

## CASE REPORT

# Central neurological abnormalities and multiple chemical sensitivity caused by chronic toluene exposure

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**Abstract** Multiple chemical sensitivity (MCS) is a syndrome in which multiple symptoms occur with low-level chemical exposure; whether it is an organic disease initiated by environmental exposure or a psychological disorder is still controversial. We report a 38-year-old male worker with chronic toluene exposure who developed symptoms such as palpitation, insomnia, dizziness with headache, memory impairment, euphoria while working, and depression during the weekend. Upon cessation of exposure, follow-up neurobehavioural tests, including the cognitive ability screening instrument and the mini-mental state examination, gradually improved and eventually became normal. Although no further toluene exposure was noted, non-specific symptoms reappeared whenever the subject smelled automotive exhaust fumes or paint, or visited a petrol station, followed by anxiety with sleep disturbance. During hospitalization for a toluene provocation test, there was no difference between pre-challenge and post-challenge PaCO<sub>2</sub>, PaO<sub>2</sub>, SaO<sub>2</sub> or pulmonary function tests, except some elevation of pulse rate. The clinical manifestations suggested that MCS was more relevant to psychophysiological than pathophysiological factors.

**Key words** Multiple chemical sensitivity; neurobehavioural test; provocation test; toluene.

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## Introduction

Multiple chemical sensitivity (MCS), also known as idiopathic environmental intolerance, twentieth-century disease, environmental illness and ecological illness, has several definitions and might be considered a phenomenon rather than an illness [1]. No single physiological test has been found to correlate with the

various symptoms. In 1999, consensus criteria were proposed for MCS [2], suggesting it to (i) be a chronic condition that (ii) has symptoms that recur reproducibly in response to (iii) low levels of exposure of (iv) multiple unrelated chemicals, (v) to improve or resolve when incitants are removed and (vi) to involve multiple organ systems. Although MCS had been studied extensively, a unifying mechanism to explain the pathogenesis is still obscure. Whether a psychogenic origin can separately explain all the associated symptoms is currently under debate. Here, we describe a patient who developed MCS after laboratory test-documented central neurological deficits caused by chronic toluene exposure. A toluene-specific challenge test was also performed to determine whether pathophysiological or psychophysiological factors are more important in causing the patient's symptoms.

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## Case report

A 38-year-old man worked as a glue stirrer in a shoe-making factory for almost 12 years. While working, he mixed a large amount of organic solvents with glue and stirred them into a dilute and even form. After mixing the liquid, he had to pour it into smaller containers. About 4 years before his first clinic visit to our hospital, he developed symptoms such as palpitation, insomnia, dizziness with headache, memory impairment, euphoria while working, and depression during the weekend. The patient visited our occupational medicine clinic in February 1998 because his symptoms began to interfere with his daily activities. On examination, he was found to be a well-nourished and well-developed man, with normal blood pressure (120/60 mmHg). Neurological examination revealed no focal signs, except for a mildly increased sway and a mild tremor of both hands. There was no history of trauma, head contusion, allergy, psychoneurosis, diabetes or hypertension. The patient had smoked about one pack of cigarettes per day for 15 years and consumed alcohol occasionally. His family and social history were unremarkable. He had always worked with solvents, although there were ventilation systems in the workplace and he wore personal protective equipment at times, but he reported he could always smell solvents. Environmental monitoring data were not available.

