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Trauma exposure and posttraumatic stress disorder in delinquent female adolescents

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Background: Although juveniles within the justice system have high psychiatric morbidity, few comprehensive investigations have shown posttraumatic stress disorder (PTSD) in female delinquents. Here, we aim to describe the nature and extent of PTSD and trauma exposure and to clarify the relationships among comorbidity and psychosocial factors in juvenile female offenders. **Method:** Sixty-four girls were randomly interviewed using structured tools. Self-report measures were used to assess depression, eating behaviour, impulsivity and parental attitude. **Results:** The PTSD prevalence was 33%, and 77% of the female juvenile offenders had been exposed to trauma. The offenders with PTSD showed a significantly high psychiatric comorbidity. Depression and adverse parenting were associated with PTSD development, and abnormal eating was also correlated with PTSD symptoms. Marked differences in the frequency and intensity of PTSD evaluation depending on the type of comorbidity and trauma were observed. **Conclusions:** Incarcerated young females in Japan have serious trauma-related problems, and the degree of depression is a strong predictor of PTSD development and symptoms. This study highlights the importance of adequate diagnosis and treatment of PTSD in delinquent female adolescents. **Keywords:** Trauma, female, delinquency, comorbidity, depression, eating disorder, posttraumatic stress disorder. **Abbreviations:** CAPS: Clinician-Administered PTSD Scale for DSM-IV; MINI-kid: Mini-International Neuropsychiatric Interview for Children and Adolescents; DSD: DSM Scale for Depression; BIS-11: Barratt Impulsiveness Scale 11th version; EAT-26: Eating Attitudes Test-26; PBI: Parental Bonding Instrument; IES-R: Impact of Event Scale-Revised.

Juvenile female offenders have high rates of trauma exposure. For instance, Cauffman, Feldman, Waterman, and Steiner (1998) showed that most incarcerated females are exposed to multiple types of trauma. Recent studies have revealed that witnessing a violent crime and being confronted with traumatic news are the most frequently reported sources of trauma in female juvenile offenders (Dixon, Howie, & Starling, 2005). In particular, a high lifetime PTSD incidence (67%) has been observed among young women in custody (Cauffman et al., 1998) compared with the general population's incidence range of 1–14% (American Psychiatric Association, 1994). It has been documented that chronic exposure to violence results in the numbing of feelings or substance use and increased risk-taking behaviours, including violent activities, in an attempt to cope with or adapt to the feeling of being unsafe (Crimmins et al., 2000). Additionally, Giaconia et al. (1995) found that those with any history of PTSD symptomatology (14.5%) were more likely than those without to have behavioural or emotional problems, interpersonal problems, academic failure, suicidal behaviour, and health problems. Based on the previous studies (Ruchkin, Schwab-Stone, Koposov, Vermeiren, & Steiner, 2002; Dixon et al., 2005), there is evidence that juvenile offenders with PTSD experience higher

rates of comorbid psychiatric disorders than those without PTSD. In particular, evidence suggests that young female offenders with PTSD have more co-morbidity than those without PTSD, with depression, substance abuse/dependence, psychoses and eating disorders occurring significantly and more frequently. Reasonably, it could be speculated that there is a mutual relevancy among juvenile offences including illicit drug use or delinquency, trauma exposures including adverse parenting, and psychological behavioural problems including mood liability, abnormal eating behaviours, or impulsivity.

In Japan, although there has been extensive research on the frequency of PTSD in incarcerated juvenile delinquents (Yoshinaga, Kadomoto, Otani, Sasaki, & Kato, 2004), there is little comprehensive and structured research on PTSD development, including several psychosocial measurements in female juvenile delinquents. The aims of this study are (1) to describe the nature and extent of trauma exposure and PTSD, (2) to clarify the point prevalence of PTSD, (3) to examine the relationship between psychiatric comorbidity and PTSD (traumatic exposure), (4) to analyse the associations between PTSD diagnosis and socio-demographic factors, depressive symptoms, impulsivity, abnormal eating behaviour and parenting attitude, (5) to determine the risks and factors that can be used to predict PTSD development, and whether PTSD

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symptoms correlate with psychosocial factors, and (6) to clarify the factors related to PTSD evaluations in female juvenile offenders who have never been under psychiatric medication in Japan.

Methods

Subjects

The subjects were 64 female juvenile offenders consecutively recruited from a female juvenile detention center in Japan as follows: from October 2004 to June 2006, 181 delinquent adolescents were incarcerated in a detention centre. Among these offenders, we excluded those who had already received neuroleptics (i.e., major tranquilisers, antidepressants, lithium, methylphenidate, and anticonvulsants) or those who were in a severe physical or psychiatric condition. That design was intended to avoid bias caused by medications which induce reduction of symptoms, when a structured interview was conducted for determining natural prevalence, to obtain reliable informed consent, and to consider the physical situations under a burden of this investigation. Seventeen cases (9%) were excluded on the basis of medication, and the total number of final candidates who received randomisation was 164. No subjects were excluded because of severe physical or psychiatric illness, and only subjects with a psychiatric history were included in the study. Finally, 64 subjects completed the initial screening interview and reporting questionnaires; however, two subjects refused to participate in the succeeding comprehensive interview. The subjects' ages ranged from 16 to 19 years (mean = 17.2, S.D. = 1.0) and the ethnicity of all the subjects was Japanese. Before incarceration, approximately half (55%) of the offenders were not living with their immediate family. Sixty-one percent of the offenders had dropped out of school before grade 10 (16 years old), and 33% had not been admitted to high school (15–18 years old). The other offenders are currently enrolled in high school.

Regarding their offence profile, 41% of the offenders were detained for drug-related crimes, 30% for violent crimes (e.g., assault, robbery), and 22% for pre-delinquent behaviour (e.g., prostitution or 'sugar daddy business'). Approximately 10% of the female delinquents were multiple offenders, and 60% had been arrested at least twice.

Procedures

This investigation was conducted as part of the regular medical service for maintaining the mental health of offenders in reformatory schools. Written informed consent was obtained from all the subjects, and the institutional head and chief director of the correction centre (Haruna Joshi Gakuen, covered by the Tokyo Regional Office of Correction Bureau, Ministry of Justice, Japan) approved the study. The subjects were individually approached by the first author (M.A.), who explained the nature of the study and provided an information sheet and a consent form. The interviewers (M.A., T.U. and Y.I.) emphasised that the procedure was voluntary and that the subjects could

withdraw at any time. All the subjects were interviewed within approximately one month of their detention. During assessment, each interviewer was unaware of the subjects' offence and socio-demographic information. Within one week of their interview, the participants were asked to complete five self-rating questionnaires.

Measures

General. The interviewers assessed the background characteristics corresponding to the subjects' demographics, history of use of any illegal drugs, and trauma exposure of the subjects. Information on age, criminal history, recidivism history, family composition, living conditions, history of psychiatric visits and admission to a psychiatric hospital, family alcohol or drug problems, educational attainment and intelligence quotient (IQ; already measured in a juvenile classification home) was recorded.

As regards their history of illegal drug use, the subjects were asked whether they had used any of the following illegal drugs: stimulants, cocaine, anaesthetics, hallucinogens, inhalants, marijuana or psychotropic drugs. Information on the start and frequency of drug use, and the dose of the drug use was also obtained.

The traumatic event checklist of the Clinician-Administered PTSD Scale for DSM-IV (CAPS; Blake et al., 1995) was used to obtain the subjects' trauma history. The subjects were asked whether they had experienced any of the 12 possible traumatic events on the list and whether they had experienced any trauma in addition to those on the list. Information on the onset, frequency and duration of each trauma was also obtained.

Structured interviews. Consequently, psychiatric diagnosis was determined using the Japanese version of the Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI-kid). We measured CAPS score only for the subjects who fulfilled the criteria of PTSD, as determined using the MINI-kid.

