CASE REPORT

Paradichlorobenzene (toxin)-induced leucoencephalopathy

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SUMMARY

A 40-year-old woman with a history of polysubstance abuse, hypertension, depression and anxiety with panic attacks admitted to the emergency room at the request of her primary physician owing to progressive decline in her mental status associated with anorexia and generalised pruritic skin rashes. Initial outpatient workup and that during two previous hospital admissions including thyroid function and syphilis tests, urine toxicology screen and brain imaging studies were unremarkable. Repeat MRI of the brain during her third hospital admission showed diffuse periventricular and white matter disease. This prompted further questioning of family members which revealed chronic ingestion of mothballs and toilet cakes containing paradichlorobenzene in the patient leading to toxin-induced leucoencephalopathy consistent with her neurological symptoms of altered mental status, ataxic gait, cogwheel rigidity in the arms and characteristic skin rashes. Subsequently, a feeding tube was placed to address her worsening nutritional status and she was discharged home in a stable state.

BACKGROUND

Leucoencephalopathy from ingested toxins is a rare cause of mental status changes and may be overlooked unless a careful exposure history is obtained.

CASE PRESENTATION

A 40-year-old woman with a medical history of hypertension, depression, anxiety with panic attacks, cocaine, alcohol and tobacco abuse presented to the emergency room with a 4-month history of progressive decline in her mental status and a generalised pruritic rash. Her symptoms started with an itchy rash on her hands which spread to involve her limbs, trunk and ear lobes. Over a period of 10–12 weeks, she became more somnolent and less interactive with decreased appetite. She was initially evaluated by her primary care physician with a complete blood count, comprehensive metabolic panel, thyroid function test and a non-contrast head CT scan, all of which were normal. Following dermatology consult, she was diagnosed with eczematous dermatitis and started on topical fluocinonide cream and oral hydroxyzine. She continued to deteriorate with increased generalised weakness, somnolence and developed an unsteady gait. She was admitted to the hospital, and further evaluation including vitamin B₁₂, folate, syphilis (rapid plasma reagin), HIV, heavy metal screening, all brain MRI and electroencephalography were all normal. Her mental status

continued to decline and over the next couple of weeks she developed slurred speech, became dependent in terms of activities of daily living and required assistance with walking and so her primary care physician referred her to the emergency room for admission and further management.

Physical examination during her third hospital admission revealed a lethargic, emaciated woman with dry skin and a widespread hyperpigmented rash predominantly over her extremities, trunk, ear lobes and neck (figure 1). She was non-verbal, but opened her eyes spontaneously. She could not follow commands, but aroused to sternal rub. Her cranial nerves appeared intact and there was no nystagmus. The patient grimaced to painful stimuli in all extremities and withdrew symmetrically. She had increased tone in all extremities with cogwheel rigidity; her knee jerks were brisk and symmetric with negative Babinski. Her coordination and gait could not be assessed.

INVESTIGATIONS

Investigations including blood alcohol level, ammonia, urine toxicology screen, cerebrospinal fluid (CSF) cultures, cytomegalovirus (CMV), cryptococcal serology, JC polyoma viral DNA, echocardiogram, carotid Dopplers and non-contrast head CT scan were all normal except for mildly elevated liver enzymes: aspartate transaminase 40 (10–31) U/ml, alanine transaminase 99 (10–41) U/ml and an erythrocyte sedimentation rate 45 mm/h. CSF analysis showed a mildly elevated protein 50 (15–45) mg/dl.

A repeat brain MRI revealed extensive diffuse white matter changes involving the periventricular areas in the cerebral hemispheres, corpus callosum

Figure 1 Hyperpigmented pruritic skin rashes.

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Figure 2 MRI of the brain without contrast. Findings of extensive diffuse T2-hyperintense signal abnormality involving the periventricular and deep white matter of cerebral hemispheres, corpus callosum, white matter tracts of cerebellum, middle cerebellar peduncles, posterior pons and cerebral peduncles.

and white tracts of the cerebellum, middle cerebellar peduncles, posterior pons and cerebral peduncles consistent with leucoencephalopathy (figure 2). On the basis of these findings, her family was questioned more closely about the possible ingestion or exposure to toxins and that is when they reported that the patient had been eating mothballs and toilet cakes over the past 2 years. They were unsure of the frequency of ingestion and why she ingested these products, but suggested it was because she liked the way these products smell.

