Screening for diabetic nephropathy: take your blinkers off

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Introduction
Proteinuria is one of several markers of kidney damage in diabetes. The excretion of specific types of protein, such as albumin or low molecular weight globulins, depends on the type of kidney disease that is present. One of the earliest changes in diabetes is an increase in glomerular filtration rate (GFR), or hyperfiltration, which is observed in patients with type 1 as well as many with type 2 diabetes and is accompanied by an increase in renal size. The next observable change is the development of albuminuria, and current UK guidance recommends annual screening with the albumin creatinine ratio (ACR) to identify early kidney disease in patients with diabetes. Patients with diabetes with persistent microalbuminuria are at greatly increased risk for development of proteinuria (albuminuria >300 mg/day). However, it is important to exclude other causes of proteinuria in patients with diabetes, especially if there is no associated retinopathy. We report a case of an 81-year-old man with type 2 diabetes mellitus who presented with lower back pain and proteinuria but who had had normal/minimal microalbuminuria on his annual screening. He was diagnosed with multiple myeloma. The case highlights the importance of proteinuria in diagnosing multiple myeloma and in multiple myeloma.

Key words: screening, diabetic nephropathy, proteinuria, albuminuria, multiple myeloma

Case presentation
An 81-year-old man with known type 2 diabetes mellitus diagnosed in 2011 and bipolar disorder, managed on lithium for the last 10 years, was admitted in August 2017 with worsening lower back pain and confusion. He had a history of chronic back pain since 2013. He had swelling of his right eye and was diagnosed with dacrocystitis by an ophthalmologist and had been treated with antibiotics but with no benefit. He was on insulin and his diabetes control had been good; his HbA1c was 53 mmol/mol (7%) in June 2017. He had no retinopathy and no neurological deficit.

Initial investigations showed a normal serum sodium and potassium, urea 4.8 mmol/L, creatinine 130 µmol/L, eGFR 49, serum albumin 46 g/L, adjusted calcium 2.86 mmol/L (2.2–2.6), phosphate 1.22 mmol/L, haemoglobin 125 g/L (130–180), normal mean corpuscular volume, lithium level normal. We could not find a serum calcium result from previous years. His eGFR in 2016 was 60 mL/min. His lumbosacral X-ray on admission showed a wedge compression fracture at L4. Hypercalcaemia secondary to lithium therapy was initially considered but excluded when the serum parathyroid hormone (PTH) level became available (0.4 pmol/L [1.6–7.5]). A myeloma screen was requested. A CT head scan, done as part of his confusion screen, showed a soft tissue lesion in the right orbit.

On reviewing his previous results, it was noted that there was a discrepancy between his urine ACR and protein/creatinine ratio (PCR) (table 1).

His serum light chains showed high free kappa light chain of 10,217 mg/L with a kappa/lambda ratio of 3,440.3. He was referred to the haematologists. A bone marrow biopsy showed a heavy plasma population and confirmed the diagnosis of multiple myeloma. He also had a biopsy of the right orbital mass which showed plasmacytoma.

Discussion
The diagnosis of diabetic nephropathy is based on the detection of proteinuria. Most patients with diabetic nephropathy also have hypertension and retinopathy. The main diagnostic procedures in a patient with suspected diabetic nephropathy include the following:

- Measurement of urinary albumin or protein
- Measurement of serum creatinine concentration and estimation of GFR
- Measurement of blood pressure
- Ophthalmologic examination

Microalbuminuria refers to albumin excretion above the normal

| Table 1 Urine protein/creatinine and albumin/creatinine ratios of patient |
|-----------------------------|-----------------------------|-----------------------------|
|                            | September 2015              | November 2014               | March 2013      |
| Urine protein/creatinine ratio (normal 0.0–30) | 102.0 mg/ mmol              | 68.8 mg/ mmol               | 54.1 mg/ mmol   |
| Urine albumin/creatinine ratio (normal 0.0–2.5) | 2.8 mg/ mmol creatinine     | 1.7 mg/ mmol creatinine     | 8.4 mg/ mmol creatinine |

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The absence of retinopathy and discordance between urine albumin and total protein excretion should alert clinicians to consider a non-diabetes cause for the proteinuria. However, concordance of chronic kidney disease with advanced diabetic retinopathy is low in subjects with type 2 diabetes, and chronic kidney disease without advanced diabetic retinopathy is more frequent than isolated advanced diabetic retinopathy, at variance with type 1 diabetes.6

Approximately 10–20% of patients taking lithium develop hypercalcaemia and hypocalciuria, and a smaller percentage have high serum PTH concentrations. Lithium increases serum total and ionised calcium and intact PTH levels within weeks, but these remain within the normal range in most subjects. Lithium can induce a continued defect in calcium-PTH regulation and normocalcemic patients can have a slightly raised serum PTH concentration and an increase in mean parathyroid gland volume.7

Findings on urinalysis in myeloma depend on the aetiology of the kidney damage:

- Myeloma cast nephropathy is characterised by the presence of large, waxy, laminated casts in the distal and collecting tubules; the casts are mainly composed of precipitated monoclonal light chains. The urine dipstick is typically negative for protein since most of the proteinuria comprises urinary monoclonal protein (Bence Jones proteinuria) rather than albumin.

### References


