

A case of sleep disorder associated with severe fever with thrombocytopenia syndrome

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Abstract

Severe Fever with Thrombocytopenia Syndrome (SFTS) commonly presents with clinical manifestations such as fever, muscle pain, headache, and gastrointestinal symptoms. To date, there have been no reports linking SFTS to sleep disturbances. This case involves a patient diagnosed with SFTS who developed sleep disorders during the treatment process, primarily characterized by nocturnal restlessness, mental agitation, talking to oneself, and even verbal aggression. No abnormalities were detected in cerebrospinal fluid examinations, electroencephalography (EEG), EEG topography, video EEG, or cranial magnetic resonance imaging. As the treatment progressed, the patient's sleep condition gradually improved and eventually returned to pre-illness levels. Subsequent follow-ups confirmed no recurrence of sleep disturbances.

Keywords: severe fever with thrombocytopenia syndrome, novel bunyavirus, sleep disorders

The patient is a 70-year-old male, a local retiree from Cangzhou, long-term rural resident. He was admitted on May 24, 2025, due to fatigue for 5 days and fever for 10 hours. His past medical history includes diabetes for 18 years, managed orally with Repaglinide Tablets 1 mg three times daily, Miglitol Tablets 50 mg three times daily, Dapagliflozin Tablets 50 mg once daily, and Metformin Hydrochloride Extended-Release Tablets 0.5 g twice daily, with fasting blood glucose controlled between 7-8 mmol/L.

Five days prior to admission, the patient experienced unexplained significant fatigue, accompanied by dizziness, nausea, sore throat, and loose stools (2 times/

day). There was no vomiting, abdominal pain, chest tightness, shortness of breath, urinary frequency, dysuria, headache, or myalgia. During this period, his temperature was not monitored, and he received no examination or treatment. One day prior to admission, as the fatigue showed no improvement, he sought consultation at Yanshan County People's Hospital. A complete blood count (CBC) revealed decreased white blood cells and platelets. He received fluid replacement and nutritional support therapy. Ten hours prior to admission, he developed a fever, with a maximum temperature of 38.2°C, accompanied by chills. Concurrently, the local hospital reported a positive result for Novel Bunyavirus nucleic acid. He was transferred

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to our hospital for further diagnosis and treatment and was admitted with a diagnosis of “Severe Fever with Thrombocytopenia Syndrome (SFTS).”

Physical Examination

Temperature 37.5°C, pulse 59 beats/min, respiration 14 breaths/min, blood pressure 115/79 mmHg. Height 178 cm, weight 78 kg, BMI 24.6. The patient is alert and in good spirits, with normal memory and calculation abilities. Speech is fluent. Both eyes are midline with no nystagmus. Pupils are equal and round, approximately 3 mm in diameter, with prompt light reflexes. Forehead wrinkles are symmetrical bilaterally. There is no deviation of the angles of the mouth upon showing teeth, and the tongue protrudes centrally. Muscle strength in all four limbs is normal, as is muscle tone. Deep and superficial sensation is normal bilaterally. Finger-to-nose and heel-to-shin tests are steady and accurate bilaterally. Tendon reflexes in all four limbs are normal. Babinski signs are negative bilaterally. There is no cyanosis of the lips. No obvious jaundice or skin rash is noted on the skin or sclera. The neck is supple without rigidity.

Breath sounds are clear in both lungs, with no significant dry or wet rales heard. Heart rate is 59 beats per minute, with strong heart sounds and a regular rhythm. No pathological murmurs are heard over any valve auscultation areas.

The abdomen is flat and soft, with no tenderness or rebound tenderness throughout. The liver and spleen are not palpable. There is no percussion pain over the liver or kidney areas. A soybean-sized lymph node is palpable in the right inguinal region, which is not adherent to surrounding tissues, is mobile, and is non-tender. No edema is present in the lower limbs.

Auxiliary Examinations

Routine Items: Complete Blood Count (CBC): White Blood Cells (WBC) $1.56 \times 10^9/L$, Platelet Count $48.00 \times 10^9/L$, Absolute Neutrophil Count $0.90 \times 10^9/L$, Absolute Lymphocyte Count $0.57 \times 10^9/L$. Coagulation Routine: Activated Partial Thromboplastin Time (APTT) 43.30 seconds, Thrombin Time (TT) 26.20 seconds. Urinalysis: Ketones 2⁺, Leukocytes (WBC) ⁺, Urine Glucose 2⁺ mg/dL, White Blood Cells 30.00/μL. Stool Routine and Occult Blood: Negative.

