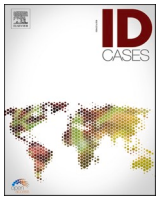
IDCases 32 (2023) e01807

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcases



Case report

Recurrent rhabdomyolysis in a patient with a history of rhabdomyolysis due to severe fever with thrombocytopenia syndrome

Masashi Nishiyama [a], Kyoko Yokota [b,*], Nobutoshi Morimoto [c]

[a] Clinical Training Center, Kagawa Prefectural Central Hospital, 1-2-1 Asahi-machi, Takamatsu, Kagawa 760-8557, Japan
[b] Department of Infectious Diseases, Kagawa Prefectural Central Hospital, 1-2-1 Asahi-machi, Takamatsu, Kagawa 760-8557, Japan
[c] Department of Neurology, Kagawa Prefectural Central Hospital, 1-2-1 Asahi-machi, Takamatsu, Kagawa 760-8557, Japan

ARTICLE INFO

Keywords:
Severe fever with thrombocytopenia syndrome
Bunyavirus
Virus infection
Sequelae
Complications
Rhabdomyolysis

ABSTRACT

Severe fever with thrombocytopenia syndrome (SFTS) is a hemorrhagic fever syndrome that is endemic to East Asia. Here, we describe a case of rhabdomyolysis, thought to have been caused by pemafibrate (which was prescribed for hyperlipidemia) or bacterial infection, in a patient who had experienced SFTS-induced rhabdomyolysis 4 years ago. This case suggests that SFTS causes muscle degeneration and can lead to recurrent rhabdomyolysis as a long-term complication.

Introduction

Severe fever with thrombocytopenia syndrome (SFTS) is an emerging tick-borne hemorrhagic fever syndrome that is endemic to East Asia, first clinically identified in China in 2009 [1]. Apart from China, cases have been reported from South Korea and Japan since 2012 and 2013, respectively [2,3], and more recently from Vietnam and Taiwan [4,5]. SFTS is caused by SFTS virus (SFTSV), a member of the *Phlebovirus* genus of the family Bunyaviridae, and ticks (e.g. *Haemaphysalis longicornis*) are considered to be a vector [1]. Furthermore, there have been reports of human-to-human transmission [6]. In recent years, there have also been cases of infection from animals, including companion animals, which pose an additional challenge to disease control [7]. Clinical features of SFTS involve a variety of symptoms such as fever, gastrointestinal, and neurologic symptoms, as well as bilocytopenia and liver dysfunction, and can include rhabdomyolysis (RM) [8]. The reported mortality rate is 12–30 % [1,9]. We encountered a patient with recurrent RM with previous history of RM due to SFTS. In recurrent RM, an underlying metabolic or muscular abnormality is presumed, but the cause is often unknown [10]. There are few reports of long-term complications of SFTS. In the present case, the previous history of SFTSV infection could have caused some kind of irreversible degeneration of the muscles, leading to the second occurrence of RM.

Case report

An 84-year-old Japanese man presented to the emergency department with a 1-week history of progressive bilateral leg weakness. He was receiving treatment for hypertension, hyperlipidemia, and benign prostatic hyperplasia. His chronic medications included amlodipine, potassium L-aspartate, aspirin, lansoprazole, sulpiride, and pramipexole, as prescribed. Pemafibrate had been added to his routine medicines 2 weeks prior to his emergency department visit, to treat his hyperlipidemia. He had a history of RM due to SFTS 4 years previously.

Blood tests revealed that his creatine kinase, creatinine, and C-reactive protein levels were elevated at 10,245 IU/L, 1.83 mg/dL, and 8.35 mg/dL, respectively. There was no evidence of dysthyroidism or an electrolyte imbalance. A urine test showed occult blood without microscopic hematuria; myoglobin was detected in the urine. Pyuria and bacteriuria were also noted. Later, the urine culture identified *Escherichia coli*.

