Tophaceous pseudogout in a patient undergoing peritoneal dialysis

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Abstract Calcium pyrophosphate dihydrate deposition disease (pseudogout) is a crystal arthritis characterized by pyrophosphate dihydrate crystal deposition in the articular cartilage or synovium. In chronic kidney disease patients, the major causes of crystal arthritis are calcium oxalate crystals and basic calcium phosphate crystals. However, pseudogout is apparently infrequent among such patients. This report describes a rare case of tophaceous pseudogout (tumoral form of pseudogout) involving the hip joint in a peritoneal dialysis patient, as revealed by CT scan and synovial fluid aspiration. Fluid aspiration and oral NSAIDs improved the clinical symptoms. This report is the first to describe tophaceous pseudogout in a peritoneal dialysis patient, which suggests that pseudogout should be suspected in dialysis patients with unexplained arthritis.

Keywords Pseudogout · Calcium pyrophosphate dihydrate deposition disease · Chronic kidney disease · Peritoneal dialysis

Introduction

Joint and bone disorders are common complications of chronic kidney disease (CKD) patients. Differential diagnoses of acute arthritis include hemarthrosis, septic arthritis, and crystal arthritis. The major causes of crystal

arthritis in CKD patients are calcium oxalate crystals and basic calcium phosphate crystals [1–3]. However, calcium pyrophosphate dihydrate deposition disease (pseudogout) is probably infrequent among such patients [1–3]. This report describes a rare case of tophaceous pseudogout (tumoral form of pseudogout) in a patient with peritoneal dialysis (PD) revealed by synovial fluid aspiration.

Case report

An 82-year-old man with fever and increasing pain in the left inguinal region was admitted to the Japanese Red Cross Medical Center Hospital in May 2012. He had been receiving PD therapy since 2003 for end-stage renal disease secondary to chronic glomerular nephritis. He had been treated with Midpeliq L (Terumo Medical Corp., Tokyo, Japan): a neutral pH biocompatible dialysis solution with lower concentrations of glucose degradation products. The final concentrations of the electrolytes and buffer were Na^+ 135 mEq/L, Ca^{2+} 2.5 mEq/L, Mg^{2+} 0.5 mEq/L, Cl^- 98.0 mEq/L, and lactate 40.0 mEq/L, with pH of 6.3–7.3. Osmolality of the 1.35 % glucose solution was 350 mOsm/L. That of the 2.5 % glucose solution was 414 mOsm/L. The PD regimen was automated peritoneal dialysis with four 3-h exchanges using 7.2 L of 1.35 % glucose dialysate and 2.5 L of 2.5 % glucose dialysate. They were mixed during automated peritoneal dialysis. The glucose concentration was about 1.9 %. His kidney and peritoneal Kt/V were 1.8–2.0. His normalized protein catabolic rate (nPCR) was ~ 0.7 . He was treated with peritoneal dialysis for the first 5 years. Subsequently, he was transferred to combination therapy in 2008 because of anuria. The regimen of combined therapy was daily PD (7 days per week) and hemodialysis (HD) once a week. He

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Table 1 Laboratory data and dialytic factors on admission

Laboratory data	
RBC	321 ($10^4/\mu\text{L}$)
Hb	9.9 (g/dL)
Ht	30.2 (%)
PLT	33.7 ($10^4/\mu\text{L}$)
WBC	7800 (/ μL)
TP	6.4 (g/dL)
ALB	3.5 (g/dL)
BUN	33 (mg/dL)
Cre	8.71 (mg/dL)
UA	6.7 (mg/dL)
CRP	8.23 (mg/dL)
Ca	8.1 (mg/dL)
P	4.2 (mg/dL)
iPTH	290 (pg/mL)
ALP	401 (IU/L)
Bone specific ALP	21 (IU/L)
Fe	23 ($\mu\text{g/dL}$)
TIBC	165 ($\mu\text{g/dL}$)
Ferritin	259 (ng/mL)
TSH	2.87 ($\mu\text{IU/mL}$)
FT3	2.4 (pg/mL)
FT4	0.77 (ng/mL)
$\beta 2\text{MG}$	24.6 (mg/L)
Dialytic factors	
Modality	PD+HD
PET category	Low average
D/P Cr	0.56
Weekly Kt/V(peritoneum)	1.9
nPCR	0.6

