An older man with low back pain and no acute injury

Commentary by **GRAHAME ELDER** MB BS, PhD, FRACP

Could renal osteodystrophy be the cause of this man's increasing low back pain without an acute injury?

Case scenario

Sam is a 59-year-old abattoir worker who presented with low back pain that has been increasing over the past couple of years. He had decided to apply for the disability pension. There had been no acute back injury.

Sam appeared to have a good range of lower spinal movement and he was not overweight, but he had been treated for hypertension and insulin dependent diabetes mellitus (type 1 diabetes). His diabetes was poorly controlled and apparently rarely monitored. A spinal x-ray reported only minor spondylitic changes, but the radiologist commented that there was increased bone density in the lumbar vertebrae. It was suggested that he could have renal osteodystrophy.

Associate Professor Elder is a Staff Specialist in the Department of Renal Medicine, Westmead Hospital and a member of the Osteoporosis and Bone Biology Program, Garvan Institute, Sydney, NSW.

What is the basis of this condition? Could it be the cause of Sam's increasing low back pain? How should he be managed?

Commentary

The basis of renal osteodystrophy

The term renal osteodystrophy (ROD) describes the histomorphometric changes in bone that occur as a consequence of chronic kidney disease (CKD). A diagnosis of ROD can only be made accurately by performing a bone biopsy after tetracycline labelling (tetracycline being used to provide information on mineralisation).

ROD starts to develop early in patients with CKD when quite small reductions in the glomerular filtration rate lead to an imbalance between the amounts of dietary phosphate ingested and urinary phosphate excreted. Bone cells (osteocytes and osteoblasts) detect this imbalance and release fibroblast growth factor 23, a hormone that increases phosphaturia and reduces the kidney's ability to produce calcitriol, the most active form of vitamin D. Reduced calcitriol levels decrease vitamin D-dependent uptake of phosphate from the gastrointestinal tract, so that together these changes tend to restore phosphate balance (Figure 1). However, another major action of calcitriol is to inhibit parathyroid hormone (PTH) production. Consequently, the reduced calcitriol production also results in secondary hyperparathyroidism, which may worsen as CKD progresses. This is not an inevitable progression because drugs that are commonly used in CKD management, such as calcium and calcitriol, can suppress the release of PTH and development of hyperparathyroidism.

PTH is a major driver of bone turnover, but the level achieved and the circadian nature of normal PTH production determine whether this hormone exerts anabolic or catabolic effects on bone. PTH levels in patients with CKD are often very high and noncircadian, leading to impaired bone architecture and weak