Biochemistry: Aspartate Aminotransferase (AST) 106.40 U/L, Total Protein 51.50 g/L, Albumin 30.00 g/L, Glucose 12.02 mmol/L, Sodium (Na⁺) 133.20 mmol/L, Calcium (Ca²⁺) 1.89 mmol/L, Phosphorus (P) 0.81 mmol/L.

Cardiac Markers: B-type Natriuretic Peptide (BNP): 61.38 pg/mL; Troponin I: 0.11 ng/mL; Myoglobin: 137.48 μg/L; Creatine Kinase-MB Isoenzyme (CK-MB): 29.50 U/L; Lactate Dehydrogenase (LDH): 693.90 U/L; α-Hydroxybutyrate Dehydrogenase (α-HBDH): 455.00 U/L.

Inflammatory Markers: C-reactive Protein (CRP): 2.84 mg/L; Procalcitonin (PCT): Within normal limits; Interleukin-6 (IL-6): 86.85 pg/mL.

Other Markers: D-dimer: 4.85 mg/L; Blood Gas Analysis: pO₂: 108.50 mmHg, pCO₂: 30.70 mmHg, Na⁺ 129.40 mmol/L, Ca²⁺ 1.04 mmol/L, GLU 10.56 mmol/L; Glycated Hemoglobin (HbA1c): 8.50%; Fungal (1,3)-β-D-glucan Test (G Test) and Galactomannan Test (GM Test): Negative.

Etiological Tests: Severe Fever with Thrombocytopenia Syndrome Bunyavirus Nucleic Acid Test: Positive (7.66×10^2 TCID₅₀/mL); Hepatitis B Surface Antibody

(HBsAb): >1 000.00 mIU/mL; HIV Antibody: Negative; Brucella Antibody: Negative; Epidemic Hemorrhagic Fever Antibody: Negative; Cytomegalovirus IgM (CMV-IgM): Negative.

Electrocardiogram (ECG): Sinus bradycardia, heart rate 58 beats/min.

Imaging Studies:

Cardiac Ultrasound (Echocardiogram): Trace tricuspid regurgitation, impaired left ventricular diastolic function, no significant abnormality detected in left ventricular systolic function.

Color Doppler Ultrasound of Superficial Lymph Nodes: Enlarged lymph node in the right groin.

CT Plain Scan (Chest + Abdomen): Bronchitis, with a few scattered linear opacities in both lungs. Calcified nodule in the lateral basal segment of the right lower lobe. Multiple small diverticula in the colon. Small amount of pelvic fluid and a small amount of abdominal exudate.

Treatment course

After admission (2025-5-24), the patient was treated with Favipiravir for antiviral therapy (Day 1: 1.6 g Q12H; Days 2 to 5: 0.6g Q12H); Ulinastatin to suppress the cytokine storm (200,000 units Q8H); Omeprazole for acid suppression (20 mg QD); Compound Glycyrrhizin for liver protection and enzyme reduction (60 ml QD); Ceftriaxone to prevent bacterial infection (2 g QD); Coenzyme Q10 10 mg three times daily + Trimetazidine 20 mg three times daily for myocardial nutrition; insulin for glycemic control; and other symptomatic and supportive treatments.

Due to recurrent fever and significant generalized pain, Methylprednisolone 40 mg/day was added on 5-27 to reduce systemic inflammatory response. On 5-28, the patient developed sleep disturbances, waking frequently at night with sleep durations of only 1-2 hours each time, and experienced incoherent speech. These symptoms resolved during the daytime, with normal communication possible. Examination revealed decreased memory and calculation ability, but normal orientation. When inquiring with family members about the patient's sleep condition prior to the onset of the illness, they reported that the patient typically fell asleep around 22:00 each day and woke up around 5:00 the following morning. The sleep schedule was regular, with no history of insomnia or difficulty falling asleep. Therefore, the current sleep disturbance is considered to be associated with the novel Bunyavirus infection. Butylphthalide capsules were added to scavenge oxygen free radicals, improve cerebral energy metabolism, and reduce neuronal apoptosis.

