Cerebellar Atrophy as a Delayed Manifestation of Chronic Carbon Disulfide Poisoning

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Abstract: A 70-year-old man developed a slowly progressive cerebellar syndrome after having been exposed to carbon disulfide (CS2) in a viscose rayon plant for 27 years. Ataxia, dysmetria, dysarthria and adiadochokinesia appeared 7 years after retirement from work (at age 54), and were later accompanied by cognitive deterioration, dysmnesia, spatio-temporal disorientation, emotional lability, and paranoid-obsessive disturbances. Brain computed tomography (CT) and magnetic resonance imaging (MRI) showed advanced global cerebellar atrophy, and a picture of less severe cerebrocortical atrophy. The case illustrates the possibility of chronic toxic encephalopathy among patients with previous long-term exposure to CS2. In such instances, cerebellar damage may develop as an exceptional, delayed manifestation of neurotoxicity: brain imaging techniques can significantly contribute to the diagnosis and follow-up, in addition to occupational anamnesis and neuropsychiatric evaluation. The patient presented also serves as a reminder that neurodegenerative disorders of apparently unknown origin sometimes derive from occupational toxic exposures suffered in the past. The clinical manifestations may appear several years after retirement from work, when the effects of toxic damage combine with age-related neuronal loss to overcome the brain functional reserve.

Key words: Carbon disulfide, Cerebellum, Neurotoxicity, Neuroimaging, Occupational disease, Viscose rayon

Carbon disulfide (CS2) has been extensively employed as an industrial solvent and reagent since the early 19th century. Nowadays, the compound is utilised in the production of rayon and cellophane from wood pulp (viscose process) and, to a smaller extent, in the pesticide and chemical industries1). CS2 is a systemic toxicant, and a wide range of adverse health effects (including neuropsychiatric, cardiovascular, ocular, gastrointestinal, endocrine, and reproductive disorders) has been observed in exposed workers2–4). The nervous system (both peripheral and central) represents the main target for CS2 toxicity: clinical manifestations of occupational poisoning (resulting from chronic exposure) include polyneuropathy, cranial neuropathy, mental deterioration, pseudobulbar palsy, and movement disorders, both in the form of pyramidal (hemiplegia) and extrapyramidal (parkinsonism, choreoathetosis) syndromes2–4). Cerebellar involvement has been described in very few cases5–8).

Thanks to the improvement of workplace hygienic conditions, overt CS2 neurotoxicity is encountered exceptionally in the current clinical practice. As a consequence, CS2-induced encephalopathy has been investigated only sporadically with modern neuroimaging diagnostic techniques, such as brain computed tomography (CT) and brain magnetic resonance imaging (MRI).

We report the clinical and neuroimaging findings of a case of occupational CS2 poisoning evolving with severe cerebellar atrophy.

The patient is a 70-year-old man, who had been employed
in a viscose rayon plant from age 20 to age 47 (1951–1978). He had been occupied in the churn room (viscose preparation) for 5 years, and in the bleaching department for 13 years. During the last period of employment (9 years), he worked as a deliveryman. Most of the time, this job was also carried out in areas contaminated with CS₂. Personal exposure data are not available. During the ‘70s, measured CS₂ air levels from the factory ranged from 10 to 60 mg/m³ (3–19 ppm)\(^9\). The patient occasionally abused of alcoholic beverages and was a lifelong smoker (10–20 cigarettes/day).

The subject was first hospitalized at age 44 with clinical and electromyographic findings indicative of mild peripheral polyneuropathy. He also presented cephalea, loss of libido, and gastroduodenitis. Chronic CS₂ poisoning was suspected, and the patient was referred to the Italian Institute for Insurance against Work Accidents (INAIL), which recognized the occupational origin of the disease. The peripheral neuropathy eventually recovered, however the patient returned to hospital at age 47 (the same year of retirement from work), due to the appearance of a mild and transitory right pyramidal syndrome, accompanied by vertigo, impotentia coeundi, and chronic dyspepsia.

A slowly progressive cerebellar syndrome (presenting with ataxia, dysmetria, dysarthria, and adiadochokinesia) developed starting from age 54. A brain CT (performed at age 55) revealed cerebellar atrophy with dilation of the fourth ventricle. The motor, balance and coordination disturbances worsened in the following years, and the patient developed a neurogenic bladder, complicated by an episode of acute urinary retention (age 63).

Currently (age 70), the patient is almost unable to walk and lives on a wheelchair continuously assisted by his wife. Recent neuropsychiatric evaluation showed further worsening of the cerebellar syndrome, as well as cognitive deterioration (total MODA score: 53/100), severe dysnesia, spatio-temporal disorientation, emotional lability, and paranoid-obsessive disturbances. Brain CT and MRI (Fig. 1) demonstrated advanced global cerebellar atrophy with marked dilation of the vermian and pericerebellar liquoral spaces, as well as a picture of less severe cerebrocortical atrophy. Echographic examination of the cardiovascular system was unremarkable, with the exception of a small (maximum diameter: 23 mm) aneurisma of the abdominal aorta.