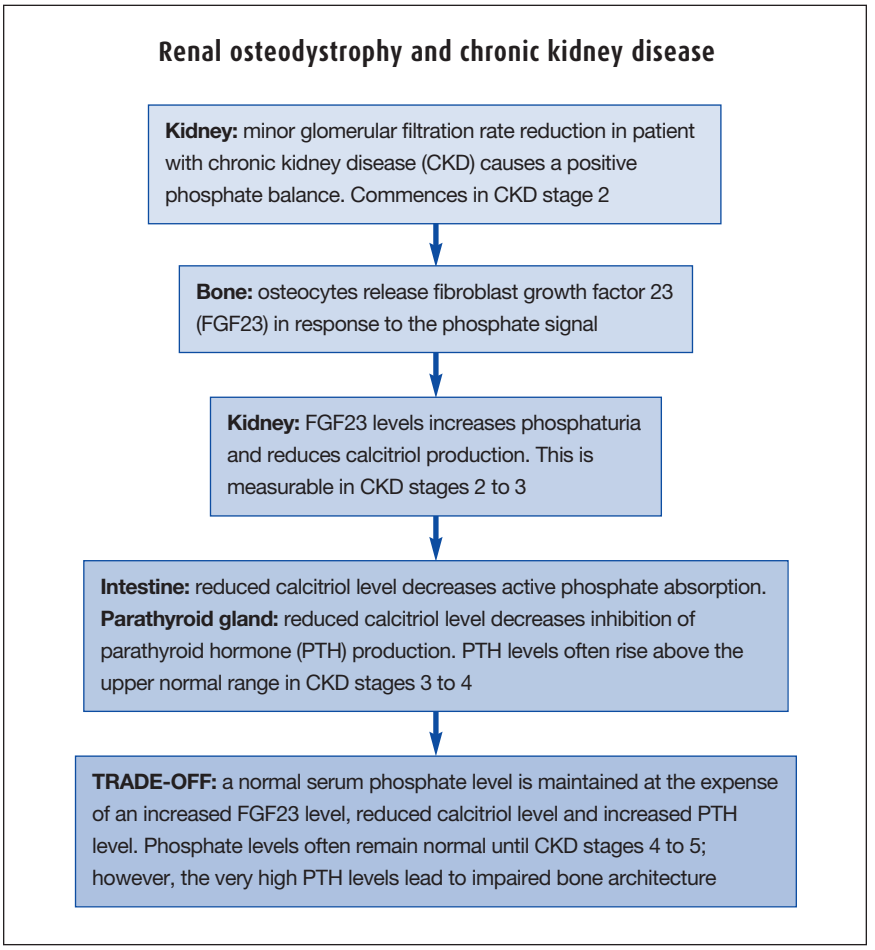

Figure 1. Development of renal osteodystrophy as a consequence of chronic kidney disease, showing hormonal interactions between the kidneys, bone, intestine and parathyroid glands.

bones that can fracture readily. A pattern of increased bone density on lateral spine x-ray – often called the 'rugger jersey spine' – is characteristic of the more extreme bone changes associated with CKD-related hyperparathyroidism. These changes are caused by osteosclerosis towards the endplates at the upper and lower vertebral margins and reduced bone density towards the middle of the vertebra (Figure 2). It is rare to see 'rugger jersey spine' before patients reach CKD stage 5 or require dialysis. However, earlier stages of hyperparathyroidism or mixed pathology with associated mineralisation disturbances may present a more diffuse increase in density on x-ray. If renal function has been abnormal for some time, this diffuse density increase may be noticeable in patients with CKD stages 3 or 4.

Could ROD be the cause of Sam's increasing low back pain?

Low back pain present for many years is not characteristic of ROD and ROD is uncommon compared with other musculoskeletal causes of back pain. Nevertheless, bone and muscular pains are features of ROD and the associated abnormal bone quality increases the risk of vertebral crush fractures. So the answer is yes, ROD could be the cause, but it is unlikely.

In the later stages of CKD when ROD is symptomatic or detected radiologically, other symptoms of severe CKD caused by fluid overload and anaemia would also be expected. To quickly exclude ROD as a possibility, the serum creatinine level and estimated glomerular filtration rate (eGFR) should be checked. If they are normal, then ROD is not the cause.

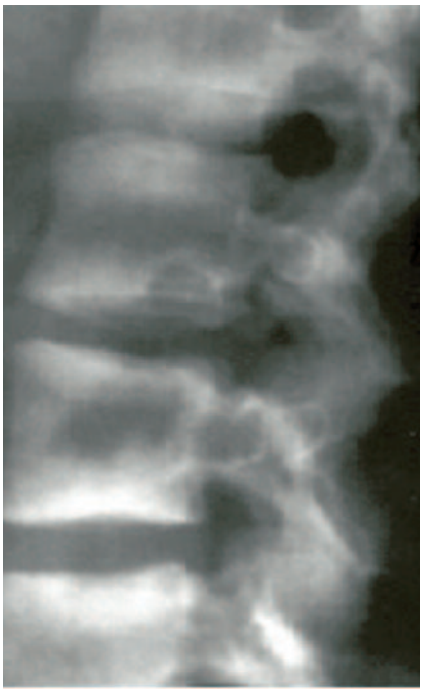

Figure 2. A spinal x-ray of CKD-associated hyperparathyroidism showing alternating sclerotic and lucent bands suggestive of rugby jersey stripes.

If the eGFR is reduced, it is reasonable to check a PTH level together with levels of serum calcium, phosphate, 25-hydroxyvitamin D and alkaline phosphatase. Although alkaline phosphatase is a liver enzyme, it is also produced by osteoblasts, so when other liver function tests are normal, increases in alkaline phosphatase can be due to increased osteoblastic activity caused by secondary hyperparathyroidism. If the eGFR is less than 60 mL/min/1.73 m^2 and PTH and alkaline phosphatase levels are elevated, ROD remains a possibility. Calcium and phosphate levels may be normal or abnormal, depending on the stage of CKD. Reduced levels of 25-hydroxyvitamin D are common in the

general population and in patients with CKD. Reduced 25-hydroxyvitamin D levels should be excluded as a cause of mild secondary hyperparathyroidism but this would not cause an increase in lumbar vertebral bone density.

