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**Brief Report****Psychogenic periodic fever**R.J. Timmerman<sup>a</sup>, J. Thompson<sup>a</sup>, H.M. Noordzij<sup>b</sup> and J.W.M. van der Meer<sup>a,c</sup>*Departments of<sup>a</sup> Infectious Diseases and<sup>b</sup> Clinical Psychiatry, University Hospital, Leiden, Netherlands*

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The present report concerns a 35-yr-old Caucasian male who had suffered from episodic fever of unknown origin over a period of 13 yr. Extensive investigation covering all the known causes of fever of unknown origin did not yield a diagnosis. Finally, a psychogenic cause was considered, and treatment with a psychotropic drug and relaxation therapy led to complete disappearance of the febrile periods. *Neth J Med* 1992;41:158–160.

Key words: Psychogenic fever; Episodic fever; Fever of unknown origin

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**Introduction**

Episodic fever persisting for many years is a diagnostic challenge. The fact that many diseases can be the cause necessitates frequent and repeated investigations. In most cases, a diagnosis is finally reached, but often only after a long and painful odyssey through the medical knowledge available [1]. It has not been firmly established that the cause of episodic fever may be psychogenic in nature, but we have found some indications in the literature that psychogenic fever can occur [1–3].

In this paper we describe a patient with recurrent febrile episodes of psychogenic origin which persisted over a period of 13 yr.

**Case Report**

A Caucasian male, born in 1953, had had recurrent attacks of fever since 1974. In 1972 he was treated for a duodenal ulcer, and in 1974 an atrial septal defect was closed with a Teflon patch. Since that operation he had had febrile episodes lasting 2 to 3 days and occurring at approximately monthly intervals. A typical episode started with a feeling that the tongue and throat were swollen, and this was accompanied by headache and myalgia. The patient then began to hyperventilate and developed chills. His temperature rose to 40°C and he sometimes lost consciousness for a couple of minutes. During the next 24–48 h his temperature gradually dropped. After about a week of general malaise he was able to resume his work as a typographer.

Since 1979 the patient had been admitted several times for analysis of these attacks. Extensive and repeated investigations into possible causes of fever of unknown origin carried out during and between attacks did not lead to a diagnosis. A complete neurological work-up was also negative.

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*Correspondence to:* R.J. Timmerman, Gemini Ziekenhuis, Dept. of Internal Medicine, Huisduinerweg 3, 1782 GZ Den Helder, Netherlands.

<sup>c</sup> *Present address:* Dept. of Internal Medicine, University Hospital, Nijmegen, Netherlands.

Slight neutrophilia was occasionally observed during an attack.

In 1986 the patient was referred to our hospital, where a few new data were added to his medical history. He had no contact with fumes or gases, and episodic fever did not occur in the family history. Three abortive attacks were observed. During these attacks, the patient had fever up to 39°C and hyperventilated. The next day his temperature was normal. On a single occasion a slightly elevated peripheral blood neutrophil count ( $13.5 \times 10^9/l$ ) was found. The level of C-reactive protein did not rise. Despite many attempts, we failed to find an infectious focus or evidence pointing to another disease. Familial Mediterranean fever was unlikely, because the results of a noradrenaline provocation test were negative [4]. Serum IgD was normal, which excluded the hyper-IgD periodic fever syndrome [5]. There was no evidence for familial Hibernian fever [6]. Neurological examination showed no abnormalities and an electroencephalogram was normal. An endocrinological work-up to detect a hypothalamic origin was inconclusive [7,8]. Porphyria and amyloidosis were excluded. The effect of antipyretic drugs on the attacks was equivocal: the temperature declined similarly with and without these drugs. Prolonged administration of colchicine, domperidone, and chlorpromazine had no effect.

While in hospital in 1987, the patient mentioned that he feared losing his job because of his repeated absence due to the recurrent periods of illness. His wife said on that occasion that her husband had an unceasing fear that he had a serious disease. He agreed to psychiatric consultation. His psychiatric history revealed that his development had been normal, despite the knowledge of having a heart problem. He remembered that having been on a waiting list for 2 yr he was summoned for heart surgery on very short notice. When he was told afterwards that the operation had been just in time, this had frightened him. The first attack of fever occurred shortly after discharge from the hospital.

The fever always developed within 8 h of a stressful situation at home or at work which aroused his anger. During this type of stressful

situation, the patient experienced a feeling that this tongue and throat were swollen, a constricted sensation in a band around his head and aching muscles. During psychiatric examination he gave the impression of being a nervous man without further psychopathology.

This prompted us to perform a hyperventilation test [9], which provoked the above-named symptoms. The patient panicked slightly, but was able to reduce the symptoms by breathing into his cupped hands for 3 min. Approximately 4 h later his temperature rose to 38.5°C and returned to normal within 12 h. The patient showed a pattern of clearly defined panic attacks without phobia but accompanied by hyperventilation; this was not caused by any other somatic or psychiatric disturbance. On the basis of the DSM III classification system, the diagnosis panic disorder (300.01) was made [10].

It was then decided not to keep the patient in hospital. He was treated with clomipramine [11] in an increasing dose up to 50 mg t.i.d. and the possible connection between the fever, the panic attacks and the heart operation was discussed in three sessions. He received relaxation training via an audiotape which he was instructed to listen to twice daily. After discharge the patient continued the prescribed medication and received support from his family doctor. During the subsequent 3 months he suffered two hyperventilation attacks followed by fever (up to 39°C) lasting 12 h. On both occasions the family doctor instructed him to listen to the relaxation tape. On two occasions he fainted at work during a hyperventilation attack; this was not followed by fever. He was then referred to a psychotherapist, to undergo 25 sessions of focal insight-giving psychotherapy. During the subsequent 2 yr he never panicked, nor did he experience hyperventilation or fever. The patient is still taking 25 mg clomipramine t.i.d.

## Discussion

We presented a case of episodic fever of 12 yr' duration in a 35-yr-old patient.

We do not know whether the elevated temperature in this patient was a true fever, i.e., a condition with a raised hypothalamic set-point, or

a hyperthermia, i.e., a condition with a normal set-point. The slight neutrophilia indicates that the attacks were associated with an acute phase response, albeit a mild one. This finding would argue for fever rather than for hyperthermia. It is of interest that Kluger et al., who provided evidence that stress-induced fever can occur in rats, demonstrated that a rise in temperature could be prevented by cyclooxygenase inhibitors [12]. This implies a pathogenetic role for one or more endogenous pyrogens, such as interleukin-1  $\alpha$  and  $\beta$ , tumour necrosis factors  $\alpha$  and  $\beta$ , interleukin-6, and interferon  $\alpha$ , which could be produced either by mononuclear phagocytes or by cells of the central nervous system, for example [13]. In our case, however, treatment with the cyclooxygenase inhibitor ibuprofen had no distinct effect on the patient's temperature.

The results of investigations concerning other causes of episodic fever were all negative. The diagnosis psychogenic fever was based on the psychiatric history, the positive results of the provocation test, and the positive effects of therapy.

We do not attribute the absence of febrile periods to an antipyretic effect of clomipramine since the patient has developed fever while on treatment with this drug.

This case suggests a psychogenic origin of the episodic fever in this patient, especially since relaxation therapy and psychotropic medication led to disappearance of the febrile episodes.

On these grounds, we think that in patients with episodic fever who have been examined at length without finding an organic substrate, a psychogenic origin must be considered.

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