

CASE REPORT

WEIL'S DISEASE WITH ELEVATED PLASMA D-DIMER

K Ohnishi, Y Kato and K Hayakawa

Department of Infectious Diseases, Tokyo Metropolitan Bokutoh General Hospital, Sumida City, Tokyo, Japan

Abstract. We report a case of Weil's disease manifesting elevation of plasma D-dimer in the acute phase. Later, in the convalescent phase after treatment, the plasma levels of D-dimer returned to normal. Plasma D-dimer can be used as a marker of fibrin formation and degradation. Based on our observations, we conjecture that fibrin formation and fibrinolysis may occur in the acute phase of Weil's disease.

INTRODUCTION

Weil's disease is an acute febrile zoonosis, but the disease is very rare in Japan at present. The causative organisms of Weil's disease, *Leptospira interrogans* serovars Icterohaemorrhagiae and Copenhageni, are carried in the urine of wild mice and rats and transmitted to humans through contact with skin. Weil's disease is thus mainly recognized as an occupational disease affecting persons who come into contact with mice and rat urine.

Plasma levels of D-dimer are elevated in some infectious diseases (Ohnishi and Kato, 2002; Shilon *et al*, 2003). Thrombus formation is followed by activation of the fibrinolytic system and D-dimer is formed by plasmin-mediated proteolysis of cross-linked fibrin. Fibrin and fibrinogen degradation products (FDP) are known to be elevated in Weil's disease (Edwards *et al*, 1985), but we are aware of very few reports describing or investigating plasma D-dimer levels in patients with Weil's disease (Raing *et al*, 1990; Theilen *et al*, 2002).

Here we report a recent case of Weil's disease in a patient who contracted the infection at his workplace in Tokyo and manifested el-

evated plasma D-dimer in the acute phase.

CASE REPORT

A 35-year-old Japanese man who had been living in eastern Tokyo and working as a sewer worker was referred to our hospital on February 18, 2004 because of 5 days of fever, myalgia, and increasing jaundice. On admission to our hospital he presented with mild confusion, a body temperature of 38.3°C, pulse of 130/minute, and blood pressure of 100/60mmHg. Jaundice and conjunctival suffusion were identified. Abdominal tenderness and muscular tenderness throughout the entire body were noted. No remarkable findings were noted on examinations of the heart and lungs. Laboratory data on admission showed a white blood cell (WBC) count of 14,700/mm³ (normal range: 6,500±3,800/mm³) with 91% neutrophils, 4% lymphocytes, and 5% monocytes. Other laboratory findings were as follows: platelet (Plt) count, 1.2x10⁴/mm³ (normal range: 13~35x10⁴/mm³); D-dimer, 4.9 µg/ml (normal range: <1.0 µg/ml); FDP, 4.2 µg/ml (normal range: <5.0 µg/ml); prothrombin time (PT), 86.8% (normal range: 75~120%). Serum levels of C-reactive protein (CRP), total bilirubin (T-Bil), creatine phosphokinase (CK), blood urea nitrogen (BUN), and creatinine (Cre) were 43.43 mg/dl (normal range: <0.30 mg/dl), 5.2 mg/dl (normal range: 0.2~1.1 mg/dl), 219 IU/l (normal range: 30~185 IU/l), 47 mg/dl (normal 7~20 mg/dl), and 4.0 mg/dl (normal range: 0.4~1.1 mg/dl), respectively.

Correspondence: Dr Kenji Ohnishi, Department of Infectious Diseases, Tokyo Metropolitan Bokutoh General Hospital, 4-23-15 Kohtohbashi, Sumida City, Tokyo 130-8575, Japan.

Tel: 81-3-3633-6151; Fax: 81-3-3633-6173
E-mail: infection@bokutoh-hp.metro.tokyo.jp

Table 1
Laboratory values in a patient with Weil's disease.

	February						March			May	
	18	19	20	21	22	23	25	28	1	15	6
D-dimer ($\mu\text{g/ml}$)	4.9	10.3	8.4	11.1	12.8	13.9	10.9	10.7	7.1	3.3	0.5
FDP ($\mu\text{g/ml}$)	4.2	15.2	9.5	14.1	18.3	21.6	16.8	13	5.9	1.4	0.0
PT (%)	86.8	70.2	94.3	106.5	104.8	113.8	100	90.4	90.4	88	108.2
BUN (mg/dl)	47	69	60	78	61	78	79	54	41	12	10
Cre (mg/dl)	4.0	5.7	3.6	4.1	3.3	3.7	4.2	3.1	2.4	1.1	0.7
ALT (IU/l)	30	33	41	35	30	30	24	58	70	74	31
LDH (IU/l)	168	342	488	494	492	501	375	328	317	153	127
Plts($\times 10^4/\text{mm}^3$)	1.2	1.5	2.1	2.5	2.5	3.9	8.7	33.2	43.4	82.3	35.2

FDP, fibrin and fibrinogen degradation products.; PT, prothrombin time; BUN, blood urea nitrogen; Cre, creatinine; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; Plts, platelets.

Weil's disease was suspected based on the patient's symptoms, findings on physical examination, and laboratory data on admission. The patient received administrations of daily doses of 1 g of streptomycin intramuscularly from February 18 to 21 and daily doses of 2 g of ampicillin intravenously from February 19 to 25. The patient lapsed into anuric renal failure, and his renal function slowly recovered under management with hemofiltration. The results of blood examination on April 16, 2004 were as follows: WBC of $6,100/\text{mm}^3$, Plt of $40.1 \times 10^4/\text{mm}^3$, CRP of 0.53 mg/dl, T-Bil of 1.1 mg/dl, CK of 30 IU/l, BUN of 8 mg/dl, Cre of 0.7 mg/dl, alanine aminotransferase (ALT) of 19 IU/l, and lactate dehydrogenase (LDH) of 123 IU/l. The patient was discharged on April 19, 2004. The diagnosis was confirmed by amplification of the *flaB* gene of *Leptospira* from the DNA extract of the patient's blood on February 18 and an elevation of serum antibody in *L. interrogans* serovar Icterohaemorrhagiae/Copenhageni detected with the standard microagglutination assay (<1:10 on admission, rising to 1:80 after 7 days). Elevated plasma levels of D-dimer and FDP were identified during the hospital stay. Table 1 shows the plasma levels of D-dimer, FDP, and PT; the serum levels of BUN, Cre, ALT, and LDH; and the number of platelets.

DISCUSSION

Plasma D-dimer and FDP were both elevated in our patient in the acute phase, and the D-dimer returned to a normal level during the convalescent phase. Physicians have not been interested in plasma levels of D-dimer in patients with Weil's disease, and to our knowledge, elevated plasma D-dimer has been reported in the acute phase of only 2 patients with Weil's disease (Raing *et al*, 1990; Theilen *et al*, 2002). D-dimer is thought to be eliminated primarily by the liver (Pizzo and Pasqua, 1982). However, ALT and PT were in the normal range in our patient while elevated D-dimer were observed, and these findings may indicate that formation of D-dimer may have been accelerated. The plasma level of D-dimer can be used as a marker of fibrin formation and degradation (Bick and Baker, 1982), and D-dimer assay is thought to

be helpful in the diagnosis and management of patients with diseases associated with fibrinosis (Wilde *et al*, 1989). The observation of elevated plasma D-dimer noted in our patient and the 2 patients with Weil's disease previously reported (Raing *et al*, 1990; Theilen *et al*, 2002) may indicate that fibrin formation and fibrinolysis characteristically occur during the acute phase of Weil's disease.

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