

CASE REPORT

Psychogenic fever due to worry about COVID-19: A case report

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Funding information

The authors have no funding source to disclose concerning this report. This work was supported by JSPS KAKENHI Grant Numbers JP19K17927

Abstract

Psychogenic fever is stress-related hyperthermia that is recognized as a psychosomatic condition. We treated a 46-year-old Japanese man who was worrying about the coronavirus infection (COVID-19) and had a fever with a maximum temperature of 38.1°C. The patient was tested twice for SRAS-CoV-2 using polymerase chain reaction (PCR), but both tests were negative. All tests were negative for organic diseases, including infections, allergy/collagen diseases, endocrine disorders, malignancies, and drugs-induced conditions. The more he doubted the COVID-19 in him, the more he complained of the already known various symptoms, such as smelling disorder. The patient believed firmly that he had COVID-19 because PCR can be false negative. Finally, the patient was treated with the anxiolytic, loflazepate, at 4 mg/day. This treatment was highly effective. The patient's serum IL-6 was 1.1 pg/ml (≤ 4.0). The patient was diagnosed with psychogenic fever due to irrational worry over coronavirus. Such typical cases should be treated with an anxiolytic.

KEYWORDS

case report, COVID-19, hyperthermia, psychogenic fever, pyrexia, SARS-CoV-2

1 | INTRODUCTION

Psychogenic fever is an increase in body temperature associated with psychological stress. In a patient with psychogenic fever, the brain coordinates the heat production response to psychological stress.¹ However, the mechanism through which psychological stress increases a patient's body temperature is not yet fully elucidated. This condition is also referred to as "stress-induced hyperthermia" because the pathogenicity is induced and attenuated by psychological stress.¹ Psychogenic fever was first described in 1930,² and its incidence is 3.6% in nosocomial patients.³ Psychogenic fever is non-inflammatory, that is, evoked by a pathway other than the arachidonic acid pathway. However, the pathogenicity of psychogenic fever is not well understood. Acute psychological stress-induced hyperthermia is a pathogenic pathway leading to pyrexia.¹

2 | CASE PRESENTATION

This case involves a 46-year-old Japanese man who was worrying about the new coronavirus infection (COVID-19) in April 2020 in Japan. The patient was febrile on April 15, 2020. Japan's state of emergency over the coronavirus had begun a week earlier on April 7, 2020. The patient visited the outpatient clinic in our hospital on April 21, 2020 with a complaint of low-grade fever below 37.4°C, which is borderline for the suspicion of COVID-19. The patient was worried that he might be infected with the coronavirus and requested to be performed the PCR test for SARS-CoV-2. The SARS-CoV-2 test was performed and the outcome was negative, and the patient was convinced to go home. The next day, the patient visited the outpatient clinic again to determine whether the febrile sickness was due to other causes. A blood test showed

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no inflammation (WBC 7,200/ μ l and CRP 0.01 mg/dl). The patient was screened for infections, rheumatoid diseases, endocrine disorders, malignancies, and allergic diseases, and all the results were negative. He was then prescribed acetaminophen for the fever.

The patient returned to the outpatient clinic 6 days later because acetaminophen did not ameliorate his fever, which had increased to 38.1°C (Figure 1). Non-steroidal anti-inflammatory drugs were not used in this case. The patient felt that his smell was slightly faint and his taste sense was intact. The more he doubted the COVID-19 in him, the more he complained of the already known various symptoms, such as smelling disorder and fatigue. The patient had no complaints of chills, shivering, and sweating due to the fever. His facial expression was unremarkable, and his speech was calm. The patient expressed fear for the effect of the infection, little irritation, no anxiety to dying, and no suicidal ideation. He had never been in contact with an infected or a febrile person. The patient was just worried that he could put other persons at risk of being infected he was infected with SARS-CoV-19 virus. Due to a broadcast announcing “PCR false-negative cases” in a certain population, the patient was afraid that he had COVID-19, which could affect everyone around him, including his family, neighbors, and colleagues. Although he tested negative for COVID-19, he determined that the test was not always reliable. The patient requested for a second PCR test for SARS-CoV-2, which was also negative. In addition, the patient had a history of psychological treatment for depression 2 years ago and had been treated using the antidepressant paroxetine for several years. The patient was treated with loflazepate, a benzodiazepine anxiolytic, at 4 mg/day, and the fever rapidly decreased to below 37.0°C approximately 12 h after the anxiolytic treatment (Figure 1). We used loflazepate for 16 days and the patient's pyrexia responded well for a few weeks during weekly or biweekly follow-up in the outpatient clinic. During the follow-up period, he continued to check his vital signs including body temperature in the same frequency.

