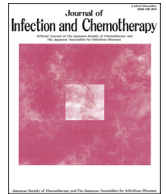




Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: <http://www.elsevier.com/locate/jic>

Review Article

Pathophysiology of severe fever with thrombocytopenia syndrome and development of specific antiviral therapy

Masayuki Saijo

Department of Virology 1, National Institute of Infectious Diseases, Toyama 1-23-1, Shinjuku, Tokyo, 162-8640, Japan

ARTICLE INFO

Article history:

Received 23 March 2018

Received in revised form

22 June 2018

Accepted 12 July 2018

Available online xxx

Keywords:

Severe fever with thrombocytopenia syndrome
SFTS

Favipiravir

Ribavirin

Viral hemorrhagic fever

Pathophysiology

ABSTRACT

Severe fever with thrombocytopenia syndrome (SFTS) caused by SFTS virus (SFTSV), a novel phlebovirus, was reported to be endemic to central and northeastern PR China and was also to be endemic to South Korea and western Japan. SFTS is an emerging viral infection, which should be categorized as a viral hemorrhagic fever disease as Crimean-Congo hemorrhagic fever (CCHF) is caused by CCHF virus. SFTS is a tick-borne viral infection. SFTSV is maintained between several species of ticks and wild and domestic animals in nature. Patients with SFTS show symptoms of fever, general fatigue, and gastrointestinal symptoms such as bloody diarrhea. The severely ill SFTS patients usually show gastrointestinal hemorrhage and deteriorated consciousness. The case fatality rate of SFTS ranges from 5 to 40%. Pathological studies on SFTS have revealed that the mechanisms behind the high case fatality rate are virus infection-related hemophagocytic syndrome associated with cytokine storm, coagulopathy due to disseminated intravascular coagulation causing bleeding tendency, and multi-organ failure. Favipiravir was reported to show efficacy in the prevention and treatment of SFTSV infections in an animal model. A clinical study to evaluate the efficacy of favipiravir in the treatment of SFTS patients has been initiated in Japan. SFTSV is circulating in nature in PR China, Korea, and Japan, indicating that we cannot escape from the risk being infected with SFTSV. The development of specific therapy and preventive measures is a pressing issue requiring resolution to reduce the morbidity and mortality of SFTS patients.

© 2018 Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

Contents

1. Introduction	00
2. Characteristics and life cycle of SFTSV and route of SFTSV infection to humans	00
2.1. Characteristics of SFTSV	00
2.2. Tick species involved in SFTSV transmission to humans	00
2.3. Human-to-human infections	00
3. Clinical characteristics of SFTS	00
3.1. Clinical manifestations	00
3.2. Association between viremia level and prognosis	00
3.3. Pathophysiology	00
3.4. Mechanism of CNS-associated symptoms appearing in SFTS patients	00
3.5. Pathophysiologies leading to a poor prognosis	00
4. Animal model and evaluation of the efficacy of antiviral agents favipiravir and ribavirin in treating SFTSV infections	00
4.1. General issues	00
4.2. In vitro antiviral activity of favipiravir against SFTSV	00
4.3. In vivo efficacy of favipiravir against SFTSV infection in IFNAR-KO mice	00
4.4. Favipiravir therapeutic study	00
5. Specific and promising antiviral drug therapy for SFTS	00

E-mail address: msaijo@nih.go.jp.<https://doi.org/10.1016/j.jiac.2018.07.009>

1341-321X/© 2018 Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

6.	Supportive therapies for SFTS patients	00
6.1.	Steroid pulse therapy	00
6.2.	Plasma exchange	00
7.	SFTS and CCHF	00
8.	Summary	00
	Funding	00
	Acknowledgements	00
	References	00

Abbreviations

ALT	alanine aminotransferase
AST	aspartate aminotransferase
CCHF	Crimean-Congo hemorrhagic fever
CCHFV	CCHF virus
CNS	central nervous system
DPRK	Democratic Peoples' Republic of Korea
HLH	hemophagocytic lymphohistiocytosis
IFN	interferon
IFNAR	interferon alpha receptor
IFNAR-KO mice	IFNAR-KO C57BL/6 mice
IHC	immunohistochemistry

IL	interleukin
IP	interferon- γ -induced protein
KO	knockout
LDH	lactate dehydrogenase
MIP	macrophage inflammatory protein
NP	nucleocapsid protein
PE	Plasma exchange
PR China	the People's Republic of China
sCD40L	soluble CD40 ligand
SFTS	severe fever with thrombocytopenia syndrome
SFTSV	SFTS virus
sIL-2RA	soluble IL-2 receptor alpha
TCID ₅₀	50% tissue culture infective dose

1. Introduction

Severe fever with thrombocytopenia syndrome (SFTS) was discovered as an emerging infectious disease epidemic to the People's Republic of China (PR China) [1,2], South Korea [3], and Japan [4,5]. SFTS is endemic to East Asia, PR China, South Korea possibly including the Democratic Peoples' Republic of Korea (DPRK), and Japan (Fig. 1). The causative agent of SFTS is a novel

phlebovirus of the family *Bunyaviridae*. It has been officially named SFTS virus (SFTSV) in the genus *Phlebovirus* of the family *Phenuiviridae* in the 10th Report released in 2016 from the International Committee on Taxonomy of Viruses (https://talk.ictvonline.org/ictv-reports/ictv_online_report/).

Crimean-Congo hemorrhagic fever (CCHF) is also a tick-borne viral infection caused by CCHF virus (CCHFV, genus *Nairovirus*, family *Phenuiviridae*). CCHF is endemic to Africa, Europe, the

(A) SFTS



(B) CCHF



Fig. 1. SFTS- and CCHF-endemic regions. SFTS is endemic to East Asia whereas CCHF is endemic to Africa, Europe, the Middle East, and Central and South Asia, including the Xinjiang Uyghur Autonomous Region of PR China.

Download English Version:

<https://daneshyari.com/en/article/8957925>

Download Persian Version:

<https://daneshyari.com/article/8957925>

[Daneshyari.com](https://daneshyari.com)