Fever, Skin Rash, Jaundice and Lymphadenopathy after Trichloroethylene Exposure : A Case Report

THIRABHATRA CHITTASOBHAKTRA, M.D.*,
PENPUN WATTANAKRAI, M.D.**,
ABHASSANEE SOHONSLITDSUK, M.D.***,
WINAI WANNANUKUL, M.D.*,
CHUTIMA PRAMOOLSINSAP, M.D.***,
PRAWAT NITIYANANT, M.D.****

Abstract

Trichloroethylene, a chlorinated hydrocarbon has been reported to cause many adverse health effects. This paper describes a female patient presenting with rather unusual manifestation secondary to trichloroethylene (TCE) exposure, i.e. hepatitis and generalized dermatitis. The diagnosis was confirmed by positive skin patch testing with 50 per cent TCE solution. After withdrawal from the exposure site, her symptoms improved and liver function test returned to baseline level after a three-months period of follow-up. TCE induced immunologic reaction has been postulated as the pathological process of this illness.

Trichloroethylene (TCE), first synthesized in 1864, has been widely used in industrial operations as a degreaser, fabric dry-cleaning agent. Structurally, TCE is an unsaturated chlorinated hydrocarbon with molecular formula as Cl_2C = CHCl. It is colorless, noninflammable and highly fat soluble(1). Routes of absorption are inhalation, ingestion and minimally *via* skin absorption. The adverse health effect of TCE previously reported involve the central nervous system, peripheral nervous system, skin, liver, kidney and heart. Hepatitis from industrial exposure to TCE is rare, since in the group of 288 cases of industrial "poisoning" from TCE, only five showed evidence of hepatitis signs and symptoms(2). When combined with generalized dermatitis, there are only a few reports in the literature. Ten years' review (1986-1996) in Ramathibodi Hospital, neither hepatitis nor dermatitis has been reported. This article describes a patient with hepatitis and generalized dermatitis after industrial exposure to TCE.

CASE REPORT

A 18-year-old female was referred to

* Department of Medicine,
** Division of Dermatology,
*** Division of Gastroenterology & Tropical Medicine, Department of Medicine,
**** Department of Pathology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

Ramathibodi Hospital for evaluation of work up about her illness: prolonged fever, jaundice and skin rash. She was previously healthy and started working for two months in a factory manufacturing socks. Her duty was to spray TCE for cleaning dirty spots on the socks. The working environment was poorly ventilated and she had been working without any protection.

One month before admission, she developed high grade fever and erythematous maculopapular rash. She also had nausea, vomiting and icteric sclera, so she was admitted at a general hospital. Physical finding revealed moderate jaundice, hepatomegaly and generalized exanthematous rash distributed on her face, trunk and extremities. She was treated as Salmonella infection with oral pefloxacine, however, her fever and hepatitis persisted. The rash became hyperpigmented and started to peel off two weeks after admission. Her past history was unremarkable. She did not take any regular medication, alcohol and never received blood transfusion nor had previous jaundice because the diagnosis was not established, she was referred to Ramathibodi Hospital for further evaluation. Physical examination revealed low grade fever, moderate jaundice and generalized hyperpigmentation with residual desquamation on her face, trunk, extremities especially on palms and soles. Hepatomegaly and enlarged left cervical lymph node was noted. Other findings were unremarkable.

CBC showed Hematocrit 34 per cent, WBC 10,700 cells/mm^3, Neutrophil 77 per cent, Lymphocyte 15 per cent, Eosinophil (Eo) 4 per cent, Monocyte 4 per cent and Platelet count 355,000 cells/mm^3. Liver function test revealed total bilirubin 30.3 mg/dl, direct bilirubin 16.5 mg/dl, aspatate aminotransferase (AST) 115 U/L, alanine aminotransferase (ALT) 56 U/L, alkaline phosphatase (ALP) 113 U/L, albumin 38.8 g/L and total protein 61.1 g/L. The serological studies of hepatitis A, B, C viruses were negative. Other studies included Weil-Felix titer, Widal titer, Melioid titer and anti-HIV were all negative. The serum screening for fluorescent antinuclear antibody (FANA) was negative.