He was diagnosed with RM along with acute kidney injury and urinary tract infection. The patient was treated with antibiotics and intravenous fluids. Pemafibrate was withdrawn as it was suspected to be the most likely cause of RM; sulpiride and pramipexole were also withdrawn. His condition improved gradually, and he was discharged on the 16th day of hospitalization (Fig. 1).

* Correspondence to: Center for Infectious Disease Education, Kagawa University Hospital, 1750-1, Miki-cho, Kita-gun, Kagawa 761-0793, Japan.
E-mail address: kyokota1018@gmail.com (K. Yokota).

https://doi.org/10.1016/j.idcr.2023.e01807
Received 10 February 2023; Received in revised form 17 May 2023; Accepted 22 May 2023
Available online 23 May 2023

Discussion

Here, we report a case of a man who experienced two episodes of RM over 4 years. The first episode was caused by SFTS, and the second is suspected to have been caused by fibrates. Before the onset of SFTS, the patient had no history of RM, other myopathies, or metabolic diseases. Therefore, this case suggests that SFTS-induced RM may cause muscle degeneration as a long-term sequela and increase susceptibility to other factors that can cause RM.

The reported risk factors for RM related to fibrates include combination therapy with other drugs (including statins), chronic kidney disease, diabetes mellitus, and hypothyroidism [11,12]. The mechanism of fibrate-induced RM is thought to be multifactorial, with the most probable mechanism being an interplay among pharmacokinetics, drug interactions, dosage, and predisposing medical conditions. In addition, it is assumed that fibrates may exacerbate potential mitochondrial myopathies and promote physiological changes in the skeletal muscles [13].

We also could not exclude the possibility of the second episode of RM being related to urinary tract infection due to *E. coli*. In a study of 103 cases of RM related to bacterial infection, 78.6 % cases had at least one additional risk factor for RM, such as diabetes or statin use, suggesting that bacterial infection in combination with other factors might have played a role in the development of RM [14]. The patient was unaware of fever but was aware of muscle weakness prior to admission. A large amount of residual urine was reported at the time of admission, and we believe that muscle weakness due to RM may have led to urinary tract infection as a result of difficulty in urinating.

Several infections, including SFTS, have been reported to cause RM [15–18]. Two mechanisms of virus-induced RM have been proposed—direct viral invasion of myocytes and release of toxins or cytokines affecting the muscle [19]. Concerning SFTS, it has been hypothesized that a cytokine storm may damage muscle cells, resulting in RM [18]. Severe viral infection may result in long-term irreversible muscle degeneration. Furthermore, fibrates have been shown to directly damage muscle cells in patients with undiagnosed myopathy [13]. Therefore, it is plausible that in this case, the SFTS 4 years previously caused degeneration in the muscle and was an underlying factor in the subsequent development of fibrate-induced RM.

Melli et al. [10] reported that 11 % cases of RM are recurrent, of which only 10 % are associated with underlying myopathy or metabolic abnormalities. Most recurrent cases of RM have no known cause. Recurrence could be coincidental; however, it could also be due to an unknown myopathy or metabolic abnormality that is difficult to diagnose, or an acquired factor, as suspected in this case. In this case, it is possible that fibrates, bacteria, or both, triggered the second episode of RM. It is reasonable to assume that the presence of muscle damage from a previous severe viral infection contributed to the RM recurrence.

In conclusion, this case suggests that RM due to SFTS is a risk factor for RM recurrence. Hence, careful follow-up should be performed after prescribing antihyperlipidemic drugs to patients with a history of RM due to SFTS. The long-term sequelae of some viral hemorrhagic fevers, such as Ebola hemorrhagic fever, are becoming increasingly apparent [20]. This case indicates the need for further studies on the long-term complications of SFTS.

CRediT authorship contribution statement

Masashi Nishiyama contributed to the clinical management and writing of the manuscript with substantial contribution to the discussion section. Kyoko Yokota contributed to organize the overall structure of the manuscript and discussion part. Nobutoshi Morimoto contributed to the management of the clinical treatment and the discussion section. All authors contributed to the writing of the final manuscript.