The Mini-International Neuropsychiatric Interview (MINI) was developed by Sheehan et al. (1998); it is organised into diagnostic modules. On the other hand, the MINI-kid was developed for children and adolescents; it is used in screening 23 axis-I DSM-IV disorders. For most modules of MINI, two to four screening questions are used to rule out the diagnosis when answered negatively. Positive responses to screening questions are examined by further investigation of other diagnostic criteria. We obtained permission to use the official Japanese version from Dr Otsubo (Showa University, Japan), the original translator of the MINI-kid.

CAPS is a structured clinical interview designed for assessing adults for the 17 symptoms of PTSD outlined in DSM-IV along with five associated features (i.e., guilt, dissociation, derealisation, depersonalisation, and reduction in awareness of surroundings). CAPS provides a means of evaluating self-reports of exposure to potential criterion-A events, current and/or lifetime DSM-IV diagnosis of PTSD, the frequency and intensity of each symptom, the impacts of the 17 PTSD symptoms on social and occupational functions, and the

overall severity of PTSD. CAPS consists of standardised prompt questions, supplementary follow-up (probe) questions, and behaviourally anchored five-point rating scales corresponding to the frequency and intensity of each symptom assessed. The Japanese version is currently used widely, and we administered it with permission from Dr Asukai.

Before the investigation, raters were trained using the standard manual of the MINI-kid (Otsubo et al., 2005). The CAPS interview took about 2 hours, and the raters were also trained using a videotape of the Japanese version of CAPS (Asukai, Hirohata, Kato, & Konishi, 2003).

Self-rating questionnaires. Five questionnaires were used in the study, which included the Japanese version of the DSM Scale for Depression (DSD), the Japanese version of the Barratt Impulsiveness Scale 11th version (BIS-11), Eating Attitudes Test-26 (EAT-26), the Parental Bonding Instrument (PBI) and the Impact of Event Scale-Revised (IES-R).

DSD (Roberts, Roberts, & Chen, 1995) is used in dimensionally evaluating depressive symptoms and diagnose major depressive episode according to the DSM criteria. The questionnaire for this scale is based on the *Diagnostic Statistical Manual for Mental Disorders*, 4th edition, with 27 items for identifying depression symptoms such as 'feel very sad'. EAT-26 (Garner, Olmsted, Bohr, & Garfinkel, 1982) is used in assessing a broad range of symptoms and provides a total score for disturbed eating attitudes and behaviours. It contains three factors as follows: dieting, bulimia and food preoccupation, and oral control. BIS-11 (Patton, Stanford, & Barratt, 1995) is a short questionnaire designed for measuring impulsiveness and has three factors, namely, motor impulsivity, no planning, and inappropriate attention. It has 30 items and impulsiveness level is calculated by summing the scores for each item. PBI (Parker, Tupling, & Brown, 1979) has been widely used in evaluating the parental situations of subjects all over the world. It was developed to assess paternal and maternal parenting attitudes recognised by offenders. It provides two dimensional scores, namely, care and overprotection. IES-R (Weiss & Marmar, 1997) was used to assess only the participants who had experienced traumatic events, and these offenders were asked about their most stressful event. The IES-R has 22 items, seven of which have been added to the original 15 items of IES. These assess hyperarousal symptoms such as anger and irritability, heightened startle response, difficulty in concentrating and hypervigilance, and the intrusion scale assesses a dissociative-like re-experience and true flashbacks. Eight items are used in assessing avoidance according to DSM-IV. Respondents are asked to rate each item according to the past seven days. The reliability and validity of each Japanese version has already been confirmed (Doi, Roberts, Takeuchi, & Suzuki, 2001; Ujiie & Kono, 1994; Someya et al., 2001; Kitamura & Suzuki, 1993; Asukai et al., 2002).

Statistical analysis

We used descriptive statistics, that is, the χ^2 test and analysis of variance (ANOVA), to investigate the associations of the respective evaluable factors with

PTSD diagnosis or exposures only to a traumatic event; logistic regression analysis to estimate associations and risks for the prediction of a PTSD diagnosis (PTSD score, 1 point) among the subjects who had trauma exposure using all factors as independent variables, and multiple linear regression analysis to determine correlated factors with the IES-R scores using dimensional scores as independent variables; non-paired t-test (two-tailed) to characterise CAPS ratings in detail in female offenders with PTSD; and Bonferroni's correction to avoid α error with multiple comparisons. A probability level of .05 or less was considered statistically significant. We used the Japanese version of SPSS for statistical analysis (SPSS Japan, Inc.).

Results

Trauma exposure and PTSD prevalence

Figure 1 shows the statistics of trauma exposures in the juvenile female offenders; 76.5% of the participants experienced a traumatic event. Most of the participants were exposed to multiple types of traumas, with sexual abuse being the most frequently reported trauma (54.7%). Being a victim of violence (45.3%), being confronted with traumatic news and childhood maltreatment, excluding neglect, (32.8%) were also frequently reported.

As evaluated using the MINI-kid, 21 (32.8%) of the juvenile female delinquents were diagnosed as currently having PTSD, whereas 43.7% were diagnosed as currently not having PTSD despite having experienced traumatic events. Afterwards, CAPS was used to assess the 21 subjects; 19 completed the interview but two were unable to complete the interview owing to mental instability. Fifteen (29.7%) of these 19 subjects were diagnosed as having full PTSD, two as suffering from partial PTSD, and the other two as currently not having PTSD.

PTSD and comorbidity

Table 1 shows a comparison of comorbid psychiatric diagnosis among the female offenders with PTSD, without PTSD and without trauma exposure. Those with PTSD have significantly higher comorbidities with depression ($\chi^2 = 12.1$, $p = .002$), panic disorder ($\chi^2 = 14.8$, $p = .001$), agoraphobia ($\chi^2 = 8.3$, $p = .016$), separation anxiety disorder ($\chi^2 = 13.0$, $p = .002$), social phobia ($\chi^2 = 17.7$, $p = .000$), obsessive-compulsive disorder ($\chi^2 = 9.0$, $p = .011$), conduct disorder ($\chi^2 = 6.2$, $p = .045$) and psychotic disorder (current episode) ($\chi^2 = 7.3$, $p = .027$) than those not exposed to trauma. Those with PTSD were more likely to report comorbidities of panic disorder, social anxiety disorder, social phobia and psychotic disorder including a lifetime episode ($\chi^2 = 8.0$, $p = .018$) than those without PTSD. In addition, those with PTSD indicated a significantly higher risk of suicidal
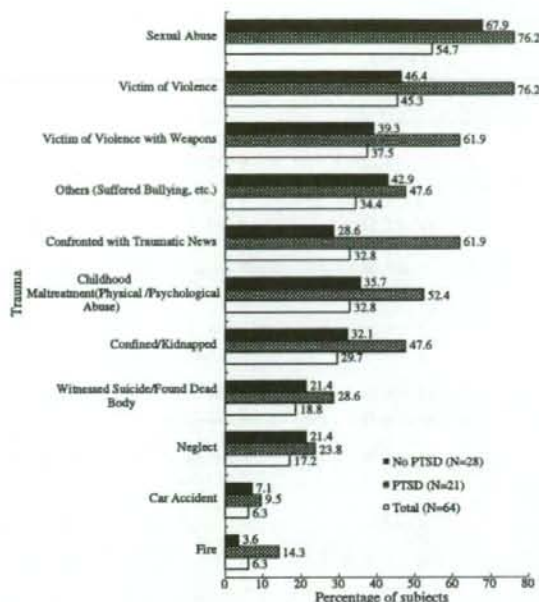
Figure 1 Trauma exposure of female offenders with and without PTSD for each trauma type. Overall, 76.5% of the subjects experienced a traumatic event. Most of the participants were exposed to multiple types of trauma, with sexual abuse being the most frequently reported type of trauma (54.7%)

tendency than those without trauma experience ($\chi^2 = 9.3$, $p = .009$).

