Short report

Repeated facial palsies after chlorocresol inhalation

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SUMMARY A 42-year-old woman who experienced more than 50 attacks of left-sided facial palsies after exposure to chlorocresol was studied. Only muscles around the left side of the mouth were affected. On neurophysiological testing during chlorocresol provocation the only abnormality was a loss of motor units during maximal contraction of the left orbicularis oris muscle. This could be explained by a peripheral as well as a central effect. Extensive electrophysiological examination without chlorocresol provocation excluded a preexisting generalised nerve disorder and other diagnostic procedures did not give evidence of pathology involving the left facial nerve. A hyperreactive mechanism causing a transient block of the left facial nerve is proposed.

Neurotoxicity due to occupational exposure to chemicals can be ascribed to two main categories: (1) the diffuse cerebral damage related to carbon disulphide¹ and other organic solvents,² and (2) the polyneuropathy caused by acrylamide,³ hexacarbone^{4,5} etc. Only rarely has more selective nervous system affection been reported, such as multiple cranial nerve palsies, mainly of the fifth nerve^{6,7} after exposure to trichloroethylene. We describe a case of relapsing left-sided facial palsy associated with occupational exposure to chlorocresol.

Case report

The patient, a right-handed 42-year-old woman was referred because of recurring left-sided facial palsy. During the last 6 months of her 5 years employment at the sterilising department of a large pharmacy she had about 50 episodes of left-sided facial palsy. These episodes lasted from 15 minutes to 3 hours and were usually preceded by a feeling of pins and needles in the left side of the face. During and after an attack she felt unwell with a slight headache. All attacks were similar to each other and most occurred at work. It was eventually discovered that a slightly raised air concentration of chlorocresol evoked an attack. She also noticed that fresh air outside stopped the attack within 15 minutes. Only three

attacks occurred when not at work. One was in a supermarket, another half an hour after swallowing a tablet of pondocillin, and a third at home when a colleague wearing her work clothes came straight from work to see her. For the last two months she had noticed a slight feeling like pins and needles in her left arm. On examination a diminished sensibility to touch and pin-prick was found in the left side of her face and neck. The rest of the neurological examination was normal. In particular, there was no facial weakness. The general physical examination was also normal.

The effect of exposure to chlorocresol was studied. A few drops of a 0.1% concentration of chlorocresol diluted in water was poured into a sink, the cold tap was turned on to ensure a water born aerosol and the patient was placed near the sink. After approximately 3 minutes a partial left-sided

Fig Before and after a chlorocresol provocation test showing a partial left-sided facial palsy.

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Received 4 February 1986.

Accepted 24 March 1986

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facial palsy occurred preceded by a feeling of pins and needles in the left cheek and temporal region. The weakness only affected the left orbicularis oris which was severely paretic. The philtrum was pulled 3–5 mm to the right (fig). There was no weakness of eye closure nor of the musculature of the forehead. The tear production of the left eye was unaffected. The rest of the neurological examination remained normal. After half an hour the facial palsy gradually resolved. We repeated the provocation test with chlorocresol three times in connection with various diagnostic procedures. The clinical result of all these tests was identical: a partial left-sided facial palsy affecting the mouth. The EMG of the paretic left orbicularis oris showed a severe reduction of motor unit potentials at maximal effort. There were no signs of denervation and the mean duration of 22 motor unit potentials was normal. EMG of the right orbicularis oris was normal. The latency of the normal muscle action potentials of the orbicularis oris evoked after stimulation of the facial nerve at the stylomastoid foramen on the left and right, was normal. Without provocation with chlorocresol the following neurophysiological examinations were normal: nerve conduction studies of the median and tibial nerves, quantitative EMG of the left and right orbicularis oris, frontalis and quadratus labii inferioris muscles, latency to frontalis and quadratus labii inferioris after supramaximal stimulation of the right and left facial nerve just below the stylomastoid foramen, muscle action potentials of the above mentioned muscles, blink reflexes, vibratory threshold (biotesiometry), VEPs and SEPs along the median and tibial nerves. The otoneurological examination before chlorocresol provocation was normal including hearing and vestibulocaloric examination. The stapedius reflex was normal before and during provocation. Gustatory testing was not carried out.

The sterile department where the patient worked consisted of two rooms located at the centre of a large pharmacy building. She carried out preparation of drugs that had to be bottled under sterile precautions. After having experienced a number of facial palsies while at work in the sterile rooms, she noticed that the palsy occurred every time she poured water on a filter for preparation of ampoules containing heparin and chlorocresol. She then tried to expose herself to heparin and chlorocresol separately, and discovered that only exposure to chlorocresol provoked the facial palsy. No other employees at work had experienced any facial or other nerve palsies.

A skin prick test with a standard allergen panel showed no positive reactions. Moreover, the serum concentrations of the immunoglobulins IgA, G, M, E and blood eosinophils were normal. An *in vitro* leucocyte stimulation test with chlorocresol was negative.

A CT scan of the skull, tomography of the facial canals and routine laboratory tests including liver function tests were normal. Measurement of the air concentration of chlorocresol at her work was not carried out.

