Toxic Leukoencephalopathy

This information sheet is intended for clinicians in British Columbia.

What is toxic leukoencephalopathy?

Toxic leukoencephalopathy is a structural alteration of white matter in the brain, secondary to toxic agents.

What toxic agents are involved?

A large number of agents have been associated with toxic leukoencephalopathy: **recreational drugs** (ethanol, heroin injected or smoked, cocaine, ecstasy); **organic solvents** (toluene); **environmental toxins** (carbon monoxide, arsenic, carbon tetrachloride); **antineoplastic agents** (cranial irradiation, methotrexate, carmustine, cisplatin, cytarabine, fluorouracil, levamisole, fludarabine, thiotepa, interleukin-2, interferon alpha); i**mmunosuppressive drugs** (cyclosporine, tacrolimus); **antimicrobial agents** (amphotericin B, hexachlorophene).

What is the link with heroin?

Leukoencephalopathy after inhaling heroin was first reported from Amsterdam in 1982. Since then, cases have been reported in both Europe and North America. Cases have been associated with smoking heroin by a method known as "chasing the dragon." This refers to the process of heating heroin on aluminum or tin foil with a flame and inhaling the white smoke, or pyrolysate, with a small tube.

A systematic literature review performed in 2019 found that between 1994 and 2018 among the 50 people who used heroin who developed leukoencephalopathy, inhalation was the most popular route (60%), followed by intravenous injection (30%) and snorting (10%). [1]

How many cases of toxic leukoencephalopathy have been seen in British Columbia?

From December 2001- July 2003, 20 cases of toxic leukoencephalopathy were identified in the Vancouver Coastal Health region. No cases were reported in BC in 2004; but from September 2005-August 2006, seven further cases were identified in Victoria.[2] Twenty (74%) of all cases were male and two couples were identified. Among the 2003 cases, the duration of smoking heroin varied from one to 30 years.[2] In 2020, a few cases of toxic leukoencephalopathy were identified in Vancouver and Vancouver Island regions.

How does "chasing the dragon" lead to toxic leukoencephalopathy?

The etiology of toxic leukoencephalopathy is unknown but is thought to be due to toxic contaminants in the heroin, or toxic properties of heroin generated through the smoking process. There is no evidence to indicate a genetic predisposition. The practice of chasing the dragon is not uncommon; however the associated leukoencephalopathy has been rarely reported.

What are the symptoms and signs?

The symptoms may be delayed after exposure, and usually progress over weeks or months. Cases present with a variety of neurobehavioural signs and symptoms: confusion, inattention, memory loss, psychiatric disturbance, abulia (lack of initiative and drive), visuospatial deficits, speech abnormality, spasticity, Babinski sign, cerebellar dysfunction, myoclonus, bradykinesia, dystonia, stupor and coma.

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What are the findings on imaging and pathology?

Magnetic resonance imaging (MRI) shows diffuse, symmetric white matter hyperintensities in T2-weighted images of the brain. Common areas affected include the cerebrum, cerebellum, and brainstem, and more specifically, in the periventricular and subcortical white matter, pyramidal tracts, lemniscal pathway, pons, and corpus callosum. The hallmarks on the MRIs of those who inhaled heroin were posterior to anterior involvement of the cerebral white matter and lesions in the posterior limbs of the internal capsules, cerebellum and brainstem. In contrast, those who injected heroin intravenously had more frequent lesions in the subcortical U fibers and the genu of the internal capsules.[1]

In contrast computerized tomography (CT), may show bilateral hypodensities in the cerebrum, cerebellum, brainstem, corpus callosum, and deep white matter. Brain biopsy reveals spongiform or vacuolar degeneration of white matter, with relative sparing of subcortical (U) fibres. Findings include demyelination, axonal swelling, and axonal loss.

What are the outcomes of toxic leukoencephalopathy?

The typical course of disease described in the literature is progressive; usually progressing through three stages over weeks to months. The first stage is primarily cerebellar, symptoms include: motor restlessness, cerebellar ataxia with speech issues. Secondly, additional symptoms such as myoclonic jerks and dance-like movements as well as progressive weakness and hyperactive reflexes may occur. Finally, approximately 25% of patients reach stage three with spasms, loss of the ability to move or speak and in some eventual death.[4]

The case fatality rate in BC case reports was high, 13 out of 27 cases (48%) identified in 2001-2006 are known to have died. Survivors may recover or have permanent brain injury.[2] In a systematic review of 50 people who use heroin, clinical improvement was observed in 60% of patients, the overall mortality rate was 12%. Higher mortality was observed in patients who used the inhalation route (16.7%).[3]

What is the treatment for toxic leukoencephalopathy?

Research indicates that supportive supplements and vitamins (Vitamin E, Vitamin C, and coenzyme Q10) can be used to facilitate neurological recovery.[3]

How can toxic leukoencephalopathy be prevented?

Avoidance of toxic agents is the best protection against toxic leukoencephalopathy. Currently, we do not fully understand the relationship between heroin use and this condition.

References

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