress, and illness. These episodes tended to resolve spontaneously and were not associated with any other symptoms. He had noticed that his urine occasionally becomes dark during these episodes. He had not been previously diagnosed with any significant medical condition. He denied any history of prescription medications or supplements taking. His family history was unremarkable for liver disease or any hereditary conditions. He was a non-smoker and did not consume alcohol. He practiced an active lifestyle and followed a balanced diet. He worked as a software engineer and had experienced occasional stress related to his job.

On physical examination, the patient appeared healthy and was afebrile. His sclerae were mildly icteric, and there was no palpable hepatosplenomegaly. The examination was otherwise unremarkable, with no hepatomegaly, splenomegaly, or abdominal tenderness. His vital signs were within normal limits.

7.1 What constitutes the initial diagnostic workup for the case?

Laboratory investigations revealed elevated total bilirubin levels, measuring 2.8 mg/dL (normal range: 0.3-1.2 mg/dL), and elevated indirect (Unconjugated) bilirubin levels, measuring 2.5 mg/dL (normal range: 0.2-0.8 mg/dL). Other LFTs, including ALT and AST, were within normal limits, with ALT at 23 U/L (normal range: 7-56 U/L) and AST at 22 U/L (normal range: 10-40 U/L). In addition, the complete blood count (CBC) and other routine blood tests were unremarkable. Also, the patient was followed up after three months, and laboratory investigations showed persistent elevation of total bilirubin (2.7 mg/dL) and indirect bilirubin (2.4 mg/dL). Other LFTs remained normal, including ALT (21 U/L) and AST (20 U/L).

7.2 Considering the clinical and laboratory findings, what is your definitive diagnosis?

Based on the clinical presentation and laboratory findings, he was diagnosed with Gilbert's Syndrome. It is a benign, inherited condition characterized by intermittent, mild unconjugated hyperbilirubinemia, often exacerbated by fasting, stress, or illness^[30,31].

7.3: Would you outline your recommended management and provide advice for the patient.

He was reassured about the benign nature of Gilbert's Syndrome. He was advised to maintain a healthy lifestyle, including regular meals and stress management. Follow-up appointments were scheduled to monitor his condition and ensure there were no other underlying issues^[30,31]. He is educated about the factors that can trigger jaundice and the importance of staying hydrated and managing stress. He was also informed that, in most cases, no specific treatment is required for Gilbert's Syndrome. He was encouraged to seek medical attention if he experienced any new or concerning symptoms^[30,31].

CASE 8: JAUNDICE WITH EXTRAPYRAMIDAL SIGNS

A 15-year-old male, presented to the clinic with increasing fatigue and a sense of weakness over the past six months. He noticed that his skin and the whites of his eyes had taken on a yellowish hue, and he began to have episodes of abdominal pain and discomfort and presence of dark urine. Additionally, he had been experiencing personality changes, with mood swings and irritability. His friends and family had observed these changes and encouraged him to seek medical attention. He had no known chronic medical conditions and is not currently

taking any medications. He had no history of trauma, surgeries, or recent illnesses. There was no known family history of liver disease or other significant medical conditions.

On physical examination, the patient appeared fatigued and had visible icteric. His abdomen was soft but tender in the right upper quadrant. Neurological examination reveals subtle extrapyramidal signs, including a resting tremor and dysarthria.

8.1 What constitutes the initial diagnostic workup for the case?

To investigate the cause of his symptoms, the following diagnostic tests were ordered:

LFTs revealed elevated levels of ALT and AST (69 U/L, normal range: 10-40 U/L), indicating liver cell damage, elevated total bilirubin levels (3.9 mg/dL, normal range: 0.3-1.2 mg/dL), particularly direct bilirubin (0.8 mg/dL, normal range: 0.1-0.4 mg/dL), suggestive of impaired bilirubin excretion, elevated ALP levels (52 U/L, normal range: 7-56 U/L). While, PT and international normalized ratio (INR) were slightly prolonged, suggesting impaired liver synthesis^[32,33].

8.2 What additional diagnostic tests or procedures would you recommend for further evaluation in this case presentation?

The primary care physician ordered CBCs (hemoglobin of 9 gm/dl), peripheral blood smear showed evidence of hemolysis and the presence of schistocytes, with an elevated reticulocyte count (7.2%, normal range: 0.5-2.5%). G6PD quantitative study showed a reduced enzyme activity level (3.2 U/g, normal range: 4.5-13.5 U/g). The haptoglobin level was low (< 10 mg/dL, normal range: 30-200 mg/dL), and lactate dehydrogenase (LDH) was elevated (650 U/L, normal range: 105-333 U/L)^[32,33].

