

613 From deadly fatal to easily overlooked among Karp strain: Diversity of clinical features of Scrub typhus in Fukushima, Japan

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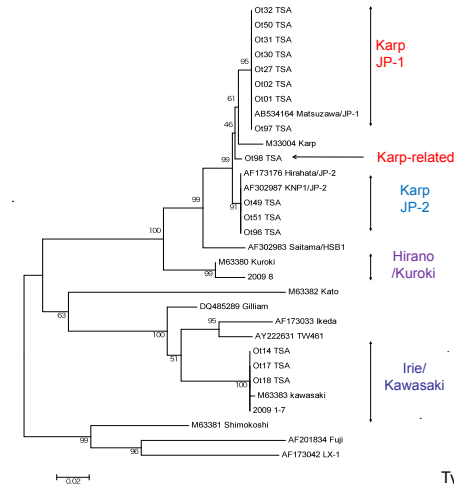
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Background Scrub typhus (ST) is endemic in Fukushima, where the highest number has been reported from 2006 to 2011 in Japan. In 2009, One fatal case of ST had reported with delay of diagnosis and treatment. This study aimed to determine clinical features among strains (Karp, Irie/Kawasaki, Hirano/Kuroki) in this endemic area.

Table 1. The stereotyped classification : "summer type" and "autumn-winter type" scrub typhus in Fukushima, Japan

	The summer type		The autumn-winter type
Serotype	Karp		Kawasaki, Kuroki
Phylogenetic type	JP-1/Matsuzawa	JP-2/KNP1	Kawasaki, Kuroki
Vector	<i>L. Intermedium</i>	<i>L. pallidum</i>	<i>L. scutellare</i>
Regional distribution	North, middle and east coast (Abukuma mountains) of Fukushima		South to middle of Fukushima
Virulence	Relatively severe in delayed diagnosis		Relatively mild
Prognosis	Occasionally fatal with DIC		Relatively good

Figure 1. Phylogenetic tree constructed using the sequences of TSA (Type-specific antigen) for 56-kDa gene (434bp)



Methods All patients diagnosed between 2008 and 2015 at the Ohta Nishinouchi general hospital (1,036-bedded tertiary care cancer centre in Fukushima, Japan) and affiliated hospitals are retrospectively reviewed.

Results There were 48 cases of scrub typhus during the study period. Twenty-one cases of Karp-related (44%), nineteen cases of Kawasaki (40%) and eight cases of Kuroki (16%) are diagnosed. The average age of the patients was 69 years old (range, 37-90). Women are dominated (M:F=17:31).

•These 48 cases were categorized as follows:

Categorized type	Clinical features
1 (Typical/Mild)	Triad (fever, rash and eschar) without sequelae
2 (Typical /Severe)	Triad, DIC with shock state, bleeding tendency Needed intensive management
3 (Atypical / Severe)	Proceeded major organ involvement
4 (Atypical /Mild)	Without triad, lacking major symptoms

Table 2. The diagnosis of Scrub Typhus

Serological tests (Indirect immunoperoxidase IgG/IgM) are performed to all cases.

Karp (n=21)	Diagnosis		Specimens for PCR		
	Serology	PCR			
JP-1/ Matsuzawa	11	11	Eschars		
JP-2/KNP1	3	3	Eschar, blood		
Karp-related (Ots8)	1	1	Eschar		
Karp (genotype unknown)	6	0	Eschar-like skin (1)		
	(NE 1)	(ND 1)	(NP 4)		
Kawasaki/ Kuroki (n=27)	Diagnosis		Specimens for PCR		
Serology	PCR	PCR NP NE			
Irie/Kawasaki (n=19)	19	9	9	1	Eschars, skin, joint fluid
Hirano/Kuroki (n=8)	8	1	4	3	eschar

NE: No eschar, ND: Not detected, NP: Not performed

Table 3. Categorized clinical features (Type 1 to 4) and Serological types

Categorized Type	Clinical features	Serological types		
		Karp (21)	Kawasaki (19)	Kuroki (8)
1 (Mild/Typical)	Triad without sequelae	○ 57% (12/21)	○ 58% (11/19)	○ 37.5% (3/8)
2 (Severe/Atypical)	Fatal, bleeding tendency	⊙ 14% (3/21)	× 0% (0/19)	× 0% (0/8)
3 (Severe/Atypical)	Prominent organ involvement	○ 19% (4/21)	○ 16% (3/19)	× 0% (0/8)
4 (Mild/Atypical)	Under-diagnosed Overlooked	△ 10% (2/21)	○ 26% (5/19)	○ 62.5% (5/8)

Discussion

•The determination of virulence mechanism of *O. tsutsugamushi*, host-mediated pathogenic mechanisms is unresolved (1). The virulence of JP-1 /Matsuzawa and JP-1/ Arato had regarded not enough to kill mice (2). On this case series, the two cases of JP-1/Matsuzawa showed the severe clinical course with shock state, bleeding tendency with DIC. The relationship between the clinical features, severity and serotypes is also not clear. The further investigation is needed.
 •The 5 cases of ST without eschar were found in this study (10%, 5/48): one of Karp, one of Irie/Kawasaki and 3 of Hirano/Kuroki. The "eschar negative scrub typhus" would be existed even if complete physical examination were performed, as previous study mentioned as 13% (3). Each serotypes (Karp, Irie/Kawasaki and Hirano/Kuroki) presented without eschar, which figures as one of the various clinical features of diversity in ST in Fukushima. It may play as atypical clinical presentation secondary to relatively low-virulence of serotype Hirano/Kuroki rather than Karp in Fukushima.

Conclusion

•The clinical features of each strains (Karp, Irie/Kawasaki and Hirano/Kuroki) of ST in Fukushima, Japan found to have a diversity in severity, typical and atypical presentation.
 •Serotype of Karp has wide clinical features from fatal to mild cases compared with Irie/Kawasaki and Hirano/Kuroki.
 •The virulence of Karp (especially JP-1) in Type 2 should be noted.
 •Atypical presentation of ST should not be missed as differential diagnosis of fever in this endemic area

References

- 1) Paris DH (1), Shelle TR, Day NP, Walker DH. Unresolved problems related to scrub typhus: a seriously neglected life-threatening disease. Am J Trop Med Hyg. 2013 Aug;89(2):301-7.
- 2) Urakami H, Takahashi M, Misumi H, Okubo K, Enatsu T, Tamura A. Detection, isolation and characterization of *Orientia tsutsugamushi* in *Leptotrombidium intermedium*. Med Entomol Zool 2000; 51:169-77
- 3) Ogawa M, Hagiwara T, Kishimoto T, et al. Scrub typhus in Japan: epidemiology and clinical features of cases reported in 1998. Am J Trop Med Hyg 2002; 67:162-5.
- 4) Kelly DJ, Fuerst PA, Ching WM, Richards AL. Scrub typhus: the geographic distribution of phenotypic and genotypic variants of *Orientia tsutsugamushi*. Clin Infect Dis. 2009 Mar 15;48 Suppl 3:S203-30.

