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Clinical Significance of Blood Coagulation Factor XIII Activity in Adult Henoch-Schönlein Purpura

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Abstract

Background: A correlation between decreased blood coagulation factor XIII activity and the severity of organ disorders in pediatric Henoch-Schönlein purpura (HSP) has been demonstrated, but possible correlations in adult HSP have not been thoroughly investigated.

Objectives: To investigate the association between factor XIII activity with varying clinical severities of HSP and the severity of organ disorders and to examine the efficacy of factor XIII substitution therapy.

Methods: The distribution of purpura and the severities of joint, abdominal, and renal symptoms were scored in 44 adults with HSP. Plasma factor XIII activity was measured with the latex agglutination immunoturbidity method.

Results: Reduced factor XIII activities were correlated with clinical severity scores (the total of all scores), organ disorder severity scores (the total score excluding the purpura score), joint symptom scores, and abdominal symptom scores but not with renal disorder scores. Factor XIII activities were increased in patients during posttreatment remission. Factor XIII substitution therapy was performed in 7 patients with severe organ disorders. Consequently, joint and abdominal symptoms markedly improved, but renal symptoms did not.

Conclusion: Measurement of plasma factor XIII activity in adult HSP is clinically useful because it indicates disease severity and the severity of digestive tract and joint disorders. Factor XIII substitution therapy is effective for joint and abdominal symptoms but not for renal symptoms. Further investigation of the effect of this treatment on renal symptoms is necessary.

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Key words: adult Henoch-Schönlein purpura, blood coagulation factor XIII, clinical severity, organ disorders, substitution therapy

Introduction

Henoch-Schönlein purpura (HSP) is a systemic vasculitis caused by the deposition of immunoglobulin (Ig) A-dominant immune complexes in small blood vessels of the glomeruli or skin or both. Purpura and symptoms in the joints, digestive organs, and kidneys are of varying severity. HSP most frequently develops in children, particularly those aged 5 to 6 years[1]. Although HSP in adults has a lower incidence it is more likely to cause or

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aggravate renal damage and, therefore, requires active treatment and careful monitoring[2,3].

In 1977, Henriksson et al.[4] reported reduced blood coagulation factor XIII activity in children with HSP accompanied by abdominal and joint symptoms; moreover, they showed that the transfusion of a fibrinogen preparation containing abundant factor XIII with an antiplasmin agent improved gastrointestinal hemorrhage in a case of severe HSP. A correlation between reduced plasma factor XIII activity and the severity of multiple organ disorders, especially abdominal symptoms, has been shown in pediatric HSP in several case studies[5,6] and a case-control study[7], and factor XIII substitution therapy markedly improved abdominal symptoms, joint symptoms, and renal dysfunction[6,7]. Two epidemiological studies[8,9] of changes in symptoms and laboratory values in children with HSP have shown that reduced plasma factor XIII activity is a risk factor for progression to renal dysfunction.

In 5 adults with HSP and markedly reduced plasma activities of factor XIII, factor XIII substitution therapy was effective against abdominal symptoms[10–12]. However, no controlled studies or case series have been reported, and reliable evidence regarding the significance of factor XIII therapy is lacking. Therefore, we investigated the association between plasma factor XIII activity and the severity of HSP, as determined on the basis of the severity of renal disorders, abdominal symptoms, and joint symptoms, in 44 adults and evaluated the clinical significance of plasma factor XIII activity.

Subjects and Methods

1. Patients

The subjects were 44 patients with HSP who were 20 years or older (29 men and 15 women aged 20–84 years; mean age: 51.2 years) and who presented at our outpatient clinic from September 2004 through March 2011 (**Table 1**) with multiple palpable purpural lesions of the lower extremities and other areas of the body. Histologic examination of skin biopsy specimens showed leukocytoclastic vasculitis of cutaneous small blood vessels, and direct immunofluorescence studies of biopsy specimens of either the skin or kidney showed positivity for IgA, which is included in the Chapel Hill Consensus Conference diagnostic criteria[13]. All cases met the criteria proposed by Helander et al.[14].

2. Methods

(1) Clinical severity scores

The distribution of purpura and the severity of joint symptoms (arthralgia, joint swelling), abdominal symptoms (abdominal pain, bloody stools), and renal disorders (urinary protein, urinary occult blood) were each scored on a 4-point scale from 0 to 3 following the method of Fukui et al.[7] (**Table 2**). The total of these scores was defined as the clinical severity score, for which values of 1 to 5, 6 to 10, and 11 or more were defined as mild, moderate, and severe, respectively. The total of the scores for joint and abdominal symptoms and for renal disorders was defined as the organ disorder severity score.