In viscose rayon manufacturing, CS₂ reacts with alkali cellulose to form cellulose xanthate. Subsequent steps include filtration, spinning, washing, bleaching, drying, and packing. Workers may be exposed to CS₂ during all phases of the industrial process\(^3\). The subject described had been employed for several years in both viscose making and bleaching, that is in the departments which have been historically associated with the highest number of Italian occupational poisoning cases\(^3\). Most of his clinical features (i.e., cephalea, vertigo, peripheral neuropathy, hemiparesis, mental deterioration, digestive and genitourinary disturbances) are also consistent with previous reports\(^2\text{--}^4\). Cerebellar damage, however, has

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**Fig. 1.** Representative magnetic resonance scans showing diffuse atrophy of the cerebellum and, to a lesser extent, of the cerebral cortex.
Ethanol is notoriously neurotoxic, and both cerebral and cerebellar atrophy have been documented in chronic alcoholics\(^\text{15}\). Experimental studies indicate that CS\(_2\) and ethanol combined affect the nervous system to a greater extent than each of these compounds alone\(^\text{16}\). The subject described presents a history of occasional alcohol abuse. To which extent such drinking habit acted synergistically with the occupational exposure to CS\(_2\), influencing the development of the encephalopathy and the predominance of cerebellar damage, is difficult to determine. A strong influence seems unlikely since, with the exception of the transitory polyneuropathy suffered at age 44, the patient did not develop other medical conditions possibly related to ethanol consumption (e.g., nutritional disorders, anemia, hepatopathy).

The clinical picture of chronic CS\(_2\) poisoning may worsen after cessation of the exposure\(^2, 3\). Accordingly, both in the patient described by Frumkin\(^\text{8}\) and in the present case, the cerebellar syndrome appeared after retirement from work and subsequently progressed. The subject followed by us also developed cerebrocortical atrophy and cognitive deterioration, configuring a picture of diffuse encephalic degeneration. This is noteworthy, since there is controversial evidence that occupational chemical exposure participate in the etiopathogenesis of some neurodegenerative disorders (e.g., Alzheimer’s disease) which are usually labelled as “idiopathic”\(^\text{17}\). It has been postulated that some neurotoxic insults may not be reflected in any immediate clinical manifestation, and that this type of damage may deplete reserve capacity, making the brain more vulnerable to additional injury. Moreover, physiological loss of neurons with aging may be accelerated, resulting in functional changes several years after the toxic exposure has ceased\(^\text{18}\). It should also be noted that some individuals may be genetically predisposed to increased vulnerability to industrial chemicals\(^\text{19}\).

In the patient described, both CT and MRI showed a picture of diffuse and progressive cerebellar atrophy which was particularly pronounced in the cerebellum, according with the clinical picture. Focal or diffuse brain atrophy in CT scans following chronic CS\(_2\) exposure was also documented in previous reports\(^6, 7, 20, 21\). A MRI study was performed by Peters et al.\(^5\), who showed a pattern of central demyelization in two out of four CS\(_2\)-poisoned patients. Huang et al.\(^\text{21}\) described ten viscose rayon workers with polyneuropathy and neuropsychiatric disturbances: brain MRI abnormalities (mild cerebrocortical atrophy and/or multiple lesions of the basal ganglia and corona radiata) were present in seven of them. In the case reported by
Frumkin\(^8\), MRI revealed advanced cerebellar atrophy and prominent atrophy in the posterior tracts and nuclei of the pons. Finally, Hageman et al.\(^22\) reported the case of a painter who developed dementia and parkinsonism after over 40 years of exposure to CS\(_2\) in a viscose rayon factory: brain MRI showed generalized cerebral atrophy and white matter hypodensity. On the basis of these observations, it appears that the neuroimaging findings of CS\(_2\) encephalopathy are rather variable. Nevertheless, brain imaging can be useful (i) to exclude other brain diseases (e.g., neoplasms) that may show similar clinical features; (ii) to evaluate cerebellar damage, when present; and (iii) for follow-up observations.

In conclusion, although CS\(_2\) poisoning is almost exclusively of historical importance, clinicians should be aware of the possibility of chronic toxic encephalopathy among patients with previous long-term exposure to this chemical. In such cases, cerebellar atrophy may develop as an unusual, delayed manifestation of neurotoxicity, in addition to the more common manifestations of the disease (e.g., mental deterioration): careful occupational anamnesis, serial neuropsychiatric evaluation, and brain imaging techniques (CT and MRI) can significantly contribute to the diagnosis and follow-up.

More generally, the case presented is a reminder that neurodegenerative disorders of apparently unknown origin might derive from occupational toxic exposures suffered in the past. The clinical manifestations may appear even decades after retirement from the job at risk, when the effects of toxic damage combine with age-related neuronal loss to overcome the brain functional reserve.

References


