Case report

Deferiprone, iron overload in a renal transplant patient

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Learning Point for Clinicians

Iron overload in kidney transplant patients is uncommon and there is little experience of use of chelator therapy. This case suggests that deferiprone was safe and effective in reducing ferritin levels and removing cardiac iron with no short term detriment to transplant function. Deferiprone may offer renoprotection to excessive iron.

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Regular red blood cell transfusion is the mainstay of treatment in patients with symptomatic refractory anaemia. Repeated transfusions result in accumulation of iron in the heart, liver and pancreas which lead to the production of reactive oxygen species, which may lead to cellular dysfunction, and in the longer term to cell necrosis and apoptosis. Iron chelation therapy reduces this tissue iron deposition.

Three iron chelating agents are available. Parenteral (intravenous or subcutaneous) deferoxamine reduces myocardial and liver iron concentrations and is excreted mainly by the kidneys.\textsuperscript{1} Desferrioxamine is associated with acute kidney injury and acute tubular dysfunction (mainly proximal).\textsuperscript{2} Deferasirox, an oral iron chelator with primarily hepatobiliary excretion,\textsuperscript{1} is as effective in treating iron overload but has been associated with acute kidney injury, an increased incidence of reversible Fanconi syndrome and transient rises in serum creatinine (SC).\textsuperscript{2} Deferiprone is licensed for the treatment of patients with thalassaemia major when deferoxamine therapy is contraindicated or inadequate and is effective in removing intracellular iron from the heart and other tissues.\textsuperscript{2} It has been associated with 1–2% agranulocytosis, and potentially increased liver enzymes.\textsuperscript{3,4} Chelator use has not been described in transplant patients or those with significant renal impairment.

A 73-year-old man with end stage renal disease of unknown aetiology received a deceased donor renal transplant in 1988 with a baseline SC 175 µmol/l. In 2004, he developed anaemia of chronic disease (ACD) (SC: 292 µmol/l) and received intermittent blood and iron transfusions due to a background history of ischaemic heart disease. The anaemia persisted despite adequate iron levels and darbepoetin alpha was commenced (40–100 µg). By July 2009, darbepoetin alpha failed to treat the anaemia. Switch to high dose epoetin beta had no effect on haemoglobin necessitating further blood transfusions. Erythropoietin antibodies and three bone marrow biopsy/aspirates showed a mild increase in plasma cells consistent with mild monoclonal gammopathy of uncertain significance and features consistent with ACD. Parathyroid hormone was only mildly elevated. He required transfusions on a 2 weekly basis.

Serum ferritin (SF) levels climbed secondary to regular transfusions over a period of 18 months,
and by May 2011 had reached >4000 ng/ml. In September 2011, he was admitted for ablation following diagnosis of supraventricular tachycardia due to possible iron accumulation within the myocardial tissue. Blood transfusions were now fortnightly, and by January 2012 SF was >7800 ng/ml (Table 1). T2* MRI prior to commencement of chelation therapy showed a myocardial value of 23 ms (normal range > 20 ms), and liver T2* of 10 ms (normal > 6 ms). The SC had risen to 338 µmol/l. Deferiprone was commenced at 2 g three times a day and subsequently reduced to 1 g three times a day (due to an estimated glomerular filtration rate calculated using the MDRD equation (eGFR) of 16 ml/min).

He tolerated deferiprone, and SF decreased >3000 ng/ml over the following 6 months. There was no significant adverse effect on renal function (Table 1) and there was a 125 mg/mmol (16%) reduction in proteinuria. This reduction in proteinuria may in part be related to removal of iron from the renal parenchyma or a reduction in free (labile) iron affecting oxidative stress pathways. Agarwal et al.5 have previously demonstrated that iron infusions may in part lead to proteinuria in patients with renal dysfunction and Shah et al. have shown beneficial effects of chelation with deferiprone on eGFR and proteinuria.6 The T2* for the heart increased to 42 ms, indicative of decreased iron concentration, whereas the liver value remained unchanged at 10 ms. Deferiprone is frequently associated with an improvement in cardiac function before an improvement in cardiac iron is detected.

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### References