CASE REPORT

Resolution of NASH with weight loss documented by hepatic MRI

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SUMMARY

A 57-year-old Asian woman with type 2 diabetes mellitus, hypertension, obesity, dyslipidaemia and history of breast cancer, was referred to the cardiovascular health and lipid centre for evaluation and management of dyslipidaemia and NASH (Non-alcoholic steatohepatitis) in 2010. She originally had a detailed work up at the liver clinic for elevated liver enzymes, with no associated symptoms. Initial hepatic MRI on 22 January 2007 showed diffuse fatty infiltration quantitated at 15%. We counselled her on lifestyle modifications, including dietary measures and exercise, geared toward weight loss. Over the next 2 years, she lost 24.5 lbs; repeat hepatic MRI on 22 December 2011 showed 6% hepatic fat, which is within the normal range. This case demonstrates the efficacy of significant weight loss in the improvement and resolution of NASH. We believe that this is the first case report documenting this through liver MRI.

BACKGROUND

Non-alcoholic fatty liver disease (NAFLD) is a metabolic disorder closely related to insulin resistance and obesity.^{1 2} This close association has led to the likely consideration of NAFLD as the hepatic manifestation of metabolic syndrome.^{3 4} NAFLD comprises a spectrum of disease that ranges from benign hepatic steatosis to inflammatory changes with or without fibrosis. Non-alcoholic steatohepatitis (NASH) may progress to cirrhosis and hepatocellular carcinoma (HCC). Bugianesi *et al*⁵ demonstrated that features consistent with metabolic syndrome were observed more frequently in patients with HCC superimposed on cirrhosis of unknown aetiology.⁶ NASH refers to the presence of hepatic steatosis when no other cause of secondary hepatic fat accumulation (most commonly, heavy alcohol consumption) is identified. It has a high prevalence and is seen worldwide. It is also the most common liver disorder in developed nations, where major risk factors include central obesity, type 2 diabetes mellitus, dyslipidaemia and metabolic syndrome.^{6 7} Through this case of metabolic syndrome and NASH, we demonstrate the significant impact of lifestyle changes leading to weight loss on fatty infiltration of the liver.

CASE PRESENTATION

A 57-year-old Asian woman presented with type 2 diabetes mellitus, hypertension, obesity, dyslipidaemia and a history of breast cancer. She was initially evaluated at the liver clinic for elevated liver enzymes, with no associated symptoms. She denied the use of any over the counter medications, herbal

products or oestrogen. She had no history of nicotine or alcohol use and no family history of liver disease or diabetes, and no personal history of autoimmune disorders. Her medications included amlodipine, metoprolol succinate, letrozole, omeprazole, calcium carbonate-vitamin D and multivitamins.

On physical examination, waist circumference was 36 inches, there was no hepatosplenomegaly or any stigmata of chronic liver disease. Thereafter, the patient was referred to the cardiovascular health and lipid centre for management of her type 2 diabetes, dyslipidaemia and NASH.

INVESTIGATIONS

Liver disease work up revealed negative serologies for hepatitis B and C, a mildly positive antismooth muscle antibody test (1:20), negative antinuclear antibody, antimitochondrial antibody, ceruloplasmin, α one antitrypsin, insulin level and iron studies.

Hepatic MRI on 22 January 2007 showed diffuse fatty infiltration with a fat fraction percentage of 15% (figure 1).

TREATMENT

In addition to having type 2 diabetes, the patient also had four components of metabolic syndrome: increased waist circumference, hypertension, elevated glucose and high triglyceride. We counselled her on dietary modalities to lower low-density lipoprotein (LDL), advised her to exercise at least 30 min for at least 5 days a week and gave her behavioural tips to reduce portion size to help lose weight. These tips in our clinic have resulted in an average weight loss of 10.8 lbs at a mean follow-up of 1.75 years.⁸ The tips stress on having breakfast every morning, putting down the fork between bites during meals and taking a sip of water, drinking a glass of water before each meal and, if dining outside, taking half of the restaurant meal home. Type, duration and number of sessions of exercise per week were assessed at baseline. The physician gave the patient exercise prescriptions and she followed-up with a dietician at regular visits. Of note, LDL-cholesterol (C) was 111 mg/dL on 18 August 2011 (table 1) when pravastatin 10 mg was started, with follow-up LDL-C of 85 mg/dL on 13 October 2011 (table 1).

