Does she have a fatty liver?

Ken Sikaris, *MBBS, FRCPA, BSc (Hons), FAACB, is Director of Chemical Pathology, Melbourne Pathology, and Senior Fellow, St Vincent's Hospital Clinical School, Melbourne University, Victoria.*
Prithi Bhathal, *MBBS, PhD, FRCPA, is Professorial Research Fellow, Department of Pathology, Melbourne University, and Consultant Pathologist, Melbourne Pathology, Victoria.*

Case history

A 31 year old woman complains of weight gain and irregular periods. She also has a strong family history of type 2 diabetes. She is not on any medications and denies any alcohol consumption. Her weight is 85 kg but her height is only 170 cm in comparison. She has a waist circumference of 93 cm and her blood pressure on this occasion is 140/90.

As well as thyroid function and sex hormone tests, you request routine biochemistry including lipids and a fasting glucose.

Investigations

Thyroid function tests (TFT), luteinising hormone (LH), follicle stimulating hormone (FSH), testosterone and oestradiol tests are within normal limits.

Liver function tests (LFT)		
Protein	78 g/L	(65–85)
Albumin	43 g/L	(35–48)
Bilirubin	8 umol/L	(<15)
Alkaline phosphatase (ALP)	72 IU/L	(<110)
Gammaglutamyl transpeptidase (GGT)	36 IU/L	(<30)
Alanine aminotransferase (ALT)	48 IU/L	(<30)
Asparate aminotransferase (AST)	35 IU/L	(<30)
Lipids		
Total cholesterol	5.4 mmol/L	(<5.5)
Triglycerides	1.8 mmol/L	(<2.0)
HDLC	1.0 mmol/L	(>1.0)
LDLC	3.2 mmol/L	(<3.5)
Fasting glucose	5.8 mmol/L	(<5.5)

Question 1

Would you consider any of the LFT abnormalities to be significant?

Question 2

What is a fatty liver?

Question 3

How can a diagnosis of fatty liver be made?

Question 4

Does this woman have the metabolic syndrome?

Question 5

What other investigations are required?

Question 6

How would you manage this woman?

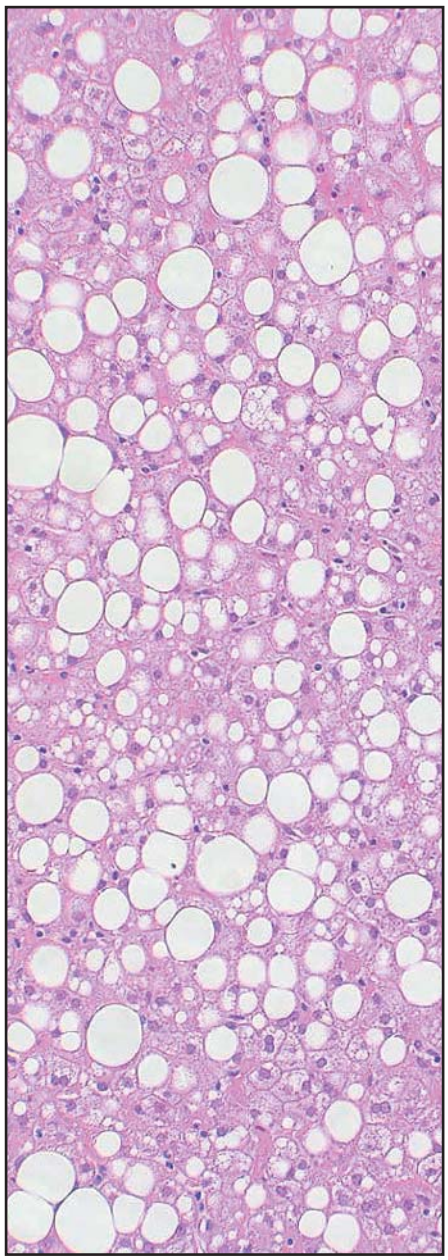

Figure 1. Steatosis: Liver cells filled with fat vacuoles

Answer 1

Although the liver enzymes (ALT, AST and GGT) are only mildly elevated, all levels are high for a woman of this age. Note that many laboratories do not quote age and sex related reference intervals for liver enzymes (as recommended in recent guidelines[1]) and subtle but significant abnormalities may be missed.

Answer 2

Fatty liver (or hepatic steatosis) is an accumulation of triglycerides in the liver (>5% of the liver weight) that is often seen in alcoholism, but may also be seen in nonalcoholic patients. Both are characterised by elevated liver enzymes,[2] although when the ALT/AST ratio is high, nonalcoholic hepatic steatosis is more likely,[3-4] as in this case. Hepatic steatosis (fatty liver) can progress to steatohepatitis (fat and centrizonal inflammation) usually with fibrosis (when AST levels are often higher). Nonalcoholic hepatic steatohepatitis can progress to cirrhosis and its strong association with insulin resistance and the risks of the metabolic syndrome are vitally important.

Answer 3

Fatty liver is firstly a diagnosis of exclusion. Rule out common causes of subclinical hepatitis such as chronic viral hepatitis and consider autoimmune hepatitis (antismooth muscle/actin antibodies). Alcohol and other toxins, including prescribed medications and herbal therapies should also be excluded. In men of this age also consider the possibility of genetic haemochromatosis. Ultrasound can show evidence of fatty liver when the subtle changes in echogenicity have been properly calibrated for. Computerised tomography (CT) and magnetic resonance imaging (MRI) may also show changes, but findings can also be nonspecific. Liver biopsy is currently the only way to diagnose the progressive form of fatty liver disease (namley steatohepatitis). Advanced imaging techniques such as proton magnetic resonance spectroscopy are ideal but are generally confined to research studies. There are many risk factors for fatty liver disease and all are related to metabolic syndrome[5-6] (previously called 'Syndrome X').

Answer 4

The USA National Cholesterol Education Program (NCEP) has established diagnostic guidelines for the metabolic syndrome.[7] This patient satisfies almost all the criteria. Furthermore, although her fasting glucose is not ≥6.1, neither is it below 5.5 (the cutoff recommended by Diabetes Australia) (Table 1).

Answer 5

Although other investigations may reveal further abnormalities (eg. fasting insulin, oral glucose tolerance test [OGTT], ultra sensitive C-reactive protein [CRP], urate), they will probably not significantly alter the diagnosis or management. A low level of sex hormone binding protein (SHBG) is a particularly good predictor of insulin resistance, especially in women. Polycystic ovary syndrome, a condition that has a strong relationship with obesity and insulin resistance, is often biochemically associated with low SHBG and a high LH/FSH ratio (>2.5).

Answer 6

Clear guidelines are available for the clinical and therapeutic intervention for hypercholesterolaemia, hypertension and diabetes. Until formal studies of new therapies of metabolic syndrome are completed (eg. metformin, thiazolidinediones, alpha glucosidase inhibitors) therapy will largely be based on diet and weight reduction, which are effective in improving both the features of the metabolic syndrome and fatty liver.

Conflict of interest: none declared.

Table 1. Adult treatment panel (ATPIII) criteria for metabolic syndrome (any three will satisfy a diagnosis)

	Women	Men
Fasting glucose	≥6.1 mmol/L	
Fasting triglycerides	≥1.69 mmol/L	
Fasting HDLC	<1.29	<1.04
Waist circumference	>88 cm	>102 cm
Blood pressure	≥130/88 mmHg	

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