

Case Report

Treatment of An Acute Severe Cadmium Poisoning Patient Combined with Multiple Organ Dysfunction Syndromes by Integrated Chinese and Western Medicines: A Case Report*

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Cadmium (Cd), a toxic heavy metal commonly found in the environment, can cause toxic reactions at a dose of 30 mg. Cd is absorbed into the body mainly through the respiratory tract, digestive tract, and skin.⁽¹⁾ About 10%–50% of Cd absorption is inhaled dust, then about 5%–10% of ingested Cd is absorbed by body, which depending on particle size.⁽²⁾ As known, most of Cd poisoning reaction is chronic, and acute Cd poisoning, especially high doses of acute poisoning, is very rare in clinic. Due to its airless and tasteless characteristics, Cd poisoning is hidden, and it is easy to be misdiagnosed in hospitals. However, Cd poisoning is particularly dangerous because it progresses rapidly and can cause death within hours. In order to better understand the treatment of Cd poisoning, we report a successful treatment case of a young man with multiple organ failure due to Cd poisoning. The patient gave a written informed consent, and the case report was approved by the Ethical Committee of Guangdong Provincial Hospital of Chinese Medicine.

Case Presentation

Initial Stage

A 23-year-old man was presented with abdominal pain, shortness of breath, and unconsciousness on May 16th, 2017. After rapid physical examination, the results showed heart rate of 220 beats/min, blood pressure (BP) of 60/40 mm Hg, blood oxygen saturation (SPO₂) 80%. Emergency physicians considered the diagnosis as multiple organ dysfunction syndromes (MODS), and performed urgently tracheal intubation and ventilator assisted ventilation, then transported the patient to the intensive care unit (ICU).

In the ICU, physical examination showed that the patient was slightly unconscious, bilateral pupil size was equally, diameter was about 3 mm, light reflection was sensitive. In blood gas analysis,

oxygen partial pressure (PO₂) 18.5 mm Hg, partial pressure of carbon dioxide (PCO₂) 28.8 mm Hg, and blood lactate (LAC) 11.4 mmol/L. The coagulation was very bad, D-dimer was over 20,000 mg/L FEU, prothrombin time (PT) 58.6 s, prothrombin activity (PTA) 12%, prothrombin international normalized ratio (INR) 6.74, fibrinogen (Fib) 1 g/L, activated partial thromboplastin time (APTT) 63.8 s. Myocardial enzyme spectrum indicated myocardial injury, such as creatine kinase (CK) 754 U/L, creatine phosphokinase isoenzyme (CK-MB) 28 U/L, lactate dehydrogenase (LDH) 7038 U/L, brain natriuretic peptide (BNP) 1934.4 pg/mL, and high-sensitivity cardiac troponin (hs-cTnI) 0.043 μg/L. Blood routine is shown in Appendix 1, white blood cells (WBCs) 15.59 × 10⁹/L. Serum creatinine was 171 μmol/L, which indicated mild renal insufficiency. However, liver function was very poor, glutamic pyruvic transaminase (ALT) 2289 U/L, glutamic-oxalacetic transaminase (AST) 2639 U/L, total bilirubin (TBIL) 62.3 μmol/L, and blood ammonia (NH₃) 87 mmol/L (Appendix 2).

Deterioration Stage

During ICU hospitalization, the patient's condition changed rapidly and deteriorated. He was in coma, with BP 64/35 mm Hg, BNP > 5000 pg/mL, PT 58.7 s (Appendix 3), APTT > 180 s, TBIL 518 μmol/L (Appendix 4), creatinine 429 mmol/L (Appendix 5),

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estimate glomerular filtration rate (eGFR) 15.59 mL/min/1.73 m². Electrocardiogram (ECG) indicated supraventricular tachycardia. Cardiac color ultrasound showed that ejection fraction (EF) was 21%, heart enlarged and the wall motion weakened. The X-ray showed pulmonary congestion, pulmonary interstitial edema, enlargement of the heart, and a small amount of pleural effusion on both sides. Head, chest, abdominal and pelvic CT showed (1) no abnormal density in head; (2) lung congestion, heart enlargement, attention to cardiac dysfunction; (3) a small amount of pericardial effusion; (4) intestinal pneumatosis, flake high density in pelvic cavity, considering the intestinal contents; (5) pelvic effusion. All of above, the patient suffered from severe MODS.