PD peritoneal dialysis, HD hemodialysis, PET peritoneal equilibration test, D/P Cr dialysate-to-plasma ratio of creatinine

experienced one episode of mild peritonitis in 2006. He was dialyzed adequately and his peritoneal function was mostly preserved (his dialysate-to-plasma creatinine value of peritoneal equilibration test results was constant around 0.5–0.6), which enabled him to continue long-term PD therapy [4, 5]. His serum level of phosphate (4.2–6.8 mg/dL, average 5.0 mg/dL), calcium (8.5–10.1 mg/dL, average 9.3 mg/dL), and intact parathyroid hormone (49–490 pg/mL, average 286 pg/mL) were controlled using phosphate binders (calcium carbonate 1000 mg/day and lanthanum carbonate 750 mg/day), calcimimetics (cinacalcet hydrochloride 25 mg/day) and administration of vitamin D3 analog. His other medications included low-dosage aspirin and pitavastatin calcium 1 mg/day, and eicosapentaenoic acid ethyl ester 1800 mg/day. He had a stroke caused by cerebral infarction in 2000. He had been receiving leuprorelin acetate for prostate cancer since 2006.

Fig. 1 Computed tomography showing tumoral mass near the left hip joint space

For 3 weeks before admission, he had a history of fever and had difficulty walking because of increasing pain in the left inguinal region. An examination revealed a palpable tumor in the left groin area, which was painful when palpated. His left hip flexion was limited. He had no history of trauma in this region. Examination of the other joints yielded no abnormal findings.

Laboratory data and dialytic factors on admission are presented in Table 1. His white blood cell count, serum calcium, phosphate, and uric acid were in the normal range. C-reactive protein was elevated to 8.23 IU/mL (normal, <0.3). A CT scan revealed a capsule-like structure surrounding a low-density area along the internal iliac muscle in the dorsal area of the left femoral artery and vein in the groin (Fig. 1). The differential diagnosis included bacterial abscess, tophaceous gout, or amyloidosis related to the long-term dialysis. Synovial fluid was aspirated from the swollen region, examination of which revealed the presence of CPPD crystals with negative cultures. According to the clinical, radiological, and laboratory findings, the patient was diagnosed as having tophaceous pseudogout. After his diagnosis, he started taking non-steroidal anti-inflammatory drugs (NSAIDs), after which his symptoms were resolved. 7 days after synovial fluid aspiration, he showed signs of recurrence and underwent another fluid aspiration. His pain was well controlled after the second aspiration. He was discharged on the tenth hospital day. The level of CRP fell to normal 4 months after discharge (Fig. 2). At 15 months, no symptom of disease recurrence was found.

Discussion

CPPD disease is characterized by crystal deposits in the articular cartilage or synovium. In fact, CPPD disease

Fig. 2 Clinical course of the present case. *NSAIDs* non-steroidal anti-inflammatory drugs, *CRP* C-reactive protein

presents various clinical manifestations, from absence of symptoms to severely destructive arthropathy [6, 7]. A tumoral form of CPPD disease (tophaceous pseudogout), a rare presentation of CPPD disease, has also been reported [8]. The optimal method for diagnosing pseudogout necessitates aspiration and pathologic examination of the synovial fluid from a swollen or painful joint [6, 7]. The CPPD crystals are typically rhomboidal, but small or long rods and even squares might be observed [3, 8]. An X-ray of the joint might be taken to ascertain whether calcium-containing deposits are present in the cartilage, creating a condition known as chondrocalcinosis. Other potential causes of symptoms such as gout, rheumatoid arthritis, and infection must be ruled out. In the current case, fluid localization was determined by CT scan. Furthermore, CPPD crystals were confirmed in aspirated fluid.

Some cases of CPPD disease in CKD patients have been described in the literature. Braunstein et al. [9] reported that radiologic findings of 6 cases among 28 long-term dialysis cases resembled CPPD disease, but they were not diagnosed pathologically. Chalmers et al. [10] described that 1 out of 61 PD patients had CPPD disease, but that study lacked individual patient information. Summary information from reports in the literature of acute pseudogout in CKD patients diagnosed using synovial fluid aspiration is presented in Table 2 [1–3, 11, 12]. Various joints are affected, including the wrist, shoulder, knee, hip, and elbow. Two patients were pre-dialysis patients. Most of the patients experienced CPPD disease within 1 year from the initiation of dialysis. Only two cases (including the current case) of long-term dialysis were found. Patient ages were 39–82 (average 59.3 years old), which seems younger