On the first clinic visit, neuropsychological tests were performed. The Chinese version of the Cognitive Ability Screening Instrument (CASI, version 2.0) [3] showed deficits in the items of abstract thinking, remote memory and recent memory, and he had a low total score. The result of the Mini-Mental State Examination (MMSE) [4] was also below the normal range of the general population [5] (see Table 1). The Wechsler Adult

Intelligence Scale—Revised (WAIS-R) revealed abnormalities in visual-motor coordination and digit span, but was otherwise normal (PIQ = 89, VIQ = 93, FIQ = 90). The Wechsler Memory Scale—Revised (WMS-R) showed defects in verbal memory (81), general memory (87) and attention/concentration (85), but normal abilities in visual memory (105) and delayed recall (93). The patient was removed from work in May 1998 and stayed at home without any formal job. He was also advised to avoid contact with any organic solvent. Upon cessation of exposure, he gradually improved, as indicated by the CASI and MMSE scores, over 31 months of follow-up (see Table 1). Subjective symptoms also improved quickly. However, despite no further chemical contact, palpitation, headache and dizziness occurred whenever he smelled automotive exhaust or paint, or visited a petrol station. As a consequence, the associated symptoms became 'conditioned' and refractory, and sometimes the patient developed symptoms while simply preparing to go to a petrol station or watching others painting. According to his clinical presentations, a temporal relationship between exposure and disease was very clear, and no other causes of such neurological damage could be identified. MCS was diagnosed, and we prescribed tranquillizers and advised him to consult a psychiatrist. At the same time, after a full explanation and agreement with informed consent, our patient was hospitalized for provocation tests with 100% toluene. We found some elevation in the pulse rate (from 80 to 100), but no other abnormal findings in his electrocardiogram, blood pressure, or respiratory rates, and no difference between pre-challenge and post-challenge PaCO<sub>2</sub>, PaO<sub>2</sub>, SaO<sub>2</sub> or pulmonary function tests. In December 1999, after medical removal and symptomatic treatment for 19 months, the patient performed neurobehavioural tests again and only mild impaired ability in attention was

**Table 1.** Scores of follow-up neurobehavioural tests (CASI and MMSE) by duration after the patient stopped exposure

|                                    | Month(s) after stopping toluene exposure |      |      |      |      |    |
|------------------------------------|--|------|------|------|------|----|
|                                    | 0  | 1    | 3    | 4    | 19   | 31 |
| Remote memory (10)                 | 9  | 10   | 10   | 10   | 10   | 10 |
| Recent memory (8.5–12)             | 6  | 5.5  | 7.5  | 9.5  | 10.5 | 9  |
| Attention (7–8)                    | 8  | 8    | 8    | 8    | 7    | 8  |
| Mental manipulation (7–10)         | 8  | 8    | 8    | 8    | 10   | 10 |
| Orientation (17–18)                | 17                                       | 18   | 18   | 18   | 18   | 18 |
| Abstract thinking (7–12)           | 6  | 8    | 7    | 9    | 9    | 10 |
| Language (9–10)                    | 10                                       | 9    | 9    | 10   | 10   | 10 |
| Drawing (9–10)                     | 10                                       | 10   | 10   | 10   | 10   | 10 |
| Verbal fluency (6–10)              | 6  | 10   | 7    | 8    | 9    | 10 |
| CASI (85.5–100)                    | 80                                       | 86.5 | 84.5 | 90.5 | 93.5 | 95 |
| MMSE (25–30)                       | 25                                       | 22   | 26   | 27   | 30   | 29 |
| Headache and insomnia <sup>a</sup> | ++++                                     | +++  | +    | +    | +    | +  |

Values in parentheses are reference data from standardized general population [5]. Italics are those below normal range.

<sup>a</sup>Subjective symptoms reported by the patient. ++++ extremely severe, +++ severe, ++ moderate.

shown. WAIS-R revealed improved and nearly normal results (PIQ = 94, VIQ = 96, FIQ = 95). He went back to work with advice to avoid organic solvent exposure and to have regular psychiatric consultation. Despite the results of the neurobehavioural tests and WAIS-R showing recovery to normal functioning, the associated symptoms, such as dizziness, headache, anxiety and insomnia, continued to bother him, especially when exposed to a number of volatile chemicals.

While the patient applied for compensation for occupational disease, the diagnosis of toluene central neuropathy with MCS became a matter of contention between the patient and his company. His conditions were later determined as work-related by the Council of Labour Affairs in June 2001. This is the first established case of work-related MCS in Taiwan.

