CASE REPORT

Hereditary haemochromatosis presenting with diabetic ketoacidosis

S. Adam¹,², S. Grecian¹ and A.A. Syed¹,²

From the ¹Diabetes and Endocrinology, Salford Royal NHS Foundation Trust & University Teaching Hospital, Salford M6 8HD, UK and ²Faculty of Medical and Human Sciences, The University of Manchester, Grafton Street, M13 9PL, Manchester, Oxford UK

Address correspondence to Dr S. Adam, Core Technology Facility, University of Manchester, Grafton Street, M13 9PL, Manchester, Oxford UK. email: s.adam@doctors.org.uk

Learning points for clinicians

• Hereditary haemochromatosis is the most common inherited disorder in Caucasians
• The classic clinical triad includes cirrhosis, diabetes and hyperpigmentation
• It can sometimes present atypically with acute emergencies such as diabetic ketoacidosis
• Early recognition and treatment can reduce long term complications and mortality

Case presentation

A previously healthy 53-year-old Caucasian man presented to the emergency department with vomiting, lethargy and blurring of vision for five days and polydipsia, polyuria and weight loss of 6 kg over a month. He was dehydrated and deeply tanned (Figure 1A). On direct enquiry he recalled that his father and paternal uncle were also dark and died in their fifties from heart disease. He had no history of blood transfusions, alcohol use or smoking. He had hepatomegaly without stigmata of chronic liver disease, heart failure or endocrine disease. Initial investigations showed an arterial pH of 7.1 (normal, 7.35–7.45) and bicarbonate 11.2 (21.0–28.0) mmol/l, ketonuria (4+), plasma glucose 20.7 (4.0–11.0) mmol/l, and alanine transferase 69 (0–50) U/l, bilirubin, alkaline phosphatase, prothrombin time, renal function, C-reactive protein, full blood counts, chest X-ray and echocardiogram were normal.

Following treatment for diabetic ketoacidosis (DKA), he was established on subcutaneous insulin injections. His insulin requirements were typical of pancreatic beta cell failure (albeit of non-autoimmune aetiology as islet cell and glutamic acid decarboxylase antibodies subsequently came back negative). Based on skin bronzing, hepatomegaly, diabetes and suggestive family history, hereditary haemochromatosis (HH) was suspected. Iron studies confirmed severe iron overload with a serum ferritin of 11346 (40–400) µg/l, iron 39.3 (11–28) µmol/l, transferrin saturation 92 (15–45)%, and total iron binding capacity 42.7 (45–70) µmol/l. Genotyping confirmed a homozygous C282Y mutation of the HFE gene. Ultrasound confirmed diffuse hepatomegaly and percutaneous liver biopsy showed micronodular cirrhosis with severe haemosiderosis. Pituitary function tests showed hypogonadotrophic hypogonadism and secondary hypothyroidism; magnetic resonance imaging confirmed pituitary haemosiderosis. With regular phlebotomy hyperferritinaemia reduced and skin bronzing lightened (Figure 1B). He is receiving insulin, levothyroxine and testosterone therapies. Long-term management has included monitoring of diabetic complications, alphafetoprotein levels and hepatic ultrasound scans.

Discussion

Hereditary HH is an autosomal recessive disorder affecting 1 in 200 people of northern European descent. Nearly 85–90% of patients are homozygous for the C282Y mutation in the HFE gene; however, fewer than 10% will develop clinical disease. Iron overload is diagnosed by persistently raised fasting transferrin saturation and ferritin levels. Serum ferritin alone is not a reliable predictor as it can be normal in early stages of iron overload and falsely elevated in chronic alcoholism and inflammatory conditions. Whereas the classical triad of HH includes hepatic cirrhosis, diabetes and skin pigmentation, clinical features can range from the asymptomatic to multi-system
disease including liver failure, arthritis, cardiomyopathy and endocrinopathies.¹

Diabetes mellitus occurs in 20–50% of patients with HH and results chiefly from loss of insulin secretory capacity due to pancreatic haemosiderosis but may be mistaken for type 2 diabetes.³ It is, however, rare for a patient with undiagnosed HH to present with DKA.⁴ It is important to consider secondary causes of diabetes in atypical acute presentations. Hypogonadism is the most common endocrinopathy after diabetes; the principal defect is usually pituitary haemosiderosis, which can also result in other anterior pituitary hormone deficiencies causing hypothyroidism, hypoadrenalism and growth hormone deficiency.

Phlebotomy is the mainstay of treatment for HHs;²,⁶ iron chelators can be used when phlebotomy is contraindicated; erythrocytophoresis—selective removal of red blood cells—is expensive, no superior to phlebotomy and not widely available. Early recognition and treatment of HH can reduce morbidity and premature mortality.³,⁶ Long-term management should include surveillance and treatment of complications, particularly hepatocellular carcinoma, which has an incidence of 8–10%.⁶

Conflict of interest: None declared.

References