than the age of non-CKD CPPD patients. Often, CPPD is associated with other conditions such as prior joint trauma, surgery, aging, and metabolic diseases such as hyperparathyroidism, hemochromatosis, hypothyroidism, hypomagnesemia, amyloidosis, and hypophosphatemia. Hyperparathyroidism, hemochromatosis, and amyloidosis are common complications of CKD and dialysis patients. In this case, hemochromatosis was excluded from the data of ferritin. Although the relation with amyloidosis must be considered because of the long history of dialysis, no sign of a relation was found in the radiological data. Secondary hyperparathyroidism was well controlled according to the K/DOQI or Japanese Society of Dialysis Therapy (JSDT) guidelines, but it persisted throughout his dialysis therapy, which is consistent with the previous reports of CPPD disease in CKD patients. Although the pathogenesis of CPPD disease in CKD patients, especially PD patients, remains unclear, calcium concentration of the dialysate, low fetuin, and abnormal dialysis metabolite might be associated with the disease. Tophaceous pseudogout is a rare form of CPPD that manifests in the form of a mass [8]. To our knowledge, tophaceous pseudogout has never been reported in dialysis patients. It usually occurs in the temporomandibular joint, occasionally in the perispinal tissues, but rarely in the joints of the extremities. Consequently, the involvement of the hip joint in the current case is a rare manifestation of tophaceous pseudogout.

Cooling of the joint, oral NSAIDs, and oral colchicine are effective for treating pain and disability during severe episodes. For patients who cannot receive NSAIDs for medical reasons, aspiration of the joint with subsequent intra-articular steroid injection is regarded as the treatment

Table 2 Reported cases of pseudogout (calcium pyrophosphate dihydrate deposition disease) in CKD patients

Patient no.	Age	Sex	Location	Symptoms	CKD stage	Dialysis period	Type of dialysis	ESRD cause	Ca/P	HPT	Treatment	References
1	71	M	Wrist, ankle, hip	Joint pain	5	0 months		DM	4.8/N/A	N/A	Steroid, anakinra (IL-1 inhibitor)	[11]
2	66	F	Wrist, knee	Joint pain	5D	6 months	HD	DM	9.4/2.8	Yes	Joint aspiration NSAIDs	[1]
3	57	M	Ankle	Joint pain	5D	1 months	HD	Unknown	8.4/6.2	Yes	Joint aspiration corticosteroid injection	[2]
4	41	M	Wrist, shoulder, knee, hip	Joint pain, fever	5D	18 years	HD	CGN	10.7/4.1	No	NSAIDs, steroid	[3]
5	39	M	Wrist	Joint pain, fever	5D	6 months	HD	Unknown	8.4/12.4	Yes	Not described	[12]
6	59	M	Elbow	Joint pain	5	0 months		HTN	8.3/6.2	Yes	Not described	[12]
7*	82	M	Hip	Joint pain, fever	5D	9 years	PD+HD	CGN	8.1/4.2	Yes	Joint aspiration, NSAIDs	Current case

CKD Chronic kidney disease, ESRD end-stage renal disease, Ca calcium, P phosphate, M male, F female, D dialysis, HD hemodialysis, PD peritoneal dialysis, DM diabetes mellitus, CGN chronic glomerular nephropathy, HTN hypertension, N/A not available, HPT hyperparathyroidism

* Current case

of choice [13]. In this case, fluid aspiration and NSAIDs were effective. For CKD patients before initiation of dialysis, NSAIDs are usually avoided because of the risk of decreasing kidney function. To prevent further attacks, low doses of colchicine or NSAIDs might prove effective. Nevertheless, no treatment is available to dissolve the crystal deposits. Patients should remain under careful observation because of the risk of recurrence.

This report is the first to describe tophaceous CPPD disease involving the hip joint in a PD patient. When a CKD or dialysis patient complains of joint pain, physicians often do not consider pseudogout, probably because it is rarer than crystal arthritis of other types. Pseudogout in CKD patients is rare. Few cases have been reported in the literature. Furthermore, no case of pseudogout in PD patients has been reported in the literature. Results related to the case described herein suggest that pseudogout should be suspected in peritoneal dialysis patients with unexplained arthritis.

Conflict of interest No potential conflict of interest exists in relation to this article.

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