

# Uhthoff's phenomenon as the initial symptom in neuromyelitis optica spectrum disorders: a case report

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## Case report

A 20-year-old male presented with a history of dysuria after taking a hot bath 13 days prior to visiting a urology clinic. A urinary tract infection was diagnosed. He reported difficulty urinating about 3 minutes after taking a hot bath, accompanied by a distended and painful bladder. The symptoms gradually resolved after about 30 minutes but dysuria worsened over time, especially when he took a hot bath (about 40°C, a shower or bath). Eventually his symptoms began to persist even 12 hours after bathing and a urinary catheter was inserted after 5 days. In the meantime, he developed numbness in his back and limb weakness and was transferred to the neurology department. The patient's medical, family and medication history were otherwise unremarkable.

The patient's temperature (36.6°C), blood pressure (108/72 mmHg), and pulse (76 beats/min) were normal as was respiratory, cardiovascular, and abdominal examination. Neurological examination revealed bilateral knee and ankle reflexes (notedly hyperactive), limb muscle strength (slightly decreased), and sensory system examination was normal. His pupils were isochoric and the papillary light reflex was present. No sensitive focal signs were detected and Babinski sign was negative.

His laboratory test results (complete blood count, blood sugar, lipid, hepatic, renal function, antinuclear antibodies, antiphospholipid antibodies, antineutrophil cytoplasmic antibodies, and rheumatoid factor) were normal. Routine urinalysis revealed a red blood cell count of 16/μL and white blood cell count of 16/μL. Examination of a cerebrospinal fluid sample showed a white blood cell level of  $16 \times 10^6$  L. The oligoclonal bands in cerebrospinal fluid and serum were negative, and anti-aquaporin-4 antibodies in the serum were positive.

Cerebral magnetic resonance imaging (MRI) revealed abnormal signals in the right brachium

pontis, brainstem, and left parietal lobe, with no contrast enhancement. The whole spinal MRI scan displayed abnormal signals from C6 to T1 (Fig). The patient was diagnosed with neuromyelitis optica spectrum disorder (NMOSD). Treatment included intravenous immunoglobulin (0.4 g/kg/d) and glucocorticoids (1000 mg intravenous methylprednisolone for 5 days, then changed to oral methylprednisolone 60 mg for 1 week). He recovered gradually; 5 days later, the catheter was removed and he could urinate freely. The numbness in his back and limb weakness resolved gradually. Five months later, the abnormal signals on the MRI scan were no longer present, and there was no recurrence at 1-year follow-up.

## Discussion

German professor Wilhelm Uhthoff described the phenomenon of transitory visual disturbance in 1890 in patients with multiple sclerosis (MS) occurring after physical exercise and an increase in body temperature. In 1961, G Ricklefs named this phenomenon Uhthoff's phenomenon (UP),<sup>1</sup> as Uhthoff observed the appearance of reversible optic symptoms induced by an increase in body temperature in four of 100 patients with MS and described it as the 'prominent deterioration of visual acuity during physical exercise and exhausting activity'.<sup>2</sup> Subsequent observations revealed that the physiological mechanism of visual dysfunction during heat exposure was the same as that of various other neurological symptoms experienced by MS patients. When Uhthoff researched the phenomenon, he considered exercise to be the only aetiology and ignored the importance of elevated body temperature. In 1950, the hot bath test was developed based on this phenomenon and was used to diagnose MS. Nonetheless because of the non-specific nature and potential complications of the hot bath test, it was replaced in 1980 by other diagnostic tests such as cerebrospinal fluid analysis