On 5-29, the patient's nighttime sleep remained poor. Family members reported significant nocturnal agitation, while daytime mood was relatively stable. Considering potential steroid side effects and the possibility of viral infection-related aseptic meningitis, Methylprednisolone was discontinued, and Mannitol 125 ml Q6H was administered to reduce intracranial pressure.

Electroencephalogram (EEG) and brain mapping were performed: Interictal abnormal waves: During quiet wakefulness, 6-8 Hz medium-amplitude mixed rhythmic activity was observed in the bilateral parieto-occipital regions, with poor regulation and modulation. Multiple 5-6 Hz slow wave rhythms were noted across all leads. Occipital rhythm inhibition was incomplete upon eye opening. A 2-hour video EEG (VEEG) showed interictal abnormal waves: Paroxysmal medium-low amplitude 6.5-7 Hz theta waves were observed

in the frontopolar and frontal regions, all abnormal.

Brain MRI plain and enhanced scans showed: 1. Mild white matter rarefaction and age-related brain changes. 2. Left-sided mastoiditis.

On 5-30, the patient’s sleep condition showed no improvement. A lumbar puncture was performed: CSF pressure was 180 mmH₂O. CSF routine: Colorless and transparent, Pandy’s test negative, nucleated cell count 4×10⁶/L, polymorphonuclear cells 25%, mononuclear cells 75%. CSF biochemistry: Protein 0.05 g/L, Glucose 3.5 mmol/L, Chloride 127 mmol/L. CSF mNGS testing was negative. The nucleic acid test for the novel Bunyavirus in the cerebrospinal fluid was negative. A panel of ten autoantibodies for autoimmune encephalitis was negative.

On 5-30, a repeat test for Novel Bunyavirus nucleic acid turned negative, and Favipiravir was discontinued.

Following consultations with the Cognitive Disorders and Sleep Disorders departments on 5-31, a diagnosis of sleep disorder was considered. Both departments recommended administering Olanzapine 5 mg QN (nightly) and Eszopiclone 3 mg QN orally. Haloperidol injection was suggested for PRN (as-needed) use to manage severe agitation. After starting Olanzapine and Eszopiclone, the patient’s sleep showed some improvement.

On the night of 6-2, the patient experienced a recur-

rence of sleep disturbances, manifesting as mental excitement, talking to himself, and getting out of bed to move around the room independently. To rule out drug-induced behavioral abnormalities, most medications were discontinued, with only Olanzapine, Eszopiclone, and Omeprazole continued.

By 6-4, the patient’s sleep had improved compared to before. There were no further episodes of incoherent speech or significant agitation. On 6-5, sleep continued to improve further, with longer sleep durations (3-4 hours per episode), reduced frequency of waking, and no recurrence of incoherent speech or significant agitation. On 6-6, sleep markedly improved, with each sleep period lasting about 6 hours. No further abnormal behaviors occurred, and calculation ability and orientation were normal. The patient’s condition improved, and he was discharged on 6-7.

Follow-up

A telephone follow-up was conducted one month after the patient’s discharge. The patient reported no recurrence of sleep disturbances since leaving the hospital, and their sleep patterns had essentially returned to pre-illness levels.

Discussion

Severe Fever with Thrombocytopenia Syndrome (SFTS) is a tick-borne disease caused by the novel

Table 1. Monitoring of Various Indicators During Treatment.										
Data	5.24	5.25	5.27	5.28	5.29	5.30	5.31	6.2	6.4	6.6
WBC*10 ⁹ /L	1.56	2.51	5.00	6.58	4.66	5.21	4.73	3.93	4.69	4.39
NE*10 ⁹ /L	0.90	1.46	1.05	2.34	1.61	1.60	1.37	1.24	1.62	1.90
LY*10 ⁹ /L	0.57	0.92	3.52	3.40	2.32	2.72	2.47	2.09	2.58	2.03
PLT*10 ⁹ /L	48	52	41	61	89	124	150	214	151	245
CK(U/L)	302		1434	1211	641	442	371	147	101	75
LDH(U/L)	693		1182	1098	755	584	548	426	462	318
HBDH(U/L)	455		810	764	566	478	444	367	375	262