On the day that the patient's fever was the highest, serum IL-6 was 1.1 pg/ml (≤ 4.0). This IL-6 value is indirect evidence for non-inflammatory psychogenic fever in this case.

During this episode of fever, he consulted a psychiatrist and was diagnosed as depressive mode based on his mental status. He had never experienced a fever episode of unknown origin, and he was having psychogenic fever for the first time. We did not check for the antibodies against the SARS-CoV-2 virus. We performed the third PCR test for SARS-CoV-2 1 month after the episode according to his demand, but the result was still negative.

3 | DISCUSSION

Pyrexia is usually a thermoregulatory response to a stimulus, such as infection. Thus, a systemic inflammatory response causes fever. Pyrexia is treated to preserve brain function and maintain homeostasis, including maintenance of cardiovascular function.⁴ If fever is neglected, mortality would be elevated in patients with infection and organic disease. However, treatment indication and intervention for pyrexia are not always clear. Generally, an anxiolytic should be effective in patients with psychogenic fever. In our case, an anxiolytic was effective (Figure 1). The recurrence of pyrexia should be anticipated due to psychogenic factors, because anxiety and stress are often chronic contiguous conditions in psychiatric patients. In our patient, the risk factor of psychogenic fever was chronic stress.¹ Stress-related psychosomatic symptoms are sometimes variable in different clinical situations and scenarios. In addition, in an experimental model, repeated chronic stress enhanced hyperthermia response to a novel stress. Due to this point, emerging infectious diseases including COVID-19 can easily evoke symptomatic conditions in an anxiety background.⁵ In our case, continuous fear sensation for COVID-19 in addition to other social stressors triggered a febrile response.

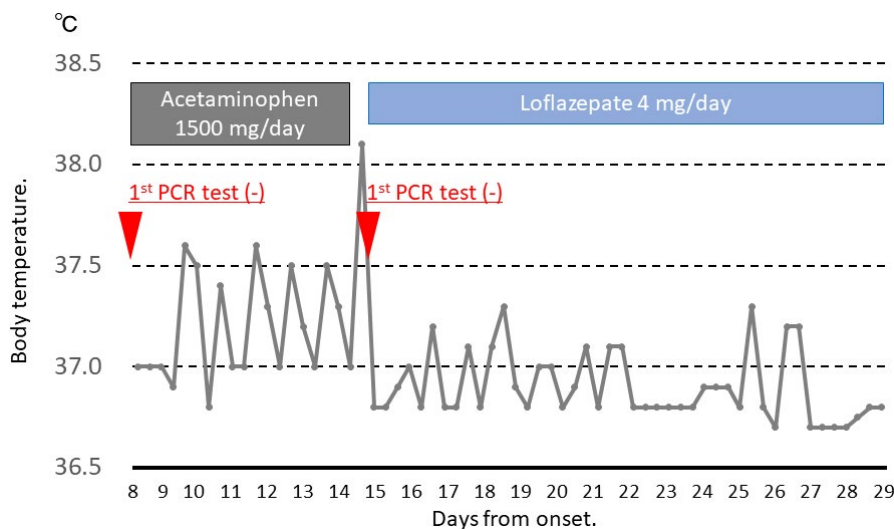


FIGURE 1 Patient's clinical course. The patient's body temperature (Celsius) was measured three times a day during his daily life. The patient was tested twice for SARS-CoV-2 (PCR test) during his clinical course

In patients with infection, fever can develop in response to the infection or the stress of the infection.⁶ Thus, different treatments may be appropriate. In an experimental setting, Vinkers CH et al.⁶ reported that diazepam, but not aspirin, was effective in attenuating psychogenic fever, and vice versa for inflammatory fever. Both benzodiazepines and non-steroidal anti-inflammatory drugs, such as aspirin, or antipyretics, such as acetaminophen, can be used.