Left cervical lymph node and liver biopsies were done. The pathological finding of the lymph node revealed reactive hyperplasia. The liver microscopically showed intact fairly lobular architecture. Liver cell cords appeared irregular with double-cell thickness. Large liver cell with multiple nuclei were occasionally seen. Recent liver cell necrosis with polymorphonuclear cell infiltration in the centrilobular zone were noted (Fig. 1). Focal loss of liver cells in this area was observed (Fig. 2). The portal tracts were densely infiltrated by lymphocytes and some polymorphonuclear cells. The histopathological findings were compatible with chronic toxic hepatitis[3].

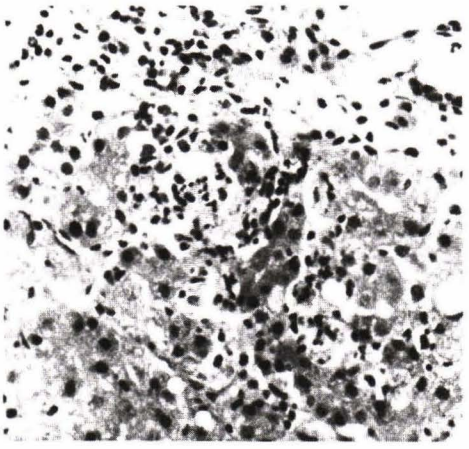

Fig. 1. Recent necrosis of liver cells with polymorphonuclear cell infiltration in the centrilobular zone. H & E, x 150.

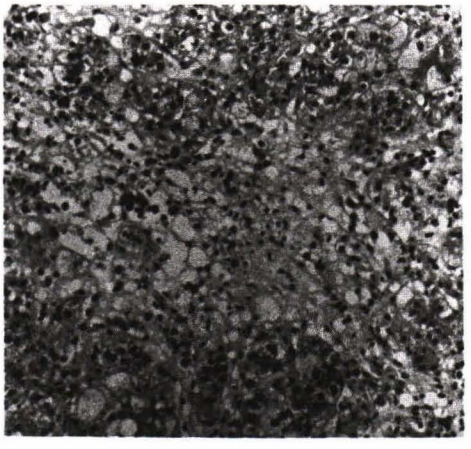

Fig. 2. Focal liver cell loss (arrow) in the centrilobular zone. H & E, x 65.

