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Case Report

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Occupational and Environmental Exposure to Phthalates as a Problem of Modern Society

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Summary

Nowadays people come into contact with various chemical substances contained in numerous products. These include phthalates, commonly used for instance in cosmetics, paint, and paint thinners. This paper presents a case of a 37-year-old male patient who suffered from very severe nervous system damage with tetraparesis after having used a paint thinner containing diisononyl phthalate at work for more than ten years. Brain MRI revealed scattered focal lesions in both cerebral hemispheres, typical of cytotoxic oedema. A follow-up examination conducted after 2 years showed persistent lesions and more severe cortical atrophies. Decreased cognitive function and operating memory disturbances were also observed in the patient. His mental processes display features of sluggishness and lack flexibility. Clinical presentation of the patient indicates severe nervous system damage in long-term contact with phthalates.

Key words: *Phthalates; Nervous system damage*

Introduction

Nowadays human life is connected with coming into contact with various chemical substances contained in numerous products. Their safe use depends on the type and concentration of compounds contained in them, including phthalates. Phthalates are organic compounds present in many commonly used products, such as cosmetics, toys, food wrap, paint, varnish, and thinners. They are widely used in the production of plastic and lubricants and are found in thinners.

Phthalates are present in plasticisers added to paint and thinners commonly used in the production and repair of technical equipment.

In 2005 the European Parliament (Directive 2005/EC) banned manufacturing and distribution of toys and cosmetics for children containing certain phthalates. However, there are no legal regulations concerning the use of phthalates in products for adults. There is no obligation to list these substances among ingredients on the packaging. Consequently, consumers do not know whether a given product contains phthalates or not. These compounds are easily absorbed into the body and after a prolonged exposure may cause a number of health problems.

Aim of the study

To present diagnostic difficulties and problems in treatment of a patient with nervous system damage in phthalate poisoning.

Case Description

A 37-year-old male patient with tetraparesis and speech disturbances (aphasia), having scattered lesions of unknown aetiology in the central nervous system, was admitted to the Department of Rehabilitation of the Military Medical Institute in Warsaw in August 2011 to undergo rehabilitation.

First manifestations of the disease were observed in November 2010 when speech disturbances and limb strength decreases appeared. At the time the patient was diagnosed and treated at the Department of Neurology and Department of Oncology of the Regional Hospital and then at the Nervous System Cancer Department at the Cancer Centre in Warsaw. Numerous lesions in both cerebral hemispheres were found in the patient during the stay. Stereotactic biopsy results did not indicate the presence of neoplastic cells. As regards the aetiology, tests for bacteria, fungi, toxoplasmosis, toxocariasis, and cysticercosis gave negative results. Other diseases were excluded: vasculitis, sarcoidosis, granulomatosis with polyangiitis, and tuberculosis. Carotid and vertebral arteries were patent with smooth wall outlines and the blood flow was normal. Treatment with steroids resulted in very severe complications: sepsis, respiratory failure in bilateral pneumonia, which required the use of a ventilator, and steroid-induced diabetes. The patient was treated for many months at various hospital departments.

On admission to the Department of Rehabilitation, 10 months after first manifestations of the disease appeared, the following was observed: moon face and muscle atrophies, especially in forearms, arms, and shins (typical of Cushing's syndrome). Neurological examination revealed abnormalities; the patient was oriented to time and person, had speech disturbances (aphasia), slight horizontal-rotational nystagmus when looking to the left, anisocoria (R>L), central paresis of nerve VII on the right, and slurred speech. He suffered from tetraparesis with decreased muscle tone in the upper limbs: the score of the left limb was 3 points and of the right limb – 2 points on Lovett scale. As regards the lower limbs, there was abnormal flexion in the hip and knee joints as well as abnormal plantar flexion and extension of the feet. The score was 1 point on Lovett scale on both sides and there were weak reflexes in the triceps on the left. There were no other tendon and periosteal reflexes, no plantar reflexes, and Babinski's sign was observed on the right. The patient was immobilised and required help in the activities of daily living.

Accessory investigations included magnetic resonance imaging conducted on 21 March 2011 by Dr. Ewa Skrobowska (Figure 1).

