

Parkinson's disease in occupational exposure to joss paper, a report of two cases

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Abstract

We report two genetically unrelated ethnic Chinese women, aged 63 and 60 years, who developed Parkinson's disease at the age of 55 and 53 years respectively. Both cases were working in the same joss paper shop for 15 years prior to the onset of Parkinson's disease. There was no family history of Parkinson's disease and exposure to other chemical or toxic agents. Biochemical analysis of joss papers revealed the presence of heavy metals such as lead, copper, zinc, and mercury, which has been implicated in the pathogenesis of Parkinson's disease. The Parkinson's disease in these two cases was attributed to occupational exposure to joss paper. Joss paper has not been associated with the development of Parkinson's disease previously.

INTRODUCTION

Joss paper is a ceremonial paper used in China and other parts of Asia. It is burned during religious ceremony to pay respect to the ancestors. It consists of thin, rough, usually rice paper, often with metallic leaf attached. There are two main types of joss paper. The first type (Figure 1) has metallic leaf in the centre of the page with orange colouring that makes the metal leaf look like gold. Printed over the leaf is a red block print with Chinese writing and patterns. The second type (Figure 2) has two pieces of metallic leaf on both sides of the page. One side has the orange colouring that makes the metal leaf look like gold. The other side is left uncoloured so that the leaf is silver in colour. Previously, joss paper commonly used in Malaysia was manufactured locally. Since 1990, with rising import from China, the local production of joss paper had ceased.

Until today, the tradition of burning joss paper is still widely practiced by the ethnic Chinese in Malaysia. Despite this, there have been no previous reports of health problems associated with joss papers in the literature. We present two genetically unrelated cases of Parkinson's disease with occupational exposure to joss paper.

CASE REPORTS

Case one and two were ethnic Chinese women, aged 63 and 60 years respectively. Both women were previously of good health. Case one started to have slowly progressive right-sided stiffness and slowness of movement in 1994, at the age of

55. Case two developed right-sided stiffness and tremor of hand in 1996, at the age of 53. Case one had one sibling, and Case two nine. Both had no parental consanguinity or family history of Parkinson's disease.

During their first presentations, physical examination revealed right-sided cogwheel rigidity and bradykinesia. Case two also had resting tremor. Their facial expression was reduced. The cognitive function such as memory and language was normal. There were no other abnormal neurological signs suggestive of parkinsonism-plus syndromes. The following investigations were negative: full blood count, serum urea and electrolytes, liver function test, VDRL (Venereal Disease Research Laboratory), serum ceruloplasmin, copper, serum complement factors, anti-nuclear factor, anti-double stranded DNA antibody and chest Xray. MR imaging study of brain in the second patient did not show any abnormality while Case one declined MR imaging.

Both patients were started on levodopa and had good clinical response at a total daily dose of 400 to 600 mg. They subsequently developed peak dose dyskinesia with choreoathetosis involving cervical and limbs muscles, wearing-off phenomenon and early morning foot dystonia after being treated with levodopa for eight and six years respectively. In 2002, Case two underwent bilateral deep brain stimulation of subthalamic nuclei with significant symptomatic improvement, with increased "on" period and reduction in dyskinesia. Her total daily requirement of levodopa was also reduced by about 60%.

Case one and two had been working in a joss paper shop since 1974, and were both wives of the shop owner. Their work involved selling joss papers and joss sticks that were supplied by local manufacturers. Whereas the joss sticks were sealed with plastic coverings, the joss papers were usually sold in bundles without wrappings. There were two other workers in the shop, but only Cases one and two were directly handling the joss papers. Other than the joss papers, both patients were not exposed to other chemical or toxic agents. In 1988, they stopped working with the joss paper when the shop closed down for economical reasons. The other two workers remained healthy till to date.

Samples of joss papers available at a joss paper shop, which were imported from China was sent for chemical analysis by the Standard and Industrial Research Institute of Malaysia Limited (SIRIM) laboratory. The metallic contents of the metallic leaves of both types of joss paper, Specimen A (Figure 1) and Specimen B (Figure 2) were analysed. The laboratory techniques used were: Flameless Atomic Absorption Spectroscopy for determination of mercury, and Inductively Coupled Plasma Optical Emission Spectroscopy for determination of arsenic, cadmium, copper, lead, selenium, tin and zinc. As the standard reference for the level of heavy metals in joss papers was not available, the results of the chemical analysis were compared with that recommendation from the SIRIM¹ as shown on Table 1. The concentration of lead in the joss paper Specimen A was found to exceed the maximum level allowed by the SIRIM. Tin,

copper, zinc, arsenic, and other heavy metals were also found in the joss papers.

