—Short Communications—

Low levels of IL-1ra versus IL-1 levels in prostatic fluid
are not a cause of prolongation of prostatitisTaiji Nishimura, Hiroyuki Abe, Hiroshi Ito, Kazunori Ikeda,
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We have investigated the significance of leukocytosis^{1,2)} and its prolongation³⁾ in prostatic fluid (PF) from prostatitis patients. In a previous paper we reported an increase in the survival rate of peripheral blood monocytes (PBMC) when cultured with macrophages in PF from nonbacterial prostatitis (NBP) patients, possibly due to cytokines secreted from the macrophages, because elevated interleukin (IL-1) β levels in culture medium were observed⁴⁾.

Recent papers have reported that the balance between the production of IL-1 and IL-1 receptor antagonist (ra) probably influences the regulation of the host response and the severity and prolongation of inflammatory reactions in some diseases⁵⁾, and that the balance is necessary for homeostasis of the mononuclear phagocytosis system⁶⁾, because IL-1ra limits the extent of the potentially deleterious effects of IL-1⁷⁾. The inhibitory action of IL-1ra results from binding of IL-1ra to the IL-1 receptor Type I with an affinity comparable to that of IL-1 α or IL-1 β , thus competing with IL-1 α or IL-1 β for binding this receptor. This binding, however, does not result in signal transduction⁵⁾. An excess of 10 to 100 times more IL-1ra than IL-1 is needed to abrogate the biologic effects of IL-1 on target cells by 50%⁷⁾. High dose administration of IL-1ra to affect cartilageproteoglycan synthesis disturbance caused by IL-1 is considered for clinical application⁸⁾.

Herein we have attempted to clarify whether low levels of IL-1ra vs. IL-1 are a cause of prolongation of prostatitis, especially NBP and prostatodynia. Generally prostatitis is classified into four groups: acute bacterial prostatitis (ABP), chronic bacterial prostatitis, NBP and prostatodynia. The latter two are most common in prostatitis and usually take a long course. In prostatodynia, patients have similar complaints as in NBP, but there is no leukocytosis in prostatic fluid. Because of a shortage of cases of prostatitis, female acute bacterial cystitis (ABC), which is the most common disease in out-patient urology clinics, was also studied for the understanding of data obtained in the present study of prostatitis. No studies of the relation between IL-1 and IL-1ra in the urological field are to be found in the literature.

IL-1 β and IL-1ra concentrations in urine after prostatic massage (VB3: Voided bladder 3) in prostatitis and catheterized urine from female ABC patients were determined by using enzyme-linked immunosorbent assay kits (R & D Systems INC. Minneapolis, MN, USA)

Table IL-1 β and IL-1 ra level (pg/ml) in VB 3 or urine from prostatitis patients and catheterized urine from female ABC patients

	IL-1 β	IL-1 ra
ABP (n=2) case 1	196	3,920
case 2	14	1,357
NBP (n=5)	14 in 1, ND in 4	1,316 $\pm$ 569*
Prostatodynia (n=6)	ND	582 $\pm$ 391
ABC (n=13)	68, 46, 27, 22 and 21 in 1 and ND in 8	2,535 $\pm$ 2,977

ABP: Acute bacterial prostatitis, NBP: Nonbacterial prostatitis, VB 3: Voided bladder 3, ABC: Acute bacterial cystitis, ND: Not detected, *: $p=0.032$ vs. Prostatodynia and $p=0.385$ vs. ABC.

according to the manufacturer's instructions.

In a study of two ABP cases, significant increases of IL-1 β and IL-1ra were observed in one and slight increases of both cytokines were observed in the other (Table). Both cases were cured within 2 weeks by administration of antibiotics. In 6 cases with nonbacterial prostatitis (NBP), no significant increases of IL-1 β or IL-1ra were observed and only a slight increase of IL-1 β was noted in one case (Table). Average IL-1ra level in NBP was similar to that in ABP case 2 and was higher than that in prostatodynia ($p=0.032$). It was not statistically different from that in ABC ($p=0.385$). In prostatodynia, IL-1 β was not detected in any case.

In female ABC patients, more than 10^7 E. coli per ml was recovered from catheterized urine in all 13 cases and subjective and objective symptoms disappeared within a week after administration of oral antibiotics for three days. Increases of IL-1 β levels were observed in 5 cases (Table). IL-1ra levels tended to be high when IL-1 β levels were high.

In conclusion, in NBP, 1) IL-1 β , which is believed to elicit deleterious effects in inflammatory tissues, was not detected in 4 cases and was slightly elevated only in one case, 2) average IL-1ra levels were not low compared with those in ABP or female ABC cases, which were cured quickly with antibiotics, 3) in a case of NBP in which IL-1 β was detected, IL-1ra vs. IL-1 ratio was 103, which was comparable to that in two ABP and five ABC cases with elevated IL-1 β , where the ratios were from 20 to 97 and from 34 to 280, respectively. From these results, we speculated that low levels of IL-1ra vs. IL-1 secreted in prostatic fluid are unlikely to be a cause of prolongation of NBP or prostatodynia.

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