In addition to pyrexia, other symptoms should be considered when diagnosing psychogenic fever. Given that a definitive diagnosis is difficult, there are very few reports concerning psychogenic fever.^{5,7–10} Psychogenic fever is underdiagnosed and underestimated because the association between stress and fever is obscure and difficult to prove.⁷ A search for English language publications in the PubMed database using the keywords “stress-induced hyperthermia” and “case report” revealed only five articles (up until July 7, 2020). In addition to fever, psychogenic stress can cause other psychosomatic symptoms, including visual⁷ and consciousness disturbances (catatonia).⁸ Psychogenic fever can be distinguished from inflammatory responses to infections based on the cytokine profiles.⁵ Although psychogenic fever is common in cancer patients,⁹ it is often difficult to diagnose the cause of fever in these patients. Psychogenic fever can rise to as high as 39.7°C.¹⁰ Even a spiked fever, more commonly associated with sepsis, can be induced by psychological stress. However, psychological interventions, including anxiolytics, neuroleptics, and electroconvulsive therapy, relieve fever symptoms dramatically in many cases.^{5,7–10}

The mechanism of psychogenic fever is unclear, although several mechanisms have been investigated. The present consensus is that inflammatory mediators are not involved in the pathogenesis of psychogenic fever.¹ In patients with psychogenic fever, inflammatory mediators are not expected to increase. However, stress can induce increased levels of serum inflammatory mediators, such as prostaglandin E₂, IL-1 β , and IL-6.⁵ Acute psychological stress has been shown to influence IL-1 β .¹¹ Furthermore, Steptoe et al.¹² reported that IL-6 was elevated by 56% after mental stress. Despite experimental and clinical research, the association between psychogenic hyperthermia and inflammatory cytokines is still not well understood. In our case, IL-6 did not increase in the hyperthermia episode. We advocate that psychogenic fever is not associated with the immunological inflammatory milieu. However, the association between inflammatory mediators and psychogenic fever should be further investigated in specific situations and stress conditions.¹

As a final consideration, we discuss the disease category for psychogenic fever. Psychogenic fever is not identified as an established clinical entity in the DSM-5 or ICD-11. The ICD-11 proposed to eliminate many clinically significant components of the syndrome.¹³ The DSM-5 working group considered, but rejected such a circumscribed approach.

Nevertheless, due to this policy, psychogenic fever has not been listed as an independent clinical entity in the DSM-5. If the ICD-11 argument was extended to medical diseases, one would never include fever, pain, or edema as indicators of any diagnosis because they are found in many different diseases.¹³ In this case, the symptom of pyrexia alone cannot be diagnosed as a dependent clinical entity in any disease category. However, in clinics, we are required to record patients' complaints and treat symptomatic patients. Thus, psychogenic fever should be recognized as a stand-alone sickness.

ACKNOWLEDGEMENT

NA. Published with written consent of the patient.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

OI managed the patient's case, contributed to the literature search, and wrote the manuscript. MU made substantial contributions to the concept and design of this report. OI qualified the patient's data and suggested important intellectual content. MU was involved in the supervision of the manuscript and managed the research. All authors approved the final version of the manuscript.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The subject has given his written informed consent to publish the case (including publication of images). The case report was approved by the institute's committee on human research.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patients for publication of this study.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

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How to cite this article: Imataki O, Uemura M. Psychogenic fever due to worry about COVID-19: A case report. *Clin Case Rep*. 2021;9:e04560. <https://doi.org/10.1002/ccr3.4560>