□ CASE REPORT □

A Case of Tuberculous Peritonitis in a Hemodialysis Patient with High Serum Soluble Interleukin-2 Receptor and CA-125 Levels

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Abstract

A hemodialysis patient with tuberculous peritonitis with hypercalcemia and high serum soluble interleukin-2 receptor (sIL-2R) and CA-125 levels is reported. An 82-year-old woman who had been on hemodialysis therapy for 6 years was admitted to our hospital for evaluation and treatment of hypercalcemia. Laboratory examination and radiologic studies revealed markedly increased serum sIL-2R and CA-125 levels and exudative ascites, with high levels of adenosine deaminase (ADA) and CA-125, which was suggestive of malignancy or tuberculosis. She was finally diagnosed as having tuberculous peritonitis based on positivity for *Mycobacterium tuberculosis* in ascitic fluid. The ascites subsided with normalization of hypercalcemia and a marked decrease in serum sIL-2R and CA-125 levels in response to anti-tuberculosis treatment. This case indicates that serum sIL-2R and CA-125 levels can rise to levels suggestive of malignancy in tuberculous peritonitis, and that they can be used to monitor the response to anti-tuberculosis treatment.

Key words: tuberculous peritonitis, hemodialysis, soluble interleukin-2 receptor (sIL-2R), CA-125

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Introduction

Patients with chronic renal failure have an increased incidence of tuberculosis due to decreased cellular immunity. Although extrapulmonary tuberculosis is rare in the general population, its frequency has been reported to be 37.7-51.6% of tuberculosis infections in dialysis patients (1, 2). Tuberculous peritonitis is one of the most prevalent forms of extrapulmonary tuberculosis. Because its diagnosis and treatment are often difficult, a high index of suspicion and aggressive evaluation are needed in the clinical setting. The case of a patient with tuberculous peritonitis presenting initially with hypercalcemia is presented; serum soluble interleukin-2 receptor (sIL-2R) and CA-125 measurements were useful for monitoring the disease activity.

Case Report

An 82-year-old woman with end-stage renal failure due to nephrosclerosis had been undergoing hemodialysis (HD) since 2003. In mid-September 2010, she was admitted to our hospital because of hypercalcemia and elevated C-reactive protein (CRP) with complaints of abdominal discomfort. On admission, her height was 145.0 cm, and her weight was 38.2 kg. Her temperature was 36.6°C, heart rate was 63/min, and blood pressure was 139/75 mmHg. Chest radiography showed mild cardiac enlargement. Abdominal computed tomography (CT) showed the presence of multiple enlarged mesenteric lymph nodes and a moderate amount of ascites.

The patient's laboratory findings on admission conducted prior to a HD session are summarized in Table 1. Briefly, the patient showed anemia, hypoalbuminemia, renal dysfunction, hypercalcemia, and elevation of C-reactive protein.

Table 1. Laboratory Findings on Admission

Peripheral blood		Blood chemistry		Serological study	
WBC	5400 / μ L	TP	6.0 g/dL	CRP	11.19 mg/dL
Neutro	85.9%	Alb	2.9 g/dL	ANA	(-)
Lymph	5.2%	BUN	22.9 mg/dL	IgG	854 mg/dL
Mono	7.0%	Cr	4.97 mg/dL	IgA	110 mg/dL
Eosino	1.3%	UA	3.6 mg/dL	IgM	50 mg/dL
Baso	0.6%	Ca	12.9 mg/dL	C3c	115.2 mg/dL
RBC	357×10^4 / μ L	P	4.3 mg/dL	C4	53.3 mg/dL
Hb	10.5 g/dL	AST	20 IU/L	CH50	25.2 U/mL
Ht	34.5%	ALT	17 IU/L	RF	<7.0 IU/L
Plt	26.5×10^4 / μ L	Na	137.5 mEq/L		
		K	3.9 mEq/L		
		Cl	98.5 mEq/L		
		Intact-PTH	90 pg/mL		
		sIL-2R	9170 U/mL		
		CA-125	385 U/mL		
		ACE	13.6 IU/L

Figure 1. Clinical Course. Abbreviations: HD: hemodialysis, CRP: C-reactive protein, sIL2-R: soluble interleukin 2 receptor, INH: isoniazid, EB: ethambutol hydrochloride, REF: rifampicin, PZA: pyrazinamide**Table 2. Laboratory Findings of Ascitic Fluid**

Appearance	Turbit	Blood chemistry	
Cytology	Class II	TP	3.9 g/dL
		Alb	1.8 g/dL
		LDH	192 IU/L
pH	8.0	ADA	42.8 IU/L
Specific gravity	1.028	(normal range 6.8-18.2 IU/L)	
Hematology		Serology	
WBC	1300 /mm ³	CA-125	304 U/mL
neutrophils	11.0 %	<i>Mycobacterium tuberculosis</i>	
lymphocytes	80.0 %	Culture	positive
monocytes	7.0 %	PCR	negative
macrophages	2.0 %		

Serum CEA, CA 19-9, and SCC levels were within normal limits (data not shown), whereas soluble interleukin-2 receptor (sIL-2R) and CA-125 levels were increased to 9,170 U/mL (normal range: 145-519 U/mL) and 385 U/mL (normal range: <35 U/mL), respectively. Both the sputum smear and polymerase chain reaction (PCR) analysis were negative for *Mycobacterium tuberculosis*. The tuberculin skin test was nonreactive. QuantiFERON-tuberculosis (QFT) testing was indeterminate.