OUTCOME AND FOLLOW-UP

Over 2 years, the patient lost 24.5 lbs by walking 1–2 h daily, decreasing portion sizes and following a low fat and low carbohydrate diet. Repeat hepatic MRI on 22 December 2011 showed no evidence of fatty liver with a fat fraction percentage of 6%

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Figure 1 Hepatic MRI showing fat fraction percentage of 15% (high)—before 22 January 2007.

(normal is 4% with SD of 5%; [figure 2](#)). The 4 month duration of statin treatment was unlikely to affect liver fat so dramatically; thus, we believe the 2 years of lifestyle modifications and significant weight loss were responsible for the resolution of NASH. [Table 1](#) shows the patient's labs, statin medication and exercise during this time period. Of note, glycated haemoglobin (HbA1c) decreased from 6.9 to 6.1, probably also due to weight loss.

DISCUSSION

This patient had 15% hepatic fat when she weighed 167 lbs ([figure 1](#)). The fact that the percentage of hepatic fat decreased

to 6% after losing 24.5 lbs ([figure 2](#)) strongly suggests that obesity was responsible for NASH in this case. We believe that this is the first case report documenting this through serial liver MRIs. Of note, the patient's liver function tests also improved and became normal with weight loss. HbA1c also decreased from 6.9 to 6.1.

Prevalence estimates for NAFLD vary widely depending on the population studied and the definition used. The worldwide prevalence for NAFLD is estimated at 6.3–33% and is lower for NASH, ranging from 3% to 5%.⁷ NAFLD is highly prevalent in persons with type 2 diabetes mellitus, with an ultrasound study showing an estimate of 69% and up to 50% in patients with dyslipidaemia attending lipid clinics.⁷ From its official recognition as a distinct entity in 1980, due largely to the study published by Ludwig *et al*,⁹ where biopsy specimens of patients with NASH of unknown cause were reviewed, NAFLD was identified as being causally related to obesity. A review study of autopsy records of 207 obese patients was carried out by Wanless *et al*, and found that the severity and prevalence of hepatic steatosis was proportional to the degree of obesity. The validation of this relationship to insulin resistance and obesity in other studies^{1 2 10} has led to the prescription of dietary modifications and increased physical activity as the first line of treatment for NAFLD.⁷ Lifestyle interventions combining dietary restriction, behaviour modification and exercise improve liver function tests and reduce steatosis when a reduction in weight/body mass index of 7–9% is achieved.^{11–13} Palmer and Schaffner¹¹ retrospectively evaluated 39 overweight patients who were screened to exclude any other conditions affecting the liver. The most common hepatic enzyme elevation was of alanine aminotransferase, and they found that its activity improved by 8.1% for every 1% reduction in body weight. Ueno *et al*¹² studied 25 obese Japanese participants and divided them into treated and control groups. Fifteen underwent a programme of restricted diet, in which calories were based on ideal body weight, and exercise for 3 months. No interventions were performed in the control group. Patients in the treated group showed a significant decrease in weight, aminotransferases, total cholesterol and fasting plasma glucose levels. In addition, steatosis was significantly improved on liver biopsy in these patients. The 10 patients in the control group did not show any of these biochemical and histological changes. Forty-eight patients with chronically elevated liver enzymes and clinical, radiological and histological findings of fatty liver were prospectively studied by Knobler *et al*.¹⁴ Sixty-four per cent of the patients evaluated

Table 1 Labs, weight, statin and exercise trends

Date	Total cholesterol	LDL	HDL	TG	HbA1c	ALT/AST	Wt (lbs)	Statin	Exercise
11 March 2006	211	125	54	159	6.9	59/36	167	None	30 min walk daily
22 January 2007	1st Hepatic MRI showed diffuse fatty infiltration with a fat fraction percentage of 15% (high)								
21 April 2010	206	129	55	109	6.8	41/31	158	None	30 min walk daily
18 August 2011	186	111	47	141	6.3	13/17	143.6	None	1 h walk daily
13 October 2011	165	85	58	112	6.2	14/19	145.6	Pravastatin 10 mg daily	1 h walk daily
22 December 2011	2nd Hepatic MRI showed no evidence of fatty liver with a fat fraction percentage of 6% (normal)								
19 April 2012	149	63	56	150	6.1	11/17	140.6	Pravastatin 10 mg daily	1–2 h walk daily