(2) Measurement of plasma factor XIII activity

Plasma factor XIII activity was measured with the latex agglutination immunoturbidity method of Yamada et al.[15]. Briefly, plasma was reacted with latex beads sensitized with sheep polyclonal antibodies against human factor XIII (Hexamate Factor XIII, Roche Diagnostics GmbH, Basel, Switzerland), and factor XIII activity was measured as the absorbance of agglutinated latex beads at 540 nm. The first international standard for factor XIII plasma (National Institute for Biological Standards and Control code: 02/206) of the World Health Organization was used to confirm a standard range, and 0.91 IU/mL (91% activity) and 0.93 IU/mL (93% activity) of the plasma were prepared by confirming activity as previously described[16]. The mean factor XIII activity measured in 106 healthy subjects was 73.2% to 142.4%, and values within 70% of this level were regarded as the normal range. The measurement range was 2.3% to 140%, and when the level exceeded 140%, the sample was diluted. Factor XIII activity was measured at the first visit in all patients and during the active pretreatment phase and the posttreatment remission phase in 14 patients. In 7 patients who underwent factor XIII substitution therapy, factor XIII activity was measured several times during the observation

Table 1 Patient backgrounds and outcomes of the treatment

Case	Age (years)/sex	CSS	ODS	JSS	ASS	RDS	PS	Factor XIII	Treatment	Outcome
1	73/F	6	6	2	4	0	1	57%	PSL, factor XIII	CR
2	38/M	8	6	2	4	0	2	59%	PSL, factor XIII	CR
3	48/M	14	12	5	1	6	2	49%	PSL, factor XIII, PP	PD
4	20/F	14	13	4	4	5	1	52%	PSL, factor XIII, PP	PR
5	29/M	11	9	2	2	5	2	23%	PSL, factor XIII, PP	PR
6	68/M	8	6	0	5	1	2	23%	PSL, factor XIII	CR
7	53/M	6	4	0	4	0	2	51%	PSL, factor XIII	CR
8	28/F	11	9	1	6	2	2	33%	PSL	CR
9	68/F	10	7	2	5	0	3	45%	PSL	PR
10	71/M	8	6	2	1	3	2	58%	PSL	CR
11	56/F	4	2	0	2	0	2	56%	No medication	CR
12	24/M	3	0	0	0	0	3	69%	No medication	CR
13	71/F	2	1	1	0	0	1	66%	No medication	CR
14	67/M	2	0	0	0	0	2	27%	No medication	CR
15	70/M	12	10	1	3	6	2	28%	PSL, PP	PD
16	70/M	10	7	0	1	6	3	57%	PSL, mPSL pulse,	PR
17	38/M	9	7	2	0	5	2	69%	PSL	CR
18	51/M	9	7	2	0	5	2	80%	PSL, mPSL pulse	PR
19	57/F	9	6	2	2	2	3	77%	PSL	CR
20	69/F	8	6	2	4	0	2	67%	PSL	PR
21	84/M	7	5	0	0	5	2	65%	PSL	PR
22	82/F	7	6	0	0	6	1	117%	PSL	PR
23	39/M	6	4	4	0	0	2	40%	PSL	CR
24	36/M	6	5	0	0	5	1	136%	PSL, mPSL pulse	PR
25	43/M	6	4	1	2	1	2	43%	PSL	CR
26	65/M	6	3	0	0	3	3	72%	No medication	PR
27	34/F	6	3	2	1	0	3	136%	No medication	CR
28	30/M	5	3	2	1	0	2	53%	No medication	CR
29	30/M	4	2	2	0	0	2	69%	No medication	CR
30	72/M	4	2	0	1	1	2	68%	No medication	CR
31	79/M	4	2	0	0	2	2	60%	No medication	CR
32	60/F	4	3	0	0	3	1	118%	No medication	PR
33	20/F	4	2	2	0	0	2	94%	No medication	CR
34	75/F	3	2	2	0	0	1	68%	No medication	CR
35	22/F	3	2	2	0	0	1	69%	No medication	CR
36	49/M	2	0	0	0	0	2	103%	No medication	CR
37	36/F	2	0	0	0	0	2	78%	No medication	CR
38	60/M	2	0	0	0	0	2	77%	No medication	CR
39	34/M	2	0	0	0	0	2	105%	No medication	CR
40	23/M	2	0	0	0	0	2	132%	No medication	CR
41	61/M	1	0	0	0	0	1	85%	No medication	CR
42	53/M	1	0	0	0	0	1	121%	No medication	CR
43	61/M	1	0	0	0	0	1	101%	No medication	CR
44	34/M	1	0	0	0	0	1	80%	No medication	CR

CSS = clinical severity score; ODS = organ disorder score; JSS = joint symptom score; ASS = abdominal symptom score; RDS = renal disorder score; PS = purpura score; PSL = prednisolone; mPSL = methylprednisolone; PP = plasmapheresis; CR = complete response; PR = partial response; PD = progressive disease

period (see below).