In terms of treatment, the patient was treated with opening the vein channel, and monitored with pulse-induced contour cardiac output (PiCCO, PC8500, Pulsion, Germany) technique, which showed severe cardiogenic shock in the patient, dopamine (Harvest, Shanghai, China) and noradrenaline (Grand Pharmaceutical, China) injections were given to maintain BP, tracheal cannula and breathing machine were used to assist ventilation, continuous renal replacement therapy (CRRT, Gambro, Prisma-Flex, Sweden) was used to improve renal function. Intra-aortic balloon pump (IABP, Datascope CS100, America) was applied for the treatment of cardiogenic shock, vitamin K was given by intravenous drip to prevent bleeding, a large amount of plasma was transfused or exchanged in order to improve coagulation and liver function.

The patient was comatose, with cold perspiration, limbs convulsion, and pulse of slight desire. Syndrome differentiation of Chinese medicine (CM) was deficiency of yang qi. The CM therapeutic methods aimed at reviving the yang for resuscitation. The patient was treated with Sini Decoction (四逆汤) for 7 days (from May 17th to May 23th, 2017), which consists of *Aconitum Carmichaelii* 20 g, *Zingiber officinale* 20 g, and *Glycyrrhiza uralensis* 20 g in order to improve the heart function.⁽³⁾

Decubation Stage

After all these treatments, due to unknown cause of MODS, poisoning related index was carried out by a thorough inspection. On May 19th, the Occupational Health Monitoring Center of Guangzhou

detected Cd in the blood and urine following with diagnosis corrected for severe Cd poisoning, which induced MODS. The concentration of Cd in urine was 323.1 μg/L (Appendix 6), and 27.8 μg/L in blood. According to the test of Cd, CaNa₂EDTA (1 g/day, KingYork, Tianjin, China) was used to prevent metal toxicity for 2 courses of treatment. Three days was a course of treatment and the interval was one day.

Gradually, the patient was conscious, the limbs were warmed, and shortness of breath was improved. In addition, the patient had jaundice symptoms. The principle of CM should be supplementing qi and dispelling jaundice. Thus, the patient was treated with not only qi-tonifying drugs including *Astragalus membranaceus*⁽⁴⁾ and ginseng,⁽⁵⁾ but also with the jaundice-eliminating drugs including *Artemisia capillaris*,⁽⁶⁾ *Artemisia apiacea*⁽⁶⁾ and *Rheum officinale*.⁽⁷⁾ The CM treatment lasted for 20 days (from May 24th to June 12th). The patient was successfully extubated and without CRRT on June 8th, 2017. And the concentration of Cd in urine and blood was decreased to 2.1 and 2.3 μg/L, respectively. Then the patient was taught to practice Baduanjin exercise every day (Appendix 7). At the beginning, Baduanjin exercise was practiced 15 min once, thrice a day, and lasted for 10 days (from June 9th to June 18th). In the process of time, the patient could take Baduanjin exercise 30 min once, thrice a day until July 6th. At the same time, the patient was also given metoprolol tartrate (12.5 mg, twice a day for long-term usage, AstraZeneca, England) for reducing myocardial oxygen consumption. After a comprehensive treatment, the patient could move without impediment, and was restored from sickness, finally discharged from hospital on July 7th, 2017.

Three weeks after discharge, the patient returned to the hospital for reexamination. The blood test showed WBC 6.03 × 10⁹/L, serum creatinine 84 μmol/L, ALT 8 U/L, AST 25 U/L, TBIL 34 μmol/L, BNP 297.7 pg/mL, PT 13.5 s and APTT 32.8 s. Cardiac color ultrasound showed that EF was 48%, and the left ventricular, left atrium and right ventricle were slightly enlarged. The X-ray showed no abnormality.

