

The patient, a 70-year-old man with chronic renal failure and class III heart failure was admitted to the hospital on 26 July 2010 with turbid peritoneal dialysate, non febrile, having mild abdominal pain and positive Rebound sign at the physical examination. Leucocyte cell count showed the presence of 1200 leucocytes/ $\mu\text{l}$  (neutrophil count of 90%) in the peritoneal dialysate but subsequent culture of the fluid resulted negative. Treatment started with vancomycin 15mg/kg/5 days i.p. and aztreonam 2gr/d i.p. for a total of 20 days. On 30 July 2010 cell count was 50 leucocytes/ $\mu\text{l}$  and the patient was discharged.

3 days later however, at the first control visit, the peritoneal dialysate was turbid anew, the patient presented the same clinical findings and cell count revealed the presence of 300 leucocytes/ $\mu\text{l}$ . A Gram positive, spherical microorganism that occurred in tetrads with circular, smooth, glistening and yellow colonies was recovered from the peritoneal dialysate. The microorganism was identified as *Kocuria varians* by the VITEK 2 system. The isolate was susceptible to gentamycin, erythromycin, clindamycin, tetracycline, glycopeptides and linezolid while it was resistant to levofloxacin by the disc diffusion method. Following laboratory report, the patient was treated with vancomycin alone (15mg/kg/5 days i.p. for a total of 20 days).

Turbidity of the peritoneal dialysate did not reappear until 27 August 2010 when the patient was admitted to the hospital with generalized abdominal pain, positive Rebound sign and cell count of 550 leucocytes/ $\mu\text{l}$ . *K. varians* was isolated for the second time and removal of the peritoneal catheter followed by insertion of a new one in a different position was considered. Culture of the removed catheter was positive for *K. varians*. Vancomycin i.p. was administered, subsequent cultures were negative and the patient remained in good clinical condition since then.

Infections related to *K. varians* are uncommon but this species may act as opportunistic pathogen in immunocompromised patients with underlying diseases. Furthermore, *K. varians* is a biofilm forming bacterium<sup>4</sup> thus probably complicating the antimicrobial treatment of catheter related infections. Erroneous identification of coagulase-negative Staphylococci as *Kocuria* spp. is possible and can be excluded with certainty only with the application of genotypic assays such as 16S RNA.<sup>1</sup> In the present case the Vitek 2 system using the new GP identification card<sup>5</sup> reported a “very good identification” for all three isolations. This case report aims on emphasizing the importance of careful consideration of the laboratory and clinical procedures when rarely pathogenic microorganisms are isolated in the peritoneal dialysate of patients undergoing CAPD.

#### Conflicts of interest

The authors declare that there is no conflict of interest associated with this manuscript.

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## Asymptomatic polyostotic Paget's disease associated with secondary hyperparathyroidism in a peritoneal dialysis patient

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#### To the Editor,

Paget's disease (PD) is a focal bone remodelling disorder that can affect one or more bones.<sup>1</sup> It is the second most common bone disease after osteoporosis, and its diagnosis usually derives from routine biochemical analyses, when elevated alkaline phosphatase (AP) levels are observed, or during imaging tests for other reasons.<sup>1-3</sup>

The incidence of PD in patients with chronic kidney disease (CKD) is unknown. Few cases have been described in the medical literature,<sup>4-8</sup> and in some of them PD was masked by secondary hyperparathyroidism (SHP),<sup>4-6</sup> making its diagnosis quite difficult. With this in mind, we present the first case of a patient on peritoneal dialysis with coexisting polyostotic PD and SHP.

Our patient was a 72-year-old male with a history of arterial hypertension and gouty arthritis, who was diagnosed with CKD of unknown aetiology in 1990 and referred to our hospital in December 2007. In February 2008, he started continuous ambulatory peritoneal dialysis. Before starting dialysis, the patient had elevated parathyroid hormone (PTH) and AP levels. He was diagnosed with SHP and initially received cinacalcet and calcitriol, followed by paricalcitol and cinacalcet. However, PTH levels remained high despite high drug doses, and were accompanied by persistently high AP levels.

In May 2011, he underwent computed tomography imaging for inclusion on the kidney transplant waiting list, and a sclerotic lesion was observed in the right iliac bone. A bone scintigraphy showed increased uptake of the radio-tracer in the cervical spine, first finger of the right hand, left ulna, right sacroiliac joint, and, to a lesser extent, the external malleolus of the left ankle. Bone scans confirmed the presence of sclerotic lesions in the cervical spine, left ulna, and right sacroiliac joint (Figure).

During the follow-up period, the patient remained asymptomatic, without bone pain, fractures, or other complications. He was diagnosed with polyostotic PD. Given the absence of current indications for treatment, the patient is under periodic follow-up with strict surveillance and receives cinacalcet and calcifediol for SHP.