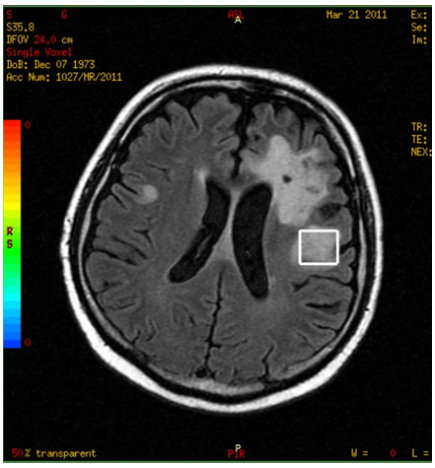

Figure 1: *Brain MRI (21 March 2011).*

The scan revealed abnormal focal lesions in both cerebral hemispheres with intensified and coalescent lesions in the left frontal lobe. The lesions were hyperintense on T2-weighted and FLAIR images. Diffusion-weighted imaging showed that central parts of the lesions were hypointense while the oedema around the lesions was hyperintense, which is typical of cytotoxic oedema. There was a biopsy scar in the left frontal lobe. The ventricular system had no widenings and dislocations. Pericerebral fluid collections and the other structures were normal.

Laboratory data reveal no significant changes, except for abnormalities observed in the period of severe complications.

Taking into consideration the history which indicates that the patient worked for more than ten years in equipment repair where he used a cleaning and maintenance fluid with which he came into direct contact through the skin and airway system for several hours every day, samples of the fluid used by the patient were tested. The laboratory test was conducted at the Department of Forensic Toxicology of the Institute of Forensic Research in Cracow (head – Prof. Maria Kała, Dr habil.). As a result of chemical and toxicological examination of the material received in the form of colourless liquid, the following substances were found: ethyl alcohol (concentration – 95.7%) and compounds used as additives (so-called plasticisers) in the process of plastic manufacturing, mainly diisononyl phthalate (DINP).

Diisononyl phthalate is a substance used in the production of coatings, printing ink, paint, glues, polymers, lubricants, and for diluting organic peroxides. It is also used during the production of phthalate paint, laminates, synthetic gum arabic, PVC, and as a thinner for cleaning systems.

In the body it is metabolised to monosteres and partially to alcohol. The end product is phthalic acid. It should not be used as a substance with a concentration greater than 0.1% in terms of weight with respect to the plasticised material in toys and in conditioning products for children.

This chemical substance is not classified as dangerous, according to Annex I to Directive 67/548/EEC. In order to secure the substance in a workplace it is recommended to maintain proper airing of the room and use individual means of protection, such as protective glasses, gloves, and shoes. Persons who use the product must be periodically trained and taught about its dangerous features.

In 2011 and 2012, during the stays at the Department of Rehabilitation of the Military Medical Institute, each stay lasting several weeks, the patient underwent comprehensive physical therapy and rehabilitation adjusted to his needs and abilities. It included low frequency magnetic field therapy, laser therapy, muscle electric stimulation, massage, individual rehabilitation, occupational therapy, and neurophysiological therapy. The aim of physical therapy was to achieve independence, active sitting, strengthening of the trunk and limb muscles, vertical positioning in a vertical stander, and improved cardiovascular and respiratory performance.

Speech disturbances affected mostly language and had the form of amnesic aphasia. According to the Goodglass and Kaplan scale score, intensity of the deficits was 3. Therapy concerned language functions and the improvement of communication skills.

A follow-up MRI scan of the head (Figure. 2) revealed:

The examination conducted in three planes using SE and TSE sequences, T1-, T2-weighted and FLAIR images, and DWI+ADC as well as T1-weighted images with intravenous contrast administration revealed status post stereotactic biopsy in the left frontal area. Single hyperintense focal lesions of a vascular character were found in the white matter of both cerebral hemispheres on T2-weighted and FLAIR images. No new lesions were found. The corpus callosum was hyperintense. Several small hyperintense lesions were revealed on T2-weighted and FLAIR images in cerebellar hemispheres and peduncles. No abnormal enhancement was seen after intravenous contrast administration. There were cortical atrophies. (Dr. Radosław Maciak)

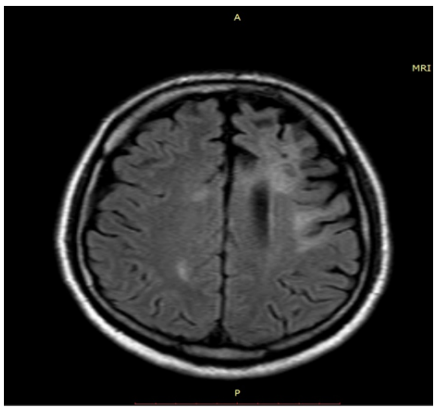

Figure 2: *MRI (7 February 2013).*

Out-patient physical therapy and rehabilitation has been continued up to now. Between November 2010 and October 2013, the patient did not come into contact with phthalates.