Comparisons of self-questionnaires

Table 2 shows a comparison of the mean scores in the self-rating questionnaires (DSD, EAT-26, BIS-11 and PBI) between the female offenders with PTSD, without PTSD, and without trauma experience by one-way ANOVA and post-hoc comparison. The female offenders with PTSD showed significantly higher scores in DSD ($F[2,60] = 8.4$, $p < .01$), total EAT-26 ($F[2,61] = 6.8$, $p < .01$), and two subscales of EAT-26 (diet factor ($F[2,61] = 4.6$, $p < .05$) and bulimia/food preoccupation factor ($F[2,61] = 6.2$, $p < .01$)) than those without PTSD or trauma experience. The oral control subscale scores in EAT-26 of the female offenders with PTSD were significantly higher than those of the female offenders without trauma experience ($F[2,61] = 3.4$, $p < .05$). There were no statistically significant differences in impulsiveness and parental attitude among the groups.

Prediction of PTSD diagnosis and symptomatology

Logistic regression analysis of all the factors including categorical and dimensional items such as independent variables enabled us to identify three significant predictors and respective risks for the development of PTSD among 47 subjects who had trauma exposure (Table 3). The scores in DSD sig-

nificantly predicted the development of PTSD ($p < .01$), and its odds ratio was 1.1. Additionally, lower maternal protection and maternal care scores assessed using the PBI were selected as risk factors for PTSD diagnosis. This logistic model was statistically highly significant ($\chi^2 = 15.8$, $p = .001$).

To determine the predictive factors of the severity of PTSD-related symptoms, stepwise multiple regression analysis was conducted with IES-R total score as a dependent variable. A statistically significant model was obtained with two correlation factors ($R^2 = .66$, $F[2,45] = 43.3$, $p < .001$), and the DSD ($\beta = .73$, $p < .001$) and EAT-26 oral control scores ($\beta = .17$, $p < .08$) were entered as significant related factors.

Features of PTSD in female offenders determined using CAPS

To classify the characteristics of PTSD symptom profiles according to the type of traumatic event or comorbidity, we compared CAPS score including the frequency and intensity scores of three criteria between the subjects with and without comorbidity, and those with and without respective trauma experiences. Table 4 shows detailed comparisons only of the variables that were statistically significant as determined by Bonferroni's correction (p < .0062; .05/repeated numbers).

The comorbidity of panic disorder significantly increased the intensity scores of criteria B and

Table 1 Comparison of comorbid psychiatric diagnoses of female offenders with PTSD, without PTSD and without trauma exposure

Diagnosis (determined using MINI-kid)	I PTSD (N = 21) N (%)	II No PTSD (N = 28) N (%)	III No Tex (N = 15) N (%)	$X^2(df = 2)$
Depression	11 (52.4)	7 (25.0)	0	12.1**(I > III)a
Dysthymia	7 (33.3)	6 (21.4)	1 (6.7)	3.6
(Hypo)manic episode				
Current	3 (14.3)	1 (3.6)	0	3.7
Past	12 (57.1)	14 (50.0)	4 (26.7)	3.5
Panic disorder	9 (42.9)	2 (7.1)	0	14.8***(I > II, I > III)a
Agoraphobia	7 (33.3)	3 (10.7)	0	8.3* (I > III)a
Separation anxiety disorder	11 (52.4)	6 (21.4)	0	13.0**(I > II, I > III)a
Social phobia	11 (52.4)	3 (10.7)	0	17.7***(I > II, I > III)a
Specific phobia	5 (23.8)	4 (14.3)	2 (13.3)	1.0
OCD	8 (38.1)	4 (14.3)	0	9.0*(I > III)a
Alcohol				
Abuse	14 (66.7)	18 (64.3)	7 (46.7)	1.7
Dependence	16 (76.2)	16 (57.1)	7 (46.7)	3.5
Substance				
Abuse	13 (61.9)	14 (50.0)	11 (73.3)	2.3
Dependence	10 (47.6)	12 (42.9)	9 (60.0)	1.2
Tic disorders				
Tourette	1 (4.8)	0	0	2.1
Motor	0	1 (3.6)	0	1.3
Vocal	0	0	0	–
Transient	1 (4.8)	0	0	2.1
ADHD				
Combined	8 (38.1)	5 (17.9)	1 (6.7)	5.5
Inattentive	0	4 (14.3)	2 (13.3)	3.2
Hyperactive/Impulsive	1 (4.8)	1 (3.6)	0	.7
Conduct disorders	17 (81.0)	22 (78.6)	7 (46.7)	6.2*(I > III, II > III)a
Oppositional defiant disorder	1 (4.8)	2 (7.1)	0	1.1
Psychotic disorder				
Current	9 (42.9)	5 (17.9)	1 (6.7)	7.3*(I > III)a
Lifetime	11 (52.4)	6 (21.4)	2 (13.3)	8.0*(I > II)a
Mood disorders with psychotic features	2 (9.5)	2 (7.1)	0	1.4
Anorexia nervosa	3 (14.3)	2 (7.1)	3 (20.0)	1.6
Bulimia nervosa	5 (23.8)	1 (3.6)	2 (13.3)	4.5
Generalised anxiety disorder	1 (4.8)	1 (3.6)	0	.7
Adjustment disorders	0	1 (3.6)	0	1.3
Pervasive developmental disorder	0	2 (7.1)	0	2.7
Suicidal tendency	15 (71.4)	13 (46.4)	3 (20.0)	9.3**(I > III)a

Note. PTSD = posttraumatic stress disorder; Tex = trauma exposure; OCD = obsessive-compulsive disorder; ADHD = attention deficit/hyperactivity disorder. a: Significant difference between groups by Fisher's exact probability test (two-sided); *p < .05; **p < .01; ***p < .001, two-tailed.

B + C + D of the PTSD subjects. Concerning the differences in the type of traumatic event, the experience of being a victim of violence significantly influenced the intensity scores of criteria D and B + C + D. The experience of witnessing suicide or finding a dead body significantly affected the increases in the frequency scores of criteria B.

Discussion

In this study, we found that experiencing traumatic events is very serious and common in female juvenile delinquents, and that the prevalence of PTSD is remarkably high in juvenile female Japanese offenders. These findings are consistent with those on young females under detention in Western countries (Dixon et al., 2005; Abram et al., 2004; Cauffman et al., 1998).

Previous research studies have shown that female offenders are usually exposed to multiple traumatic events; in particular, sexual abuse is one of the most serious forms of victimisation among female children and adolescents. Many researchers have identified PTSD as a core manifestation of sexual abuse because of the high frequency with which this disorder and related symptoms appear in sexually assaulted children (Kendall-Tackett, Williams, & Finkelhor, 1993). The results of this study also supported the notion that trauma from sexual abuse trauma is obviously high in young female offenders in Japan.

