

# The Masqueraders presenting a multi-system disease Unusual and atypical clinical features of Scrub Typhus in Fukushima, Japan

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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. Atypical clinical presentation of ST makes the diagnosis difficult followed by treatment delay which is unfortunate because ST is eminently treatable.

**Methods:** We reviewed the clinical features of ST in adults from 2008 to 2017 at Ohta Nishinouchi General Hospital, a major teaching hospital in Fukushima, Japan.

**Results:** 55 cases (serotype Karp 24, Irie/Kawasaki 21, Hirano/Kuroki 10) of ST were confirmed by elevated IgM and IgG in paired sera and PCR positivity within eschars. Complications were documented in 13% (7/55: 4 Karp and 3 Irie/Kawasaki), cardiovascular (4 cases of paroxysmal atrial fibrillation), neurological (2 cases of syncope, encephalitis) and metabolic/electrolyte abnormalities (hyponatremia /SIADH). In terms of atypical clinical features, the cases without triad (fever, rash and eschar) were found in 31% (17/55). The cases of "eschar negative scrub typhus" were found in 11% (6/55: Karp 1, Irie/Kawasaki 1, Hirano/Kuroki 4). Patients without fever and rash were 18% (10/55: Karp 2, Irie/Kawasaki 6, Hirano/Kuroki 2) and 9% (5/55: Karp 2, Irie/Kawasaki 1, Hirano/Kuroki 1). Severe cases complicated with shock and DIC (7%, 4/55) including one fatal case (2%, 1/55: Hirano/Kuroki). Besides the typical cases with triad 53% (29/55), the unusual complications and atypical features were found in total 40% (22/55).

**Conclusion:** The diagnosis of ST becomes a clinical challenge if typical features are absent. In an endemic area, atypical presentation of ST involving multi-system disease is common.

**Table 1. Serotypes, Phylogenetic types and Vectors of ST**

	The summer type		The autumn-winter type
Serotype	Karp		Irie/Kawasaki, Hirano/Kuroki
Phylogenetic type	JP-1/Matsuzawa	JP-2/KNP1	Kawasaki, Kuroki
Vector chigger mites	<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
Preference to human	"Slow biter" to soft skin after migration		"Quick-biter" without migration

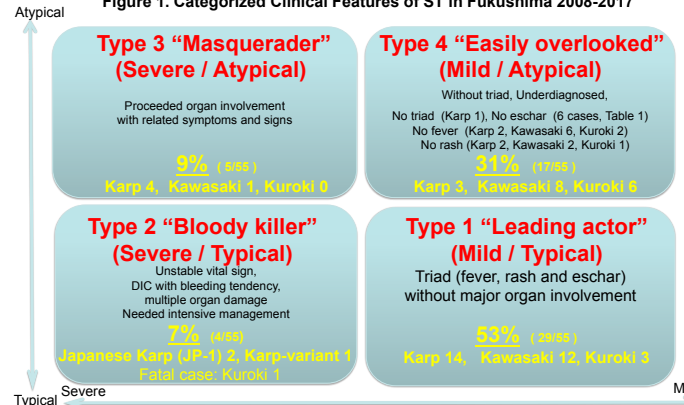
L: *Leptotrombidium*

**Table 2. Clinical overview of "non-eschar" ST (11% 6/55)**

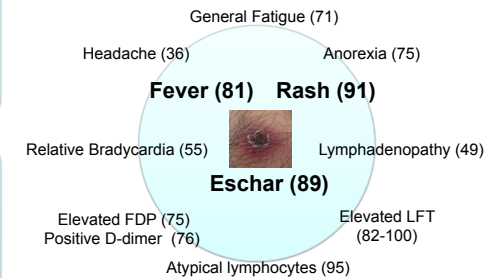
Age/ Sex	Serotypes	Serology titer (IP IgG/IgM)	Fever (°C)	Rash Distribution	Treatment	PD/HD/DTT	VNT	Comorbidities /CCI	Prognosis /From onset to death (Days)
62/M	Karp	-/2560 2560/5120	37.1	None	None	6/N/N	2	DM, HTN, Adrenal tumor /1	Survival
72/F	Hirano/Kuroki	10240/20480 10240/10240	39.4	Neck, chest	None	0/N/N	4	HTN, DLP/ 0	Survival
52/F	Hirano/Kuroki	2560/20480 20480/20480	38.5	Scalp	DOXY po:10D	0/5/5	2	ITP/ 0	Survival
68/M	Irie/Kawasaki	80/640 5120/5120	38.7	chest	DOXY po: 7D	5/2/7	1	PD, Autoimmune bullous disease / 1	Death (PD, PNA) / 1642
62/F	Hirano/Kuroki	1280/-	40.0	Trunk	MINO po:14D	0/7/7	6	HTLV-1 positive (fb ATL) / 0	Survival
85/M	Hirano/Kuroki	10240/2560 20480/5120	37.5	Trunk	MINO iv:8D DOXY po:5D	5/17/23	2	Bladder Ca, AA, ILD / 2	Death (ILD) / 279

