

CASE REPORT

세탁소를 운영하는 부부에서 동시에 발생한 담낭암: 담낭암과 벤젠과의 연관성

심광연, 차상우, 엄옥현, 전창균, 정승원, 장재영, 조영덕

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Simultaneous Occurrence of Gallbladder Cancer in a Laundry Couple: Association between Gallbladder Cancer and Benzene

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Gallbladder (GB) cancer occurs predominately as a biliary tract malignant tumor. It generally has a very poor prognosis, and early detection is often difficult. A variety of carcinogens have been implicated as an important cause for GB cancer. Benzene is a well-known carcinogen for hematologic malignancy, and its casual relationship with GB cancer has been suggested. We report a case of two patients who had operated a laundry cleaning facility together and later simultaneously got GB cancer after prolonged benzene exposure. (*Korean J Gastroenterol* 2013;61:107-109)

Key Words: Gallbladder neoplasms; Benzene

INTRODUCTION

Gallbladder (GB) cancer occurs primarily in elderly individuals aged 70 or older. Initial clinical symptoms associated with GB cancer are nonspecific, and metastasis occurs quickly. In cases where the diagnosis has been delayed making radical resection difficult, median average survival duration is generally less than 6 months.¹ The gallstone, GB polyp, porcelain GB, anomalous pancreatobiliary union (APBU), and the race etc. are the risk factors of GB cancer. Exogenous cancer-causing material can accumulate in the GB and GB cancer carcinogenesis.

CASE REPORT

A 60-year-old man with no significant past medical history was admitted for a 2-week history of jaundice due to unknown etiology. On physical exam, generalized jaundice was observed, and a mass was palpated in his right upper quadrant abdomen.

Laboratory finding showed a total/direct bilirubin 18.4/9.9 mg/dL, AST/ALT 183/331 IU/L, ALP 700 IU/L, GGT 537 IU/L, and CA19-9 of 4,980 U/mL. Abdominal ultrasonography and CT were showed a thickened GB wall with a GB mass invading through the hepatic segments 4 and 5 (Fig. 1). Intrahepatic bile duct (IHD) dilatation was observed due to mass infiltration. In addition, because multiple lymph no-

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Fig. 1. Abdominal CT finding of first patient (husband). A 6×7 cm sized hypoechoic mass lesion (arrow) in gallbladder and infiltration into the liver parenchyma.

des had invaded the abdominal cavity, the patient was diagnosed with stage IV GB cancer. GB cancer was confirmed with ultrasonography guided tissue biopsy, and pathology revealed an undifferentiated adenocarcinoma.

Another patient was a 52-year-old female, the first patient's wife who worked together with the first patient in the laundry cleaning business for 40 years. She was admitted hospital because of jaundice. Her laboratory findings showed total/direct bilirubin 9.8/6.4 mg/dL, AST/ALT 172/497 IU/L, ALP 411 IU/L, GGT 1,304 IU/L, and CA19-9 of 613 U/mL. Based on CT findings, a 2.2 cm mass lesion was observed in the GB body wall (Fig. 2). The mass lesion infiltrated the surrounding bile duct, spreading into the duodenal bulb and lymph nodes within abdominal cavity. Metastasis of GB cancer to lymph nodes was also diagnosed based on PET-CT showing increased ^{18}F FDG absorptions in the GB surrounding and lymph nodes around porta hepatis and celiac trunk. Urine phenol-benzene and t.t-muonic acid-benzene testing was used to measure the body benzene concentration in both patients. Both patients' urine phenol-benzene was calculated to be 12.895 and 2.489 mg/g creatinine (normal range <50 mg/g creatinine, 10 ppm standard), respectively. Their urine t.t-muonic acid-benzene was 0.057 mg/g creatinine for the first patient and, 0.058 mg/g creatinine for the second patient (normal range <1 mg/g creatinine, 10 ppm standard). To relieve first patient's obstructive jaundice, percutaneous transhepatic bile duct drainage of both IHDs were performed. However, he died 40 days later despite of the best supportive treatment. Endoscopic retro-



Fig. 2. CT finding of second patient (wife). A 2×2 cm sized mass lesion (arrow) in the gallbladder body with enhanced wall thickening.

grade biliary drainage of both IHDs using plastic stents was performed in the second patient. She died 100 days later in spite of the best supportive treatment.