Subsequently, a high blood level of paradichlorobenzene (PDCB) of 3.8 µg/dl (<0.02 µg/dl) was found.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis after the MRI included toxic or metabolic encephalopathy, progressive multifocal leucoencephalopathy and inborn errors of metabolism. Inborn errors of metabolism were less likely because in most cases it presents earlier on in life. Progressive multifocal leucoencephalopathy is specifically associated with JC polyoma virus. She had no significant metabolic abnormality with normal CSF analysis so the suspicion was for toxic leucoencephalopathy from the PDCB in the mothballs and toilet cakes. She also had a dermatosis which has been described in other case reports of PDCB ingestion.

TREATMENT

There is no specific antidote for PDCB so the patient was treated with supportive care including intravenous hydration, vitamin supplementation, percutaneous endoscopic gastrostomy (PEG) tube feeding, topical fluocinonide for the skin rashes and physical therapy.

OUTCOME AND FOLLOW-UP

The patient was discharged home with a PEG tube and home physical therapy. Her family was strongly advised to avoid further exposure of patient to mothballs or toilet cakes.

At a clinic visit 4 weeks after discharge, she was talking and eating and was able to transfer.

DISCUSSION

Leucoencephalopathy is a central nervous system disorder in which the white matter suffers progressive damage caused by a variety of agents including cocaine, heroin, PDCB, antimicrobials, antineoplastic agents, radiation treatment, immune modulators, environmental and industrial toxins. Infections such as HIV, polyoma virus and CMV also cause white matter disease.

PDCB is a common ingredient in diaper pail and toilet bowl deodorisers and moth repellents. It is also used as a fumigant and as an intermediate compound in the chemical synthesis of certain pesticides, dyes and resins. Even though its actual mechanism of toxicity is not known, it rapidly distributes in human tissues, especially in adipose tissue and may cause renal or hepatic toxicity, gastrointestinal upset and central nervous system toxicity. It is eliminated through the kidneys, and so can be measured in the serum or the urine.

Chronic PDCB exposure is usually associated with hepatic toxicity, neurotoxicity is less common. However, there are some case reports of PDCB causing neurotoxicity involving a wide range of neurological symptoms: anorexia, depression, ataxia with gait disturbances, tremors, hypo or hypertonia, muscle weakness and speech deficits. In these cases, exposure to PDCB has been prolonged over a period of more than a year.¹⁻⁶ All of these cases, except one, were in patients with a psychiatric history. The exception was in twin girls who had been sniffing and ingesting mothballs as a recreational drug.⁶ Three of these cases report a similar dermatosis like our patient with ichthyotic hyperpigmented lesions.^{1 3 6} There are only three reported cases of PDCB neurotoxicity that are associated with a high serum concentration of PDCB; in the other cases, the diagnosis was inferred from the clinical presentation and history of PDCB ingestion.²

There is no specific antidote for PDCB toxicity nor PDCB-induced leucoencephalopathy and so patient was treated with supportive care including the removal of the patient from further exposure to toxin. These cases demonstrate that some recovery will occur over many months, but often some permanent neurological impairment remains.¹⁻⁵

Our patient's diagnosis of PDCB-induced leucoencephalopathy eluded us until her repeat MRI of the brain showed diffuse white matter disease. This prompted further exploration of her history leading to the revelation by her family of her pica of mothballs and toilet cakes for 1-2 years. The patient also had mutism at the time of her third hospital admission which was a barrier to good physician-patient communication.

Learning points

- ▶ In patients presenting with altered mental status and a new rash, think of toxic exposures.
- ▶ In a patient with leucoencephalopathy, take a good exposure history particularly in psychiatric patients.
- ▶ Patients may recover from the long-term neurological effects of paradichlorobenzene if removed from exposure.

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Competing interests None.

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