Normal laboratory limits:

- ▶ Total cholesterol (Total Chl): <200 mg/dL.
- ▶ Low-density lipoprotein (LDL): <100 mg/dL (goal for this patient per ATPIII guidelines).
- ▶ High-density lipoprotein HDL: 40–60 mg/dL.
- ▶ Triglyceride (TG): 0–149 mg/dL.
- ▶ Alanine aminotransferase (ALT): 0–40 IU/L.
- ▶ Aspartate aminotransferase (AST): 0–40 IU/L.
- ▶ Glycated haemoglobin (HbA1c): 4.8–5.9%.

Figure 2 Hepatic MRI showing fat fraction percentage of 6% (normal)—after 22 December 2011.

were overweight or obese, 44% had diabetes mellitus, 29% had impaired glucose tolerance and 17% were hyperinsulinaemic. Dietary intervention was the primary mode of weight loss, along with the use of oral lipid-lowering and hypoglycaemic medications when appropriate. Weight loss (mean 3.7 kg) was achieved along with normalisation of liver enzymes in 50% of patients. This effect of weight loss on NAFLD was further seen in a case series of 36 obese patients who underwent paired liver biopsies. The first biopsy was performed at the time of laparoscopic adjustable gastric band placement and the second biopsy was performed after weight loss (mean loss of 34.0 ± 17 kg), at a mean interval of 25.6 ± 10 months after the procedure.¹⁵ There was NASH in 23 and steatosis in 12 patients, initially. Weight loss postsurgery resulted in a significant improvement in liver histology with greater improvement seen in patients with a diagnosis of metabolic syndrome prior to surgery. Proton MR spectroscopy has been used to confirm and quantify the effectiveness of weight loss on hepatic steatosis.¹³ A 10% loss of body weight via dietary modifications alone or in combination with increased physical activity results in a 44–58% reduction in hepatic triglyceride concentration in overweight adults. Therefore, these measures are currently the first line of treatment for NAFLD.⁷ In this process, physical activity appears to have an independent significant effect. Kantartzis *et al*¹⁶ showed that although reduction in hepatic fat was a function of weight loss, cardiorespiratory fitness independently predicts hepatic fat content. In a study by St George *et al*,¹⁷ of 141 participants, patients who increased or maintained physical activity to ≥ 150 min/week over 3 months had remarkable improvements in liver enzymes, and this effect was independent of weight loss. Cardiorespiratory fitness is thought to modulate liver steatosis by increasing insulin sensitivity via a reduction of peripheral lipolysis, stimulation of fatty acid oxidation and inhibition of lipid synthesis.^{16–18} While weight loss is beneficial in NAFLD, rapid

weight loss can worsen liver disease^{19–20} and patients have to be cautioned about this. The related pathogenesis appears to be rapid massive mobilisation of fatty acids from visceral stores, which on reaching the liver may be hepatotoxic. Therefore, an initial target weight reduction should be 10% of baseline weight and should not exceed 1.6 kg/week.¹⁹ In a recent randomised control trial by Promrat *et al*,²¹ the effects of lifestyle modifications with a combination of diet, exercise and behavioural changes with a goal of 7–10% weight reduction was analysed on the change in NASH histological activity score (NAS) after 48 weeks of intervention. They concluded that weight reduction achieved through the aforementioned measures led to improvement in NASH liver histology. A significant study associating NASH MRI findings with histopathology by Elias Jr *et al*²² showed moderate correlations with histological grades of steatosis and MRI stages of fibrosis.

This case demonstrates the efficacy of significant weight loss in the improvement and resolution of NASH. We believe that this is the first case report documenting this through serial liver MRIs.

Learning points

- ▶ Lifestyle measures including weight loss and exercise play a key role in the management of non-alcoholic steatohepatitis.
- ▶ Weight loss may have been the most important factor in the current case.
- ▶ Adult Treatment Panel III recommended therapeutic lifestyle measures as first-line therapy in the management of metabolic syndrome, and the current case supports this.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Reminder of important clinical lesson

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