DISCUSSION

Cd exposure can cause wide-ranging deleterious health reactions in humans and animals, which can damage pulmonary, renal, hepatic, skeletal, reproductive and cardiovascular functions.^(8,9) Heavy

metals like Cd are potentially toxic at different cellular levels for which exposure is not acceptable.⁽¹⁰⁾ Cd toxicity induces tissue injury through creating oxidative stress,⁽¹¹⁻¹³⁾ changing in DNA expression,^(14,15) inhibition or upregulation of transport pathways particularly in the proximal S1 segment of the kidney tubule.^(16,17) Therefore, the toxic effects of Cd poisoning are through multiple systems and pathways. The organs failures in those patients are associated with the cardiovascular system, renal, hepatic and coating, which made diagnosis difficult and management complex.

Cd is transported throughout the body, through oral ingestion or inhalation of Cd, especially stored in liver and kidney.^(18,19) These two organs absorb approximately 50% of the Cd burden.^(18,19) The excretion of Cd will be the half-life of 25 years.⁽²⁰⁾ The long biological half-life of Cd in humans (10–30 years) can cause bone disease, nephrotoxicity, carcinogenicity, and many other poisoning effects.⁽¹⁸⁻²⁰⁾ The most severely damaged organs of patients precisely are liver and kidney, which lead to their slow recovery.

There is no consensus of opinion in the literature regarding treatment of Cd toxicity. The common strategy for heavy metal poisoning is mostly chelation therapy to promote heavy metal excretion. However, efforts to find a safe and effective drug for removing Cd from kidneys have largely failed. The chelators for Cd toxicity are themselves described to have different safety and efficacy.⁽²¹⁾ So far, the chelation therapies for Cd toxicity have not been approved for clinical application.^(22,23) Chelators such as CaNa₂EDTA have been reported to have protective effects against heavy metal poisoning. But CaNa₂EDTA can induce renal toxicity and kidney damage.⁽²⁴⁾ Because of the deficiency of specificity, CaNa₂EDTA therapy is not a recommended drug for the treatment of Cd poisoning.⁽²⁵⁾ However, for the patient's rehabilitation, in addition to the adjuvant treatment of the ICU machine, CaNa₂EDTA was also important especially in the excretion of Cd.

Combining with the history, the disease belonged to "the poisoning disease" of the category of CM. Based on CM theory, qi permanently protects the body and prevents the attacks from the disease. Baduanjin exercise is a traditional Chinese health Qigong routine created by an ancient physician for health promotion. The Baduanjin sequential therapy

is a cardiac rehabilitation exercise developed by our intensive care medicine team, which consists of the sitting and standing forms. Baduanjin sequential therapy meets the characteristics of modern low intensity and long time aerobic exercise. In addition, Baduanjin exercise can systematically mobilize movable joints and muscles, enhance cardiopulmonary functions, and concurrently modulate mind and spirit, ultimately achieving the integration of the mind and body.^(26,27) This patient was taught with the sitting form of Baduanjin exercise,⁽²⁸⁾ which included 8 postures. The patient practiced Baduanjin exercise every day and was restored from sickness.

In conclusion, acute severe Cd poisoning combined with MODS is a challenging clinical problem, especially to a doctor with no experience in treating the disease. Therefore, a diagnosis should be made quickly and treatment decisions of organ supporting need a deep consideration. Given the ubiquity of Cd in the environment and the multi-system toxicity of Cd as discussed previous, the CaNa₂EDTA treatment was benign in clinical protocols, though toxicity of kidneys needed to be monitored. The role of CM in treating patients with poisoning was not negligible, especially in the early rehabilitation of patients.

Conflict of Interest

The authors declare that they have no competing interests. None of the authors received funding from the relevant drug manufacturers in this research.

Author Contributions

Zhou YS and Zeng RX drafted this manuscript; Zhang MZ supervised article quality; Guo LH made critical revision of the manuscript and contributed to the rationalization of the study. All authors read and approved the final manuscript.

Electronic Supplementary Material Supplementary material (Appendixes 1–7) is available in the online version of this article at <http://dx.doi.org/10.1007/s11655-020-3089-4>.

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