While secondary care physician (hepatologist) ordered serum ceruloplasmin levels showed decreased in its level, while 24-hour urinary copper excretion was significantly elevated. Abdominal ultrasound showed hepatomegaly with evidence of hepatic steatosis. Genetic testing confirmed a mutation in the ATP7B gene, establishing the diagnosis of Wilson's disease^[32,33].

8.3 Based on the available information, what is the definitive diagnosis for this case?

Based on his clinical presentation, laboratory findings, and genetic testing results, Michael Johnson is diagnosed with Wilson's disease.

8.4 What recommendations and management strategies would you provide for this patient?

The patient was advised to avoid triggers that can exacerbate hemolysis, such as infections, certain medications (e.g., sulfonamides, dapsone), and fava beans. He also started folic acid supplementation to support red blood cell production^[32,33]. The patient was closely monitored, and blood transfusion was considered if there was evidence of severe anemia.

He started copper chelation therapy to reduce copper accumulation in his liver and other tissues and provided Zinc supplements were prescribed to block the intestinal absorption of copper. He was advised to avoid high-copper foods and sources, such as shellfish and liver^[32,33].

Regular follow-up appointments were scheduled to monitor his liver function and copper levels and assess his response to treatment and laboratory investigations showed an improvement in hemoglobin levels (10.5 g/dL), total bilirubin (1.8 mg/dL), and liver function tests (AST 35 U/L, ALT 24 U/L). The patient was advised to continue with regular follow-up and to maintain a healthy lifestyle to prevent hemolysis^[32,33].

CASE 9: JAUNDICE AND NOCTURNAL PRURITIS

A 55-year-old expatriate female, presented to the clinic with complained of persistent fatigue, nocturnal itching, sleep disturbance, jaundice, and upper right quadrant abdominal discomfort over the past six months duration. She was concerned about these symptoms and their impact on her daily life. She reported no fever, abdominal pain, or changes in her bowel habits. Her medical history was unremarkable, and she was not taking any medications or supplements. She had not taken any medications, had no history of trauma, surgeries, or significant past illness. She didn't smoke or use illicit drug or consuming alcohol.

On physical examination, the patient appeared fatigued, and had visible jaundice, with the presence of two spider angioma (small, dilated blood vessels with a central red dot) on the anterior chest wall. Presence of signs of skin pruritis. Palpate the spleen and liver for presence of hepatosplenomegaly.

9.1 Which fundamental diagnostic test would you suggest as essential in this case?

To investigate the cause of her symptoms, the following LFTs were revealed elevated levels of ALP (435 U/L, normal range: 40-129 U/L), GGT (314 U/L, normal range: 0-55 U/L), and total bilirubin (3.9 mg/dL, normal range: 0.3-1.2 mg/dL), and elevated levels of both AST (98 U/L, normal range: 10-40 U/L) and ALT (74 U/L, normal range: 7-56 U/L), while her albumin levels were slightly decreased^[34,35].

9.2 What additional diagnostic tests or procedures would you recommend for further evaluation in this case presentation?

The additional diagnostic test is an autoimmune screen which showed positive antimitochondrial antibody (AMA) at a titer of 1:640. Abdominal ultrasound revealed mild hepatomegaly and evidence of bile duct dilation.

A liver biopsy was performed, demonstrating chronic inflammation and destruction of the intrahepatic bile ducts, confirming the diagnosis of primary biliary cirrhosis (PBC)^[34,35].

9.3 Can you provide the diagnosis and outline the recommended management plan for this case?

Based on her clinical presentation, laboratory findings, positive AMA, imaging results, and liver biopsy, Mary Walker is diagnosed with primary biliary cirrhosis (PBC)^[34,35].

She was referred to hepatologist and started on ursodeoxycholic acid (UDCA) therapy to slow the progression of the disease and to alleviate symptoms such as pruritus. The patient was advised to avoid alcohol and to maintain a healthy lifestyle to support liver function^[34,35].

The patient was followed up after three months, and laboratory investigations showed a significant improvement in ALP (223 U/L), GGT (143 U/L), total bilirubin (1.4 mg/dL), AST (48 U/L), and ALT (32 U/L). The patient's AMA titer had also decreased to 1:160. The patient was advised to continue with regular follow-up and to undergo periodic imaging studies to monitor the progression of liver disease.

