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Primary Biliary Cholangitis as a Differential Diagnosis in Abnormal Liver Function Tests Performed In a Primary Care Setting.

DR AMEER MUHAMMAD KHAN
CONSULTANT FAMILY PHYSICIAN PRIMARY HEALTHCARE CORPORATION QATAR

DR ASIF PARVEZ MALIK
CONSULTANT FAMILY PHYSICIAN PRIMARY HEALTHCARE CORPORATION QATAR

Abstract
Chronic liver disease and cirrhosis are leading causes of morbidity and mortality across the world. Primary biliary cholangitis (PBC), previously known as primary biliary cirrhosis is a chronic autoimmune disease resulting in the destruction of the small bile ducts in the liver. This case study looks at the differential diagnosis of abnormal liver function tests with a special emphasis on primary biliary cholangitis. Annual routine blood tests performed in primary care almost always include a liver function test which if abnormal require close monitoring or warrant further investigations. It is imperative to identify the cause of abnormal liver function tests and to initiate management early in the process to prevent the development of chronic liver disease and ultimately fibrosis and cirrhosis.
Keywords: Primary Biliary Cholangitis, Diagnosis, Abnormal Liver, Primary Care Setting

الملخص:

يعتبر مرض الكبد المزمن وتليف الكبد من الأسباب الرئيسية للحالات المرضية والوفيات في جميع أنحاء العالم. إن التهاب الأقنية الصفراوية الأوليّ (PBC)، المعروف سابقاً باسم تليف الكبد الصفراوي الأوليّ، هو أحد أمراض المناعة الذاتية المزمنة التي تؤدي إلى تدمير القنوات الصفراوية الصغيرة في الكبد. تبحث دراسة الحالة هذه في التشخيص التفريقي لاختبارات وظائف الكبد غير الطبيعية مع التركيز بشكل خاص على التهاب الأقنية الصفراوية الأوليّ. تشمل اختبارات الدم الروتينية السنوية التي يتم إجراؤها في مرحلة الرعاية الأولية بشكل دائم تقريباً اختبار وظائف الكبد والذي يتطلب مراقبة دقيقة أو يتطلب مزيداً من الفحوصات في حال كان غير طبيعي. من الضروري تحديد سبب اختبارات وظائف الكبد غير الطبيعية وبدء العلاج في وقت مبكر من العملية لمنع تطور أمراض الكبد المزمنة والتشمع والتليف الكبدي في نهاية المطاف.

الكلمات المفتاحية: التهاب الأقنية الصفراوية الأولي، التشخيص، الكبد غير الطبيعي، وضع الرعاية الأولية.

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Introduction and Case Presentation:
This case study looks at a young fit and healthy 41-year-old female Caucasian retail worker who presented with symptoms of lethargy and non-specific low back pain symptoms. In terms of etiology of liver dysfunction, she was not overweight, her BMI was 22. She had no past medical history nor a family history of autoimmune conditions nor of any other significant medical problems. She enjoyed cycling, was a non-smoker, and rarely consumed alcohol, except on special occasions. In terms of drug therapy, she did not use any illicit drugs, and was not taking any regular prescribed nor over the counter medication. In terms of symptoms she had general lethargy but no pruritis. She was happily married and had two young children. There was no recent history of travel. She put her lethargy down to her long shifts at work, and not sleeping properly. She suspected her low back pain could have been due to the repetitive bending and lifting she performed in her capacity as a retail worker. Her examination was unremarkable, she had full range of movement of her spine, and had minimal tenderness along her right lumbar paraspinal muscles, but no bony spinal tenderness. Her abdomen was soft and nontender, and her sclerae were clear, there was no sign of jaundice or hepatomegaly. Her vital signs were normal, and she did not complain of any change in the color of her stool or urine. She was diagnosed with musculoskeletal low back pain and prescribed some ibuprofen and paracetamol for her pain. She was advised to perform gentle exercise and avoid any heavy lifting. Our practice had a policy of performing routine screening blood tests on all our patients who were above the age of 40 to rule out any chronic conditions. She happily agreed to this.

Investigations
Her screening blood tests showed some mild liver dysfunction: bilirubin 16, GGT 133, ALP 116, AST 45, ALT 63,
Other results included a positive AMA, vitamin D of 22mmol/l, serum iron 34.8 (normal <30) normal TSH, FBC, BSL, HbA1c, folate, lipid profile, ENA, ds DNA, EUC, negative ANA, LKM, hepatitis A, B and C serology. Abdominal ultrasound showed a fatty looking liver and a non-obstructing renal calculus.
Further investigations included a repeat of her AMA. She also had a DEXA scan given the higher risk of osteoporosis in the setting of PBC especially in view of her low vitamin D. She had a full liver database including a full iron profile. She also had a non-invasive liver fibrosis marker test completed.
Results: AMA positive, liver database and iron profile normal, DEXA scan showed no evidence of osteoporosis. Her non-invasive fibrosis marker (APRI index, HEPA score, liver wave elastography) suggested no evidence of advanced liver fibrosis, bilirubin 10, albumin 41, PT 11. Significantly positive anti-mitochondrial antibodies support a diagnosis of primary biliary cholangitis. Fibrous markers were unremarkable and suggest that she does not have significantly advanced disease and the normal bilirubin is a good prognostic feature.