Our findings that female offenders with PTSD show higher psychiatric comorbidity including depression and anxiety disorders are similar to a previous finding in male delinquents (Ruchkin et al., 2002). The other study showed that incarcerated male individuals with PTSD show more pronounced

Table 2 Comparison of self-rating questionnaire scores of female offenders with and without PTSD, and without trauma exposure

Variable	I PTSD (n = 21)		II No PTSD (n = 28)		III No Tex (n = 15)		F	p value
	Mean	s.d.	Mean	s.d.	Mean	s.d.		
DSD	64.4	18.9	48.9	15.1	44.5	12.8	8.4 (I > II, I > III)*	.001
EAT-26								
Diet	13.3	9.2	7.3	6.2	6.5	8.5	4.6 (I > II, I > III)*	.014
Bulimia/food preoccupation	4.6	4.8	1.5	2.2	1.3	2.4	6.2 (I > II, I > III)*	.003
Oral control	3.5	2.4	2	2.4	1.5	2.8	3.4 (I > III)*	.040
Total	21.4	13.5	10.8	8.8	9.3	12.6	6.8 (I > II, I > III)*	.002
BIS-11								
Iat	20.7	5.7	19.9	4.6	20.6	3.8	.2	.801
Im	28.5	6.8	27.7	5.3	28.5	5.9	.1	.865
Inp	29.2	4.3	29.9	5.9	32.1	4.9	1.4	.244
Total	78.4	13.1	77.5	13.3	81.3	11.1	.4	.647
PBI								
p-care	20.5	9.2	15.6	9.7	14.1	7.9	2.6	.082
p-op	22.8	7.0	24.3	7.3	25.4	8.1	.6	.545
m-care	13.1	9.9	10.7	9.3	13.5	8.7	.6	.545
m-op	23.3	7.7	26.1	7.0	27.5	8.8	1.4	.245

Note. PTSD = posttraumatic stress disorder; Tex = trauma exposure; DSD = DSM Scale for Depression; EAT-26 = Eating Attitudes Test-26; BIS-11 = Barratt Impulsiveness Scale-11; Iat = attentional impulsiveness; Im = motor impulsiveness; Inp = non-planning impulsiveness; PBI = Parental Bonding Instrument; p-care = paternal care factor; p-op = paternal overprotection factor; m-care = maternal care factor; m-op = maternal overprotection factor.
*Bonferroni's post-hoc multiple comparison.

Table 3 Logistic regression analysis of PTSD diagnosis of female offenders with trauma exposure

Variable	B	Std. error	Odds Ratio	p value	95% CI
DSD Score	.08	.03	1.09	.003	1.03–1.15
PBI Maternal care	−.11	.06	.90	.081	.79–1.01
Maternal op	−.16	.09	.85	.070	.72–1.01

Note. N = 47; Model Fit: $\chi^2 = 15.8$, df = 3, p = .001.
DSD = DSM Scale for Depression; PBI = Parental Bonding Instrument.

distress, anxiety and depression (Steiner, Garcia, & Matthews, 1997). Dixon et al. (2005) reported that female offenders with PTSD more frequently show comorbid depression, anxiety disorders, psychoses and eating disorders than those without PTSD. In particular, depression and mostly panic disorder or social phobia are associated with trauma-related symptoms. Depression is prevalent among female juvenile offenders similarly to the depression observed among the general adolescent population. In adolescence, this depression is often characterised by irritability, aggression or suicidal ideation. Confinement may trigger depressive symptoms; however, these mood swings frequently predate arrest. In consideration of unusual situations in detention centres, incarceration might precipitate major depression among vulnerable individuals. The experience of traumatic events, such as sexual abuse and violence, could enhance vulnerability to psychosocial stressors. Thus, it may be speculated that many female offenders with PTSD easily create a vicious cycle of trauma and depression. In addition, the risk of suicide was obviously high in female

delinquents in our study, which is in agreement with the findings of Dixon et al. (2005). Sanislow, Grilo, Fehon, Axelrod, and McGlashan (2003) suggested that it is helpful to examine impulsivity and the history of drug abuse when assessing suicidal risk in detained adolescents. Although in this study we did not present distinct links between suicidal risk and impulsivity or substance use, further analysis of these issues is necessary. Moreover, a study of the prevalence of dissociative disorders in young offenders is also important (Carrion & Steiner, 2000). As a trauma spectrum, dissociation has a special relationship to sexual assault, which is common in female delinquents (Plattner et al., 2003). Dissociation is another important issue to be solved in this series of investigation in Japan.

Dimensional analysis revealed close associations of PTSD with depressive symptoms and eating problems. We emphasise that abnormal eating behaviours including binge eating and purging are relevant symptoms in female delinquents with PTSD. From the significant differences in ANOVA, eating abnormalities as assessed using EAT-26 seem to have a strong relationship with PTSD or trauma-related problems. In addition, only a trauma experience does not reflect the comorbidity of depression and abnormal eating behaviours. Thus, it should be noted that the comorbidities of depression and eating problems are defined by PTSD development.

The results of the logistic and linear regression analyses indicate that depression is the most important symptom that correlates with PTSD development and related symptoms assessed using the IES-R. The correlation between PTSD and depression was previously suggested in several

Table 4 Comparison of CAPS score between PTSD offenders with and without comorbid diagnosis, and those with and without respective trauma experiences

Comorbidity and trauma	Frequency score				Intensity score			
	B	C	D	B + C + D	B	C	D	B + C + D
CAPS: Mean (s.d.) (N = 19)	10.1 (5.4)	15.5 (6.6)	13.0 (5.2)	38.6 (16.0)	11.2 (5.3)	14.3 (6.0)	10.8 (4.3)	36.4 (14.2)
Panic disorder								
+(N = 8)	13.6 (5.1)	19.9 (4.3)	15.3 (3.3)	48.8 (11.6)	14.9 (4.8)	18.3 (3.4)	13.4 (2.8)	46.5 (9.6)
−(N = 11)	7.5 (4.3)	12.4 (6.2)	11.4 (5.9)	31.3 (15.0)	8.5 (4.1)	11.5 (6.0)	9.0 (4.3)	29.0 (12.5)
t (df = 17)	2.8	2.9	1.7	2.7	3.1*	2.9	2.5	3.3*
Victim of violence								
+(N = 15)	11.3 (5.6)	17.4 (5.7)	14.3 (4.8)	42.9 (14.7)	12.7 (5.0)	16.0 (5.1)	12.2 (3.1)	40.9 (11.4)
−(N = 4)	5.8 (1.0)	8.5 (4.8)	8.3 (4.3)	22.5 (9.6)	5.5 (1.0)	8.0 (5.4)	5.8 (4.4)	19.3 (10.3)
t (df = 17)	1.9	2.8	2.3	2.6	2.8	2.8	3.4*	3.4*
Witnessing Suicide/Dead Body								
+(N = 5)	15.6 (4.0)	20.2 (3.9)	16.8 (2.6)	52.6 (9.3)	16.0 (3.1)	19.2 (3.3)	14.8 (1.1)	50.0 (5.3)
−(N = 14)	8.1 (4.8)	13.9 (6.6)	11.6 (5.3)	33.6 (15.1)	9.5 (5.0)	12.6 (5.9)	9.4 (4.0)	31.5 (13.1)
t (df = 17)	3.2*	2.0	2.1	2.6	2.7	2.4	2.9	3.0

Note. CAPS = Clinician-Administered PTSD Scale for DSM-IV; B = re-experience symptom; C = avoidance/numbing symptom; D = hyperarousal symptom.
Non-paired t-test, two-tailed, *$p < .0062$ (Bonferroni's correction).

studies (e.g., Oquendo et al., 2005), and the risk of developing PTSD diagnosis is relatively high in accordance with an increase in DSD score. In addition, parental attitude assessed using PBI is selected as a relative risk factor. Affectionless-control (low degrees of care and high degrees of protection) has been popular as a candidate risk factor related to the development of several psychological disturbances or psychiatric illness (Parker et al., 1979), and little maternal care could be supported by our findings. Although this study shows that weak involvement with maternal protection may be related to PTSD development, the PBI provides responders' recognition regarding their parents' behaviours retrospectively. Actual parental attitude possibly differs from perceived assessments, and we should mention that the associations found in this study are correlations. Although depression and parenting attitude are important in discriminating a PTSD diagnosis among traumatised adolescents, we have to analyse parental influence by considering the actual familial situations of offenders and implying causations using a prospective procedure. Linear regression analysis also indicates that oral control correlates with trauma symptoms. There are only a few studies of the association of PTSD symptoms with eating problems. Conclusively, eating behaviour should be paid particular attention as one of the factors related to PTSD development. In contrast, impulsivity was not significantly related to IES-R score. This result may be caused by a ceiling effect, that is, the mean scores in the BIS-11 of the PTSD group were originally as high as those of the other groups; therefore, it might have been difficult to determine the statistical significance of differences among the groups even if there was a difference between the offenders and the control subjects. Moreover, some items of BIS are not applicable to adolescents; therefore,

other instruments for assessing impulsivity may be more useful to test our hypothesis.