(3) Relationships among factor XIII activity, HSP-associated variables, and symptoms

The following relationships between variables were investigated: the relationships of factor XIII activity to 1) the clinical severity score, 2) the organ disorder score, 3) the joint symptom score, 4) the abdominal symptom score, 5) the renal disorder

Table 2 Scoring system for symptoms in Henoch-Schönlein purpura

Symptoms		0	1	2	3
Purpura		Absent	Lower limbs only	Upper and lower limbs and gluteal region	Four limbs and trunk
Joint symptoms	Arthralgia	Absent	Tender	Markedly tender	Nonpalpable because of pain
	Joint swelling	Absent	Mild	Moderate	Severe
Abdominal symptoms	Abdominal pain	Absent	Mild	Moderate	Severe
	Bloody stools (immunological fecal occult blood, ng/mL)	<100	100–999	1,000–9,999	≥10,000
Renal disorders	Urinary protein (test paper method)	−	± to +	+ +	+ + +
	Urinary occult blood (test paper method)	−	± to +	+ +	+ + +

score, and 6) the purpura score; and the relationships of the organ disorder score to 7) the purpura score, 8) the peripheral white blood cell (WBC) count, 9) the C-reactive protein (CRP) level, and 10) the serum IgA level.

(4) Comparison of factor XIII activities, clinical severity scores, and organ disorder scores in the active pretreatment phase and the posttreatment remission phase

In 14 patients (patients 1 to 14, including 8 men and 6 women aged 20–73 years; mean age: 51 years), the factor XIII activities, clinical severity scores, and organ disorder scores were measured in the active pretreatment phase and the posttreatment remission phase (**Table 1**). In addition, we analyzed the correlation between (pretreatment factor XIII-posttreatment factor XIII)/pretreatment factor XIII and (pretreatment clinical severity score-posttreatment clinical severity score)/pretreatment clinical severity score.

(5) Treatment protocol

For patients with organ disorder scores of 0 to 3, only rest with no medication was prescribed. For patients with organ disorder scores of 4 or more, systemic corticosteroids were administered in accordance with the treatment protocol (**Table 3**). If abdominal symptoms or renal symptoms or both did not improve with corticosteroid therapy and if factor XIII activity was less than 70%, a factor XIII preparation was added to the treatment. If these treatments were ineffective, corticosteroid pulse therapy or plasmapheresis or both were performed.

(6) Criteria for determining the outcome of the study

If the clinical severity score was 0 by the end of the study, the outcome was considered a complete response (CR). If clinical severity score was 2 or more points lower after treatment than before treatment, the outcome was considered a partial response (PR), and if the clinical severity score had increased by 2 or more points, the outcome was considered progressive disease (PD). Finally, if the clinical severity score changed by only ±1 between before and after treatment, the outcome was considered stable disease (SD).

(7) Observation of symptoms after the end of the study

After the end of the study, all 44 patients were observed for symptoms for 6 months. If relapse occurred, then the follow-up period was extended for another 6 months. Observations of any patient who died during the follow-up period were concluded at the time of death.

(8) Administration of a factor XIII preparation

Freeze-dried blood coagulation factor XIII derived from human plasma (Fibrogammin P, 60 U/mL, CSL Behring, King of Prussia, PA, USA) was slowly administered intravenously at a dosage of 20 U/kg/day for 3 days to 7 patients who showed factor XIII activities less than 70% and who did not respond to

Table 3 Treatment protocol

Organ disorder scores	Treatment
0–3	Rest with no medication
4–7	Prednisolone was administered at a dosage of 0.5 mg·kg^{-1}·day^{-1}. If the organ disorder scores did not decrease within 1 week, the prednisolone dosage was increased to 1 mg·kg^{-1}·day^{-1}. If the organ symptoms did not improve with the above treatment, a factor XIII preparation was administered at a dosage of 20 U·kg^{-1}·day^{-1} for 3 days in patients with less than 70% of normal factor XIII activity. If these treatments were ineffective, corticosteroid pulse therapy or plasmapheresis or both were performed.
8–18	Prednisolone was administered at a dosage of 1 mg·kg^{-1}·day^{-1}. If the organ disorder scores did not decrease within 1 week, a factor XIII preparation was administered at a dosage of 20 U·kg^{-1}·day^{-1} for 3 days in patients who showed less than 70% of normal factor XIII activity. If the organ symptoms did not improve with the above treatment, corticosteroid pulse therapy or plasmapheresis or both were performed.

corticosteroid therapy.

