

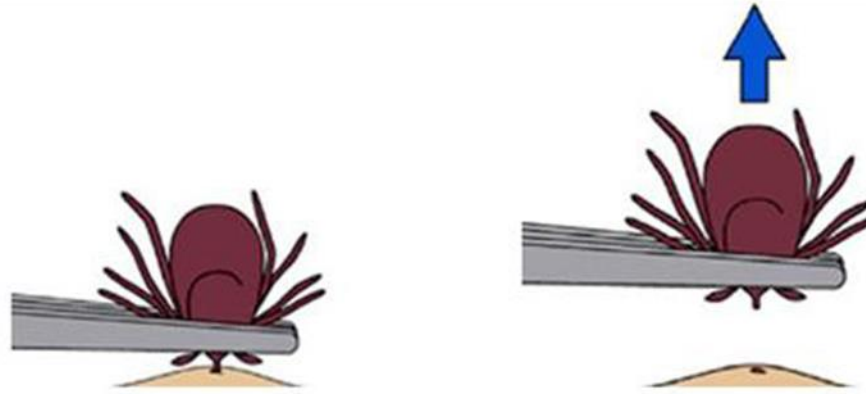
Disease review

Severe Fever with Thrombocytopenia Syndrome (SFTS) vs
Scrub typhus

삼성창원병원

소화기내과 이동규

Severe Fever with Thrombocytopenia syndrome



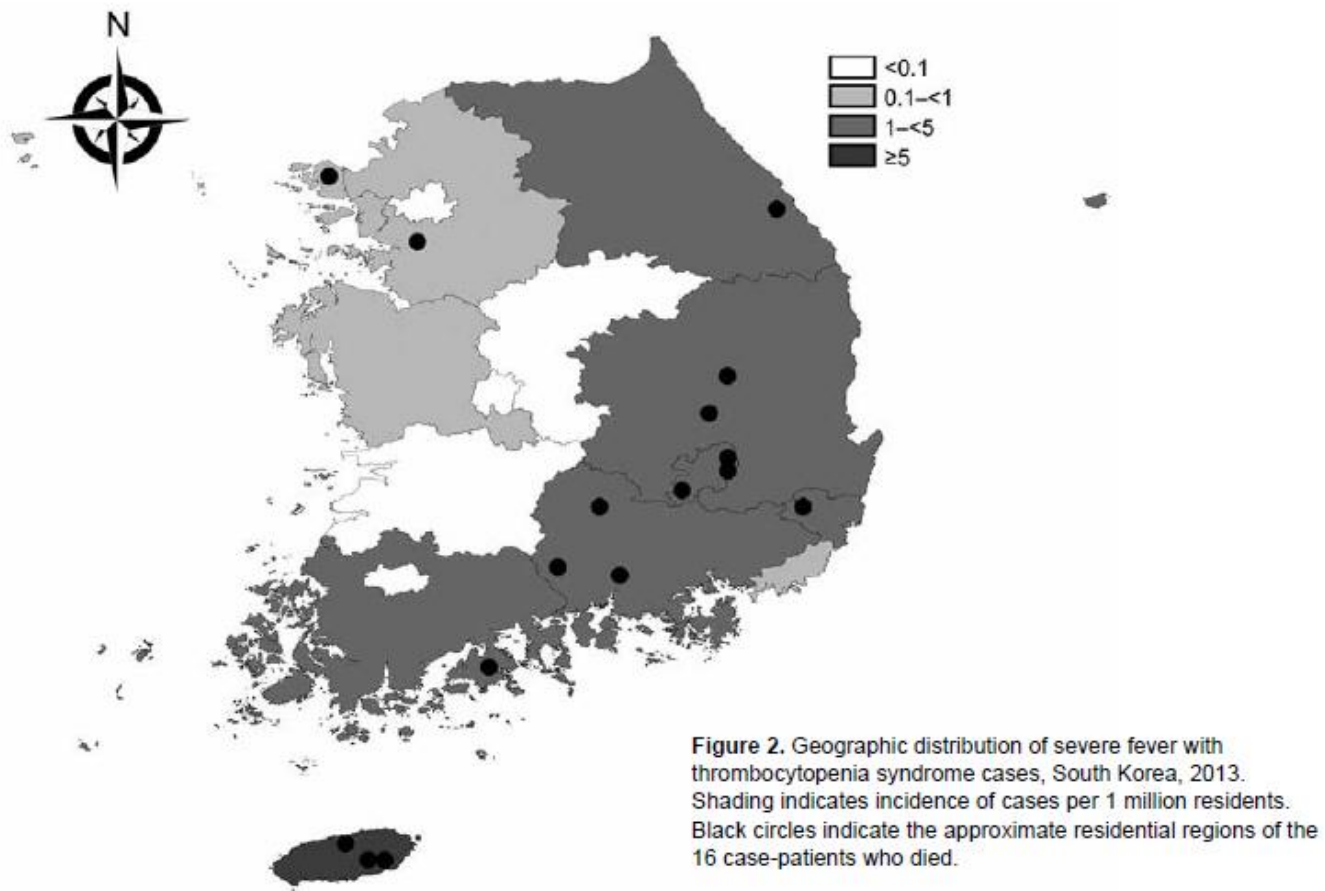
Severe Fever with Thrombocytopenia syndrome