### DISCUSSION

PD is a bone remodelling disorder characterised by a marked increase in bone reabsorption mediated by osteoclasts, followed by a compensatory increase in bone formation. The newly synthesized bone has altered biomechanical properties and structure and induces clinical complications such as pain and bone deformities, secondary osteoarthritis, fractures, headache, stenosis of the spinal canal, neurological compression symptoms, and sarcomatous degeneration.<sup>1-3</sup> The prevalence of this disease in the



**Figure 1.** Paget's disease in chronic kidney disease.

X-ray of the left forearm (A) and cervical spine (B) showing sclerosing lesions on vertebrae and the left ulna (arrows).

general population ranges between 1.5% and 4.5% in individuals older than 40 years, and increases with age, with a slight predominance in males and its distribution varies depending on the geographical region.<sup>2</sup> Follow-up of disease progression with periodical measurements of AP helps to determine the extent and level of activity of the disease.<sup>1</sup> The primary treatment is bisphosphonates, drugs capable of regulating osteoclast activity.<sup>2</sup> Randomised studies have suggested that these drugs are capable of reducing bone pain and decreasing AP levels.<sup>1</sup> Scientific evidence does support treating patients with bone pain, neurological complications, hypercalcaemia due to prolonged immobilisation, patients that undergo elective orthopaedic surgery, and patients with localised activity in the base of the cranium, the spinal column, and long bones.<sup>2</sup>

Treatment in asymptomatic patients is a controversial topic. The PRISM study<sup>9</sup> was a randomised trial that sought to standardise AP that compared the efficacy of bisphosphonates in an intensive treatment regimen that sought to normalize AP levels against symptomatic treatment in patients with bone pain. It analysed a cohort of 1324 patients and found that intensive treatment did not provide any clinical advantages (in terms of incidence of fractures, need for

orthopaedic surgery, quality of life, bone pain, and auditory thresholds) compared to symptom management. As such, additional studies are needed to evaluate whether the effects of bisphosphonates translate into clinical benefits for the patient, and therefore, treating asymptomatic patients is not recommended.

In patients with advanced CKD, the prevalence of PD is unknown. Until now, only 5 cases have been reported in the medical literature (Table), four of which were on haemodialysis (HD)<sup>4-6,8</sup> and one on peritoneal dialysis.<sup>7</sup> In three of the patients on HD, SHP masked PD, and the diagnosis was made based on persistent AP elevation following parathyroidectomy.<sup>5,6,8</sup> With respect to the treatment of these patients, one received intravenous and nasal calcitonin<sup>7</sup> and the other two, intravenous bisphosphonates (Table).<sup>5,8</sup> The indications for treatment were bone pain in two cases and a slight, long-standing fever in another case that was resolved upon treatment. No patients had adverse effects from treatment.

It is unclear the safety of bisphosphonates in CKD patients on dialysis.<sup>10</sup> Some cases have been described of successful treatment of dialysis patients with bisphosphonates, but they very few

**Table 1.** Cases of Paget's disease in patients with chronic kidney disease on dialysis that have been described in the medical literature

Author	Year	No. cases	Gender/age	Type of RRT	Extent of the PD	Secondary hyperparathyroidism	Symptoms/treatment
Ringe JD <sup>4</sup>	1985	1	F/48	HD for 1 year	Diagnosed following parathyroidectomy	Severe Aluminium-induced osteomalacia	Bone pain No treatment
Lorho R <sup>6</sup>	1998	1	M/83	HD for 6 years	Monostotic: pelvis Diagnosed by elevated parathyroidectomy	Severe, treated with alfacalcidol and parathyroidectomy	None documented
Etemadi J <sup>8</sup>	2008	1	F/77	HD for 2 years	Monostotic: cranium Diagnosed by elevated AP in the absence of SHP	No	Bone pain Oral bisphosphonates (alendronate)
Wu L <sup>7</sup>	2009	1	F/77	Dialysis peritoneal for 3 months	Monostotic: lumbar spine Neurological involvement by stenosis of the L3-L4 vertebral canal PD of 10 years	ND	Radicular syndrome Intravenous and nasal calcitonin Surgical decompression in the lumbar spine
Ciandolo G <sup>9</sup>	2010	1	F/69	HD for 3 years	Monostotic: cranium/ Diagnosed by slight longstanding fever	Severe, treated with sevelamer, cinacalcet, and paricalcitol	Slight fever Intravenous bisphosphonates (clodronate)

PD: Paget's disease F: female; AP: alkaline phosphatase; HD: haemodialysis; SHP: secondary hyperparathyroidism; M: male; ND: no data; RRT: renal replacement therapy.

cases and the majority of the patients were on HD. Since bisphosphonates are taken up by the bones at a rate of 50%-80%, they are capable of reducing bone remodelling, and this could lead to difficulties in repairing microfractures and deteriorated bone quality.<sup>11</sup> Even in patients with CKD, the deposition of bisphosphonates in the bones is believed to be proportionally higher and is also correlated with the severity of SHP, which implies a risk of inducing adynamic bone disease in these patients.<sup>11,12</sup>

In conclusion, SHP can mask the diagnosis of PD in CKD patients, so a high level of clinical suspicion to make the diagnosis. In these cases, persistently high levels of AP originating in the bones, which tends to remain high even after parathyroidectomy, may suggest the diagnosis of PD. However, in many cases, radiological images taken for other reasons may lead to the diagnosis.

### Conflicts of interest

The authors affirm that they have no conflicts of interest related to the content of this article.

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