Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Acute tubular necrosis due to cutaneous contact with cresol

Koji Okamoto,^{1,2} Eisei Noiri,² Machiko Oka,¹ Hidekazu Moriya,¹ Takayasu Ohtake,¹ Shuzo Kobayashi¹

¹Department of Nephrology, Immunology, and Vascular Medicine, Shonan Kamakura General Hospital, Kamakura, Japan;

²Department of Nephrology and Endocrinology, Department of Hemodialysis and Apheresis, University Hospital, University of Tokyo, Tokyo, Japan

Correspondence to Koji Okamoto, okamoto5-tky@umin.ac.jp

Summary

The authors report a case of a 43-year-old woman who presented with second degree chemical burns to 9% of the total body surface area due to cutaneous contact with cresol. This was associated with acute oliguric kidney injury requiring haemodialysis. In contrast to previous reports of cresol ingestion, the patient did not have evidence of hepatic dysfunction, possibly due to a low cresol concentration in the portal vein and liver. Renal histopathology showed regional accentuated tubular necrosis and disruption of the tubular basement membrane. Renal toxicity was thought to be due to direct tubular toxicity and impaired renal blood flow.

BACKGROUND

Cresols are methylphenol organic compounds that are widely used as household cleaners and disinfectants. Most exposures to cresols are at very low concentration that are not harmful. When high concentration cresols are ingested, breathed or made skin contact, it causes chemical burn and damages the organs. A saponated cresol solution and antiseptic solutions usually contain about 50% cresols, including phenols and xylenols.¹ Cresol intoxication may occur through accidental or self-induced injury. There are 38 reports of cresol intoxication with reported damage to multiple organs including the liver, lung, brain and skin. The renal pathology was thought to be acute tubular necrosis; however, there has been no histopathological examination of the kidneys apart from an autopsy study.² In the present report, we describe a case of cresol intoxication from cutaneous absorption with subsequent acute tubular necrosis.

CASE PRESENTATION

An unconscious 43-year-old woman was brought by ambulance with second degree chemical burns due to accidental contact with cresol-containing antiseptic solution. Approximately 1 h before presentation, the patient had quarrelled with her sister. When the sister began to drink cresol antiseptic solutions, the patient got into a tussle with her sister, resulting in contact with spilt cresol on the floor at 15:00. Consequently, the patient lost consciousness and was immediately taken by ambulance to our hospital at 16:00. She had an unremarkable medical history.

On arrival in our emergency room, the patient was unresponsive with second degree chemical burns involving approximately 9% of the total body surface area (figure 1A,B) Glasgow Coma Scale 3 (in sum). The urine was red-brown to black in colour. Laboratory data showed leukocytosis with a left shift (white blood cells 10 000/ μ l), haemoglobin 14.3 g/dl, an elevated serum lactate dehydrogenase of 1542 IU/l, alanine transaminase 61 IU/l and mixed acidosis (pH 7.281, pO₂ 67.9 mm Hg, pCO₂ 48.7

mm Hg, HCO₃⁻ 22.9 mEq/l). However, there was no elevation of aspartate transaminase (20 IU/l), creatinine (Cr 0.59 mg/dl) or blood urea nitrogen (BUN 10.6 mg/dl) on admission. Urinalysis showed protein 2+ and occult blood 3+.

OUTCOME AND FOLLOW-UP

The patient received extensive gastric lavage as per protocol in cases of oral intoxication, but there was no sign of cresol in the stomach. Forced diuresis was performed immediately because of anuria. The patient was started on haemodialysis on the first day after intoxication. During the first haemodialysis, her consciousness recovered completely without any focal neurological sign.

The patient developed oliguria followed by anuria within the first 36 h after admission. Serum Cr and BUN peaked at 7.35 mg/dl and 60.9 mg/dl, respectively, 72 h after admission. Ultrasound examination revealed slightly swollen kidneys bilaterally, hyper-echoic cortical lobule and a distinct border between the cortical lobule and medulla. After the peak on the third day, the renal function gradually improved with a serum Cr of 1.4 mg/dl on the 14th day (figure 1C). There was no evidence of hepatic dysfunction. The chemical burns resolved leaving slight pigmentation after covering with a dry non-stick dressing held in place with gauze.

Ultrasound-guided needle biopsy of the kidney was performed on 17th day of hospitalisation. Seventeen glomeruli were found in the biopsy specimen; the glomeruli appeared to be normal apart from slight mesangial matrix expansion. The tubulointerstitial findings were suggestive of acute tubular necrosis with desquamated tubular epithelium, loss of brush border and thinning of the tubular epithelium, pseudo-distal tubularisation, remnants of desquamated cells and small granular substance forming debris casts in the tubular lumen, mitotic figures of tubular epithelial cells and interstitial oedema on light microscopy (figure 2A). These findings had regional accentuation. At lower magnification, regional accentuated disruption of tubular basement membrane was found on periodic acid

Figure 1 (A) Contact with cresol resulted in a light brown eschar with well-defined margins and minimal oedema. There was a disinfectant-type odour suggestive of cresol. (B) The second degree burn involved approximately 9% of the total body surface area. (C) The clinical course of renal function.

