

# A 53-year-old man with possible diabetes mellitus

Commentary by **STEPHEN M. TWIGG** MB BS, PhD, FRACP

**What are the management priorities for this patient who presents with sepsis, and at review has an enlarged liver and a glucose abnormality?**

## Case scenario

A 53-year-old man presented with a fever of 39°C and profuse sweating. He had a mild sore throat, dysuria but no loin pain, and felt generally unwell.

Urinalysis showed pus cells, and culture revealed a multisensitive *Escherichia coli*. The patient had neutrophilia and some mild elevation of bilirubin (30 µmol/L) and gamma glutamyltransferase (GGT; 65 U/L). A random blood sugar level (BSL) was 7.8 mmol/L. Both his parents had become insulin dependent diabetic late in life.

The patient responded well to amoxicillin, but an ultrasound was organised via casualty due to concerns after 48 hours that he was still unwell and obstruction to his kidneys was considered a possibility. When seen in casualty he was afebrile and admitted to some recent excess of alcohol.

At review the patient looks much better. A fasting BSL is 8.8 mmol/L, total cholesterol 4.3 mmol/L, and triglycerides 1.3 mmol/L, and liver function tests are still mildly abnormal. His liver is enlarged with ultrasound features of fatty liver, and his spleen and kidneys are also at upper limits of normal. Blood pressure is in the normal range. His BMI is 29 kg/m<sup>2</sup>. To avoid overloading the patient with too much information, initial discussion focuses only on issues related to his alcohol intake, which is generally moderate, and the diabetes, which is becoming overt.

What are the priorities for this man? Should he start taking metformin straight away? Should he be given an ACE inhibitor or an angiotensin receptor blocker (ARB)? Should he have a full diabetic workup? Is a glucose tolerance test (GTT) necessary? Is the enlarged spleen of significance? Could he already have portal hypertension, and how should this be investigated? What is a safe level of drinking for patients with diabetes?

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Dr Twigg is Endocrinologist and Associate Professor in Medicine, Royal Prince Alfred Hospital, and the University of Sydney, Sydney, NSW.

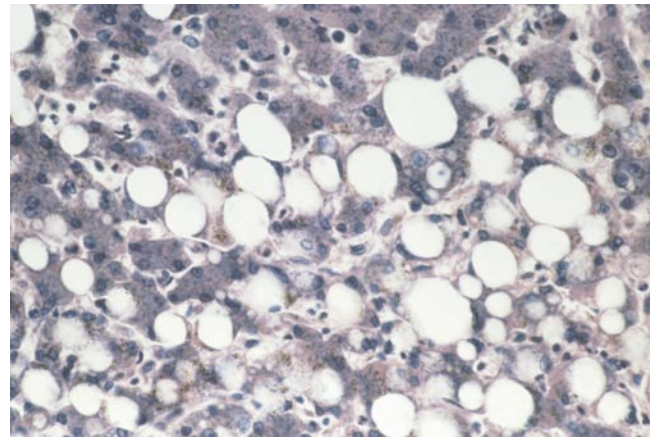


Figure. Light micrograph of a section through fatty liver. The liver cells (purple with dark nuclei) have been distended by large fat droplets.

## Commentary

The medical priorities in this man's care can be divided into four areas: management of the sepsis, assessment of his alcohol intake, hepatic assessment, and definition of the blood glucose abnormality.

### Management of sepsis

First, the *E. coli* urinary tract infection (UTI) with systemic sepsis requires management. The patient has been treated with antibiotic therapy with resolution of sepsis, and renal tract obstruction and upper tract pathology has been excluded. Although diabetes can increase susceptibility to urinary sepsis, the entire renal tract requires full investigation to determine the cause of the UTI; males, in particular, should not develop an UTI in the absence of a structural renal tract abnormality.

Bacterial prostatitis may well have been the diagnosis, which would require careful monitoring to exclude disease relapse. If this occurs, a more potent antibiotic regimen should be started (e.g. with norfloxacin for up to two weeks).

Following prompt resolution of the acute sepsis, an appropriate next step would be elective urological referral for consideration of a cystoscopy examination.

### Alcohol intake

This man's alcohol intake is of concern. A thorough history should be taken to quantitate carefully his current alcohol intake and to assess for alcohol dependence. If the latter were the case, abstinence from alcohol and commencement of formal counselling would be appropriate. If he was not thought to be alcohol dependent, moderation of alcohol intake at or below 20 g of alcohol (two standard drinks) daily would be appropriate. This individualised recommendation is more stringent than the NHMRC's standard recommendation of an intake at or below 40 g daily. This is because, although some alcohol intake can

protect against adverse cardiovascular disease outcomes, we also want to limit this patient's alcohol consumption as it may contribute to his overweight state and hypertension and, particularly over time, to an exacerbation of his liver disease.