Factor XIII activity was measured and scores for organ disorders, joint symptoms, abdominal symptoms, and renal disorders were determined before and 3 days after administration of factor XIII preparations.

(9) Statistical analysis

The relationships among HSP-associated variables and symptoms were individually subjected to nonparametric correlation analysis, and the value of the Spearman rank correlation coefficient (r_s) was defined as follows: −1.0 to <−0.7, strong negative correlation; −0.7 to <−0.4, negative correlation; −0.4 to <−0.2, weak negative correlation; −0.2 to < 0.2, no correlation; 0.2 to <0.4, weak positive correlation; 0.4 to <0.7, positive correlation; and 0.7 to 1.0, strong positive correlation. Analysis of variance was also performed, and a P value less than 0.05 was considered to indicate significance. The Shapiro-Wilk test was used for all items. Furthermore, multiple linear regression analysis, a multivariate analysis method, was performed to validate the results of univariate analysis. In the end, both analyses gave identical results.

The relationships between the distribution of purpura and organ symptom scores, WBC count and clinical severity scores, WBC count and abdominal symptom scores, CRP levels and clinical severity scores, serum IgA levels and clinical severity scores, and changes in clinical severity scores and factor XIII activities were similarly analyzed. Differences in clinical severity scores, factor XIII activities, and organ disorder scores in the active pretreatment phase and the posttreatment remission phase were analyzed with the Wilcoxon signed-rank test. The difference between means was regarded as significant if the P value was less than 0.05. All statistical analyses were performed with the standard statistical software package JMP® 7 (SAS Institute, Inc., Cary, NC, USA).

Results

Table 1 shows the treatment outcomes of the 44 patients: 31 had CR, 11 had PR, 2 had PD, and 0 had SD. Observation for 6 months after the end of the test showed that 39 patients had no relapse, but 1 patient had persistent kidney disease, 3 patients had relapse, and 1 patient died. The details of these cases are as follows. Patient 3 showed no improvement in impaired renal function despite treatment with corticosteroids, a factor XIII preparation, and plasmapheresis during the test; although dialysis was performed, renal dysfunction persisted. Patient 9 had 3 recurrences of purpura and abdominal symptoms, but corticosteroid therapy induced remission each time. Patient 15 had HSP complicated by liver cirrhosis and methicillin-resistant *Staphylococcus aureus* empyema, which was treated with corticosteroids and plasmapheresis; however, the renal symptoms did not improve, and the patient died of sepsis. Patients 27 and 37 had symptoms that improved with rest alone (CR) but had relapses of purpura 3 months after the end of

the test.

Clinical severity scores in the 44 patients ranged from 1 to 14 points (mean ± SD: 5.8 ± 3.6 points). The clinical severity score was 1 to 5 points (mild) in 21 patients, 6 to 10 points (moderate) in 18 patients, and 11 points or greater (severe) in 5 patients. Negative correlations were found between clinical severity scores and factor XIII activities ($r_s = -0.475$, P=0.0011; **Fig. 1-A**), the severity of organ disorders and reduced factor XIII activities ($r_s = -0.451$, P=0.0021; **Fig. 1-B**), and the severity of abdominal symptoms and factor XIII activities ($r_s = -0.530$, P=0.0002; **Fig. 1-D**); and a weak negative correlation was found between the severity of joint symptoms and factor XIII activities ($r_s = -0.356$, P=0.0366; **Fig. 1-C**). However, no correlation was found between the severity of renal disorder scores and factor XIII activities ($r_s = -0.107$, P=0.4884; **Fig. 1-E**). The distribution of purpura showed no correlation with factor XIII activities ($r_s = -0.230$, P=0.132; **Fig. 1-F**) or organ disorder scores (r_s=0.122, P=0.4304). There were also no correlations between peripheral blood WBC counts and organ disorder scores (r_s=0.246, P=0.1078), CRP levels and organ disorder scores ($r_s = -0.045$, P=0.7712), or serum IgA levels and organ disorder scores (r_s=0.104, P=0.503).

Data were obtained in both the active pretreatment phase and the posttreatment remission phase in 14 cases. In the posttreatment remission phase, factor XIII activities were significantly elevated compared with those in the active pretreatment phase (92.6% ± 39.1% vs. 47.7% ± 15.4%, respectively, P=0.0011; **Fig. 2-A**), whereas clinical severity scores (1.8 ± 1.7 vs. 7.6 ± 4.0, respectively, P<0.0001; **Fig. 2-B**) and organ disorder scores (1.3 ± 1.8 vs. 5.8 ± 4.1, respectively, P=0.0004; **Fig. 2-C**) were significantly decreased.