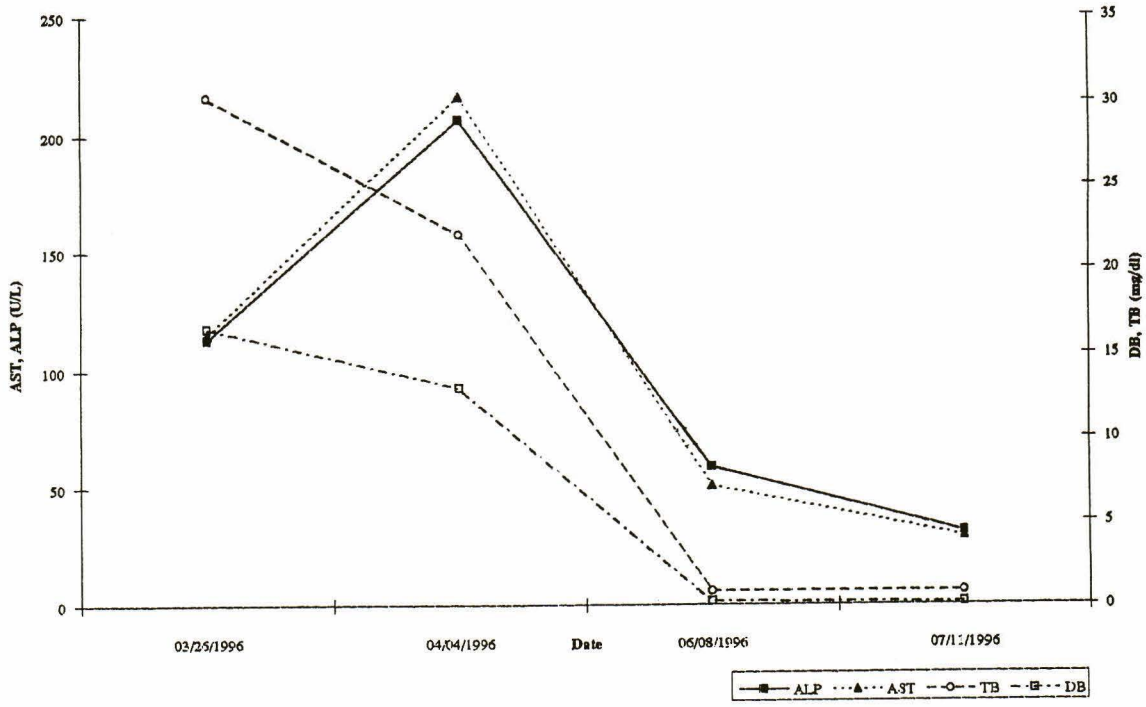

Fig. 3. Liver function tests from admission to three months follow-up.

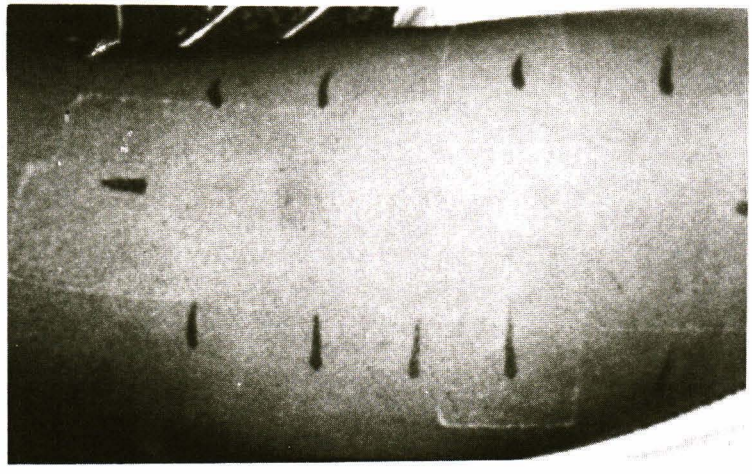

Fig. 4. Positive patch test in the patient.

She was supportively and symtomatically treated. She gradually recovered except for her jaundice, then she was discharged nine days after admission. She became clinically improved and the liver function test became normal after a three months' period of follow-up (Fig. 3). Because hypersensitivity to TCE was suspected, patch test was done one month after discharge. The patch contained different concentrations of TCE (5%, 10%, 20% and 50%) and its metabolite; trichloroacetic acid (5% TCA). The test was positive at 48 hours with 50 per cent TCE (Fig. 4) while 5 control subjects gave negative results using the same patch test technique.

DISCUSSION

The direct toxicity from TCE includes cardiovascular, nervous system, skin, renal and liver injury. It is irritant to skin and mucosa, producing dermatitis or skin burn in acute exposure and defatting change of skin in chronic dermal exposure[4]. TCE caused hepatotoxicity and renal tubular damage like other chorinated hydrocarbon such as carbontetrachloride (CCl_4)[5]. TCE also induced non-dose related diseases, such as exfoliative dermatitis. Although they were not common, there were some case reports of TCE induced exfolilative dermatitis with or without other organ involvement[6,7]. The clinical presentation of our patient was multiple organ involvement which included prolonged fever, skin rash, hepatitis (cholestatic type) and lymphadenopathy. Many systemic diseases such as viral hepatitis, salmonellosis, rickettsial infection, tuberculosis, melioidosis, and autoimmune diseases can caused this type of illness. Our investigations excluded those possibilities. Positive patch test suggested the immunologic reaction as mechanism of the illness. In animal studies, TCE can alter immunologic responses[4]. These results confirmed our hypothesis. Our findings were similar to previous reports that patch test was positive only in the high concentration of TCE[6]. The detail of mechanism is still unknown.