The management plan in the Wilson disease includes the following steps^[34,35]:

- She initiated Ursodeoxycholic Acid (UDCA) Therapy, a disease-modifying treatment for PBC, to slow the progression of the disease and relieve her symptoms.
- She was started on symptomatic relief medications and prescribed to manage her itching and discomfort.
- Regular follow-up appointments were scheduled to monitor her liver function, disease progression, and response to treatment.

CASE 10: JAUNDICE AND ASCITES

A 56-year-old retired male patient presented to outpatient clinic with 4 months history of with a history of persistent fatigue, abdominal swelling, and jaundice (yellowing of the skin and eyes). He reported a gradual onset of these symptoms and denies any recent illnesses or infections. He also noted a significant loss of appetite and weight over the past few months. He had a medical history of chronic alcohol consumption, averaging 4-5 drinks daily for the past 25 years. He mentioned no other significant medical conditions or recent travel.

Upon physical examination, the patient appeared chronically ill and malnourished. There was mild jaundice, spider nevi, and palmar erythema. Abdominal examination reveals palpable hepatomegaly with a firm, irregular edge nodular liver surface. Ascites was present, detected by abdominal percussion and shifting dullness. and the patient had leg edema. Cardiovascular and respiratory examinations were within normal limits. Also, the patient was presented with muscle wasting and significant weight loss, but there were no signs of asterixis (flapping tremor) or hepatic encephalopathy.

10.1 Which fundamental diagnostic test would you suggest as essential in this case?

Laboratory investigations reveal elevated liver enzymes, including AST (140 U/L), ALT (110 U/L), and GGT (240 U/L), indicative of liver injury. The total bilirubin level is elevated (3.5 mg/dL), predominantly direct bilirubin. Besides, the albumin level is decreased (2.8 g/dL), suggestive of hepatic dysfunction. CBC was done with mild anemia and thrombocytopenia; platelet count is low (90,000/mm³), and the prothrombin time (PT) is prolonged (18 seconds), consistent with portal hypertension. Viral hepatitis and autoimmune liver disease panels are negative. Imaging studies, including ultrasound demonstrate hepatomegaly, irregular liver surface, and ascites. No focal hepatic lesions or evidence of biliary obstruction^[36,37].

10.2 Based on the available information, what is the definitive diagnosis for this case?

Based on the clinical presentation and diagnostic workup, he was diagnosed with liver cirrhosis, likely caused by chronic alcohol consumption^[36,37].

10.3 Can you outline the recommended management plan for this case? ^[36,37]

- Abstain from alcohol consumption entirely, as it can exacerbate liver damage in cirrhosis.
- Maintain a well-balanced diet with an emphasis on protein intake and minimize sodium intake to manage fluid retention.
- Begin medications to manage complications such as portal hypertension, varices, and ascites.
- Regularly monitor for hepatocellular carcinoma through imaging studies.
- Receive vaccination against hepatitis A and B to prevent further liver damage.
- Educate close family members about the importance of liver health and routine check-ups.
- He was referred to a hepatologist for ongoing care, with a focus on managing his liver cirrhosis and its associated complications.
- His prognosis would be closely monitored through regular follow-up appointments, imaging studies, and symptom management to maintain her overall health and well-being.

10.4 What are the key distinctions in distinguishing liver cirrhosis from Biliary Cirrhosis?^[36]

Distinguishing between liver cirrhosis and biliary cirrhosis is crucial, as both conditions have distinct causes, characteristics, and management approaches. Here are some key points to help differentiate between the two:

Liver cirrhosis, often referred to as cirrhosis of the liver, is a condition where chronic liver damage results from various causes, including chronic alcohol consumption, viral hepatitis (e.g., hepatitis B and C), nonalcoholic fatty liver disease (NAFLD), or autoimmune hepatitis.

Biliary cirrhosis, specifically primary biliary cholangitis (PBC) or primary sclerosing cholangitis (PSC), is a result of autoimmune or inflammatory damage to the bile ducts. PBC is characterized by the destruction of small bile ducts, while PSC involves inflammation and scarring of both small and large bile ducts.

Liver cirrhosis is characterized by the formation of regenerative nodules surrounded by fibrous tissue. It is a result of progressive scarring of the liver parenchyma.