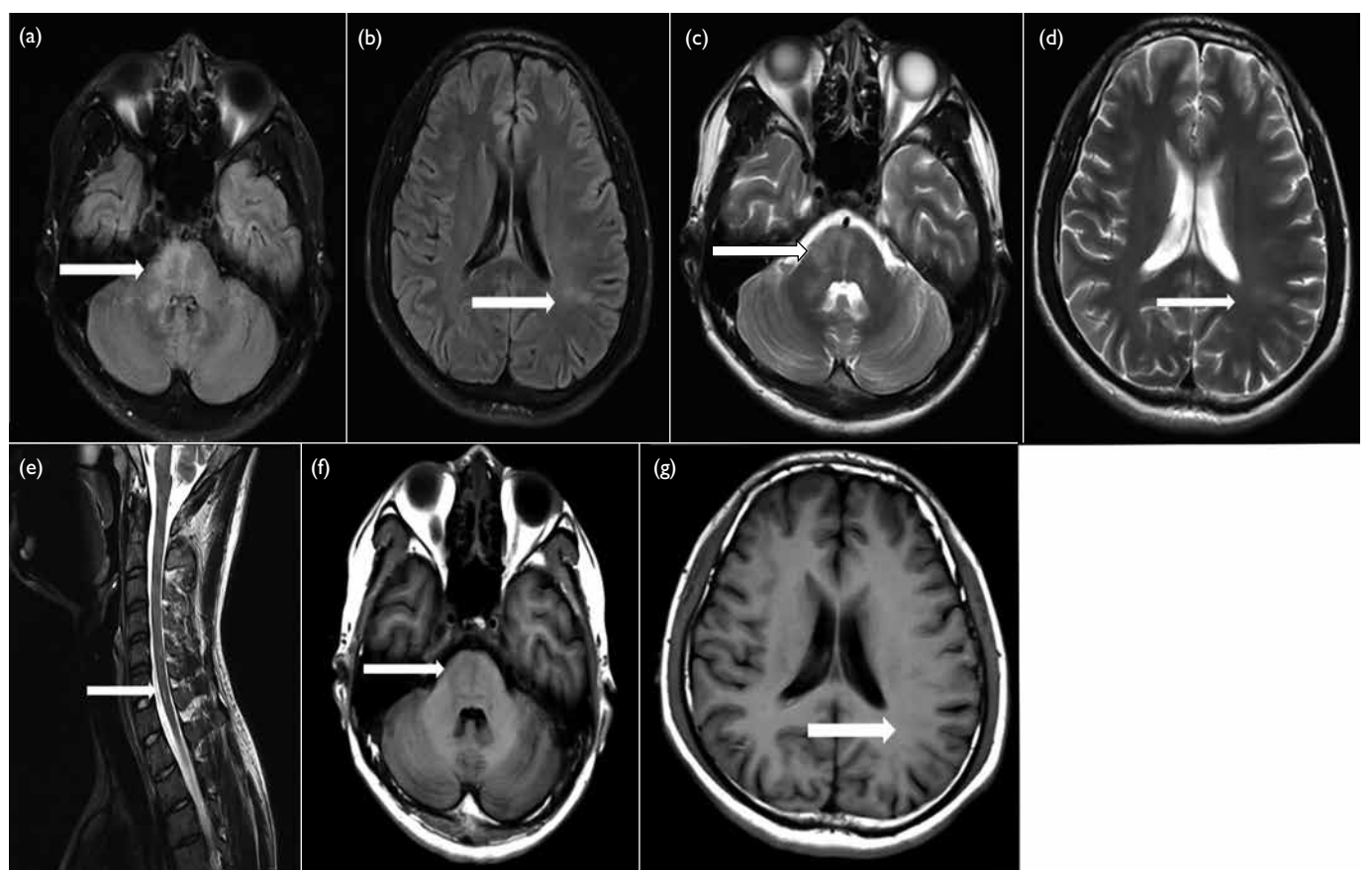


FIG. (a and b) Axial fluid attenuated inversion recovery sequence and (c and d) T2 sequence images demonstrating hyperintense signals in right brachium pontis, brainstem, and left parietal lobe (arrows). (e) T2 sequence image showing hyperintense signals from C6 to T1 (arrow). (f and g) T1 sequence images demonstrating hypointense signals in brachium pontis, brainstem, and left parietal lobe (arrows)

and MRI. The transient worsening of neurological function due to heat exposure affects the cognitive and physical functions of MS patients and affects their daily life and functional capacity. As this worsening differs to a real relapse or exacerbation of MS, it is necessary to understand this phenomenon and its pathophysiology so that suitable treatment can be administered.

Uhthoff's phenomenon is most commonly observed in individuals with MS but can also occur in those with NMOSDs.<sup>3</sup> To date, the exact mechanisms of UP have remained unclear; however they likely involve a combination of structural and physiological changes within the demyelinated axons in the central nervous system that occur in the presence of a raised core body temperature.<sup>4</sup> Factors including exercise, taking a hot bath or shower, fever, exposure to sun, menstrual cycle, psychological stress, and hot meals may worsen the symptoms in MS or NMOSD.<sup>5</sup>

A study reported UP as the first manifestation of MS in an adult male who presented with blurred vision after performing intense exercise in the fitness

room.<sup>6</sup> Another study reported three episodes of oscillopsia that occurred while a 17-year-old man participated in intense sports in summer (which was interpreted as recurrent UP); the man was finally diagnosed with radiologically isolated syndrome.<sup>7</sup> To date, no studies have reported UP as the initial symptom in individuals with NMOSDs.

The longitudinally extensive spinal cord lesions and anti-aquaporin-4 antibodies in the serum of our patient supported the diagnosis of NMOSD. Our patient first presented with dysuria after taking a hot bath and was considered a case of UP. Loss of the myelin sheath is the primary cause of UP: an elevation in the core body temperature in the context of axonal demyelination results in pore closure of voltage-gated sodium channels, thus compromising action potential depolarisation. There are a variety of heat stressors (fever, hot bath, premenstrual period, physical exercise) and clinical manifestations of UP depending on where demyelinating plaques are located.<sup>8</sup> In our patient, the rise in core body temperature during the hot bath could have aggravated the spinal lesion that

impaired the micturition centre and led to dysuria.

The patient initially visited the urology clinic and was misdiagnosed with urinary infection; due to the development of additional symptoms, he was suspected of having spinal cord lesions. Overall, urologists as well as neurologists should be aware of the phenomenon to avoid misdiagnosing diseases related to UP.

#### Author contributions

Concept or design: H Liang, C Xu.

Acquisition of data: H Liang, C Xu.

Analysis or interpretation of data: J Xu.

Drafting of the manuscript: H Liang, C Xu.

Critical revision of the manuscript for important intellectual content: J Xu.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

#### Conflicts of interest

The authors declare no conflict of interest.

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#### Ethics approval

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

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