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Case Report**Inhalational chemical exposure resulting in myelogenous leukemia**

Cesar Reis, Haley Reis, Camila Araujo, Charity Russell, Sean Welsh*, Akbar Sharip and Paul Kim

Occupational Medicine Department, Loma Linda University, Loma Linda, California, United States

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***Correspondence Info:**Dr. Sean Welsh,
Occupational Medicine Department,
Loma Linda University,
Loma Linda, California, United States***Article History:****Received:** 11/02/2017**Accepted:** 14/02/2017**DOI:** <https://dx.doi.org/10.7439/ijbr.v8i2.3939>**Abstract****Introduction:** Chronic myelogenous leukemia is a relapsing and remitting disease that may be caused by exposure to environmental toxins. In this report, we discuss a case of an individual who was occupationally exposed to chemical carcinogens over a period of 10 years and developed chronic myelogenous leukemia pursuant to this exposure.**Case Presentation:** A middle aged chemical worker presented to the emergency room with a hematopoietic syndrome. Diagnostic studies revealed laboratory findings consistent with myelogenous leukemia. Due to the patient's known repeated chemical exposures over a multi-year period preceding the hematopoietic syndrome, a qualified medical evaluator determined that the leukemia was work related.**Conclusion:** Chronic myelogenous leukemia is not generally considered an occupational disease. However, a review of the literature demonstrates that exposure to certain chemicals may result in the induction of leukemia. Several biochemical mechanisms have been proposed to account for this effect. This case illustrates that occupational history must be considered if the attribution of causation is material to the patient in the setting of chronic myelogenous leukemia. Moreover, personal protective equipment should be worn under all circumstances when working with noxious fumes in order to avoid inhalational exposures.**Keywords:** Benzene; myelogenous leukemia; environmental toxins.**1. Introduction**

Benzene is the most commonly implicated chemical carcinogen for chronic myelogenous leukemia. Benzene is a stable colorless liquid at room temperature and due to its high vapor pressure, evaporates rapidly at room temperature, making it highly flammable. Methods to detect benzene in the workplace include gas chromatography and mass spectrometry after collection in the form of charcoal. It can be measured in the mg/m³ range, but analysis can also be performed using portable direct reading instruments and dosimeters [1]. Benzene is considered a human carcinogen, with exposure to benzene in the industrial setting coming primarily from both its synthesis and use in production of other chemicals. In the occupational setting, the primary contact routes include inhalation and dermal absorption [2], but exposure can also occur through ingestion of food and

drinking water contaminated with benzene [3]. The most reported chronic effects of benzene exposure include hematotoxicity, immunotoxicity, and carcinogenicity. Its metabolites are produced in the liver and travel to the bone marrow where further metabolic activity occurs. These metabolites target stem cells, progenitor cells, and stromal cells. The first stages of benzene toxicity in the workplace shows as signs of bone marrow depression including anemia, leukopenia, or thrombocytopenia, and its symptoms follow a dose-response relationship.

Exposure to high benzene levels (160-320 mg/m³) may result in benzene toxicity [1]. In animal studies, rats exposed to benzene by inhalation had carcinogenic-related end points for chronic myelogenous leukemia after exposure to doses of 320 mg/m³ over periods of 4-7 hours

per day[4]. Benzene toxicity targets the bone marrow, resulting in changes to both humoral and cellular immunity. This dysregulation of the hematopoietic system is the main reason why chronic exposure to benzene elicits myelogenous leukemia induction. Research conducted during working hours on workers exposed to benzene, toluene, and xylenes found immunological effects including agglutinins reacting with autoleukocytes[5] and increased levels of IgM along with decreased IgA and IgG [6]. In addition, studies on chronic exposure reported increased susceptibility to allergies [7], decreased or loss of leukocytes and blood elements, enlarged spleen [8], and a reduction in circulating T-lymphocytes [9].

2. Case Presentation

A middle aged chemical worker presented to the emergency room with a hematopoietic syndrome. Diagnostic studies revealed an elevated white blood cell count with laboratory findings consistent with myelogenous leukemia. Due to the patient's known repeated chemical exposures over a period of 10 years preceding the hematopoietic syndrome, a qualified medical evaluator determined that the leukemia was work related.