- Mortality rate : 6 - 30%
- Biphasic peaks(5-6Mo, 8-9Mo)
- *H. longicornis*
 - Vector of SFTS
 - Known for other tick-borne diseases such as Lyme disease, rickettsia, and spotted fever

Epidemiology

- Single-stranded RNA virus : 3개의 분절
- Novel *Phlebovirus* species in *Bunyaviridae* family
- Retrospectively isolated in China in 2009
- In South Korea
 - first clinically detected on May 2013
- The overall prevalence of SFTS infection was 23.0% (17/74)
 - 본원 시행 결과

Epidemiology



Transmission

- Tick-borne disease
 - Vector : *H. longicornis*(작은소참진드기), *Rhipicephalu microplus*(꼬리소참진드기), *Amblyomma testudinarium* (Korea), *Ixodes nipponensis* (Korea)
 - Human-to-human transmission in cases of unprotected contact with SFTS patients or contact with infectious blood and bodily fluid
 - 잠복기 : 6-14 days

3 stages

- Febrile stage
 - Initial high serum viral load of 10^{5-6} copies/mL
 - Marked thrombocytopenia and leukopenia

- Multiple organ dysfunction stage
 - Proteinuria and hematuria
 - common and higher in fatal cases
 - 발병 7-13일 간 기간
 - 생존 환자: 혈중 바이러스 농도 감소, 혈소판 수치 회복
 - 사망환자: 혈중 바이러스 농도 증가, 10^8 , 혈소판 수치 지속 감소

- Convalescent stage

Diagnosis

- Clinical manifestation
 - History of tick bite: recall(?)
 - Fever, myalgia, arthralgia
 - **GI symptoms** : nausea, vomiting, abdominal pain, diarrhea
 - Hematologic abnormalities: Leukopenia, thrombocytopenia, bleeding tendency
 - AST, ALT, LDH, CK, CK-MB : 상승
 - SIRS, MOF, Shock, Coma
 - Neurologic Sx

Clinical manifestation

Table 2. Clinical characteristics of hospitalized case-patients with confirmed severe fever with thrombocytopenia syndrome, by outcome, South Korea, 2013*

