

# Increasing serum calcium levels and recent return from transplantation as clues to the tuberculous nature of refractory peritoneal dialysis peritonitis

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## ABSTRACT

Peritoneal tuberculosis is an uncommon complication of peritoneal dialysis in Europe. It is more common in Asian immigrants. A delayed diagnosis is frequent and impairs patient outcomes. We present two cases of peritoneal tuberculosis with common features that may help suspect the disease early countries with a low incidence. Both patients were females (of Spanish origin) who had recently restarted peritoneal dialysis following kidney transplantation. Both developed bacterial peritonitis clinically that was refractory to conventional antibiotics, despite clearance of bacteria. Both stopped calcium-containing phosphate binders because of increasing serum calcium that in one case led to frank hypercalcemia that persisted despite low calcium dialysate. Peritoneal biopsy was the first positive test in both cases. This report emphasizes the recent return from transplantation and rising serum calcium levels as features that should alert the physician of a potential underlying tuberculous peritonitis.

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**KEY WORDS:** Hypercalcemia, peritoneal dialysis, transplantation, tuberculosis

## Introduction

Tuberculosis is an uncommon cause of peritoneal dialysis (PD) peritonitis in Europe and the United States and is more frequent in Asian immigrants.<sup>[1-4]</sup> Tuberculous peritonitis symptoms are nonspecific, diagnostic tests have low sensitivity or become positive late in the course of the disease. Thus diagnosis is delayed and impacts outcomes. Familiarity with risk factors and clinical manifestations may facilitate an early diagnosis and reduce mortality.<sup>[2]</sup> We now describe two features that may help suspect the diagnosis in low-incidence countries with high transplantation rates.<sup>[5]</sup>

## Case Reports

### Case 1

A 39-year-old woman previously on PD returned to PD due to chronic allograft nephropathy. Prednisone 10 mg/day was prescribed for graft intolerance for some months. She later developed *Staphylococcus aureus* peritonitis. Despite negative cultures following antibiotics, mild intermittent fever and occasional cloudy fluid persisted for 3 months. Repeated peritoneal effluent counts contained 35-240 leukocytes/ $\mu$ L, mainly mononuclear cells, but occasionally neutrophils predominated. Peritoneal biopsy showed necrotizing granulomatous peritonitis and a single acid-fast bacillus. Two different cultures grew *Mycobacterium tuberculosis*. The patient was started on tuberculostatic treatment and switched to hemodialysis. During the episode, serum calcium levels increased, despite decreasing serum albumin levels and despite withdrawal of calcium salts: Mean  $\pm$  standard deviation serum calcium and albumin values for the 5 months prior to the peritonitis were  $8.1 \pm 0.3$  mg/dL and  $3.3 \pm 0.2$  g/dL versus  $8.9 \pm 0.4$  mg/dL ( $P < 0.004$ ) and  $2.7 \pm 0.4$  g/dL ( $P < 0.05$ ) for the next 5 months. Intact parathyroid hormone (iPTH) 85 pg/mL.

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## Case 2

A 61-year-old woman previously on PD returned to PD following stormy cadaver kidney transplantation. Immunosuppressants were discontinued. The patient was admitted with polymicrobial peritonitis. Fever persisted despite antibiotics and negative follow-up cultures. The peritoneal catheter was removed and hemodialysis was initiated. Despite discontinuation of calcitriol and calcium, hypercalcemia (calcium 10.3-10.9 mg/dL with serum albumin 2.2-2.5 mg/dL, iPTH 296.60 pg/mL) was observed and persisted for months despite low calcium dialysate. A peritoneal biopsy disclosed granulomatosis but no acid-fast bacilli. Initiation of tuberculostatic treatment led to disappearance of fever.

## Discussion

The main lesson from the above reports is that peritoneal tuberculosis should be suspected in patients with refractory peritonitis and increasing serum calcium levels, especially if returning to PD after graft loss. In addition, it illustrates the following clinical features of peritoneal tuberculosis: A) 30% of peritoneal tuberculosis can occur with other bacterial peritoneal infections, b) peritoneal leukocyte counts may even be normal or indistinguishable from bacterial peritonitis, and c) the difficult diagnosis by traditional culture methods for *Mycobacteria*.<sup>[2-4]</sup>

A comprehensive review published in 2000<sup>[4]</sup> reported a prior kidney transplant in 6% of peritoneal tuberculosis PD patients but does not mention hypercalcemia. More recent updates<sup>[2,3]</sup> also do not mention these clinical features that may alert the clinician to peritoneal tuberculosis. Two reasons may account for this omission: Peritoneal tuberculosis is more frequent in countries with low renal transplantation rates<sup>[3]</sup> and raising serum calcium levels may be obscured by end-stage renal disease (ESRD) patients trend toward hypocalcaemia, low albumin levels in PD patients and the modulation of serum calcium by dialysate calcium levels and concomitant medication.

Both patients, the only two tuberculous PD peritonitis observed in 40 years at our center, had an uneventful PD period prior to transplantation, symptoms compatible with

peritoneal tuberculosis developing shortly after the return to PD and the need to stop a stable treatment with calcium salts and/or vitamin D because of raising serum calcium levels with persistence of higher serum calcium levels for months after stopping these medications. Steroids may have contributed to the reactivation of tuberculosis. Hypercalcemia may be a feature of tuberculosis explained by macrophage conversion of calcidiol to calcitriol.<sup>[6]</sup> In conclusion, a history of recent return from transplantation and the presence of hypercalcemia or rising serum calcium levels despite discontinuation of interfering medications should alert clinicians to the possibility of tuberculous PD peritonitis.

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