In primary biliary cirrhosis (PBC), there is damage to small bile ducts, leading to chronic cholestasis. In primary sclerosing cholangitis (PSC), inflammation and fibrosis primarily affect the bile ducts, resulting in a "beaded" appearance on cholangiography.

In liver cirrhosis, there may be elevated levels of liver enzymes (ALT and AST), as well as markers of synthetic liver function (e.g., albumin, prothrombin time). Bilirubin levels can be elevated in advanced stages, and signs of hepatocellular injury are prominent.

In PBC, there are specific serological markers, including antimitochondrial antibodies (AMA), which are typically present. PSC may exhibit elevated liver enzymes but is associated with an increased risk of developing cholangiocarcinoma.

Clinical manifestations of liver cirrhosis may include hepatomegaly, splenomegaly, ascites, and hepatic encephalopathy. Signs of portal hypertension are common, such as esophageal varices.

Patients with PBC may experience pruritus (itching) due to cholestasis, while PSC patients are at risk of developing strictures in the bile ducts, leading to cholangitis. Both conditions can lead to cirrhosis.

Management of liver cirrhosis focuses on addressing the underlying cause, managing complications (e.g., variceal bleeding, ascites, hepatic encephalopathy), and promoting lifestyle modifications (e.g., abstinence from alcohol). Treatment for PBC primarily involves ursodeoxycholic acid (UDCA) to slow the progression of the disease and manage symptoms. In PSC, treatment may include endoscopic or surgical interventions to address bile duct strictures.

Complications may include hepatocellular carcinoma, portal hypertension, and end-stage liver disease. PBC can progress to cirrhosis, while PSC has an increased risk of cholangiocarcinoma.

CASE 11: SEVERE EXCRUCIATING ABDOMINAL PAIN

A 45-year-old female patient presented to the primary care clinic with one day history of severe excruciating right upper abdominal pain. She described the pain as constant, severe, and colicky in nature worsening after meals. The pain radiated to her right shoulder and back. She also reported nausea and intermittent vomiting. She denied any fever, chills, diarrhea, or recent weight loss. Her past medical history was unremarkable, and she had no known allergies.

Upon physical examination, the patient appeared uncomfortable and had tenderness and guarding in the right upper quadrant with a positive Murphy's sign (pain on inspiration during deep palpation). Her vital signs were within normal limits. Also, there was no signs of jaundice or hepatosplenomegaly.

11.1 Which fundamental diagnostic test would you suggest as essential in this case?

Laboratory investigations revealed elevated levels of liver enzymes, with aspartate aminotransferase (AST) of 124 U/L (reference range: 10-40 U/L), alanine aminotransferase (ALT) of 98 U/L (reference range: 10-40 U/L), alkaline phosphatase (ALP) of 350 U/L (reference range: 40-130 U/L), and gamma-glutamyl transferase (GGT) of 480 U/L (reference range: 9-48 U/L). The total bilirubin level was within normal limits, with a value of 0.8 mg/dL (reference range: 0.3-1.9 mg/dL). The complete blood count showed mild leukocytosis and renal function tests were normal^[38].

Abdominal Ultrasound Detect of a gallbladder stone (cholelithiasis) causing distension of the gallbladder and gallbladder wall thickening but there was no evidence of common bile duct (CBD) dilation.

Based on the clinical presentation, physical examination findings, and diagnostic workup, she was diagnosed with biliary colic due to a gallbladder stone (cholelithiasis).

11.2 Can you provide the outline of the recommended management plan for biliary colic?

The management plan for biliary colic includes the following steps^[38]:

- Pain Control: Intravenous pain relief to alleviate her acute pain, which may include analgesics and antiemetics.
- NPO (Nothing by Mouth): Mrs. Davis is kept NPO to avoid stimulating the gallbladder and to prepare for possible surgical intervention.
- Surgical Consultation: The patient is evaluated by a surgeon for possible cholecystectomy (removal of the gallbladder) due to the presence of gallstones causing symptoms.
- Monitoring: Regular monitoring of vital signs and pain levels while awaiting a surgical consultation.
- Educational Counseling: Mrs. Davis is provided with information about the procedure, potential risks, and expected recovery

CASE 12: ABDOMINAL PAIN WITH FEVER

A 55-year-old male truck driver, presented to the outpatient clinic with a two-day history of severe right upper abdominal pain. He described the pain as constant and sharp, which started after consuming a high-fat meal. The pain is associated with nausea and vomiting. He denied any history of similar episodes in the past. He had a past medical history of obesity and hyperlipidemia.