There was no correlation between the values calculated for (pretreatment factor XIII − posttreatment factor XIII)/pretreatment factor XIII and (pretreatment clinical severity scores − posttreatment clinical severity scores)/pretreatment clinical severity scores (r_s=0.139, P=0.6344).

Seven patients with severe organ involvement that did not respond to systemic corticosteroid therapy were treated with a factor XIII preparation. Consequently, factor XIII activities were rapidly elevated after treatment (126.9% ± 43.5% vs. 43.7% ± 12.4%, respectively, P=0.0014; **Fig. 3-A**), and organ disorder scores (3 ± 2.45 vs. 7.14 ± 2.27, respectively, P=0.0004; **Fig. 3-B**), joint symptom scores (0.14 ± 0.38 vs. 1.29 ± 0.95, respectively, P=0.0152; **Fig. 3-C**), and abdominal symptom scores (0.57 ± 0.98 vs. 3.57 ± 1.51, respectively, P=0.0014; **Fig. 3-D**) decreased significantly within 3 days after treatment with a factor XIII preparation. However, in 3 patients (patients 3, 4, and 5) renal disorders did not show any improvement (5.33 ± 0.58 vs. 5.33 ± 0.58, respectively; **Fig. 3-E**). These patients were further treated with corticosteroid pulse therapy and plasmapheresis. Renal function recovered in 2 of these patients (patients 4 and 5) after 3 months, but renal failure (creatinine clearance <10 mL/min) developed in 1 patient (patient 3).

Discussion

Factor XIII is an enzyme that crosslinks fibrin molecules and forms stabilized fibrin, mainly in the final step of the blood coagulation cascade[17]. Factor XIII is a transglutaminase that has many protein substrates, such as α2 plasmin inhibitor, tissue-derived collagen, and fibronectin, in addition to fibrin[18–20]. Plasma factor XIII is a glycoprotein with a molecular weight of about 320 kDa that is present as a heterotetramer (A2B2) consisting of 2 A subunits (factor XIII-A) of about 75 kDa each and 2 B subunits (factor XIII-B) of about 85 kDa each. Subunit A activates transglutaminase, and subunit B stabilizes subunit A. The heterotetramer is dissociated into 2 homodimers, factor XIII-A2 and factor XIII-B2, in the presence of thrombin and calcium ions, and active factor XIII-A is formed by cleavage of the activator peptide at the N-terminus of the factor XIII-A molecule[21,22]. In addition to its role in the formation of stabilized fibrin, factor XIII also promotes cell proliferation by crosslinking fibronectin and fibrin, thereby contributing to the wound-healing process[23].

A correlation between reduced plasma factor XIII activity and the severity of organ disorders has been shown in children with HSP[5–7], and factor XIII

