A case of C reactive protein negative peritoneal dialysis related peritonitis in patient receiving tocilizumab for rheumatoid arthritis

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Background

In recent years, the treatment of rheumatoid arthritis (RA) has been dramatically developed by induction of biologics. Although anti-IL-6 receptor antibody tocilizumab (TCZ) completely suppresses C reactive protein (CRP), inhibition of IL-6 by TCZ makes IL-6-induced fever and pain less prominent.

Conclusions

TCZ treatment may mask the typical symptoms of infection, so physicians must be aware of the potential for hidden infection when such patients present with new symptoms.

Case Presentation

A 60-year-old woman with 17-year history of RA and 4-year history of continuous ambulatory peritoneal dialysis (CAPD) for renal amyloidosis secondary to RA had been treated with etanercept + predonisolone (PSL) after induction of CAPD.

In Feburary 2013, because of exacerbation of arthritis, TCZ was induced in 4-weeks interval.

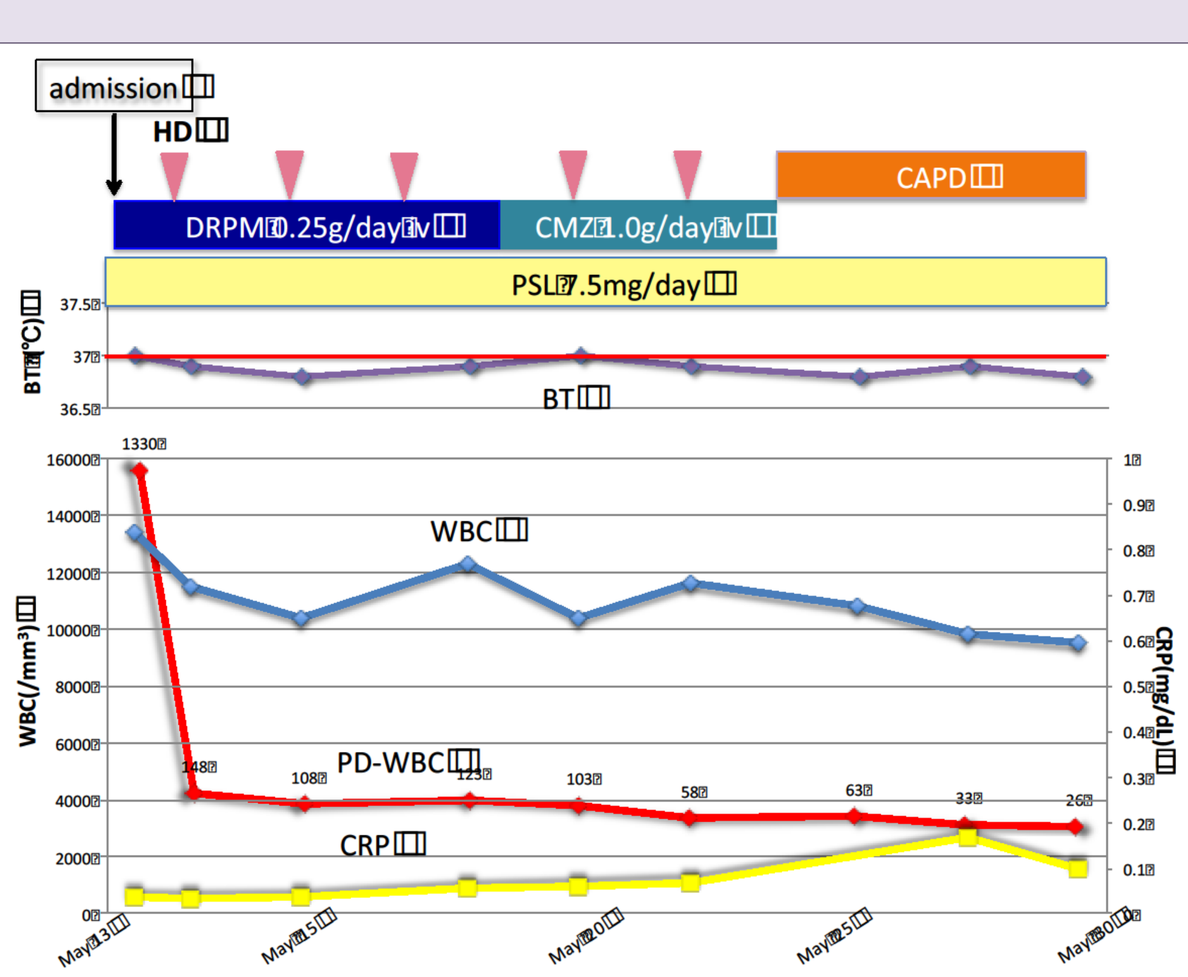
At a routine monthly visit, 18days after 4th infusion of TCZ, peritoneal fluid was cloudy and the specimen had an elevated white-cell count (WBC) (1330/mm^3, neutrophils 84%). Although blood WBC was elevated, CRP was within normal limits and she did not have any symptom, including fever, pain and nausea.