The hypercalcemia was treated with elcatonin and zoledronate, and HD with low-Ca dialysate was started (Fig. 1). The results of paracentesis performed from the pouch of Douglas on the 28th hospital day (Table 2) were turbid and

Figure 2. (A) Computed tomography (CT) of the pelvis showing a moderate amount of ascites on the 28th hospital day before starting anti-tuberculosis therapy. (B) Pelvic CT 28 days after anti-tuberculosis therapy on the 69th hospital day showing a decrease in the volume of ascites.

exudative with high levels of adenosine deaminase (ADA) and CA-125, and cytologic examination showed a marked predominance of lymphocytes and no neoplastic cells. The PCR for *Mycobacterium tuberculosis* in ascitic fluid was negative. The administration of anti-tuberculosis drugs with rifampicin (REF), isoniazid (INH), ethambutol hydrochloride (EB), and pyrazinamide (PZA) as empirical therapy was started on the 41st hospital day (Fig. 1). Two weeks after starting anti-tuberculosis drugs, the patient was eventually diagnosed as having tuberculous peritonitis based on positivity for *Mycobacterium tuberculosis* in the ascitic fluid culture (Table 2). The ascites subsided with normalization of hypercalcemia (Fig. 2) and a marked decrease in serum sIL-2R and CA-125 levels, and her general condition recovered in response to anti-tuberculosis treatment. When she was discharged from hospital after 4 weeks of anti-tuberculosis treatment, she was asymptomatic, and her CRP level was < 0.2 mg/dL.

Discussion

The most interesting aspect of this case was the considerable increase in serum sIL-2R, which was 3.5-fold higher than the mean value in a previously reported case of tuberculosis (3), and this level led us to consider the possibility of malignancy. sIL-2R, known as a surrogate marker of T-lymphocyte activation and proliferation, is detectable in the serum, and its concentration is elevated in tuberculosis (4), in which inflammatory CD4+ T-lymphocytes are activated. Studies have shown a marked elevation of sIL-2R levels in patients with active pulmonary tuberculosis, but levels similar to controls in patients with old, inactive tuberculosis (5). Thus, it is recognized that sIL-2R serves as a marker of dis-

ease activity in patients with tuberculosis (6). On the other hand, a case of tuberculous peritonitis with highly elevated serum sIL-2R levels has never been described in the literature. It is likely that many cases are left unreported. Although sIL-2R levels in ascitic fluid were not measured in the present case, high sIL-2R levels are expected, given the high levels of sIL-2R in pleural effusions in patients with tuberculous pleurisy (7-9). These studies showed that tuberculous pleurisy could be distinguished from non-tuberculous effusions with a sensitivity of 74-91% and a specificity of 93.9-100% by evaluation of pleural sIL-2R levels (7-9). Seventeen weeks after initiation of anti-tuberculosis therapy, the patient's sIL-2R level decreased from 9,170 U/mL to 1,620 U/mL, which is appropriate value for hemodialysis patients as reported by Shu et al (10).

An increased serum level of CA-125, a mucin-like glycoprotein with a molecular weight of 110 kDa, is a useful marker of ovarian cancer but can also be seen in other benign abdominal diseases such as cirrhosis, peritonitis, pancreatitis, endometriosis, uterine leiomyomas, benign ovarian cysts, pregnancy, and pelvic inflammatory disease. Thus, serum CA-125 is considered a nonspecific marker of peritoneal involvement. It has been reported that serum CA-125 levels are increased in patients with tuberculous peritonitis (11, 12). Of note, CA-125 is expressed in the coelomic epithelium, such as the pleura, peritoneum, and pericardium (13). Thus, it is considered that CA-125, which is secreted by mesothelial cells (14), drains into ascitic fluid as a result of peritonitis, and inflammation in the area destroys the blood vessels, so that CA-125 accumulates at high levels in the blood. Consistent with a previous report (15), the present patient's serum CA-125 level was elevated to 385 U/mL and normalized to 26.9 U/mL in parallel with the clini-

cal improvement. Menzin et al found no impaired metabolism or clearance of CA125 in female hemodialysis patients (16). Accordingly, serum CA-125 can be used to evaluate the efficacy of therapy in tuberculosis peritonitis, but it is not suitable for confirming the diagnosis of tuberculous peritonitis (11), as with estimation of ADA levels in ascitic fluid.

In conclusion, the present case indicates that serum sIL-2R and CA-125 levels can rise to a level suggestive of malignancy in tuberculosis peritonitis, and in addition to conventional laboratory parameters such as CRP or ESR, they may serve as an additional tool for monitoring the response to anti-tuberculosis medications.

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