The patient's condition was assessed by a follow-up examination on 7 October 2013. The patient was verbally responsive and oriented, there were no meningeal signs, and there was slight facial nerve damage. The patient moved with support on both sides. He spoke more slowly and his cognitive functions were visibly slower. The functions of visual analyser were partially disturbed. Muscle strength disturbances were observed. Limb movements were slower and the spatial movement organisation was disturbed. Disturbances of working (short-time) and visual memory were visible and results of tests assessing semantic memory were low. The patient's mental processes displayed features of sluggishness and lacked flexibility. When attempting to walk without the support, the patient was very unsure and suffered from dizziness.

Discussion

The abnormalities identified during physical examination and history-taking are connected with prolonged toxic central nervous system damage caused by phthalates contained in the fluid which the patient used for many years in his professional work. However, phthalates are present all around us. They are used in the production of creams, body lotions, moisturising lotions, nail polish, hairspray, and perfumes. Thanks to them the product effectively adheres to the body, remaining on the skin over a longer period of time, and its scent is long-lasting. Phthalates prevent stiffness and peeling off of the product and enhance its flexibility, transparency, and durability.

These compounds penetrate the body through the oral cavity, airway system, and skin. Most people in Europe and on other continents are not aware of the fact that phthalates are so common in so many everyday use products, such as soap, tinned food, receipts on thermal paper, and plastic packagings. The largest number of phthalates is absorbed with food as these substances are used in polyvinyl chloride which comes into contact with food during its processing, packaging, storing, and heating. Individual works indicate that these substances have a negative influence on the human body. In 90% of an American study population these compounds were found in urine. Andrea Canning, who decided to test her and her daughters' urine while eating available food, found high levels of phthalates in her study. After they stopped using products which might contain these compounds, follow-up tests revealed a decrease in phthalate levels in the body. When she again started eating traditional food, including microwave-heated meals and tinned food, and using traditional cosmetics and cleaners, follow-up tests once again showed a high increase in phthalate levels.

Dr Emilie Rissman, a professor of biochemistry and molecular genetics at the University of Virginia, observed anxiety states caused by phthalates in laboratory animals (mice and rats).

A group of scientists from Rochester conducted studies which indicate that these chemicals may be responsible for disturbances in the development of sexual organs in boys as well as for reducing pregnancy duration. The scientists found that children of mothers whose blood contained higher levels of phthalates were at a greater risk. The changes observed included reduced size of sexual organs and their displacement towards the anus. The changes were triggered when the number of phthalates was not very large. They were observed at a level which can be found in 25% of the American population. Professor Shanna Swan, who is the head of a group of scientists from the Centre for Reproductive Epidemiology at the University of Rochester School of Medicine, found that even a small representative sample showed an influence of phthalates on children's bodies. Studies conducted by Prof. Sharpe from Edinburgh confirm that phthalates may have a negative influence on the production of the male hormone testosterone, which is absolutely indispensable for normal development of all characteristics differentiating men from women, which takes place before birth.

The observations described in this paper, concerning a 37-year-old male patient, show that during almost 3 years following the occurrence of first manifestations of the disease, after preventing the patient from having further contact with phthalates and despite complications having such dramatic course, it was possible to improve the health status of the patient. The patient moves with difficulty, but unassisted; however, central nervous system damage is so extensive that examinations indicate abnormalities, mental processes lack flexibility, and MRI of the brain reveals cortical atrophies.

How to avoid phthalates when they are so widespread and manufacturers have no obligation to inform consumers whether or not a given product contains them? It is recommended to avoid plastic when possible and choose natural materials, such as glass, metal, and wood.

This problem is very significant and concerns all of us. It is necessary to start interdisciplinary studies in this field as the patient described suffered tragic consequences of being exposed to phthalates. This should be seen as a warning to the contemporary society.

Conclusions

Phthalates may cause severe nervous system damage. It is in the interests of people all over the world to act on the urgent need to start interdisciplinary studies concerning the influence of phthalates on the human body and promote healthy behaviour in this respect.

Author contributions: According to the order of the Authorship

Conflicts of interest: The Authors declare no conflict of interest.