Ethical approval

Our hospital do not require an ethical approval for the publication of a case report.

Consent

Written informed consent was obtained from the patient for publication of this case report.

Authorship statement

All authors meet the ICMJE authorship criteria.

Funding

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

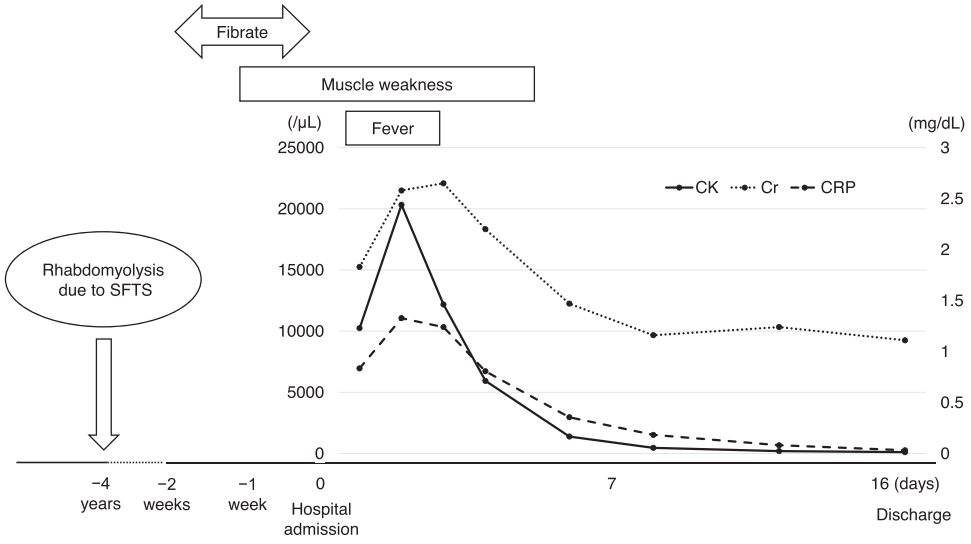


Fig. 1. Timeline of the patient's clinical course. CK, creatine kinase; Cr, creatinine; CRP, C-reactive protein.

Conflicts of Interest

None.

References

[1] Yu XJ, Liang MF, Zhang SY, Liu Y, Li JD, Sun YL, et al. Fever with thrombocytopenia associated with a novel bunyavirus in China. N Engl J Med 2011;364:1523–32. https://doi.org/10.1056/NEJMoa1010095.

[2] Kim KH, Yi J, Kim G, Choi SJ, Jun KI, Kim NH, et al. Severe fever with thrombocytopenia syndrome, South Korea, 2012. Emerg Infect Dis 2013;19:1892–4. https://doi.org/10.3201/eid1911.130792.

[3] Takahashi T, Maeda K, Suzuki T, Ishido A, Shigeoka T, Tominaga T, et al. The first identification and retrospective study of severe fever with thrombocytopenia syndrome in Japan. J Infect Dis 2014;209:816–27. https://doi.org/10.1093/infdis/jit603.

[4] Lin TL, Ou SC, Maeda K, Shimoda H, Chan JP, Tu WC, et al. The first discovery of severe fever with thrombocytopenia syndrome virus in Taiwan. Emerg Microbes Infect 2020;9:148–51. https://doi.org/10.1080/22221751.2019.1710436.

[5] Tran XC, Yun Y, Van An L, Kim SH, Thao NTP, Man PKC, et al. Endemic severe fever with thrombocytopenia syndrome, Vietnam. Emerg Infect Dis 2019;25:1029–31. https://doi.org/10.3201/eid2505.181463.

[6] Zhu Y, Wu H, Gao J, Zhou X, Zhu R, Zhang C, et al. Two confirmed cases of severe fever with thrombocytopenia syndrome with pneumonia: implication for a family cluster in east China. BMC Infect Dis 2017;17:537. https://doi.org/10.1186/s12879-017-2645-9.