DISCUSSION

Benzene is a hydrocarbon with a molecular formula of C_6H_6 . It can be present in the atmosphere, existing as a, colorless, transparent vapor without any odor or scent. It is used as a material to produce hydrocarbon compounds in dyes, organic pigments, organic chemicals, synthetic textiles, synthetic resins, agricultural pesticides, photograph chemicals, insect repellent, preservative, and insulting oils. It is absorbed primarily into the body through inhalation, although absorption through skin or conjunctival contact is possible. Approximately 50% of the inhaled benzene is not metabolized and is expelled through exhalation. The remaining 50% is metabolized through the liver, 30% being excreted through urine in a phenol form. The biological half life of benzene is 24 hours, and it is excreted within 1-2 hours. Benzene maintains high dose concentrations in tissue, 20 folds more than blood concentration because the absorbed benzene accumulates in fatty subcutaneous tissue and bone marrow.² Benzene is categorized as a carcinogen based on industry epidemiology research.³ It is also categorized as a carcinogen by the World Health Organization and affiliated International Agency for Research on Cancer.

Various researches have presented the relationship between the cancer and benzene. In 1938, the relationship be-

tween benzene and leukemia was made well known by Vigliani and Saita.⁴ A benzene in the air lead to leukemia in a group of Turkish shoe factory workers.⁵ In researches of GB cancer and benzene, 1,790 leather factory workers died of cancer, of which 13 people had GB cancer in a retrospective study.⁶ For rubber polish industry workers, using benzene and beta-naphthylamine, GB cancer risk was 4 folds more than a normal person based on a long term cohort study for 40 years.⁷ In 2001 in India, organochlorine pesticide (the organic chlorine agricultural chemical: benzene hexachloride) levels in bile were detected in 60 patients (30 GB cancer and 30 cholelithiasis). The mean biliary concentration of benzene hexachloride and dichlorodiphenyltrichloroethane, aldrin, endosulfan was found to be significantly higher in carcinoma of the GB than in cholelithiasis. High biliary pesticides concentrations suggest that these pesticides might be a GB carcinogen.⁸

A solvent is a gasoline mixture product used for dry cleaning materials that were used by the couple. Currently popular dry cleaning materials consist of benzene, trichloroethylene, perchloroethylene, and fluorine. Waste oil mixture fuel consists of diesel (20%), toluene (15%), benzene (5%), and waste oil (60%). We can assume that laundry workers using the same solvents in the same region have higher cancer prevalence rates. At 2002, industry epidemiology researchers reported that examining laundry worker's harmful exposure and workplace about 5 items (benzene, toluene, xylene, ethyl benzene, butoxyethanol) in solvents they could not exclude that using fake solvent or industrial solvent cause the cancer, although normal solvents products are not related to carcinogens. The couples worked and lived in small space of 40 m² for 40 years and were exposed to chemicals without ventilation system. Because they hanged the laundry in their house, total personal exposure was higher than other workers using benzene. Therefore, we can assume that they developed cancer because they were exposed to benzene continuously without any protective gear interspersed with periods of "momentary high dose" exposure. In the past, phenol was analyzed as the biologic exposure index. But, because sorbic acid and food additives which have similar structure like sorbic acid are changed to phenol after metabolism in the

body, they are not suitable for specific index material of benzene.

Currently, t.t-muonic acid is analyzed as a specific index material. Urinary t.t-muonic acid consistency is permissible up to a maximum level of 5 mg/g creatinine. The t.t-muonic acid urine levels in our two patients were within normal range. However, it was assumed that this carcinogenic material already accumulated in the fatty tissue or bone marrow. Two patients did not have an additional GB cancer risk factors compared to other people. Prolonged exposure to benzene was the main reason for their simultaneous GB cancer occurrence. Given that its biological half life was 24 hours, benzene body consistency in the couple already fell within the normal range.

Our report is the first report about relationship between GB cancer and benzene in Korea. But, limitation in our report is not to refer direct relation between them. So, it should be needed prospective and retrospective study to define relationship between them. We report a case of two patients who operated a laundry cleaning facility together who simultaneously got GB cancer after prolonged benzene exposure.

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