Differential Diagnosis
Impaired liver function tests are a common finding in general practice. Possible causes include chronic hepatitis C or B, acute viral hepatitis, Non-alcoholic fatty liver disease,

hemochromatosis, autoimmune hepatitis, certain medications, alcohol-related liver injury, Wilson's disease and obesity.
An isolated increased ALP and GGT raise the possibility of bile duct obstruction, primary biliary cholangitis, benign recurrent cholestasis, and infiltrative disease of the liver such as sarcoidosis, lymphoma, and metastatic disease.

Liver Panel Tests

Once an abnormal liver function test has been reported by the laboratory, it is wise to repeat the test in 4-6 weeks as up to 30% of these results will subsequently be reported as being normal. If two consecutive tests come back as abnormal then, in addition to the routine full blood count, thyroid function tests, renal function tests, one needs to do the following investigations to identify the etiology of the abnormal liver function test:
If suspecting chronic or acute viral hepatitis perform HBsAg, HBcAb, HBsAb HCV Ab. In Autoimmune hepatitis do the following tests: ANA, AMA, ASMA, SPEP, LKM. When considering Haemochromatosis, perform Fe, TIBC, Ferritin, HFE and for Alpha 1 antitrypsin deficiency perform the A1AT phenotype.

Imaging for Abnormal Liver Function Tests

These include: Diagnostic imaging studies – ultrasound and CT scan of the abdomen, Magnetic resonance imaging (MRI). A HIDA scan is useful to assess for cystic duct obstruction (acute cholecystitis) Endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous cholangiography (PTC), Magnetic resonance cholangiopancreatography (MRCP).

Management, Outcome and Follow-up

She was commenced on Ursodeoxycholic acid and Vitamin D. She attended for regular reviews with repeat liver function tests which showed an improvement in all her markers. She continued to be asymptomatic and made good overall progress. She tolerated the UCDA treatment well but initially experienced mild nausea which abated after she took it in the evening. Her lethargy also improved, and she did not develop any pruritis or jaundice. She will continue attending the liver clinic and have regular liver function tests and be monitored for any symptoms.

Discussion

Primary Biliary Cholangitis Is an autoimmune disease of the liver. It results from a slow, progressive destruction of the small bile ducts of the liver resulting in cholestasis. Further slow damage to the liver tissue can lead to scarring, fibrosis, and eventually cirrhosis.
Common symptoms are tiredness, itching and, in more advanced cases, jaundice. In early cases, there may only be changes in blood tests. It can eventually progress to cirrhosis of the liver which may lead to complications such as ascites, oesophageal varices, and hepatic encephalopathy.
PBC is a relatively rare autoimmune disease, affecting up to 1 in 3,000–4,000 people. It is much more common in women, with a sex ratio of at least 9:1 female to male. It results from a slow, progressive destruction of the small bile ducts of the liver. Most people with PBC (>90 percent) have anti-mitochondrial antibodies (AMA) against pyruvate dehydrogenase complex (PDC-E2). Most patients are currently diagnosed when asymptomatic, having been referred to the hepatologist for abnormal liver function tests performed for routine or annual screening.

Abdominal ultrasound, MR scanning (MRCP) or a CT Scan is usually performed to rule out blockage to the bile ducts which may cause secondary biliary cirrhosis because of biliary duct disease or gallstones. Given the high specificity of serological markers, liver biopsy is not necessary for the diagnosis of PBC. It is still necessary when PBC-specific antibodies are absent, or when co-existent autoimmune hepatitis, non-alcoholic steatohepatitis or where extra-hepatic comorbidities are suspected.
Medical therapy of PBC targets disease progression and symptom control. The backbone of treatment of PBC is bile acid. Ursodeoxycholic acid (UDCA) has been the only drug available until more recently when obeticholic acid (OCA), a semi-synthetic hydrophobic bile acid analogue, has been licensed in patients failing UDCA response or intolerant to UDCA. Current treatment guidelines recommend that patients with PBC who have an inadequate response to UDCA after 12 months of therapy should be considered for second line therapy.

Conclusion and Learning points

Family Physicians working in primary care routinely arrange screening blood tests for their patients. We commonly come across abnormal liver function tests, and it is important to understand how to manage these patients. If there are minimal risk factors, the patient is fit and well, it is safe to repeat these tests after a small interval. If, however, two consecutive abnormal tests are seen, it is important to have a guideline on how to manage these patients. Always remember to consider performing an autoimmune screen on these patients if all other common causes have been ruled out and consider primary biliary cholangitis in the differential diagnosis. UCDA is generally well tolerated and helps in the management of primary biliary cholangitis. It has improved the quality of life of these patients by reducing pruritis, lethargy and jaundice. In most cases it has slowed the progress of the disease preventing liver fibrosis and ultimately cirrhosis.

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