### Hepatic assessment

The patient's enlarged liver requires assessment. He does not appear to have any systemic features of chronic liver disease, and the liver ultrasound has revealed features consistent with fatty liver/steatohepatitis. The spleen is not clearly enlarged on imaging, which also helps to exclude portal hypertension. Synthetic liver function tests (INR, serum albumin, and bilirubin levels) could be performed to provide further assurance in excluding liver failure.

Due to the abnormal liver enzyme tests, including transaminase levels, and the hyperglycaemia, haemochromatosis should be excluded, initially by iron studies. If the iron saturation is elevated and/or the serum ferritin level is clearly increased, specific genetic testing for haemochromatosis is warranted.

It is most likely, however, that this patient has fatty liver (Figure) due to a combination of being overweight with an element of insulin resistance (despite the normal triglycerides) and the excessive alcohol intake. Liver biopsy should be considered only in patients in whom ongoing significant liver damage is suggested by the clinical picture and/or blood tests. If there were any doubt about the indication for such a biopsy, referral to a hepatologist would be appropriate.

### Definition of blood glucose abnormality

Finally, the blood glucose abnormality needs to be defined. At the time of this patient's acute illness, a formal random blood glucose level was within the normal range. However, once his clinical condition had clearly improved, fasting hyperglycaemia was detected, in the range where, if a second fasting plasma glucose level was at, or above, 7.0 mmol/L, the diagnostic criteria for diabetes mellitus would be fulfilled.

If this patient is shown to have diabetes on the basis of a repeat fasting blood glucose level, lifestyle intervention would be appropriate. The aim of lifestyle intervention is to achieve and maintain graduated weight loss by reduction of caloric intake and institution and maintenance of regular physical activity.

If the fasting glucose level at repeat testing is not into the diabetic range, the patient should undergo a formal 75 g oral glucose tolerance test to determine further whether diabetes is present.

Considering the strong parental family history of insulin dependence later in life, which is typical of long-standing type 2 diabetes, any diabetes mellitus in this patient is likely to be type 2 diabetes. Occasionally, due to chronically excessive alcohol intake, diabetes will be secondary to pancreatic insufficiency,

although such affected patients are nearly always under- rather than overweight.

### Therapy

For overweight or obese patients with type 2 diabetes, metformin therapy is the most appropriate monotherapy as one study has implicated it in reducing diabetes-related death and cardiovascular death,<sup>1</sup> and it could also help, minimally, in weight loss. I would start this medication if the glycaemic (HbA<sub>1c</sub>) target was not being met, to complement the patient's lifestyle management. This is presuming that he does not have risk factors for lactic acidosis contraindicating metformin use; such factors include major metabolic instability, and renal and liver failure, none of which appeared to be present during his recovery. Metformin should be started at a low dose (e.g. 250 mg twice daily, increasing after one week to 500 mg twice daily) and taken during or after meals to limit gastrointestinal side effects.

### Screening tests

In any patient with newly diagnosed type 2 diabetes, screening tests should be undertaken for end-organ damage; such patients may have had diabetes for some years before diagnosis. If microalbuminuria is present and confirmed by repeat testing, then commencement of an ARB or ACE inhibitor would be appropriate. The blood pressure target should be tight, at least <130/80 mmHg. This patient should have appropriate screening for retinopathy and fasting serum lipids with cholesterol subsets performed and managed. Smoking cessation will be required if he is a smoker. Aspirin for cardiovascular prophylaxis should be considered. Following history taking and physical examination, screening investigations for cardiovascular disease may be warranted.

As the therapeutic relationship develops with the patient (including elucidating his psychosocial state), and over the course of time, it would be hoped that this man would 'turn over a new leaf' and become a model patient, complementing lifelong lifestyle management with adherence to a judicious program of targeted medicines. MT

### Reference

1. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998; 352: 854-865 [Erratum in *Lancet* 1998; 352: 1557].

**DECLARATION OF INTEREST:** Dr Twigg delivers occasional, ad-hoc presentations on behalf of the following pharmaceutical companies: Novo Nordisk, Sanofi-Aventis, Alphapharm, Servier, GlaxoSmithKline, Pfizer and Bristol-Myers Squibb, none of which affects his commentary on the current case.