At follow-up one year after presentation, during which time she had not worked, there had only been two facial palsies both when she passed a phenoxy-producing chemical factory by car. The air concentration of chlorocresol outside this chemical factory varied from 100 to 300 ng/m³ (Mr Hans Rolskov, personal communication).

Discussion

Chlorocresol (4-chloro-3-methylphenol) is an organic substance which is crystalline at room temperature. It dissolves in water, fat and organic solvents and volatilises with steam with a characteristic odour. Its use in medicine is basically determined by its antiseptic properties. As such it is commonly used in heparin solutions,⁸ in electrode paste and in various creams used in dermatology and general skin care.⁹ The neurolytic effect of chlorocresol is utilised either alone or in combination with phenol as a nerve blocking agent.¹⁰ The anaesthetic effect usually lasts 2–4 months.¹⁰ Whereas the pharmacological and physiological effects of phenol are well studied little is known about chlorocresol. However, the basic chemical structure of phenol and chlorocresol is similar, and both have the same neurolytic and antiseptic effect. Previously reported side effects of chlorocresol includes contact dermatitis.^{9,11} To our knowledge neurological side effects of chlorocresol have not been reported in the past. The repeated provocation tests undertaken in our patient showed an obvious connection between the development of the facial palsy and exposure to chlorocresol. The patient seemed to be sensitive to very small air concentrations of chlorocresol. We did not attempt to define the lower amount of chlorocresol which could cause a facial palsy, but air analysis in the vicinity of the phenoxy producing plant, which the patient passed in her car, showed very low concentrations.

The fact that no colleagues at her work nor persons in contact with chlorocresol during the provocation tests developed any symptoms or signs of neurological dysfunction suggests the particular hyper-reactivity to chlorocresol in our patient.

The transient nature of the palsy made it difficult to localise the lesion exactly. As the facial palsy was partial, only affecting the mouth one may think of a central facial palsy. Further, the attacks were preceded by left-sided facial paraesthesias slightly extending outside the trigeminal territory down the neck, they were accompanied by headache and for some months there had been slight paraesthesias of the left leg and arm. However the possibility of a cortical lesion was not supported by the normal CT scan of the brain nor the normal EEG during a chlorocresol provocation test resulting in a typical facial palsy. Nevertheless, an affection localised to the brain stem or subcortically cannot be ruled out by the results of these tests. A partial peripheral facial palsy only affecting nerve fibres to the muscles around the mouth is another possibility. The reduction of motor unit potentials in the left orbicularis oris during the provocation test can be explained by a lower motor neuron as well as by a central affection.

The normal distal motor latency found to the left orbicularis oris does not exclude a peripheral lesion. A partial conduction block does not necessarily result in slowing of nerve conduction velocity or, if so, the block could be proximal to the stimulation site (that is, the facial canal or the intracranial portion of the facial nerve).

The normal electrophysiological examination in the left and right facial nerves when repeated 3 months later (without chlorocresol provocation) as well as the normal nerve conduction in the extremities exclude a more generalised nerve affection.

It is of interest that Schaumburg *et al*¹² in 1970 in experimental animal studies showed that low doses of phenol, a compound with a basic chemical structure similar to chlorocresol, caused a transient nerve conduction block without slowing of velocity. The conduction block followed within 5 minutes of application and recovery occurred within 10 minutes to 30 days depending on the dose used and the duration of the exposure. Nathan and Sears^{13,14} showed in experimental animal studies that phenol solutions block the conduction in nerve fibres like local anaesthetics. Recovery of conduction occurred within 20 minutes when the phenol solutions were washed away.¹⁵ Stronger phenol solutions applied to the nerve roots for longer time led to permanent fibre destruction. In a study on man intrathecal injections of phenol caused fibre degeneration in nerve roots and not in the ganglia or the spinal cord.¹⁶

There are a few reports of cranial nerve palsies (mainly fifth nerve) after industrial trichloroethylene intoxication.^{6,7} In one necropsy study severe myelin and axon degeneration was seen in the brain stem in the fifth nerve nuclei, spinal tracts and nerve roots.⁶ Trichloroethylene used in industry as a degreasing agent may contain small amounts of cresol.⁷ The special predilection that trichloroethylene has for the trigeminal nerve has been used therapeutically in patients with trigeminal neuralgia.¹⁷

Patients suffering from recurrent cranial nerve palsies were reported by Symonds¹⁸ and Steele and Vasuvat.¹⁹ However, the clinical picture in these patients was quite different from that in our case. Often the nerve palsies were multiple, they persisted for weeks or months, and only few relapses occurred. Some were related to tuberculosis, sarcoidosis or other granulomatosis like states, such as the Tolosa-Hunt-Syndrome. An external toxic aetiology seemed unlikely in any of these patients.

In conclusion we have reported a case of several facial palsies after exposure to chlorocresol. We find it most likely that the nerve palsies were due to an extreme pharmacological sensitivity causing a transient nerve block similar to transient nerve blocks evoked by phenol administration in low doses. However, it is still unanswered why the possible hyper-reactivity had such a localised and stereotyped manifestation.

We thank Dr Claus Peter Barfoed and Dr Vagn Andersen for performing otoneurological and allergic examinations, respectively. We also thank Mr Hans Rolskov who provided information about air measurements outside the chemical factory.

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