## Discussion

Many occupational studies have described central nervous system (CNS) dysfunction as an outcome of toluene exposure [6]. Decrements in functioning have been viewed as precursors of more serious CNS effects [7]. In our patient, chronic occupational toluene exposure was present without evidence of abuse. Although the symptoms were almost subjective and not pathognomonic for the diagnosis of toluene neuropathy, abnormal objective measures in the form of neuropsychological (WAIS-R, WMS-R) and neurobehavioural tests (CASI, MMSE) were observed. Whilst these findings were not specific to organic compounds and determination of the causal agent(s) was not possible, the temporal relationship between exposure and disease was very clear, and no other causes of such neurological damage could be identified. We therefore think that his condition was toluene-induced central neuropathy. These cases often cause a diagnostic dilemma because of the lack of specific and sensitive diagnostic procedures, and the fact that these conditions may become irreversible before the diagnosis can be made [8].

Despite literature on the existence of MCS, there is no unequivocal epidemiological evidence. Some researchers consider MCS to be a misdiagnosed psychological illness and that chemical exposure should not be considered as the cause of the symptoms [9]. Others propose that MCS does exist, although the prevalence generally seemed exaggerated. In 1999, investigators found 6% of adults in California and 2% in New Mexico had been diagnosed with MCS, whereas 16% in both states said they were 'unusually sensitive to everyday chemicals' [10]. MCS could be formally diagnosed in all cases in which the consensus criteria were met and no other organic disorder could account for the associated symptoms. In our case, six criteria were fulfilled, though sometimes the symptoms reappeared 'conditionally'. Psychogenic origin

alone could not explain the whole picture because of the objective evidence in the shape of neurobehavioural tests and WAIS-R, which recovered gradually after exposure ceased.

Neuropsychological assessments, especially neurobehavioural tests, have the advantage of high sensitivity but the limitation of low specificity in central neuropathy [11]. However, they are still the best methods for detecting adverse effects of neurotoxicants on the CNS insofar as there are few available biomarkers to accurately determine exposure, except for some heavy metals. Epidemiological studies have reported decrements in attention/concentration, new learning and memory, executive/psychomotor speed, and manual dexterity in individuals exposed to organic solvents [11,12]. Our patient demonstrated memory impairment and deficits in abstract thinking, coordination and attention/concentration. Whilst these symptoms could have been caused by acute exposure to organic solvents, prolonged and disproportional neurological manifestations were seen, which could not be explained as an acute effect. Such persistently refractory and reproducible conditions strongly suggested the existence of MCS in this case.

Some reports claim that patients with MCS react directly to their trigger stimuli because of some unidentified physiological abnormalities induced by previous chemical exposure [13]. Others suggest MCS is a psychological syndrome with psychometric or psychoanalytic evidence [14]. A double-blinded, placebo-controlled challenge test was suggested in resolving the controversy. Pearson [15] found MCS patients reacted similarly to the challenge chemical and to the placebo, proving that sensitivities were subjective and probably psychosomatic. Staudenmayer *et al.* [16] also reported 20 MCS patients who reacted similarly to self-identified chemicals and to placebos. Our patient, during toluene challenge, was found to have some elevation of pulse rate but no other objective data altered. There was no evidence of hyperventilation [17], or any pulmonary function changes. He complained only of palpitation, dizziness and headache. Comparative placebo challenge therefore seemed unnecessary, and we assumed that the clinical manifestations of this patient were more relevant to psychophysiological factors than pathophysiological ones.

Management of MCS patients is not easy. Attending physicians are recommended to perform compassionate evaluation, especially for those with more distressing conditions, while avoiding the use of unproven, expensive or potentially harmful tests and treatments. Establishing an effective doctor-patient relationship is extremely important. Physicians should also encourage and support the patient's efforts to return to work and a normal family and social life.

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