The results of this study indicate that the comorbidity of panic disorder enhances each intensity of PTSD symptoms, particularly the intensity of the re-experience symptom, and there is evidence that panic attacks are closely related to PTSD development (Favarelli, Webb, Ambonetti, Fonnesu, & Sessarego, 1985; Bandelow et al., 2002). Panic attacks are similar to somatic symptoms such as headache, chest pain, dizziness, or gastrointestinal complaints including criterion B (re-experience symptom) in people with PTSD. It is reasonable that the intensity criteria of PTSD had a significantly higher score as a result of the exposure to physical or psychological violence. It is also clear that witnessing suicide or finding a dead body increased the frequency scores of criterion B. We can therefore assume that trauma exposure accompanied by indirect fear of mortality enhances flashbacks or intrusion rather than arousal and avoidance.

The limitations of this study should be mentioned. The sample size of our study is small, and no comparisons with control females were conducted. Further investigation using a larger sample and a control group is required for the generalisation of the findings. We did not assess Axis-I disorders or personality traits because it is difficult to determine personality disorders in juveniles and adolescents. Some young offenders usually have personality deviations; thus, it is important to include personality assessments. Dissociation should also be evaluated as mentioned above. Although the validity of the answers to the questionnaires in this study is supported by the investigators' instruction and confirmation, methodological limitations are common in studies using self-reports. In this study, we used MINI as a screening tool. Although this tool is

convenient and comprehensive, it also has some limitations in confirming accurate diagnosis. Other reliable interview methods such as the Schedule for Affective Disorders and Schizophrenia for School-Age Children or the Diagnostic Interview Schedule for Children could also be used if respective Japanese versions become available. We were not able to establish a causal relationship between parental style, depression and PTSD only on the basis of retrospective procedures. The relationships between developmental disorders and offence patterns should be investigated in the future. Finally, we emphasise the need for prospective follow-up studies according to therapeutic approaches.

Conclusion

Incarcerated young female offenders in Japan have very serious psychiatric problems related to trauma exposure. We recommend that female delinquents be provided with not only correctional education but also mental support to prevent PTSD development among offenders in detention centres. For female offenders with psychiatric problems, treatment interventions are essential, and PTSD and comorbidity including depression or eating abnormality must be considered in the overall therapeutic strategy.

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ガンマグロブリン不応例の予測と層別化

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はじめに

川崎病は小児期に好発する原因不明の血管炎症候群であり，無治療では高率に冠動脈病変を合併することが知られている[1]。作用機序は未だ不明であるもののガンマグロブリン超大量療法（IVIG）が臨床症状や炎症マーカーの改善，冠動脈病変合併の抑制に有効であると報告され，現在標準的な治療として川崎病患者に対し広く使用されている[2]。しかし，10〜20%は IVIG により解熱しない IVIG 不応例であり，冠動脈病変合併例の大部分が IVIG 不応例に含まれる[3]。これら IVIG 不応例を初期治療開始前に予測し，より intensive な初期治療を選択することによって risk/benefit balance に優れた治療戦略をとることが可能になるかもしれない。そのような背景のもと，近年さまざまな施設から IVIG 不応例を予測するモデルが提唱された[4]〜[6]。本稿では，最近報告された IVIG 不応例を予測する新規モデル，また群馬で作成されたリスクスコアを用いた川崎病初期治療層別化の可能性について解説する。

1. IVIG 不応例の新規予測モデル

最近提唱された IVIG 不応例を，治療開始前に予測するモデルを表 1 に示す。いずれも IVIG を施行された川崎病患者の初期治療開始前患者背景，血液検査結果から IVIG 不応例に関連する独立因子を多変量解析によって抽出し，作成されたモデル

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表 1　IVIG 不応例を予測する新規スコア

群馬のリスクスコア（5 点以上：感度 76%，特異度 80%）

	閾値	点数
Na	133 mmol/L 以下	2 点
AST	100 IU/L 以上	2 点
治療開始（診断）病日	4 病日以前	2 点
好中球	80%以上	2 点
CRP	10 mg/dL 以上	1 点
血小板数	300,000/μL 以下	1 点
月齢	12 か月以下	1 点

久留米のスコア（3 点以上：感度 76%，特異度 80%）

	閾値	点数
ALT	80 IU/L 以上	2 点
治療開始（診断）病日	4 病日以前	1 点
CRP	8 mg/dL 以上	1 点
血小板数	300,000/μL 以下	1 点
月齢	6 か月以下	1 点

大阪のスコア（2 点以上：感度 77%，特異度 86%）

	閾値	点数
AST	200 IU/L 以上	2 点
総ビリルビン	0.9 mg/dL 以上	1 点
CRP	7 mg/dL 以上	1 点

である。

1）群馬のリスクスコア[4]

IVIG 1 g/kg×2 日で初期治療を施行された 750 症例を用いて作成された，7 つの変数からなる予測モデルである。スコア点数 5 点以上（11 点満点）を高リスク群とすると，78% の感度，80% の特異度で IVIG 不応例を予想することが可能であった。リスクスコアを使用するうえでいくつかの注意点がある。まず，血液検査を初診から診断時までに複数回にわたって施行した場合，好中球%・AST・CRP は最高値を，血小板数・Na は最低値をリスクスコア算出に用いる値とする。これは以

前から日本で広く用いられている原田のスコア[7]と同様の計算方法である。また，リスクスコアを作成した患者群では川崎病と診断後速やかに IVIG を施行しているため，川崎病診断病日と治療開始病日（IVIG 開始病日）は同一病日である。そのため，5 病日以前に川崎病と診断してもアスピリン投与のみで 5 病日まで待機し，5 病日以降に IVIG を投与するといった治療方針を採用している施設の患者に対して本リスクスコアを用いることはできない。リスクスコアを作成した患者群と重要な背景因子が異なってしまうため，同一のモデルで IVIG 不応例を判定することができないからである。同様の理由で 5 病日以前に川崎病と診断した患者に対して 5 病日まで待って IVIG を行い，治療開始病日の項目を 0 点にすることによってスコア点数を下げるといった人為的操作はまったく意味をなさない。

2）久留米のスコア[5]

IVIG 2 g/kg×1 日で初期治療を施行された 320 症例を用いて作成された。5 つの変数から構成される予測スコアで，3 点以上（6 点満点）を高リスク患者とすると 78％の感度，76％の特異度で IVIG 不応例を予想することが可能であった。群馬のリスクスコアとは異なり，久留米のスコアにおいて血液検査結果を入力するのは川崎病診断病日である。つまり，診断までに複数回血液検査を行っていた場合，以前のデータは考慮することなく診断病日の血液検査結果を各変数の代表値として計算する。また，群馬のリスクスコアと同様で治療開始病日と診断病日は同一病日のため，早期診断後 5 病日以降に治療を遅らせる治療待機症例に久留米のスコアを適応することはできない。

3）大阪のスコア[6]

IVIG 1 g/kg×2 日で初期治療を施行された 112 症例を用いて作成された。3 つの変数から構成され，スコア点数 2 点以上（3 点満点）を高リスク患者とすると 77％の感度と 86％の特異度で IVIG 不応例を予想することが可能であった。前述のスコアとは異なり変数ごとの重み付けはない。

これら別々のグループが作成した予測モデルは計算方法の詳細は異なっているものの，モデル内に含まれている変数や重み付けが非常に似通っている。また，予測モデル内の独立変数として選ばれたそれぞれの因子は，過去にも IVIG 不応例や冠動脈病変に関連すると多くの研究者から報告されている。これらの事実から推測すると，日本国内におけるそれぞれの予測モデルの再現性がある程度担保されていると考えてよいだろう。今後，各モデルの再現性や予測効率の検証が望まれる。