How should Sam be managed?

If Sam has renal impairment, diabetic nephropathy would be the most likely cause. This would be associated with an increased urinary albumin to creatinine ratio or overt proteinuria, and other features of diabetes such as retinopathy and peripheral neuropathy would often be present. If laboratory investigations confirmed hyperparathyroidism associated with an eGFR level of between 30 and 60 mL/min/1.73 m^2, it would be reasonable to correct any 25-hydroxyvitamin D deficiency using cholecalciferol. Nevertheless, although this may result in some reduction of PTH levels, it would not substantially influence hyperparathyroidism severe enough to cause this clinical picture. Therefore Sam should be referred to a nephrologist, with an immediate referral if his eGFR is less than 30 ml/min/1.73 m^2 (i.e. CKD stages 4 to 5).

Calcitriol, phosphate binders and, in later stages of CKD, calcimimetic drugs or parathyroidectomy may all be used to treat hyperparathyroidism and associated ROD. The pain may improve with these measures but analgesics and physical therapy will also be required.

Other possible diagnoses

ROD does not seem the most likely cause of Sam's low back pain, so once CKD has been excluded, several other diagnostic possibilities, as outlined below, need consideration.

- **Osteosclerotic prostatic metastases.** In a 59-year-old man, osteosclerotic prostatic metastases must be considered. A digital rectal examination should be performed together with a prostate-specific antigen test.
- **Myeloma and lymphoma.** Although multiple myeloma cells usually stimulate osteoclastic resorption of bone with discrete or diffuse reduction in bone density, sometimes myeloma and lymphoma cause a diffuse increase in bone density. The presence of paraproteins in the blood or urine should be excluded.
- **Vertebral compression fractures.** These fractures, including pathological fractures, can lead to an apparent increase in measured bone density, with symptoms ranging from acute pain to none. The x-ray films should be checked – a loss of vertebral height should be visible if a fracture has occurred.
- **Paget's disease.** Increased bone density in the lumbar vertebrae, with elevated alkaline phosphatase levels but generally normal PTH levels, could be caused by Paget's disease. A radionuclide bone scan will show locally increased uptake in patients with Paget's disease but a 'superscan' appearance of widespread skeletal uptake in those with secondary hyperparathyroidism caused by CKD.
- **Diabetes.** Certainly as a cause of progressive CKD, poorly controlled diabetes could be a contributor. Bone density is normal or may be increased in patients with type 2 diabetes as measured by dual-energy x-ray absorptiometry, but this would not be detected on plain x-ray. On the other hand, bone density is generally lower in patients like Sam with type 1 diabetes. The bone is more liable to fracture in patients with either type 1 or 2 diabetes than in those without diabetes.
- **Brucellosis and tuberculosis.** Brucellosis, which is more common in abattoir workers than in the general population, can affect the lumbar spine, whereas tuberculosis generally affects the thoracic spine. Fever and constitutional symptoms are generally present in these conditions and vertebral sclerosis is a late sign. However, tuberculosis and brucellosis have been largely eradicated from the Australian cattle population so a link to occupation exposure is unlikely. Sam's long clinical course reduces the possibility of other causes of osteomyelitis, although infective causes should still be considered due to his poorly controlled diabetes.
- **Other conditions.** Sarcoid, myelofibrosis, osteopetrosis, hepatitis C and many other conditions can rarely cause an increase in bone density. Sam's older age and good range of lower spinal movement exclude ankylosing spondylitis from consideration.

Finally, the low back pain might not be related to the x-ray appearance. After making sure there are no neurological deficits and discounting the contenders among the conditions listed above, referral of this patient to a multidisciplinary back pain service or a chronic pain clinic may be appropriate if the pain has been unresponsive to simple analgesia such as paracetamol and physical therapy.

Conclusion

Although bone density cannot be quantified on plain x-ray, qualitative changes can indicate underlying pathology. As in many areas of medicine, pattern recognition is important, so discussing unexpected findings with the reporting radiologist together with a careful history and some simple initial tests will often clarify the diagnosis. The term 'renal osteodystrophy' refers to a spectrum of changes that form an integral component of the 'mineral and bone disorder' of CKD. These bone changes are always associated with reduced renal function and generally with altered levels of calcium, phosphate, vitamin D and PTH. Hence it is easy to exclude ROD as a potential differential diagnosis, despite the difficulty of accurately defining its presence when CKD is present. MT

COMPETING INTERESTS: None.