Part of the patient's occupational duties included working around noxious chemical fumes multiple times per week. The chemicals were kept in large open-air vats resulting in the off gassing of noxious fumes. Personal protective equipment was not worn. These chemicals included but were not limited to benzene, toluene, xylene, and diesel fumes. The patient had repeated and persistent inhalational exposure to these chemicals over many years. After 10 years on the job, the patient developed symptoms that necessitated a visit to the local emergency department. Bloodwork was performed which revealed a hematopoietic syndrome consistent with myelogenous leukemia.

3. Discussion

3.1 Chronic Exposure to Benzene, Toluene, and Xylene

While benzene has been established as a human carcinogen by the International Agency for Research on Cancer [10], toluene and xylene may also play a part in the toxicokinetics [11]. Both xylene and toluene are aromatic and highly flammable liquids. They are not classified as carcinogenic for humans but are considered toxic and can produce target organ damage with repeated or prolonged exposure. A study in China investigating workers at a container-manufacturing plant in 2014 found gene-specific differences between control group and workers exposed to benzene, toluene, and xylene (BTX). There was a statistically significant decrease in poly (ADP-ribose) polymerase 1 (PARP1) mRNA and DNA methylation

transferases (DNMTs) in BTX-exposed workers [12]. PARP-1 is responsible for handling DNA damage and is normally constitutively expressed, and its inactivation or down regulation leads to genomic instability accelerated apoptosis [13]. DNA methylation transferases (DNMTs) might play a role in the process of DNA methylation, thereby accounting for the genomic hypomethylation found in workers exposed to BTX mixtures. The down regulation of PARP enzyme expression may represent an epigenetic pattern deviating from normal ADP-ribosylation induced by chronic BTX exposure [12]. It is well understood that chronic myeloid leukemia is characterized by the occurrence of genetic alterations due to an underlying genomic instability resulting from compromised DNA damage and repair mechanisms[14], and prolonged exposure to BTX needs to be considered as being able to impart a negative effect at the genetic level.

3.2 Diesel Fumes

Exposure to environmental chemicals has a long history linked to health complications, including cancer. However, upon closer inspection, the link between diesel exposure and leukemia appear to tell a different story. Leme and colleagues observed the cytotoxic effects of biodiesel and diesel blends on human T cell leukemia and human hepatocellular carcinoma cells. In this experiment, cytotoxic effects were found when cells were contaminated with water containing pure (at least 95%) diesel, but no such effects were found with water containing biodiesel, suggesting carcinogenic properties in diesel, but not biodiesel [19]. As a response to experimental studies suggesting the carcinogenic nature of diesel, Guo and colleagues aimed to study the link between occupations with a high exposure to diesel and various cancers; ovarian, testicular, kidney, bladder, and leukemia. Their cohort study assessed Finns born between 1906 and 1945 who were diagnosed with cancer. Relative risk and cumulative exposure were calculated, and compared between diesel exposed, and unexposed groups. The only cancer with a link to diesel ($p=0.006$) was ovarian cancer [20]. Lindquist and colleagues conducted a case-control study to investigate the association between exposure to chemicals in motor exhaust, such as petroleum gasoline and diesel, and acute leukemia. Using matched patient-control pairings, risk and odds-ratios were calculated. There were no significant differences between the groups-individuals with high exposure to motor exhaust did not have a higher risk of leukemia compared to the controls [21]. When reviewing literature to date (2004), an analysis of eighteen studies including case-control and statistical analyses, found no correlation indicating causation of leukemia from diesel[22]. Despite there being a lack of consistent data supporting a correlation with occupational diesel exposure

and leukemia, a more recent study found different effects in children. In a Chinese case-controlled study aiming to examine the link between environmental chemicals and childhood acute lymphocytic leukemia, a positive correlation was found between chemical exposure and cancer[23].

4. Conclusion

Chronic myelogenous leukemia is not generally considered an occupational disease. However, a review of the literature demonstrates that exposure to certain chemicals may result in the induction of leukemia. Several biochemical mechanisms have been proposed to account for this effect. This case illustrates that occupational history must be considered if the attribution of causation is material to the patient in the setting of chronic myelogenous leukemia. The moral of this case report is that personal protective equipment should be worn if inhalational exposure to chemicals is possible.

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