DISCUSSION

We described two patients with Parkinson's disease who had previous occupational exposure to joss papers. The typical neurological presentation, good response to levodopa and development of motor complications fulfilled the UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria for definite PD.² The levodopa-induced choreoathetosis was seen in 40% of patients after five years of therapy.³ The good response of the Case two to bilateral deep brain stimulation of subthalamic nuclei, with improvement in "on" period and dyskinesia, reduction of total daily levodopa requirement, was also similar to previous report.⁴

Parkinson's disease is believed to be the result of the interplay between genetic and environmental factors, with the relative contribution of each factor varying from one individual to another.⁵ In the present case report, genetic factor was probably not the dominant cause of their Parkinson's disease. Firstly, there was no family history of overt Parkinson's disease, particularly in Case two, who had nine siblings. Secondly, both cases were of late-onset PD, at 55 and 53 years. The mean age of onset of previously reported Malaysian case series of Parkinson's disease was 57 years.⁶ It has been known that it is the young onset Parkinson's disease with age of onset less than 40 years where genetic factor is more likely to play a dominant role.⁷ Cases one

Table 1: Comparison of results of biochemical analysis of joss paper specimens with Recommended safety limit from SIRIM, 1998.

	Concentration (microgram / gram)		
	Joss paper Specimen A	Joss paper Specimen B	Recommended safety limits of element for modelling clay and finger paint
Arsenic	1.40	0.46	25.00
Cadmium	0.10	< 0.003	50.00
Copper	8.34	1.24	not available
Lead	320.81	0.58	90.00
Selenium	0.36	< 0.01	500.00
Tin	488.26	28.88	not available
Zinc	3.42	3.94	not available
Mercury	0.02	< 0.01	25.00



Figure 1. Joss paper Specimen A



Figure 2. Joss paper Specimen B

and two, though both were wives of the same man, were not genetically related.

We believe the joss papers were the critical causative environmental factor causing the Parkinson's disease in our patients. Both cases were working with joss paper for 15 years, a long period of exposure. Among the four workers in the same shop, both workers handling the joss papers directly developed the disease whereas the other two workers who did not handle joss papers remained well. Our patients had no exposure to other known chemical or toxic agents. Among the heavy metals found to be present in the joss papers analysed, lead^{8,9}, copper^{8,9}, zinc⁸, and mercury⁸⁻¹⁰ have been implicated in the pathogenesis of Parkinson's disease, with lead in excessive amount in one of the sample tested. Iron¹¹ and manganese^{8,12} were not analysed in our patients. The substantia nigra in Parkinson's disease is oxidatively stressed¹³ and heavy metals have been suggested to be the promoters of this biochemical process by means of free radical generation.¹⁴ In addition, in vitro study has shown that heavy metals could increase the folding of α -synuclein fibrils¹⁵, the major component of Lewy

bodies.¹⁶ Another study found that heavy metals might act alone or together in the causation of the PD.¹⁷ The heavy metals can be absorbed into the body system through inhalation, oral ingestion and skin contact.¹⁸

Due to the time delay between exposure to heavy metals and clinical manifestation of Parkinson's disease, chemical screening to confirm the excessive presence of heavy metals in the patients was not possible. Chemical analysis of the actual joss papers that the patients were exposed to was also not done, as local production of joss papers had ceased since 1990. The joss papers analysed were those imported from China. The metallic content of the locally manufactured and imported joss papers may be different. Studies of environmental risk factors for a disease with long latency period such as Parkinson's disease are often difficult. This is because exposure to certain environmental factors may occur before the onset of clinical manifestations and remain unrecognised.

It is also possible that there are other unidentified environmental factors, which had acted together with the heavy metals in joss paper in triggering Parkinson's disease in our patients ("the second hit hypothesis"). The first exposure to the putative environmental neurotoxin might have damaged only a small proportion of nigrostriatal neurons, leading to a decline in dopaminergic function that was not severe enough to be clinically manifested. The second exposure to environmental neurotoxin (joss paper) could have accelerated the decline in dopaminergic function: "the second hit", leading to the appearance of clinical symptoms. In other words, the joss paper exposure could have brought forward the onset of Parkinson's disease in these two patients, who might have been likely to develop the condition in any case at a later date. It has been hypothesized that combinations of environmental factors may result in more severe nigrostriatal injury, leading to development of Parkinson's disease.¹⁹ In animal experiment, it had been shown that in the presence of Diethyldithiocarbamate, a normally nontoxic dose of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) caused nigral cell loss and dopamine depletion.²⁰

Our two patients developed typical Parkinson's disease following joss paper exposure. They were clearly different from another form of neurological syndrome that occurred following exposure to very high levels of heavy metal exposure. For example, chronic manganese intoxication in

welders resulted in a parkinsonian syndrome (manganism), which differed from Parkinson's disease in several aspects: clearer temporal relationship between the symptom onset and exposure, rapid progression, levodopa unresponsiveness, absence of reduction in fluorodopa reuptake on Positron Emission Tomography and possible resolution of symptoms by stopping the exposure to the toxin.²¹⁻²²

In view of the common practice of burning joss papers among the Chinese community in Asia, there should be greater awareness of the potential occupational hazards of selling joss papers. Chemical analysis for heavy metals in the commonly used joss papers, and systematic health survey and chemical screening of workers with long exposure to joss paper may shed further light on the hazards of joss papers.

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