Case Report

J Korean Soc Radiol 2020;81(4):985-989
https://doi.org/10.3348/jksr.2020.81.4.985
pISSN 1738-2637 / eISSN 2288-2928

대한영상의학회지

Magnetic Resonance Imaging and Clinical Features of Chlorfenapyr-Induced Toxic Leukoencephalopathy: A Case Report

클로르페나피르 중독에 의한 백색질뇌증 환자의 임상양상과 자기공명영상 소견: 증례 보고

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Chlorfenapyr is widely used as an insecticide, despite it being fatal to humans. However, chlorfenapyr-induced central nervous system toxicity has rarely been reported. We report the magnetic resonance imaging (MRI) findings in a rare case of chlorfenapyr-induced toxic leukoencephalopathy. A 71-year-old man who had ingested chlorfenapyr approximately two weeks prior visited our hospital and presented with bilateral lower motor weakness and voiding dysfunction that had developed two days before admission. Brain MRI revealed extensive bilateral white matter abnormalities involving the corpus callosum, internal capsule, brain stem, and bilateral middle cerebellar peduncle. Furthermore, spine MRI revealed diffuse swelling and hyperintensity on the T2-weighted images.

Index terms Chlorfenapyr; Leukoencephalopathy; Magnetic Resonance Imaging

Received August 1, 2019
Revised September 24, 2019
Accepted October 18, 2019

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INTRODUCTION

Chlorfenapyr has been a widely used pesticide for eradicating agricultural pests since 1995 and is classified as a moderately hazardous pesticide (Class II) based on the World Health Organization toxicity classification (1). Human intoxication with chlorfenapyr could be fatal; however, chlorfenapyr poisoning has seldom been reported, despite its widespread use (2, 3). In this paper, we present a rare case of chlorfenapyr poisoning with central nervous system involvement. This report was approved by the

Institutional Review Board of our institution.

CASE REPORT

A 71-year-old man was presented to the emergency department with bilateral lower motor weakness and voiding difficulty beginning two days prior. The patient had ingested about 100 mL of chlorfenapyr solution with suicidal intent 15 days ago. He was admitted to the hospital for six days and was discharged after improvement. Ten days after the discharge, he revisited the hospital for late-onset neurologic symptoms. His vital signs on arrival were: blood pressure, 110/60 mm Hg; heart rate, 70 beats/minute; respiratory rate, 20 breaths/minute; and body temperature, 37°C. He had an alert mental status, and his Glasgow Coma Scale score was 15. Neurologic examination revealed motor weakness in both legs (grade I). Analysis of the cerebrospinal fluid obtained from lumbar puncture did not reveal any abnormal findings.

Magnetic resonance imaging (MRI) of the brain and cervical spine were performed. Bilateral symmetric signal abnormalities in the entire cerebral and cerebellar white matter, including the corpus callosum, internal capsule, brain stem, and bilateral middle cerebellar peduncle were found. The lesion showed high signal intensity on fluid-attenuated inversion recovery (FLAIR) imaging (Fig. 1A), significant diffusion restriction on diffusion-weighted imaging (DWI), and an apparent diffusion coefficient (ADC) map (Fig. 1B). Spine MRI revealed diffuse swelling and hyperintensity in the entire cervical and the partly covered upper thoracic spinal cord on T2-weighted imaging (T2WI) (Fig. 1C). The lesion showed no contrast enhancement after intravenous injection of gadolinium (not shown). There were no non-space occupying lesions. The final diagnosis was chlorfenapyr-induced leukoencephalopathy.