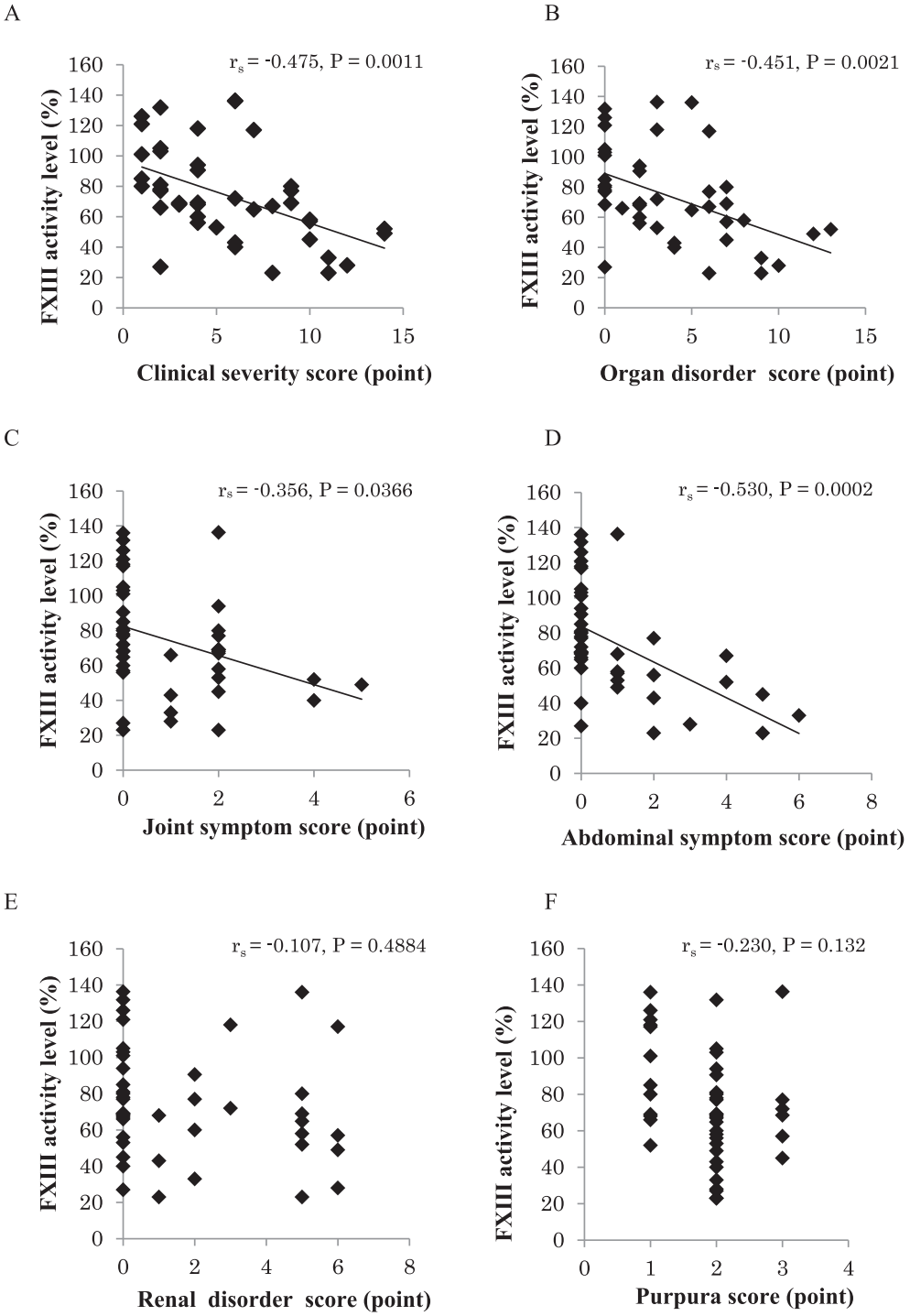

Fig. 1 Correlations of factor XIII activities with scores for clinical severity; organ disorders; joint, abdominal, and renal symptoms; and purpura distribution
Factor XIII activities were correlated with scores for clinical severity (A), organ disorder (B) and abdominal symptoms (D); weakly correlated with scores for joint symptoms (C); but not correlated with scores for renal symptoms (E) or the distribution of purpura (F).

substitution therapy markedly improves abdominal symptoms, joint symptoms, and renal dysfunction[7]. However, in adult HSP, there is a lack of reliable evidence regarding the diagnostic significance of factor XIII activity and the efficacy of factor XIII substitution therapy, because no controlled studies have been performed.