Upon physical examination, he appeared uncomfortable and in moderate distress due to the pain. His vital signs showed a mild fever of 38.5°C. Palpation of the right upper abdomen elicited significant tenderness, and Murphy's sign is positive but there were no signs of jaundice or hepatosplenomegaly.

12.1 Which fundamental diagnostic test would you suggest as essential in this case?

Laboratory investigations revealed elevated levels of liver enzymes, with aspartate aminotransferase (AST) of 145 U/L (reference range: 10-40 U/L), alanine aminotransferase (ALT) of 110 U/L (reference range: 10-40 U/L), alkaline phosphatase (ALP) of 380 U/L (reference range: 40-130 U/L), and gamma-glutamyl transferase (GGT) of 490 U/L (reference range: 9-48 U/L). The total bilirubin level was within normal limits, with a value of 0.9 mg/dL (reference range: 0.3-1.9 mg/dL). The complete blood count showed mild leukocytosis with a white blood cell count of 16,000/ μ L (reference range: 4,500-11,000/ μ L) and a left shift. Abdominal Ultrasound had shown detection of gallbladder distention and pericholecystic fluid collection, consistent with acute cholecystitis^[39].

12.2 Can you provide the outline of the recommended management plan for Acute Cholecystitis?

^[39]

- Kept the patient with NPO to rest the gallbladder and reduce inflammation.

- Put the patient on the hydration and electrolyte balance is maintained through intravenous fluids.
- **Refer** the patient to surgeon for elective cholecystectomy (removal of the gallbladder) to treat the underlying cause and prevent recurrence.
- If signs of infection are present, appropriate antibiotics are administered.
- **Monitoring:** Regular monitoring of vital signs and symptom improvement.

The patient was promptly admitted to the inpatient surgical department, where he was initiated on intravenous antibiotics for infection control and provided pain management. In order to exclude alternative pathologies, a Magnetic Resonance Cholangiopancreatography (MRCP) was conducted, revealing an absence of common bile duct stones or obstruction. After three days of conservative medical management, the patient's fever subsided, and his abdominal pain showed notable improvement. Subsequently, he underwent laparoscopic cholecystectomy, which confirmed the diagnosis of acute cholecystitis with gallstones. The postoperative period transpired without complications, and the patient was discharged on the second day following the surgery.

CASE 13: POSTPRANDIAL INDIGESTION AND BLOATING

A 47-year-old female presented to the outpatient clinic with a complaint of recurrent right upper quadrant and epigastric abdominal pain for the past six months. She had a history of laparoscopic cholecystectomy three years ago due to gallstones. Despite the surgery, her abdominal pain persisted, and she also experienced postprandial discomfort, bloating, and diarrhea. The pain was described as a dull ache in nature. The patient reported that the symptoms were usually worse after eating fatty or spicy foods.

Upon examination, the patient was afebrile, visibly uncomfortable during the examination. Abdominal examination revealed mild tenderness in the epigastric region or right upper abdominal region, but there were no signs of peritonitis or organomegaly. Blood tests were ordered complete blood count (CBC) was normal, total bilirubin: 1.2 mg/dL (Normal range: 0.2-1.2 mg/dL), direct bilirubin: 0.3 mg/dL (Normal range: 0.0-0.3 mg/dL), alanine aminotransferase (ALT): 85 U/L (Normal range: 7-56 U/L), aspartate aminotransferase (AST): 55 U/L (Normal range: 10-40 U/L), alkaline phosphatase (ALP): 150 U/L (Normal range: 40-150 U/L) and gamma-glutamyl transferase (GGT): 60 U/L (Normal range: 9-48 U/L). Other tests were normal, lipase: 40 U/L (Normal range: 8-78 U/L) and amylase: 70 U/L (Normal range: 30-110 U/L). Abdominal ultrasound showed no evidence of biliary tract obstruction or residual stones. While Endoscopic Retrograde Cholangiopancreatography (ERCP) demonstrated minor sphincter of Oddi dysfunction.

13.1 What is your diagnosis based on the laboratory investigation and clinical findings of the patient?

Based on the clinical presentation, physical examination findings, and diagnostic workup, she was diagnosed with post-cholecystectomy syndrome, primarily due to sphincter of Oddi dysfunction^[40].