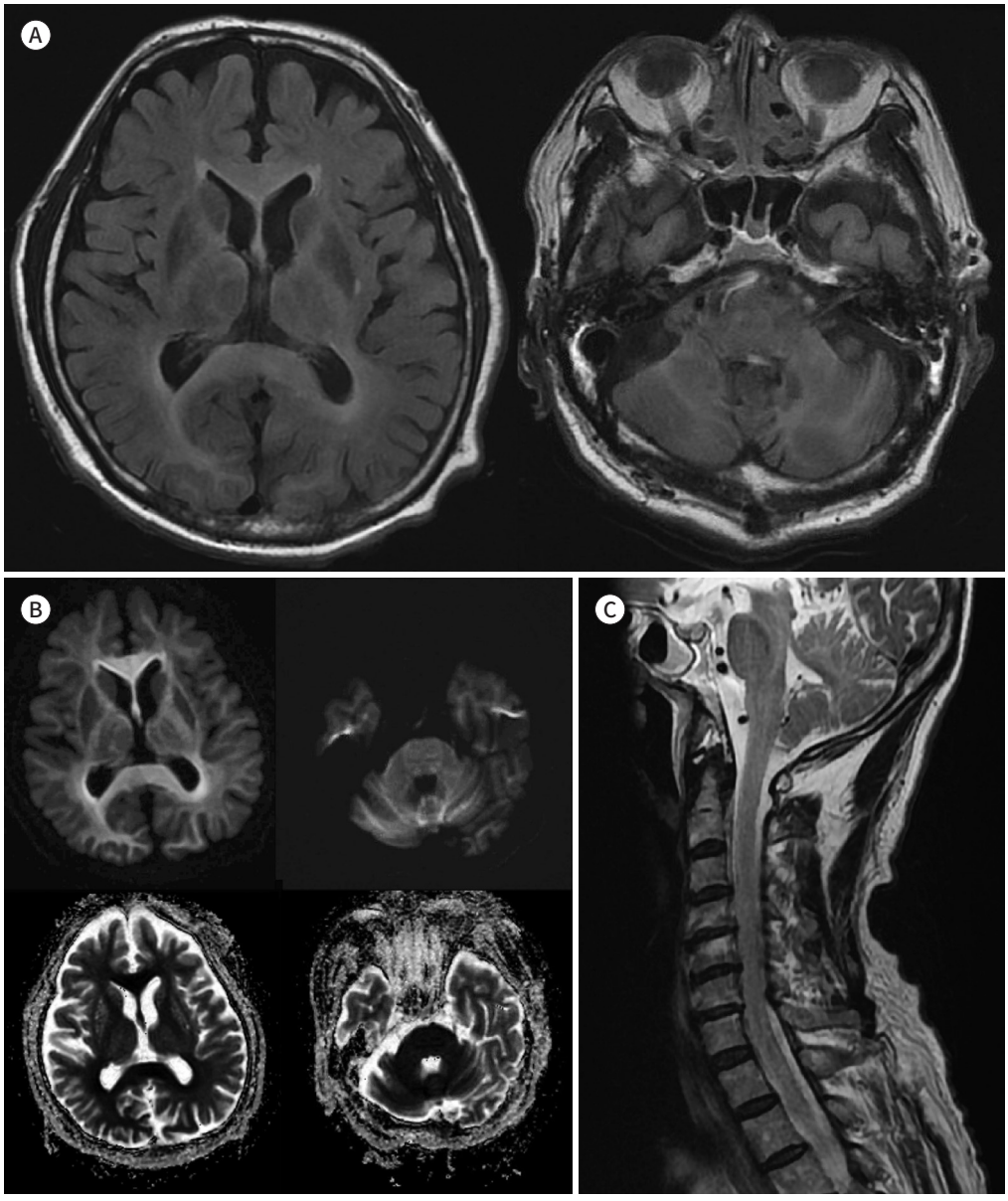
Steroid pulse therapy and other supportive conservative therapy were initiated. Three days later, his mental status deteriorated. Sustained high fever and respiratory complications developed. Endotracheal intubation was performed, and respiration was maintained using a mechanical ventilator. Two days later, his heart rate suddenly dropped, and he showed signs of sudden cardiac arrest. Cardiopulmonary resuscitation was performed for 20 min, but he passed away approximately 20 days after consuming chlorfenapyr.

DISCUSSION

Chlorfenapyr belongs to the pyrrole family, and it has no antidote. Chlorfenapyr has various mechanisms of toxicity, including dose-dependent cell membrane damage, uncoupling of oxidative phosphorylation, and disruption of acetyl coenzyme A metabolism. Thus, chlorfenapyr inhibits adenosine triphosphate (ATP) production at the mitochondrial level, triggering cellular death of the organism (4, 5). This can cause severe damage in organs with high energy requisites, such as the heart, muscles, kidney, and brain (6).