< Peritoneal Fluid >

Color	white		TP	4.3	g/dL
Turbidity	cloudy		Alb	2.4	g/dL
WBC	1330	/mm^3	UN	35.1	mEq/L
Neut.	84	%	Cr	4.4	mEq/L
Culture			Glu	115	mEq/L
	Bacillus cereus		CRP	0.035	mg/dL

< Blood >

WBC	13400	/mm^3	PCT	0.17	ng/mL
Neut.	94	%	Endotoxin	<0.8	pg/mL
Hb	10.8	g/dL	β-D glucan	9.6	pg/mL
Plt	21.0 x 10^4	/mm^3	Culture	negative	



Empiric antibiotic therapy was initiated intravenously with doripenem (DRPM). Cultures of the fluid revealed Bacillus cereus, and the treatment was subsequently changed to cefmetazole (CMZ). The WBC of blood and peritoneal fluid were improved soon. Increases in CRP observed 5 weeks after TCZ administaration (May 27) was considered to have been induced by RA flare.

Discussion

Case reports : The masking symptoms of severe infections in patients with RA receiving TCZ

No	Age (y)	M/F	Duration of RA (y)	Days after last TCZ Tx	CRP / WBC on admission	Infection focus	Symptom (+)	Symptom (-)	Pathogenic bacteria	Combined medicine
Pt.	***60***	***F***	***17***	***18***	***0.035 / 13,800***	***peritonitis***	***cloudy fluid***	***fever, pain***	***Bacillus cereus***	***PSL***
1[1)]	68	M	8	14	0.55 / 27,620	pneumonia	malaise sweat	fever sputum dyspnea	H. influenza	PSL
2[1)]	68	M	6	21	2.3 / 15,400	pneumonia	fever	sputum dyspnea	H. influenza Str. pneumonia	PSL BM SASP
3[2)]	62	F	7	20	< 0.04 / 8100	cellulitis phlegmon	local heat local pain	fever	ND	none
4[2)]	49	F	30	28	< 0.04 / 7100	cellulitis phlegmon	local heat local pain	fever	ND	PSL MTX TAC
5[3)]	78	F	38	ND	< 0.3 / 9100	pneumonia	pharyngeal pain	fever sputum dyspnea	Str. pneumonia	PSL
6[4)]	65	M	ND	ND	0.4 / 11800	synovitis	local pain swelling	fever	Sta. aureus	PSL MTX SASP

ND: no data, BM: bucillamine, TAC: tacrolimus, SASP: salfazosulfapyridine

- IL-6 is a pleiotropic cytokine with diverse biological actions, regulating the inflammation, immune response, bone metabolism, and hematopoiesis.
- In RA patient, at the local or articular level, IL-6 contributes to joint inflammation and to bone destruction via activation of osteoclasts and inhibition of osteoblast function[5)] . At the systemic level, IL-6 is a key regulator of hepatocytes in the liver, a major regulator of acute-phase protein synthesis, including CRP.
- In patient treated with TCZ, CRP used as a marker of inflammation and infection in clinical practice may remain suppressed even in the context of severe infection. Four case reports have reported the masking of symptoms of severe infections in patients treated with TCZ (table). Our patient did not have any symptom such as fever and pain, except for cloudy PD fluid, either.

References

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DOI: 10.3252/pso.eu.51era.2014