Halothane induced hepatitis and phenytoin syndrome are known as drug or chemical-induced immunologic illness. Halothane can cause acute hepatitis, high fever and rarely skin involvement. It has been postulated that some of halothane metabolites are responsible for those reactions. Since TCE is a chlorinated hydrocarbon with chemical structure closely resembling halothane, it might share some properties with halothane[7]. The positive patch test possibly could be due to TCE metabolites rather than the TCE itself. Our patient's clinical presentation was similar to the phenytoin syndrome that includes fever, rash, lymphadenopathy, hepatitis, leukocytosis, and eosinophilia[8]. The pathogenesis of this syndrome is not well established. However,cell mediated immune response may be responsible for the reaction[7].

(Received for publication on July 11, 1997)

REFERENCES

1. Ellenhorn, Matthew J. Trichloroethylene. Medical toxicology. New York, Esevier Science Publishing Company, Inc., 1988; 990-3.
2. McCarthy TB, Jones RD. Industrial gassing poisoning due to trichloroethylene, perchloroethylene, and 1,1,1 trichlorethane. 1961-80 Br J Ind Med 1983; 40: 450-5.
3. Diseases of the liver and biliary tract standardization of nomenclature, diagnostic criteria and diagnostic methodology. In : Forgarty international center proceeding No.22 DHEW Publication No. (NIH) 77-725. U.S. Government printing office, 1977; 9.
4. Poisindex : Computerized clinical information system. Trichloroethylene, 1997; Vol.91.
5. Kenna JC, Jones RM. The organ toxicity of inhaled anesthetics. Anesth Analg 1995; 81: S51-66.
6. Nakayama H, Kobayashi M, Takahashi M, et al. Generalized eruption with severe liver dysfunction associated with occupational exposure to trichloroethylene. Contact Dermatitis 1988; 19: 48-51.
7. Bond GR. Hepatitis, Rash and Eosinophilia following trichloroethylene exposure: A case report and speculation on mechanistic similarity to halothane induced hepatitis. J Toxicol Clin Toxicol 1996; 34: 461-6.
8. Dienstag JL, Isselbacher KJ. Toxic and drug induced hepatitis Harrison's Principle of Internal Medicine. 13th ed., New York, McGraw-Hill Inc., 1994: 1473-6.

ตับอักเสบและผื่นผิวหนังทั่วตัวที่เกิดจากสารไตรคลอโรเอทธีลีน : รายงานผู้ป่วย 1 ราย

ฐิรภัทร จิตต์โสภักตร์, พ.บ., วินัย วนานุกูล, พ.บ.*, เพ็ญพรรณ วัฒนไกร, พ.บ.**, ชุติมา ประมูลสินทรัพย์, พ.บ.***, อาภัสณี โสภณสฤษฏ์สุข, พ.บ.***, ประวัติ นิธิยานันท์, พ.บ.*****

รายงานผู้ป่วยหญิง 1 ราย ที่มีตับอักเสบและผื่นผิวหนังทั่วตัวโดยผู้ป่วยเกิดอาการหลังจากเข้าทำงานในหน้าที่ทำความสะอาดผลิตภัณฑ์ถุงเท้าโดยใช้สารไตรคลอโรเอทธีลีน ในรูปฟ่น

ตับอักเสบและผื่นผิวหนังทั่วตัวจากการสัมผัสสารไตรคลอโรเอทธีลีนเป็นภาวะที่พบได้น้อย กลไกการเกิดเชื่อว่ามาจากภาวะภูมิไวเกินต่อสาร ไตรคลอโรเอทธีลีน

* ภาควิชาอายุรศาสตร์,

** หน่วยโรคผิวหนัง, ภาควิชาอายุรศาสตร์,

*** หน่วยโรคทางเดินอาหาร, ภาควิชาอายุรศาสตร์,

**** ภาควิชาพยาธิวิทยา, คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี, มหาวิทยาลัยมหิดล, กรุงเทพฯ 10400