[7] Mekata H, Kawaguchi T, Iwao K, Umeki K, Yamada K, Umekita K, et al. Possible transmission of severe fever with thrombocytopenia syndrome virus (SFTSV) to a person who buried the corpus of a dead cat, which died of SFTSV infection. Jpn J Infect Dis 2023. https://doi.org/10.7883/yoken.JJID.2022.425.

[8] Xu X, Sun Z, Liu J, Zhang J, Liu T, Mu X, et al. Analysis of clinical features and early warning indicators of death from severe fever with thrombocytopenia syndrome. Int J Infect Dis 2018;73:43–8. https://doi.org/10.1016/j.ijid.2018.05.013.

[9] Zhao L, Zhai S, Wen H, Cui F, Chi Y, Wang L, et al. Severe fever with thrombocytopenia syndrome virus, Shandong Province, China. Emerg Infect Dis 2012;18:963–5. https://doi.org/10.3201/eid1806.111345.

[10] Melli G, Chaudhry V, Cornblath DR. Rhabdomyolysis: an evaluation of 475 hospitalized patients. Medicine 2005;84:377–85. https://doi.org/10.1097/01.md.0000188565.48918.41.

[11] Wu J, Song Y, Li H, Chen J. Rhabdomyolysis associated with fibrate therapy: review of 76 published cases and a new case report. Eur J Clin Pharm 2009;65:1169–74. https://doi.org/10.1007/s00228-009-0723-7.

[12] Zhou J, Li D, Cheng Q. Fenofibrate monotherapy-induced rhabdomyolysis in a patient with post-pancreatitis diabetes mellitus: a rare case report and a review of the literature. Medicine 2020;99:e20390. https://doi.org/10.1097/md.0000000000020390.

[13] Davidson MH, Armani A, McKenney JM, Jacobson TA. Safety considerations with fibrate therapy. Am J Cardiol 2007;99:3c–18c. https://doi.org/10.1016/j.amjcard.2006.11.016.

[14] Kumar AA, Bhaskar E, Palamaner Subash Shantha G, Swaminathan P, Abraham G. Rhabdomyolysis in community acquired bacterial sepsis – a retrospective cohort study. PLoS One 2009;4:e7182. https://doi.org/10.1371/journal.pone.0007182.

[15] Soni AJ, Peter A. Established association of *Legionella* with rhabdomyolysis and renal failure: a review of the literature. Respir Med Case Rep 2019;28:100962. https://doi.org/10.1016/j.rmcr.2019.100962.

[16] De Brito T, Silva A, Abreu PAE. Pathology and pathogenesis of human leptospirosis: a commented review. Rev Inst Med Trop Sao Paulo 2018;60:e23. https://doi.org/10.1590/s1678-9946201860023.

[17] Radigan KA, Nicholson TT, Welch LC, Chi M, Amarelle L, Angulo M, et al. Influenza a virus infection induces muscle wasting via IL-6 regulation of the e3 ubiquitin ligase atrogin-1. J Immunol 2019;202:484–93. https://doi.org/10.4049/jimmunol.1701433.

[18] Kim MG, Jung J, Hong SB, Lee SO, Choi SH, Kim YS, et al. Severe fever with thrombocytopenia syndrome presenting with rhabdomyolysis. Infect Chemother 2017;49:68–71. https://doi.org/10.3947/ic.2017.49.1.68.

[19] Singh U, Scheld WM. Infectious etiologies of rhabdomyolysis: three case reports and review. Clin Infect Dis 1996;22:642–9. https://doi.org/10.1093/clinids/22.4.642.

[20] Vetter P, Kaiser L, Schibler M, Ciglenecki I, Bausch DG. Sequelae of Ebola virus disease: the emergency within the emergency. Lancet Infect Dis 2016;16:e82–91. https://doi.org/10.1016/s1473-3099(16)00077-3.