The clinical course of patients who take chlorfenapyr can be divided into acute symptoms, including nausea, vomiting, rhabdomyolysis, metabolic acidosis, and renal failure, and delayed toxicity, including fever, change in mentation, and other neurologic symptoms, such as hypertonia, hyperreflexia, ataxia, nystagmus, miosis, hallucinations, convulsions, fasciculation, and paralysis (4, 5, 7).

Fig. 1. Chlorfenapyr-induced toxic leukoencephalopathy in a 71-year-old man.
A. Axial fluid-attenuated inversion recovery images show diffuse, bilaterally symmetrical, increased signal intensities in the periventricular/subcortical white matter, corpus callosum, internal capsule, cerebellar white matter, brain stem, and bilateral middle cerebellar peduncle.
B. Axial diffusion-weighted image and apparent diffusion coefficient map show significant diffusion restriction in the corresponding lesions.
C. Sagittal T2-weighted spinal image shows diffuse swelling of the spinal cord with increased signal intensity.



Chlorfenapyr takes time to convert to its active form by oxidative removal of the N-ethoxy methyl group caused by mixed function oxidases. The active, toxic form identified as 303268 or a toxic metabolite causes delayed neurological symptoms (3). This shows a possibility of delayed adverse effects of the metabolites of chlorfenapyr on vital organs that consume high energy. Therefore, patients with chlorfenapyr intoxication should be carefully observed for delayed mental status changes up to a couple of weeks after ingestion.

Although we did not have the normal findings of the patient's MRI at the time of poisoning, we can infer that there was a delayed encephalopathy as patient had no neurological symptoms (in first visiting) and showed lucid interval. This case report imply that the physicians should understand the clinical course of the disease and thus, have to apply appropriate treatment at the onset of sudden, rapidly deteriorating fatal manifestations. Brain MRI can be useful for early diagnosis of chlorfenapyr-induced toxic leukoencephalopathy and appropriate follow-up in patients who have ingested chlorfenapyr.

A few cases of chlorfenapyr-induced leukoencephalopathy in humans have been reported. The brain MRI findings were bilateral, symmetric lesions along the entire white matter tract with high signal intensity on FLAIR, diffusion restriction on DWI, and an ADC map (3, 4, 6).

Baek et al. (2) reported serial MRI findings of a reversible case of chlorfenapyr intoxication. The follow-up brain MRI obtained 71 days later revealed complete resolution of abnormal signal intensities in the brain and in the cervical to upper thoracic spinal cord, with residual hyperintensity on T2WI and atrophic changes in the spinal cord below T7.

In the present case, brain and spinal MRI showed markedly extensive and symmetric hyperintense changes on T2WI involving almost the entire white matter in the cerebrum, cerebellum, brain stem, and spine, with significant diffusion restriction. These results were similar to those of previous cases and suggestive of chlorfenapyr injuries, specifically confined to the white matter of the central nervous system. These radiologic findings are seen in mitochondrial neurogastrointestinal encephalopathies, such as Leigh's disease that can be a major differential diagnosis (8).

Author Contributions

Conceptualization, P.N.H.; investigation, P.N.H., K.J.H.; methodology, P.N.H., P.J.Y., K.S.; project administration, P.N.H.; supervision, P.N.H., P.J.Y., K.S.; validation, P.N.H., P.J.Y., K.S.; visualization, K.J.H.; writing—original draft, K.J.H.; and writing—review & editing, P.N.H., P.J.Y., K.S.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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김종혁 · 박노혁* · 박지연 · 김선정

클로르페나피르는 널리 사용되는 살충제이며 인간에게는 치명적일 수 있다. 그러나 중추신경계 침범을 동반한 클로르페나피르 중독은 거의 보고되지 않고 있다. 우리는 이전까지 드물게 보고된 클로르페나피르 중독에 의한 백질뇌병증 환자의 자기공명영상 소견을 보고하고자 한다. 약 2주 전에 클로르페나피르를 음독한 71세 남자 환자가 내원 2일 전부터 시작된 양측 하지위약감과 배뇨장애를 주소로 내원하였다. 시행한 뇌 자기공명영상에서는 뇌량, 속섬유막, 뇌줄기를 포함하는 영역에 양측성의 광범위한 뇌백질의 이상을 보였고, 척수 자기공명영상에서는 전반적인 척수에 고신호를 동반한 종창을 보였다.

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