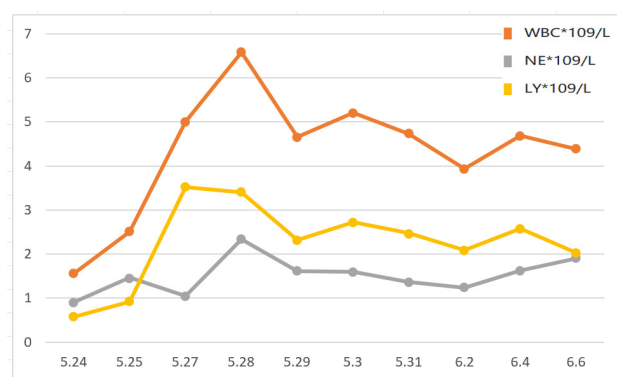


Figure 1. WBC NE LY tendency chart.

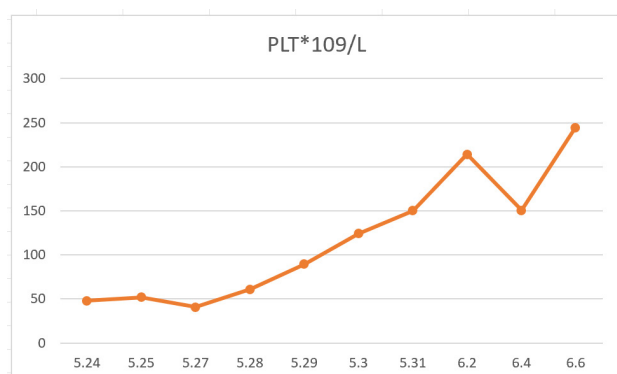


Figure 2. PLT tendency chart.

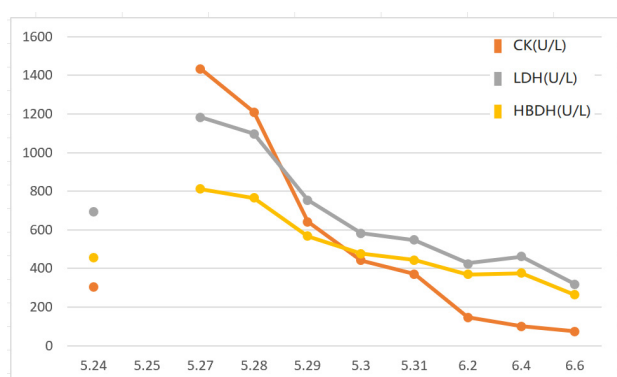


Figure 3. CK LDH HBDH tendency chart.

Bunyavirus (SFTSV). Its main symptoms include fever, thrombocytopenia, leukopenia, and gastrointestinal symptoms. Some patients are admitted with neurological symptoms such as headache and impaired consciousness as the initial presentation ^[1]. Critically ill patients may develop central nervous system symptoms like headache, drowsiness, coma, and even incoherent speech; such patients have a poor prognosis.

In this case, the patient developed sleep disturbances during treatment, and the symptoms did not resolve

even after the novel Bunyavirus nucleic acid turned negative. Although the symptoms improved with subsequent treatment, the underlying cause remains unclear. The following conditions need to be considered for differential diagnosis: Sleep disturbances caused by autoimmune encephalitis; Sleep disturbances related to post-viral inflammatory responses; Sleep disturbances induced by medications.

According to the International Classification of Sleep Disorders, Third Edition (ICSD-3), sleep disorders are categorized as follows: insomnia, sleep-related breathing disorders, central disorders of hypersomnolence, circadian rhythm sleep-wake disorders, parasomnias, sleep-related movement disorders, and other sleep disorders.

Autoimmune encephalitis, also known as antibody-mediated encephalitis, is associated with antibodies against neuronal surface proteins, ion channels, or receptors. It is characterized by prominent neurological and psychiatric symptoms ^[2], while sleep disturbances are often overlooked. In patients with autoimmune encephalitis, sleep disorders typically have a clear onset time, and multiple types of sleep disturbances may coexist in the same patient, such as disruptions in wake-sleep rhythms, non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep rhythms ^[3]. Clinically, they mainly manifest as four types: insomnia, sleep-related breathing disorders, central hypersomnolence, parasomnias, and sleep-related movement disorders.