13.2 Can you provide the outline of the recommended management plan for this condition?

The management plan for here should include the following steps^[40]:

- Sphincterotomy: An ERCP procedure was performed to cut the sphincter of Oddi, which led to significant symptom relief.
- Dietary Guidance: She received dietary guidance to avoid high-fat meals, and spicy foods and to eat small, frequent meals.
- Medication: Medications for pain management and gastrointestinal symptom control were prescribed as needed. She was prescribed a proton pump inhibitor to manage her symptoms of indigestion
- Follow-up: She was advised to have regular follow-up appointments to monitor her progress and ensure the ongoing management of her post-cholecystectomy syndrome.

CASE 14: EXTREME FATIGUE

A 35-year-old elementary school teacher, presented to her primary care physician with a two-month history of persistent fatigue, jaundice, and abdominal discomfort. She reported a general feeling of malaise and a noticeable yellowing of her skin and eyes. Her past history was insignificant, no history of smoking, illicit drug, or consuming alcohol. No history of any allergy, no history of recent travel.

Upon initial examination, the patient had jaundice, presence of mild discomfort in the right upper quadrant with mild hepatomegaly.

Laboratory tests revealed markedly elevated levels of liver enzymes, including AST and ALT. Positive for anti-smooth muscle antibodies and anti-nuclear antibodies (ANA) with significantly elevated Immunoglobulin G (IgG) levels. While she had negative for hepatitis A, B, and C. she was referred to secondary care for further assessment and evaluation.

Histopathological liver biopsy examination revealed interface hepatitis with lymphoplasmacytic infiltrates, consistent with autoimmune hepatitis. Abdominal ultrasound and CT scan confirmed hepatomegaly with no evidence of biliary obstruction or liver tumors.

14.1 what is your definitive diagnosis?

The definitive diagnosis was autoimmune hepatitis (AIH) based on her clinical presentation, laboratory findings, and liver biopsy results. The elevated liver enzymes, positive autoantibodies, elevated IgG levels, and the characteristic histological features in the liver biopsy supported this diagnosis^[41].

14.2 what is your management plan?

She was initiated on prednisone at a high dose to suppress the autoimmune response. Also, she started on the immunosuppressive Medication (Azathioprine) was added as a steroid-sparing agent to maintain remission. She had regular follow-up: monitoring of LFTs, blood counts, and to follow any side effects of medication to adjust treatment as needed. She was given nutritional counseling, osteoporosis prevention, and vaccination against hepatitis A and B^[41].

After several months of treatment, her LFTs returned to normal, and her symptoms significantly improved. She continued to have regular check-ups to monitor her condition and medication dosages. The management goal for AIH is to achieve and maintain remission while minimizing side effects associated with long-term immunosuppressive therapy.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Al-Mohanna F, Al-Adawi S, Al-Shukaili A, Al-Ismaily S. Liver disease in the Middle East: a review of the epidemiology and risk factors. *J Gastroenterol Hepatol* 2018;32(4):769-775.
2. Al-Jabri A, Al-Busaidi Z, Al-Riyami Z, Al-Rawahi N. Non-invasive tests for the diagnosis of liver disease in the Middle East. *World J Gastroenterol* 2019;25(36):5234-5242.
3. American Gastroenterological Association position statement: evaluation of liver chemistry tests. *Gastroenterol* 2002;123:1364-1366.
4. Green RM, Flamm S. AGA Technical review on the evaluation of liver chemistry tests. *Gastroenterol* 2002;123:1367-1384.
5. Lala V, Zubair M, Minter D. Liver function tests. *Stat Pearls*. 2002.
6. Harris JC, Leggio L, Farokhnia M. Blood Biomarkers of Alcohol Use: A Scoping Review. *Curr Addict Rep* 2021;8(4):500-508.
7. Pandey S, Dhiman K, Chopra P, et al. Role of abdominal ultrasound in evaluation of patients with jaundice: a hospital-based study. *J Clin Diag Res* 2016;10(3):19-22.
8. Geenes C, Williamson C. Intrahepatic cholestasis of pregnancy. *World J Gastroenterol* 2009;15(17):2049-2066.
9. Carey WD. Approach to the patient with liver disease. In *Goldman-Cecil Medicine*. Elsevier 2021;1287-1298.
10. Lok ASF, McMahon BJ. Chronic hepatitis B: update 2009. *Hepatol* 2009;50(3):661-662.
11. Kao JH. Diagnosis of hepatitis B virus infection through serological and virological markers. *Expert Rev Gastroenterol Hepatol* 2008;2(4):553-562.
12. Ralston SH, Corral-Gudino L, Cooper C, et al. Diagnosis and management of Paget's disease of bone in adults: a clinical guideline. *J Bone Miner Res* 2019;34(4):579-604.
13. Melton LJ 3rd. Epidemiology of Paget disease of bone. *J Bone Miner Res*. 2006;21(2):3-8.
14. Reid IR. Therapy of Paget's disease of bone. *Calcif Tissue Int* 2019;104(1):25-39.
15. Singer FR. Paget's disease of bone: new insights into pathogenesis, epidemiology, and management. *J Intern Med* 2019;285(2):189-204.

16. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocr Rev 2001;22(4):477-501.
17. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011;96(7):1911-1930.
18. Holick MF. Vitamin D: A D-lightful solution for health. J Investig Med 2011;59(6):872-880.
19. Weaver CM, Alexander DD, Boushey CJ, et al. Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation. Osteoporos Int 2018;29(1):1-12.
20. Webb AR. Who, what, where and when-influences on cutaneous vitamin D synthesis. Prog Biophys Mol Biol 2006;92(1):17-25.
21. Siddiqui MS, Bataller R. Alcoholic Hepatitis: A Comprehensive Review of Pathogenesis, Diagnosis, and Treatment. J Clin Med 2021;10(4):763.
22. Hatzitolios A, Savopoulos C, Lazaraki G, et al. Gamma-glutamyl transferase: a predictor of mortality in type 2 diabetes mellitus? World J Diabetes 2011;2(10):170-173.
23. Daramola A, Agrawal D, Allamneni M. Stat Pearls. Treasure Island (FL): StatPearls Publishing 2022.
24. Rinella ME. Nonalcoholic fatty liver disease: a systematic review. JAMA 2015;313(10):1069-1078.
25. Younossi ZM, Stepanova M, Rafiq N, et al. Pathologic criteria for nonalcoholic steatohepatitis: interprotocol agreement and ability to predict liver-related mortality. Hepatology 2011;53(6):1874-1882.
26. Li W, Li K, Zhao L, Zou H, Sun J. Abnormal liver function tests predict the presence of cirrhosis in nonalcoholic fatty liver disease in China. Med 2016;95(33):e4517.
27. Rinella ME. Nonalcoholic fatty liver disease: a systematic review. JAMA. 2015;313(22):2263-2273.
28. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology 2018;67(1):328-357.
29. Kleiner DE, Brunt EM, Van Natta M, et al. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. Hepatology 2005;41(6):1313-1321.
30. Chuang WL, Lee CC. Gilbert Syndrome. StatPearls. Treasure Island (FL): StatPearls Publishing 2022.
31. Horsfall LJ, Zeitouni M, Tumber N, et al. The genetics of Gilbert's syndrome revisited: lessons from 229 Gilbert's syndrome families. Liver Int 2021;41(3):492-502.
32. Cappellini MD, Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. Lancet 2008;371(9606):64-74.
33. Luzzatto L, Seneca E. G6PD deficiency: a classic example of pharmacogenetics with on-going clinical implications. Br J Haematol 2014;164(1):469-480.
34. Lindor KD, Gershwin ME, Poupon R, Kaplan M, Bergasa NV, Heathcote EJ. Primary biliary cirrhosis. Hepatology 2009;50(3):291-308.
35. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis. J Hepatol 2017;67(1):145-172.
36. Gores GJ, Lazaridis KN. Approach to the patient with liver disease. In Harrison's Principles of Internal Medicine. 2016;1:2382-2402.
37. Tsochatzis EA, Bosch J, Burroughs AK. Liver cirrhosis. Lancet 2014;383(9930):1749-1761.
38. Tazuma S. Gallstone disease: Epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). Best Pract Res Clin Gastroenterol 2006;20(6):1075-1083.

39. Glasgow RE, Yee LF, Mulvihill SJ. Diagnosis and management of acute cholecystitis. Am Fam Physician. 2019 Jun 1;99(11):635-41.
40. Al-Jiffry BO, Al-Malki TA. Post-cholecystectomy syndrome: Current perspectives. Open Access J Surg 2021;14:133-142.
41. Manns MP, Czaja AJ, Gorham JD, et al. Diagnosis and management of autoimmune hepatitis. Hepatology 2010;51(6):2193-2213.