ところで，治療開始病日と IVIG 不応例の臨床的意義はまだ不明な点が多い。なぜ治療開始病日が早いと IVIG 不応例が多くなるのだろうか？ 診断の遅れは血管炎の増悪による冠動脈のリモデリングを促進し，冠動脈瘤発生に寄与することは周知の事実あるため，多くの小児科医は川崎病をより早期に診断して IVIG を行うことが予後改善につながるとして急性期治療を行ってきた。早期治療例に IVIG 不応例が多い結果は前述の治療方針に対する大いなる矛盾であるが，早期治療例に IVIG 不応例が多い理由として 2 つの可能性が考えられる。

第 1 の仮説は早期に臨床症状がそろう患者はより重症度が高いため，IVIG が効きにくい可能性があるということである。この仮説を検証するため，前述の 750 症例を対象とし，治療開始病日以外の 6 変数を用いてスコア点数を算出したうえで，4 病日以前に IVIG 投与を行った早期治療群，5 病日以降に IVIG を行った通常治療群とを比較検討した[4]。結果，早期治療群は通常治療群に比べて IVIG 無効例（31％ vs 13％，$P < 0.001$）と冠動脈病変合併例（12％ vs 4％，$P < 0.001$）は有意に多く，またリスクスコア点数も有意に高値であった（2.9±2.5 vs 2.1±2.0，$P < 0.001$）。これらの結果からは，4 病日以前に診断された患者は 5 病日以降に診断された患者に比べて重症度が高いため，IVIG の効果が限定的であることが想定される。一方，早期に IVIG を投与すると血管炎を悪化させるといった仮説も考えられる。この仮説を証明するためには早期診断例のみを対象にして，早期治療群と待機群とに無作為割付を行う control study が必要であるが，そのような検討は未だ行われていない。このような現状で確定的なことを述べることは困難ではあるが，前述したように早期治療群がよりリスクス

コアが高値であることや，早期治療が血管炎を悪化させるといった証拠がない現時点においては，早期治療をためらう根拠は乏しく，冠動脈のリモデリングを抑制するためにより早期に血管炎を抑制する治療戦略を選択すべきであろうと筆者は考えている。

II. リスクスコアを用いた初期治療層別化の可能性

前述した予測モデルを用いることによって，およそ初期治療開始前に IVIG 不応例を予測することが可能となった。今後の課題は，これらのモデルを用いて川崎病患者の予後を改善させるために，どのような治療戦略を行うかである。

血管炎の進行に伴い，冠動脈の血管構造が破壊され遠心性の拡大をきたすという病理学的な機序を考えると，より早期に血管炎を鎮静化させ，冠動脈のリモデリングを抑制することが冠動脈病変発生を抑制するために重要である。近年ステロイド[8]，シクロスポリン[9]といった免疫抑制薬や抗TNF-α抗体 (infliximab)[10]などが初期治療として，また IVIG 不応例に対する追加治療として有用であることが相ついで報告されている。われわれは初期治療としての IVIG＋プレドニゾロン療法 (IVIG＋PSL) の有用性を検討する多施設共同前方視的無作為化比較試験を行い，IVIG＋PSL が冠動脈病変の抑制，有熱時間の短縮，CRP の早期陰性化に有用であることを報告した。そこで無作為化比較試験に参加した 178 症例にリスクスコアを後方視的に適用し，川崎病初期治療の層別化が可能か否かをシミュレーションしてみる。

1. 低リスク患者（群馬のリスクスコア 4 点以下）

IVIG のうち 70％の 62 症例，IVIG＋PSL のうち 68％の 61 症例が低リスク患者に分別された。低リスク患者における初期治療別転帰を表 2 に示す。治療抵抗例の割合，冠動脈病変の合併頻度いずれにおいても両治療群間で統計学的な有意差を認めず，冠動脈病変は IVIG の 1 例のみに認めたが，1 か月時には正常化した。また，治療開始後解熱

表 2 低リスク患者における臨床経過と冠動脈予後

	IVIG (n＝62)	IVIG＋PSL (n＝61)	P value
治療抵抗例, n (%)	3 (4.8)	4 (6.6)	0.717
初期治療不応例, n (%)	3 (4.8)	2 (3.3)	1.000
再燃例, n (%)	0 (0)	2 (3.3)	0.244
経過中の冠動脈病変合併例, n (%)	1 (1.6)	0 (0)	1.000
1 か月時の冠動脈病変合併例, n (%)	0 (0)	0 (0)	—
治療開始後解熱するまでの日数	1.0 ± 1.2	0.4 ± 1.4	<0.001
治療開始後 CRP 陰性化するまでの日数	10.0 ± 6.0	8.3 ± 4.1	0.114

表 3 高リスク患者における臨床経過と冠動脈予後

	IVIG (n＝26)	IVIG＋PSL (n＝29)	P value
治療抵抗例, n (%)	13 (50)	5 (17.2)	0.020
初期治療不応例, n (%)	13 (50)	3 (10.3)	0.002
再燃例, n (%)	2 (7.7)	2 (6.9)	1.000
経過中の冠動脈病変合併例, n (%)	9 (34.6)	2 (6.9)	0.017
1 か月時の冠動脈病変合併例, n (%)	3 (11.5)	0 (0)	0.099
治療開始後解熱するまでの日数	2.7 ± 2.4	0.9 ± 1.6	0.025
治療開始後 CRP 陰性化するまでの日数	14.0 ± 7.4	8.5 ± 3.3	<0.001

するまでの期間は IVIG＋PSL で有意に短縮していたが，治療開始後 CRP 陰性化するまでの日数は IVIG と IVIG＋PSL で統計学的な有意差はなかった。

2. 高リスク患者（群馬のリスクスコア 5 点以上）

IVIG のうち 30％の 26 症例，IVIG＋PSL のうち 32％の 29 症例が高リスク患者に分類された。高リスク患者における初期治療別転帰を表 3 に示す。IVIG に比べ IVIG＋PSL では治療抵抗例，ことに初期治療不応例が有意に低頻度であった。また，経過中の冠動脈病変合併頻度も IVIG＋PSL で有意に低頻度であり，1 か月時の冠動脈病変合併頻度も低い傾向であった。治療開始後解熱するまでの

期間，CRP 陰性化までの期間はいずれも IVIG＋PSL で有意に短縮していた。これらの結果から治療開始前にリスクスコアを用いて重症度を層別化し，初期治療を変更することによって重症川崎病患者の臨床経過，冠動脈予後を改善させることができる可能性が示された。

おわりに

IVIG 不応例の予測因子と層別化の可能性について解説した。現在，重症川崎病患者に対する免疫グロブリンと免疫グロブリン・プレドニゾロン初期併用投与の有用性を検討するランダム化比較試験（RAISE Study）が全国各地の施設に協力いただき開始された。新しい前方視的試験の実施によって川崎病初期治療層別化の有用性が検証され，新たな治療戦略が確立されることが望まれる。

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Patient Report

Kawasaki syndrome and 21-hydroxylase deficiency

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Congenital adrenal hyperplasia is a family of autosomal recessive disorders of cortisol biosynthesis.[1] More than 90% of congenital adrenal hyperplasia cases are caused by 21-hydroxylase deficiency (21-OHD).[1] Patients with 21-OHD are treated with glucocorticoids and patients with salt-wasting disease require mineralocorticoid replacement with fludrocortisone. Kawasaki syndrome (KS) is a systemic vasculitis of unknown etiology that occurs commonly in children under 5 years of age[2] and results in coronary artery abnormalities (CAA) in 15–25% of those affected.[2,3] KS is not a rare disease in Japanese children; it occurs in more than 7000 children a year.[4] In contrast, the prevalence of congenital adrenal hyperplasia is 1/15 000–20 000.[1] Because of the rarity of this disease, there are no reports of 21-OHD patients developing KS. We encountered a patient with KS who was followed with 21-OHD. The patient recovered without any coronary abnormalities on a treatment of steroid, aspirin, and i.v. γ-globulin. This case suggests the importance of adequate additional steroid therapy for congenital adrenal hyperplasia in severe inflammation, especially KS.