Characteristics	No. (%) case-patients			p value†
	Total, n = 35	Died, n = 16	Recovered, n = 19	
Fever/chills	35 (100)	16 (100)	19 (100)	1.000
Fever, n = 32				
≤39.0°C	25 (78)	9 (64)	16 (89)	0.195
>39.0°C	7 (22)	5 (36)	2 (11)	NA
Fatigue	26 (74)	11 (69)	15 (79)	0.700
Myalgia	19 (54)	9 (56)	10 (53)	1.000
Headache	12 (34)	4 (25)	8 (42)	0.476
Cough	7 (20)	3 (19)	4 (21)	1.000
Sputum	9 (26)	3 (19)	6 (32)	0.460
Lymphadenopathy on physical examination	5 (14)	1 (6)	4 (21)	0.347
Lymph node enlargement found by CT, n = 32	20 (63)	7 (54)	13 (68)	0.473
Gastrointestinal symptoms				
Overall	33 (94)	15 (94)	18 (95)	1.000
Anorexia	21 (60)	8 (50)	13 (68)	0.317
Nausea	16 (46)	5 (31)	11 (58)	0.176
Abdominal pain	9 (26)	6 (38)	3 (16)	0.245
Diarrhea	22 (63)	12 (75)	10 (53)	0.293
Vomiting	15 (43)	6 (38)	9 (47)	0.734
Diarrhea/vomiting	26 (74)	13 (81)	13 (68)	0.460
Neurologic symptoms				
Overall	27 (77)	15 (94)	12 (63)	0.047
Within 7 d after disease onset	20 (57)	14 (88)	6 (32)	0.002
Slurred speech	9 (26)	7 (44)	2 (11)	0.050
Decreased level of consciousness	26 (74)	15 (94)	11 (58)	0.022
Convulsions	8 (23)	6 (38)	2 (11)	0.105
Hemorrhagic manifestations				
Overall	12 (34)	8 (50)	4 (21)	0.090
Gross hematuria	2 (6)	1 (6)	1 (5)	1.000
Petechiae	3 (9)	1 (6)	2 (11)	1.000
Gingival bleeding	5 (14)	3 (19)	2 (11)	0.642
Hematemesis	2 (6)	1 (6)	1 (5)	1.000
Hematochezia	1 (3)	1 (6)	0 (0)	0.457
Melena	4 (11)	4 (25)	0 (0)	0.035
Treatment				
Ribavirin	9 (26)	6 (38)	3 (16)	0.245
IVIg	7 (20)	5 (31)	2 (11)	0.208
Plasmapheresis	7 (20)	4 (25)	3 (16)	0.677
CRRT	10 (29)	9 (56)	1 (5)	0.002

*NA, not applicable; CT, computed tomography; IVIG, intravenous immunoglobulin; CRRT, continuous renal replacement therapy.

†Fisher exact test was used to compare groups.

Diagnosis

- Lab diagnosis : 3 개중 최소 1개 이상
 - Viral isolation
 - Viral identification by reverse transcriptase polymerase chain reaction(RT-PCR)
 - 1-6 days after disease onset
 - Serologic detection of 4-fold increase in anti-SFTS virus immunoglobulin G titers between acute and convalescent phases

SFTS

Scrub typhus

	Ecchymosis, and purpura of extremities (<7%)	Diffuse ill-defined, erythematous maculopapules on trunk and proximal extremities
Eschar	Rare (<6%)	Present (50~70%)
Systemic symptoms	Sustained fever (>38° C), gastrointestinal symptoms (vomiting, nausea, diarrhea), <u>leukopenia</u> , <u>thrombocytopenia</u> , multiple organ failure, disseminated intravascular coagulation, central nervous system complications, and hematuria	Fever, peripheral lymphadenopathy, arthralgia/myalgia, headache, <u>transitory leukopenia</u> , <u>transitory or rare thrombocytopenia</u> , hepatic dysfunction, pneumonia, and pleurisy
Therapeutic responses to doxycycline	No	Resolution within 48 hours after oral admission of doxycycline
Risky periods related to death	1 st and 2 nd weeks after onset	None

SFTS: sever fever with thrombocytopenia syndrome

SFTS in patients suspected scrub typhus

Characteristics	SFTS PCR (+) (n=17)	SFTS PCR (-) (n=57)	p value
Male, No (%)	7 (41.2)	24 (42.1)	0.946
Age, mean \pmSD	64.2 \pm 15.5	54.5 \pm 16.4	0.033
Farming, No (%)	12 (70.6)	29 (50.9)	0.151
Fever \geq 38.3 $^{\circ}$ C	13 (76.5)	48 (84.2)	0.480
Headache	5 (29.4)	18 (31.6)	0.865
Myalgia	8 (47.1)	31 (54.4)	0.595
GI symptoms	11 (64.7)	14 (24.6)	0.002
Anorexia	10 (58.8)	5 (8.8)	<0.001
Nausea/vomiting	8 (47.1)	10 (17.5)	0.022
Abdominal pain	2 (11.8)	5 (8.8)	0.657
Diarrhea	1 (5.9)	1 (1.8)	0.409
Cough	1 (5.9)	5 (8.8)	0.580
Dyspnea	1 (5.9)	2 (3.5)	0.549
Decreased level of consciousness	3 (17.6)	-	0.010
Rash	12 (70.6)	34 (59.6)	0.414