In adults with HSP severe gastrointestinal

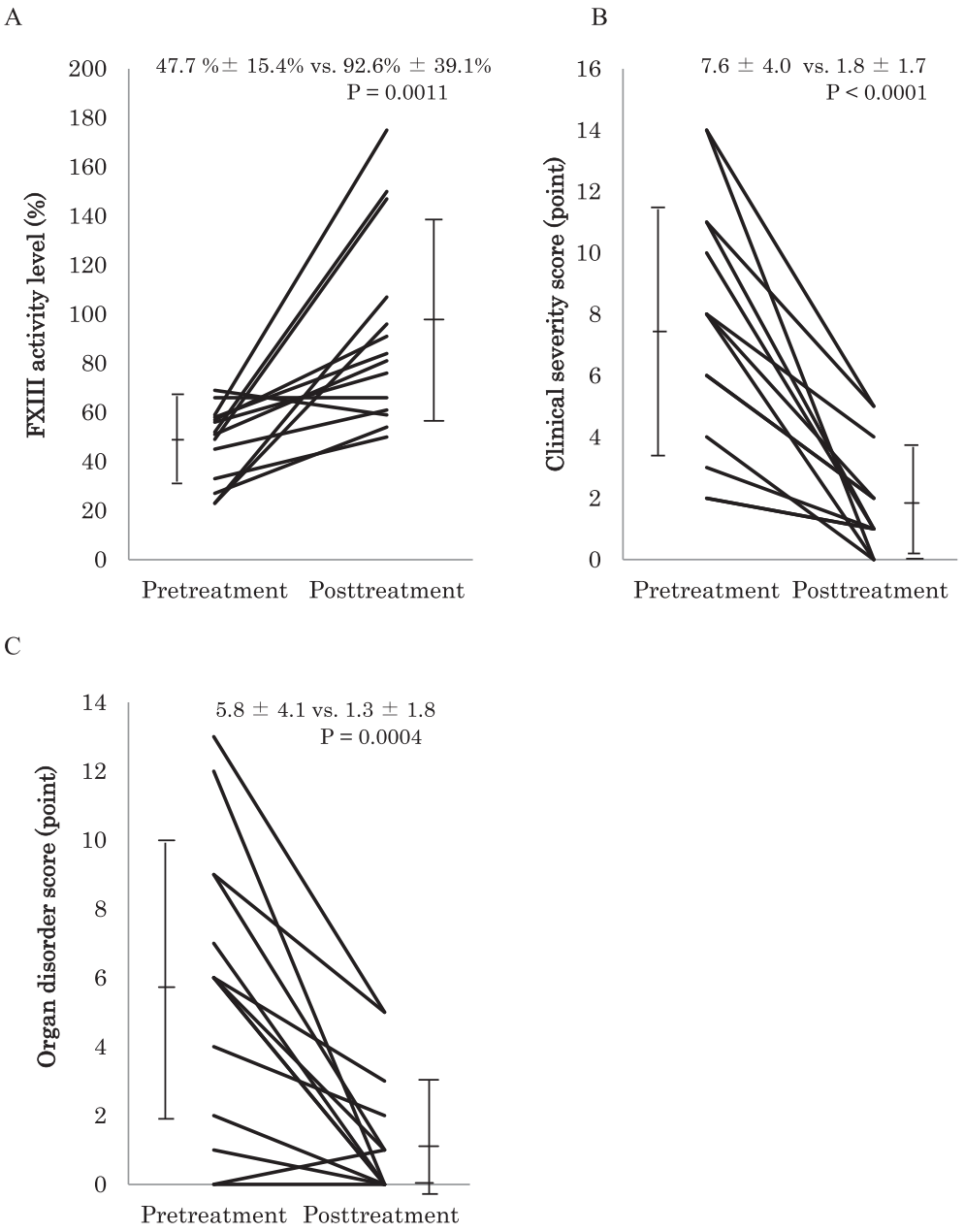

Fig. 2 Changes in factor XIII activities, clinical severity scores, and organ disorder scores from the active pretreatment phase to posttreatment remission in 14 cases
After treatment factor XIII activity levels (A) increased significantly (P=0.0011), and scores for clinical severity (B) and organ disorders (C) decreased significantly (P<0.0001, P=0.0004, respectively).

symptoms, such as colicky pain, ischemia, and massive hemorrhage, may develop, as in children with HSP[5,6]. It is noteworthy that HSP in adults is more likely to cause renal dysfunction than HSP in children and that the dysfunction tends to more severe[2,3] and to have a poorer long-term prognosis. Therefore, it is important to determine whether factor XIII activity can be used to predict the severity of HSP in adults, including abdominal disorders and renal dysfunction.

Thus, we investigated the association of factor XIII activity with disease severity and the severity of organ disorders in adults with HSP. We found that reduced factor XIII activity was strongly correlated with the clinical severity score (i.e., disease severity), the abdominal symptom score (abdominal pain, bloody stools), and the joint symptom score (arthralgia, joint swelling). However,