Insomnia related to autoimmune encephalitis presents as reduced or lack of sleep lasting for days or weeks, often accompanied by hallucinations and/or behavioral abnormalities. Sleep-related breathing disorders are associated with laryngeal obstruction and often involve stridor. Stridor usually indicates brainstem damage and increases the risk of sudden death, necessitating early recognition of this specific symptom ^[4]. Central

hypersomnolence may be accompanied by cataplexy, commonly seen in anti-Ma2 encephalitis [5]. Cataplexy manifests as sudden bilateral loss of muscle tone while awake, typically triggered by strong emotions, especially laughter. Parasomnias often occur at night, involving gentle, repetitive movements with prolonged symptom duration (minutes to hours). Sleep-related movement disorders include four types: 1) Irregular body and limb jerks, periodic limb movements during wakefulness or sleep [6]; 2) Complex, purposeful, and gentle movements with closed eyes; 3) Forceful, violent, and jerky movements accompanied by muttering or shouting [7]; and 4) Sudden awakening from sleep with confused looking around, sitting up, or talking [8]. The management of sleep disturbances related to autoimmune encephalitis primarily involves symptomatic treatment and immunotherapy. The response to immunotherapy varies depending on the specific antibodies involved.

Viral infection triggers the production of a series of inflammatory cytokines, such as interleukins, tumor necrosis factor, and interferons. These inflammatory factors play a regulatory role in the sleep-wake cycle [9]. The high expression of inflammatory factors caused by viral infection can increase vascular permeability, potentially allowing the novel Bunyavirus to cross the blood-brain barrier and enter the central nervous system, causing intracranial infection [10]. This can lead to clinical manifestations such as dizziness, headache, drowsiness, coma, psychiatric and behavioral abnormalities, and sleep disturbances. International reports have also indicated that the novel Bunyavirus can be detected in cerebrospinal fluid [11]. The viral infection may damage the blood-brain barrier, affecting the passage of various substances and leading to an imbalance in the internal environment of the central nervous system. This disruption can cause abnormal expression of molecules related to sleep/wake regulation, resulting in

sleep disorders [12]. Animal studies have demonstrated that nuclear factor- κ B (NF- κ B), activated by inflammatory cytokines, significantly suppresses the expression of clock repressors, leading to disruption of circadian rhythms in mice [13]. Furthermore, inflammatory cytokines generated by viral infection can promote the production of corticotropin-releasing hormone (CRH) [14], leading to the secretion of large amounts of glucocorticoids as an anti-inflammatory response—a mechanism of self-regulation and protection. However, excessive glucocorticoids can cause sleep disturbances.

While treating diseases, some medications can cause corresponding side effects, and sleep disturbances are a common one. Common medications that can cause sleep disorders include the following [15]: 1) Central Nervous System Agents: Selective serotonin reuptake inhibitors (SSRIs) like fluoxetine can inhibit deep sleep and REM sleep during psychiatric treatment, leading to disrupted sleep architecture. 2) Cardiovascular Agents: Beta-2 receptor blockers, such as metoprolol, used for hypertension, can inhibit melatonin secretion and interfere with normal sleep rhythms. 3) Respiratory Agents: Bronchodilators like albuterol can stimulate the central nervous system; theophylline derivatives also stimulate the CNS, causing tachycardia and leading to insomnia. 4) Hormonal Agents: Glucocorticoids can increase central nervous system excitability and disrupt melatonin secretion rhythms, leading to anxiety and insomnia. Drug-induced sleep disturbances often appear shortly after initiating the medication and typically resolve after discontinuation.

This patient had high-risk factors associated with sleep disturbances: viral infection, systemic inflammatory response syndrome, and glucocorticoid use. Therefore, the current consideration is that the patient's sleep disorder resulted from a combination of post-viral inflammatory response and medication side effects. Through

this case, we recognize that glucocorticoids should be used cautiously in patients with severe viral infections or significant systemic inflammatory responses to avoid adverse reactions such as sleep disturbances and neuropsychiatric abnormalities.

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None.

Author contributions

Liu Yang conceived and designed the study. Hanshuai Cao collected and analyzed the data. Qian Wang contributed to data interpretation and manuscript revision. All authors read and approved the final manuscript.

Conflict of interest

All authors declare no conflicts of interest.

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