Case report

The patient was delivered from healthy parents after an uncomplicated pregnancy by spontaneous vaginal delivery after 39 weeks and weighed 3590 g. Because her blood 17α-hydroxyprogesterone (17-OHP) was extremely high on the newborn mass screening program, she was referred to Kagoshima University Hospital. Pigmented skin and male genitalia with an enlarged clitoris were observed. Laboratory examinations indicated extremely high levels of adrenocorticotropic hormone (ACTH; 869 pg/mL), plasma renin activity (353 ng/mL), and 17-OHP (683 ng/mL). Additionally, hyponatremia (Na 129 mEq/L), and hyperpotassemia (K 6.2 mEq/L) were observed. We diagnosed her with salt-wasting type of congenital adrenal hyperplasia due to 21-OHD and started oral administration of both hydrocortisone and fludrocortisone acetate. After starting the treatment the patient did not have any developmental or growth problems, and

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her illness was well controlled by the outpatient clinic. There were no episodes needing hospitalization or i.v. administration of steroid although the patient sometimes fell ill.

When the subject was 5 years old she complained of fever and her mother gave her twice the usual dosage of hydrocortisone as recommended on the first illness day. On the next day she complained of fatigue and anorexia. She had lymphadenopathy and was given cefroxadine at a general clinic. On the third illness day conjunctivitis was observed. On the fourth illness day she was referred to Kagoshima University Hospital because of persistent high fever.

The subject's height was 110 cm and her weight was 20 kg. Her body temperature was 38.8°C and her heart rate was 118 beats/min. Neither cardiac murmur nor gallop rhythm was heard by auscultation. She had edema of the hands, fissured lips, rash, non-exudative conjunctivitis, right cervical lymphadenopathy, and mucosal erythema. The initial laboratory tests showed severe inflammation (white blood cell counts 12 400/μL; C-reactive protein [CRP], 18.7 mg/dL), hyponatremia (Na 128 mEq/L), and hyperpotassemia (K 5.0 mEq/L). The other laboratory tests were as follows: aspartate aminotransferase, 28 IU/L; alanine aminotransferase, 14 IU/L; total protein, 8.2 g/dL; and albumin, 4.6 g/dL. A chest X-ray showed small heart (cardiothoracic ratio 41%). Echocardiography indicated normal left ventricular wall motion (left ventricular diastolic dimension 27 mm, 77% normal, ejection fraction 72%) and normal coronary arteries.

With a diagnosis of KS, we started treatment with i.v. administration of γ-globulin (1 g/kg) and oral administration of aspirin (30 mg/kg per day). Because we suspected adrenal crisis, we also started i.v. administration of hydrocortisone, which continued until the sixth illness day, when her electrolytes improved to a sodium level of 134 mEq/L and a potassium level of 4.0 mEq/L (Fig. 1). On the sixth illness day fever and the other symptoms of KS had subsided. Her medication was continued using twice the dose of her usual oral hydrocortisone and a regular dose of fludrocortisone acetate. When the serum levels of sodium, potassium and chlorine normalized on the ninth illness day, oral hydrocortisone was reduced to the regular dosage. When the serum level of CRP decreased to the normal range on the 12th illness day, the dose of aspirin was reduced to 10 mg/kg per day. The patient was discharged on the 15th illness day with no coronary abnormalities. She did not have any abnormalities on either electrocardiogram or echocardiogram at follow-up examination.

Day of illness

| 1 | 3 | 5 | 7 | 9 | 11 | 13 | 15 |

aspirin   30mg/kg/day   10mg/kg/per day

IVGG (1 g/kg)

Hydrocortisone   100 50 25   Hydrocortisone (oral)
(i.v.mg)
25 (mg/day)   12.5 (mg/day)

fludrocortisone acetate 0.025mg/day (oral)

40°C

37°C   Body temperature

lymphadenopathy

conjunctivitis

fissured lips

rash

edema of the hands   Desquamation

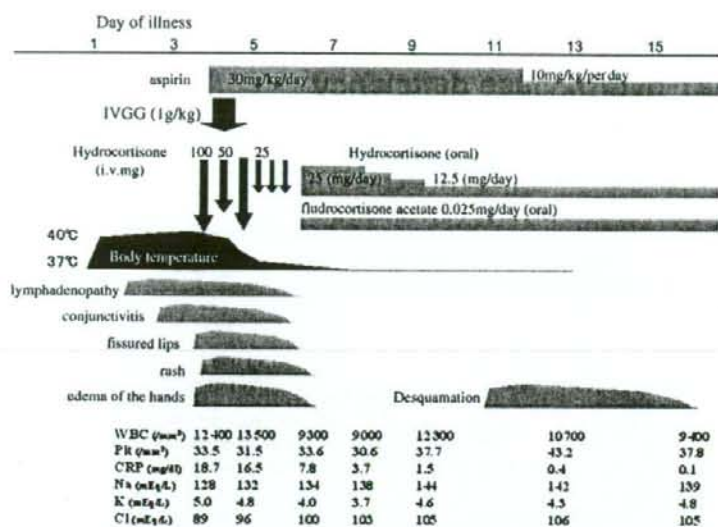|							
WBC (/mm³)	12 400	13 500	9300	9000	12300	10700	9 400
Plt (/mm³)	33.5	31.5	33.6	30.6	37.7	43.2	37.8
CRP (mg/dl)	18.7	16.5	7.8	3.7	1.5	0.4	0.1
Na (mEq/L)	128	132	134	138	144	142	139
K (mEq/L)	5.0	4.8	4.0	3.7	4.6	4.3	4.8
Cl (mEq/L)	89	96	100	105	105	106	105

Fig. 1 Clinical course. CRP, C-reactive protein; IVGG, i.v. administration of γ-globulin; oral, oral administration; Plt, platelet counts; WBC, white blood cell counts.

Her adrenal crisis was confirmed by the data on admission (extremely high levels of ACTH: 1325 pg/mL and 17-OHP: 190 ng/mL). The serum level of ACTH decreased to 63 pg/mL at discharge.

Discussion

It is important for patients with 21-OHD to supplement the steroid doses adequately when they are exposed to a stressor.[5] This patient was given twice the dosage of her usual hydrocortisone until the third illness day but she developed an adrenal crisis on the fourth illness day. It required a few days to improve her electrolyte abnormalities although we started i.v. hydrocortisone administration just after admission. The inflammation of KS may be too severe to treat with the usual recommended dose for 21-OHD patients.

We treated the present patient with i.v. administration of γ-globulin and hydrocortisone. Steroid therapy for KS has not been used for a long time because steroid therapy alone results in coronary aneurysms, thrombosis, and myocardial infarction.[6] Recently, the efficacy of steroid therapy with i.v. γ-globulin for the acute phase of KS has been reported.[7-9] The present patient was also treated with 1 g/kg i.v. γ-globulin and oral aspirin along with a total dose of 325 mg i.v. hydrocortisone. Fever subsided rapidly and coronary aneurysms were not observed. No adverse effects were observed. The present case demonstrates the efficacy of i.v. γ-globulin therapy along with the steroid in the acute phase of KS, although the main reason for the i.v. hydrocortisone was to rectify the deficiency in glucocorticoids under the stressed condition.

The incidence of KS has increased to 9992 patients per year in 2004 in the 18th nationwide surveillance for Kawasaki disease. Thus, the possibility of encountering KS patients with 21-OHD is now increasing.

Conclusion

We report a patient with KS and 21-OHD. Careful observation and adequate i.v. hydrocortisone therapy may be necessary for 21-OHD patients, when they experience severe inflammatory disease such as KS.