ST: Scrub Typhus M: Male F: Female IP: Immunoperoxidase DOXY: Doxycycline MINO: Minocycline po: per os D:Days PD: Patient delay HD: Hospital delay DTT: Days to treatment N: Not to detect VNT: Vitals number of times to the diagnosis CCI: Charlson Comorbidity Index DM: Diabetes Mellitus HTN: Hypertension DLP: Idiopathic thrombocytopenia PD: Parkinson Disease HTLV-1: Human T-cell Lymphotropic Virus fb: followed by ATL: Adult T-cell Leukemia Ca: carcinoma AA: Aortic aneurysm ILD: Interstitial Lung Diseases PNA: Pneumonia

**Figure 1. Categorized Clinical Features of ST in Fukushima 2008-2017**



**Figure 2. Clinical Features of Scrub Typhus (% of total 55 cases)**



**Table 3. Scrub Typhus as a Systemic Disease (% of total 55 cases)**

	Signs and Symptoms	Lab abnormalities	Differential /Tentative Diagnoses	Organ/system Complications
<b>Systemic, Skin</b>	Fever (81) Rash (91) Eschar (89) General fatigue (71) Conjunctival suffusion (33)	Leukocytosis (18) Elevated CRP (87)	Drug fever, Influenza, Varicella Herpes Zoster, Viral infection Japanese Spotted Fever, Murine Typhus, Tularemia	
<b>Cardiovascular</b>	Hypotension (4) Relative bradycardia (55)	Abnormal LFT AST (89) ALT (82) LDH (100)	Arrhythmia Congestive Heart Failure	Paroxysmal atrial fibrillation (7)
<b>Gastroenterology</b>	Anorexia (75) Abd pain, nausea (45) GI bleeding (1)		Peptic Ulcer Diseases Acute Hepatitis Cholangitis	Acute peptic ulcer bleeding with exposed vessel (2) Peptic ulcer (2)
<b>Neurology</b>	Headache (36) Consciousness disturbance		Meningoencephalitis Cerebrovascular diseases	Meningoencephalitis (2)
<b>Pulmonary</b>		Pulmonary infiltrations (16)	Pneumonia	
<b>Renal / Metabolic</b>		Hematuria (42) Proteinuria (51)	Renal failure (pre-renal/renal)	Acute renal failure (7) Hyponatremia/ SIADH (2)
<b>Hematology</b>	Lymphadenopathy (49)	Thrombocytopenia (29) Atypical lymphocytes (95) elevated FDP (75) Positive D-dimer (76) Hepatosplenomegaly (15)	Malignant Lymphoma Leukemia Infectious mononucleosis	DIC with bleeding tendency (7)
<b>Musculoskeletal</b>	Myalgia, Arthralgia (15)		Myositis, arthritis	Arthritis (synovial fluid PCR+) (2)

Fever > 38.0°C Hypotension: Systemic BP <70 mmHg Relative bradycardia <108 bpm (beats per minutes) on 38.3°C <132 bpm on 40°C Leukocytosis >9800/μL Elevated CRP >2.5 mg/dL AST, ALT >40 IU/L LDH >250 IU/L Hematuria and Proteinuria: urine dipstick positive Thrombocytopenia <10,000/μL Elevated FDP (Fibrin/fibrinogen degradation products) >4 μg/mL Positive D-dimer > 1 μg/mL