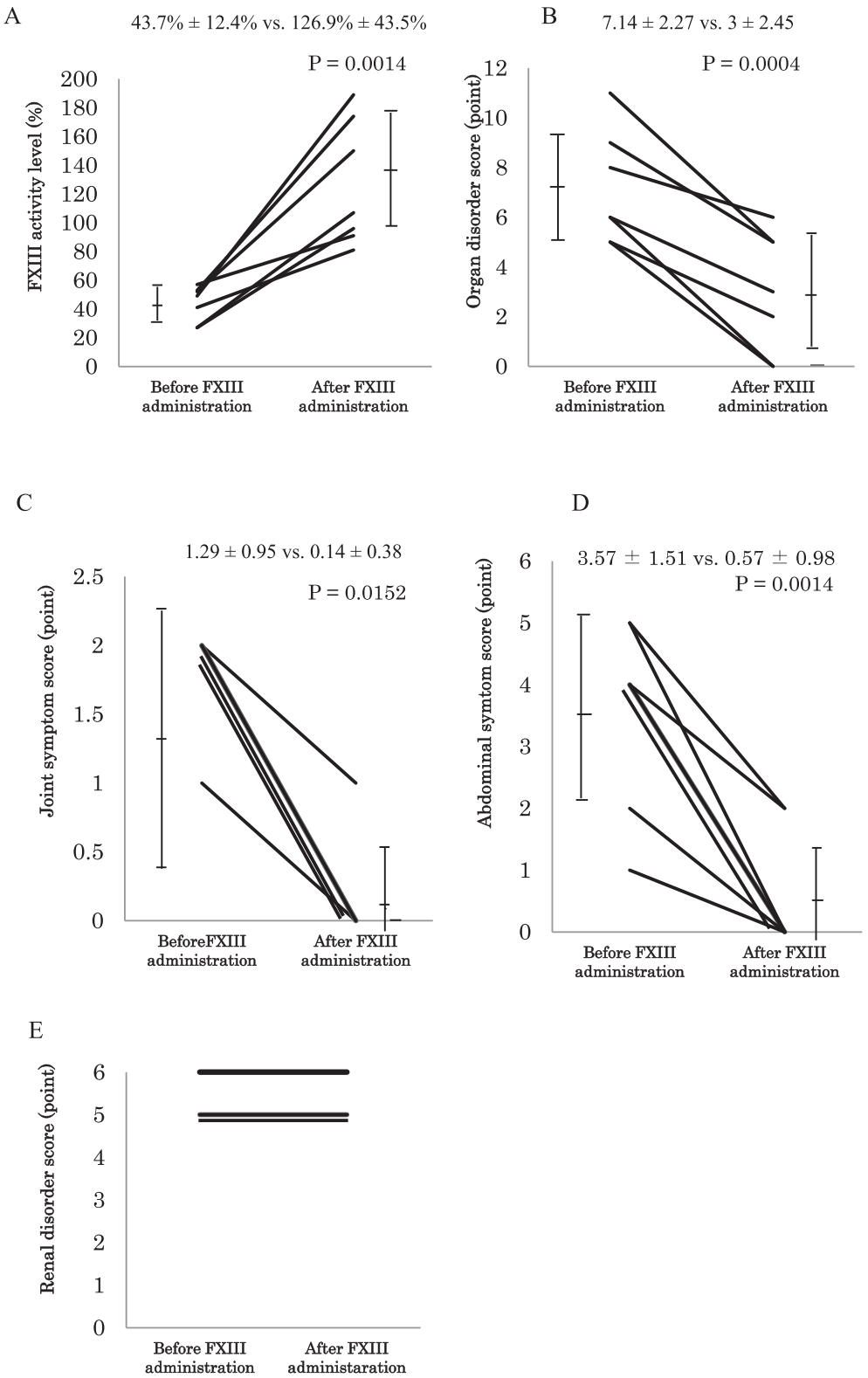

Fig. 3 Changes in factor XIII activities and organ symptoms in 7 cases after the administration of a factor XIII preparation

Factor XIII activity levels increased rapidly (P=0.0014) (A) and the organ disorder score (B), joint symptom score (C), and abdominal symptom score (D) had decreased significantly within 1 week after treatment with an factor XIII preparation in all 7 cases. However, the renal disorder score (E) showed no improvement in 3 cases.

reduced factor XIII activity was not correlated with the renal symptom score. These findings suggest that HSP is more severe and the involvement of the joints or the gastrointestinal tract or both is likely to be present when factor XIII activity is decreased, but that factor XIII activity does not predict renal dysfunction.

In addition, factor XIII activities were not correlated with the distribution of purpura, which, in turn, was not correlated with the severity of organ disorders. The severity of organ disorders was also not correlated with the peripheral WBC count or serum IgA levels. These findings indicate that the distribution of purpura, the peripheral WBC count, and serum IgA levels do not indicate the severity of organ disorders.

Changes in factor XIII activity, the clinical severity score, and the organ disorder score from the active pretreatment phase to the posttreatment remission phase were investigated in 14 cases. Factor XIII activity was significantly elevated during posttreatment remission, whereas the clinical severity score and the organ disorder score were decreased. However, changes in factor XIII activities during the disease course were not correlated with changes in the clinical severity score. This finding suggests that factor XIII activity can be used as an index of disease severity and of the severity of organ disorders, including joint and gastrointestinal involvement, but that the degree of increase in factor XIII activity does not reflect the degree of clinical improvement.

When a factor XIII preparation was administered to 7 patients who had corticosteroid-resistant HSP with abdominal involvement or renal involvement or both, abdominal and joint symptoms were markedly relieved in all patients who showed increased factor XIII activity, but renal symptoms in 3 of these patients did not improve at all. Although the number of cases was small, our findings strongly suggest that factor XIII substitution therapy is effective for joint and abdominal disorders, but not for renal disorders, in adults with HSP. A review by Zaffanello et al.[24] included a report of factor XIII substitution therapy being effective for 10 cases of pediatric HSP with renal dysfunction[7]. The discrepancy in the treatment effect between children and adults with HSP might be caused by differences in the severity of renal involvement or in the response to the drug. However, further investigations of the factor XIII treatment involving more cases are necessary to draw a more definite conclusion.

In summary, measurement of plasma factor XIII activity in adult HSP is clinically useful because it indicates the severity of the disease and the severity of digestive tract and joint disorders. Factor XIII substitution therapy may provide immediate relief of these symptoms.

Conflict of Interest: None of the authors have any coflicts of interest associated with this study.

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