Figure 2 (A) Acute tubular necrosis with desquamated tubular epithelium, loss of brush border, thinning of tubular epithelium and pseudo-distal tubularisation (Periodic acid-Schiff stain). (B) Interstitial oedema without chronic change or glomerular damage (Masson's Trichrome stain). (C) Regionally accentuated zonal disruption of the tubular basement membrane (Periodic acid methenamine silver stain). (D) Vacuolation in the tubular epithelial cytoplasm. Damaged tubules exhibit partial loss of brush border, increased nuclear:cytoplasmic ratio and cytoplasmic debris in the tubular lumen. Thinning and wrinkling of the basement membrane were found. Neutrophils were present in the tubular capillary (× 2000)

methenamine silver staining (figure 2B). The interstitium was oedematous with minimal lymphocytic infiltration. There was neither tubular atrophy nor interstitial fibrosis to suggest pre-existing chronic change. The vessels showed no specific change (figure 2C). Electron microscopy of the renal biopsy tissue showed partial loss of brush border, thinning/wrinkling of the basement membrane and focal cytoplasmic vacuolation consistent with nephrotoxic acute tubular necrosis (figure 2D). The glomerular basement membrane was intact.

DISCUSSION

In this case, myoglobin by rhabdomyolysis, haemoglobinuria by haemolytic anaemia, septic shock from bacterial infection via chemical burn could be the aetiology of acute kidney injury. However, only slight creatine kinase (232 U/l) elevation was found, and there was no decreased haptoglobin, bacteraemia nor septic shock. The acute kidney injury was thought to be due to acute tubular necrosis by cresol intoxication. The loss of consciousness was may be due to cresol or external injury due to falling her head on the floor. There were no abnormal findings on head CT. The level of consciousness was quickly recovered in 3 h and no sign of headache. The loss of consciousness was thought to be due to cresol itself. Cresol is an organic compound widely used as antiseptic solution. Blood level of cresol at 71–191 µg/ml are associated with death in cases of intoxication.^{3–4} Clinical findings include irritation and burning of the skin, mucosal lesions, heart damage, anaemia, liver and kidney dysfunction and coma. Almost all previously reported cases of peroral cresol intoxication had hepatic dysfunction. It was reported that the tissue concentration in the liver was about 7–10 times higher than that in the brain or kidney in a case of peroral cresol intoxication.² The excretion of cresol involves two steps: the initial step is cresol glucuronidation during biliary excretion, followed by excretion in the urine. In generally, cresol clearance by conventional haemodialysis is limited by protein binding and the ratio of its volume of distribution.⁵

In the present case, cresol was not detected in the gastric lavage which indicated that cresol was not absorbed orally but percutaneously. There are two previous reports of percutaneous cresol intoxication. A 7-year-old boy with percutaneous intoxication from saponated cresol had second degree chemical burns to 15% of his body surface area; this was associated with seizure and impaired renal function.⁶ In another report, a 46-year-old man with percutaneous intoxication from hot cresol solution had deep dermal burns, respiratory failure, acute renal failure and mild hepatic dysfunction.⁷ Meanwhile, in the cases with peroral intoxication, the prevalence of renal dysfunction was 28.6% and that of liver dysfunction was 62.5%.^{2–13} In addition to that, all cases with renal dysfunction were accompanied by liver dysfunction in this setting. It is possible that almost all of the gastrointestinal absorbed cresol enter the liver via the portal vein, while cutaneously absorbed cresol may enter the systemic circulation without passing through the liver. Cresols have severe permeability and protein degeneration effect like as phenol. First-pass effect defined with absorption route is most important even if the final concentration is highest in the

liver tissue. This may explain why kidney dysfunction is relatively more severe than hepatic dysfunction in percutaneous cresol intoxication.

Cresol is a known nephrotoxic substance.¹⁴ In reports of cresol intoxication, acute renal failure is often found. Foxall *et al*¹⁵ reported a victim suffering from phenol burns covering 50% of the body surface area who developed acute tubular necrosis. However, it is unclear the extent in which the biological properties of cresol are the same as those of phenol alone. Although the renal pathology caused by cresol intoxication is thought to be acute tubular necrosis, there are no reports examining the renal histopathology apart from an autopsy study. We performed a needle biopsy of the affected kidney to clarify the pathology. The pathological findings indicated that cresol intoxication caused acute tubular necrosis. There are two aspects related to this – direct tubular toxicity and impaired blood flow – factors which have been reported in the cutaneous absorption of phenol.¹⁵ Prominent vacuolation was found in the cytoplasm of tubular epithelium similar to the hepatocellular vacuolation following intoxication.¹⁶ This finding is suggestive of direct cresol toxicity. In addition, regional accentuated disruption of the tubular basement membrane was found; we presume it is due to impaired renal perfusion.

In conclusion, percutaneous cresol intoxication has a relatively lower prevalence of hepatic dysfunction but a higher prevalence of renal failure. Our case suggests that aggressive therapy similar to that given for oral intoxication may be warranted if there is extensive contact with cresol. We suggest that acute renal failure due to cresol is caused by direct toxicity to the tubular epithelium and impairment of renal perfusion.

Learning points

- ▶ Skin must be considered to be the new entrance gate through nephrotoxic agent.
- ▶ Percutaneous intoxication of cresol has relatively lower prevalence of hepatic dysfunction but more prevalence of renal failure.
- ▶ Aggressive therapies as systemic intoxication have to be done even on a small area of chemical burn from cresol.
- ▶ Acute renal failure due to cresol is caused both direct toxicity tubular epithelium and blood perfusion impairment.

Competing interests None.

Patient consent Obtained.

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