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川崎病との鑑別を要した日本紅斑熱の1例

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要 旨

　症例は4歳女児。会陰部を虫に刺された後全身に紅斑と発熱が出現し入院した。眼球結膜充血以外の川崎病主要症状を呈しており川崎病も考えられたが、刺し口を認めたため minocycline の投与を行った。症状は速やかに軽快し、その後に膜様落屑を認めた。*Rickettsia Japonica*（以下 *R. japonica*）IgM が陽性であり日本紅斑熱と診断した。日本紅斑熱で川崎病の主要症状の多くを呈する例があることの認識は重要と思われた。

[小児科臨床　61：801, 2008]

KEY WORDS　日本紅斑熱, *Rickettsia Japonica*, 刺し口, 膜様落屑, 川崎病

はじめに

　日本紅斑熱は *R. japonica* を保有するマダニに刺咬されることで発症する高熱，発疹，刺し口を3徴候とする4類感染症である[1]。我々は眼球結膜充血以外の川崎病主要症状を呈し，川崎病との鑑別を要した日本紅斑熱の1例を経験したので報告する。

症 例

　症例は4歳女児。花火大会があり川岸に座って花火見物をした際に「会陰部を虫に刺された」と訴えた。家族が見てみると，会陰部に径5cmくらいの赤い腫脹が見られた（1病日）。特に治療を行わずに経過をみていたが3病日に手掌・足底と顔面の発赤が出現した。4病日の夕方には38℃台の発熱が出現し，紅斑が全身に拡がった。5病日に近医皮膚科で会陰部の刺し口を指摘され，近医小児科を紹介受診した。ツツガムシ病が疑われ，精査加療目的で同日当院に入院した。

　入院時現症：身長104cm, 体重16.5kgで入院時の体温は38.0℃だった。眼球結膜に充血を認めず口唇の発赤も認めなかった。口腔内は咽頭の発赤といちご舌を認めた。頸部リンパ節は両側に1.5cm大を数個触知した。鼠径リンパ節は両側とも1.5cm大を数個触知し圧痛を認めた。心雑音や過剰心

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図 患児の皮膚所見
A．入院時外陰部の所見．3×3 cm大の紅斑を認めた．その中央には痂皮を伴う刺し口を認めた．
B．退院当日（13病日）から出現した膜様落屑．

音を認めず呼吸音も正常だった。腹部は平坦・軟で肝脾腫を認めなかった。顔面と四肢を中心に粟粒大の紅斑を伴う小丘疹が散在していた。両足は足背から前頸骨部に紅斑を認めたが硬性浮腫は認めなかった。右大陰唇には3×3 cm大の発赤を認め、その中心には径2 mm大の刺し口を認めた（図A）。意識は清明で、神経学的所見に異常を認めなかった。

入院時検査所見（表）：白血球数は8,000/μℓと上昇はなく、C-reactive protein（CRP）は2.7 mg/dℓと軽度の上昇を認めた。肝機能や腎機能に異常は認めなかった。

入院後経過：入院時に発熱、口腔所見（いちご舌）、四肢末端の変化（手掌紅斑）、発疹、頸部リンパ節腫脹を認めており、川崎病も鑑別疾患のひとつに考えられた。しかし、病歴と会陰部の刺し口からツツガムシ病の可能性を考え、minocycline 点滴静注（3.6mg/kg/day）で治療を開始したところ翌日には解熱した。6病日に行った心エコー検査では壁運動は正常で僧帽弁逆流や心嚢液貯留を認めず、冠動脈病変も認めなかった。皮膚症状も次第に改善し9病日には消失し、炎症所見もCRP 0.4mg/dℓと改善した。リケッチア抗体価の検討では、*Orientia tsutsugamushi* 抗体価がIgM 抗体価、IgG 抗体価ともに20倍未満であったが、*R. japonica* 抗体価は IgM 抗体価が5病日に20倍、12病日に40倍、IgG 抗体価が5病日に20

表　入院時検査			
白血球数：8,000/μℓ		GT：	14IU/L
好中球：56.1%		T-Bil：	0.5mg/dℓ
リンパ球：34.8%		D-Bil：	0.1mg/dℓ
好酸球：6.2%		TP：	7.0g/dℓ
好塩基球：0.1%		Alb：	4.4g/dℓ
単球：2.8%		BUN：	7mg/dℓ
赤血球数：506万/μℓ		Cr：	0.3mg/dℓ
血色素：13.3 g/dℓ		Na：	138mEq/L
ヘマトクリット：39.1%		K：	3.6mEq/L
血小板数：17万/μℓ		Cl：	102mEq/L
AST：27IU/L		Ca：	9.6mg/dℓ
ALT：17IU/L		Glu：	105mg/dℓ
LD：315IU/L		CRP：	2.7mg/dℓ

倍未満、12病日に20倍であった。臨床経過と抗体価から日本紅斑熱と診断した。退院直前の心エコー検査も異常所見を認めず、13病日目に退院した。退院日から両手の指尖部に膜様落屑が出現した（図B）。

考　察

本例は、入院時に発熱と川崎病の主要症状の4項目を認め川崎病の可能性も考えられるが、刺し口を認めたことや minocycline の投与で速やかに解熱したことが川崎病の経過と異なっていた。最終的には *R. japonica* の抗体価の推移から日本

紅斑熱と診断した。日本紅斑熱で川崎病との鑑別を要した例の報告はない。

日本紅斑熱はリケッチア感染症で，R. japonica を保有するマダニに刺咬されることで発症する[1]。潜伏期は2～8日で，高熱，発疹，刺し口が臨床的3徴候である[1]。2～3日の発熱の後に顔面と四肢に米粒大から小豆大の辺縁不整形の紅斑が多数出現し，紅斑は搔痒感や疼痛がないのが特徴とされる[1]。手掌部の紅斑はツツガムシ病にはなく[2]，日本紅斑熱に特徴的な所見である[1]。本疾患は重症化すると播種性血管内凝固や多臓器不全などの重篤な合併症を生じることがあるため，早期に診断し，テトラサイクリン系抗生物質を投与することが重要である[1]。

本例は高熱，発疹，刺し口の三徴候を認めたため，リケッチア感染症の診断は比較的容易であった。ただ，高熱や発疹，所属リンパ節腫脹などの日本紅斑熱の症状は川崎病の主要症状と共通しており[1]，川崎病の不全型との鑑別が必要となる場合も考えられる。本例は入院時に①いちご舌，②頸部リンパ節腫脹，③発疹，④四肢末端の変化（発赤・腫脹）を呈しており，発熱は2日目だったが，発熱を有意とすると川崎病の主要症状の5項目を呈していた。また，回復期には川崎病に特徴的な膜様落屑を認めた。

刺し口は日本紅斑熱のほぼ全例で認める臨床的診断の決め手となる所見とされているが，小さく浅いものでは刺咬後数日で消失することがある[1]。刺し口が消失する，あるいは分かりにくい

ような症例では，理学所見のみでは川崎病との鑑別が困難なことも考えられる。このような場合は川崎病と診断され，テトラサイクリンの投与が遅れ，重篤な状況を来す可能性も考えられた。刺し口がはっきりしない場合でも，マダニの生息地である野山や田畑への立ち入りの既往がある場合には本症の可能性を考慮する必要がある。

日本紅斑熱の発生は主に温暖な太平洋岸沿いで確認されているが，交通手段が発達し人の往来が便利になった現在では，好発地域以外の地域であっても可能性は否定できない。本例でみられたいちご舌や回復期の川崎病を思わせる膜様落屑が日本紅斑熱でみられたという報告はなく，本例は特異な例である可能性はある。しかし，日本紅斑熱で川崎病の主要症状の多くを呈することがあるという認識は重要と思われた。

結　語

川崎病の主要症状を呈した日本紅斑熱の1例を経験した。日本紅斑熱で川崎病の主要症状の多くを呈する例があることの認識は重要と思われた。

文　献

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A case with Japanese spotted fever needed to be distinguished from Kawasaki disease

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