SFTS in patients suspected scrub typhus

Laboratory findings on admission	SFTS PCR (+) (n=17)	SFTS PCR (-) (n=57)	p value
Leukopenia (<4000 cells/mm ³ , n (%))	2 (11.8)	18 (31.6)	0.131
Lymphocytopenia (<1500 cells/mm³, n (%))	6 (35.5)	43 (75.4)	0.002
Anemia (Hematocrit < 30%, n (%))	3 (17.6)	4 (7.0)	0.341
Thrombocytopenia (< 10 ⁶ cells/mm ³ , n (%))	7 (41.2)	13 (22.8)	0.221
CPK, IU/L, meadian (IQR)	67 (33-132)	76 (45-128)	0.512
LDH, IU/L, mean ±SD	533±202	402 ±151	0.021
AST, IU/L, meadian (IQR)	104 (48-194)	69 (54-112)	0.210
ALT, IU/L, meadian (IQR)	70 (30-119)	53 (35-83)	0.616
PT (INR), meadian (IQR)	1.08 (1.03-1.15)	1.03 (0.97-1.09)	0.057
CRP, mg/L, meadian (IQR)	71.6 (46.4-110.4)	42.9 (23.2-80.3)	0.034
BUN, mg/dL, meadian (IQR)	12.7 (9.3-18.2)	12.7 (9.4-15.3)	0.634
Creatinine, mg/dL, median (IQR)	0.9 (0.8-1.3)	0.8 (0.6-1.0)	0.510
Albumin, g/dL, mean ±SD	2.9 ±0.7	3.3 ±0.5	0.005
Hematuria, n (%)	3 (20.0)	20 (35.7)	0.356
Scrub typhus	11 (64.7)	34 (59.6)	0.486

SFTS in Korea

Characteristics	Total, n = 35
Fever/chills	35 (100)
Fever, n = 32	
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Lymph node enlargement found by CT, n = 32	20 (63)
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Hemorrhagic manifestations	
Overall	12 (34)
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Petechiae	3 (9)
Gingival bleeding	5 (14)
Hematemesis	2 (6)
Hematochezia	1 (3)
Melena	4 (11)

Laboratory tests	Total, n = 32
Platelet count, × 10 ⁹ /L‡	38 (15–113)
Leukocyte count, × 10 ⁹ cells/L‡	1.5 (0.7–3.0)
ANC, × 10 ⁶ cells/L, n = 30‡	969 (125–3,292)
Hemoglobin, g/L‡	12.9 (9.2–16.4)
aPTT, s, n = 30	54 (35–97)
AST, U/L, n = 31	242 (63–4,567)
ALT, U/L, n = 31	77 (27–1,432)
Total bilirubin, mg/dL, n = 31	0.5 (0.2–4.0)
Amylase, U/L, n = 26	84 (40–333)
Lipase, U/L, n = 20	98 (38–692)
CK, U/L, n = 21	570 (67–4,362)
CK-MB, U/L, n = 18	6.9 (0.3–300.0)
LDH, U/L, n = 28	908 (279–4,564)
ALP, U/L, n = 31	119 (44–1,586)

Predictors of mortality

- Older age
- early neurologic symptoms
- Melena, hemorrhagic Sx(?)
- Inc ALP, ALT, LDH(?)
- High viral loads

Treatment

- No specific treatment
- Symptomatic and supportive therapy
- Ribavirin (?)-lacked evidence
- The administration of neutralizing antibodies (?)
- Plasma exchange and ribavirin (?)
- Vaccines or prophylactic drugs have not been introduced yet

Reference

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