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## Case Report

# A Case of Dilated Cardiomyopathy Associated With Chronic Toluene Exposure

Gabrielle Denault, MD,<sup>a,†</sup> Hamza Ouazani Chahdi, MD,<sup>a,†</sup> Louis Patry, MD,<sup>b</sup> and Jean-Pascal Costa, MD, MMEd<sup>c</sup>

<sup>a</sup>Faculty of Medicine, Université de Montréal, Montréal, Québec, Canada

<sup>b</sup>Department of Occupational Medicine, Centre Hospitalier de l'Université de Montréal, Montréal, Québec, Canada

<sup>c</sup>Department of General Internal Medicine, Centre Hospitalier de l'Université de Montréal, Montréal, Québec, Canada

## ABSTRACT

A 56-year-old woman working in a factory for the past 34 years presented with dilated cardiomyopathy of unknown etiology. She was exposed daily to toluene at work, without adequate protective equipment. A public health department investigation reported that toluene exposure among workers at her factory was more than 3 times the established limit. Toluene inhalation is associated with cases of cardiac arrhythmias, vasospasm, and cardiomyopathy. Occupational exposure to cardiotoxic substances should be investigated in patients with idiopathic cardiomyopathy. This case report highlights an association between a case of dilated cardiomyopathy and chronic exposure to toluene.

## RÉSUMÉ

Une femme de 56 ans, employée dans une usine pendant 34 ans, a reçu un diagnostic de cardiomyopathie dilatée de cause inconnue. Au travail, elle était exposée quotidiennement au toluène, sans équipement de protection adéquat. Une enquête effectuée par le département de santé au travail de la santé publique a révélé que les travailleurs de cette usine étaient exposés à une concentration de toluène supérieure à 3 fois la limite établie. L'inhalation de toluène a déjà été associée à des cas d'arythmies cardiaques, de vasospasmes et de cardiomyopathies. La possibilité d'une exposition professionnelle à des substances cardiotoxiques devrait être examinée chez les patients atteints de cardiomyopathie idiopathique. Cet article met ainsi en évidence un cas de cardiomyopathie dilatée associé à une exposition chronique au toluène.

A 56-year-old woman of South American origin presented to our emergency department with a 9-month history of progressive dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. Her past medical history was unremarkable except for cholecystectomy, left hilar lung calcified granulomas on a 2014 radiograph, and a family history of hypertension. Her father had passed away at age 65 years, possibly from a myocardial infarction. The patient had previously consulted her family doctor, who prescribed bronchodilators, suspecting asthma. She had no history of chest pain, palpitations, syncope, or lower-limb edema. She had lost 10 pounds in the preceding year. She had no history of digestive symptoms, upper respiratory tract infection, rheumatic fever, arthralgia,

or new rash. Her history was also negative for tobacco use, drug use, and alcohol abuse. Nutritional deficiencies were not suspected. Her pregnancies had been unremarkable. Her latest travel was 2 years earlier to South America.

Physical examination revealed a blood pressure of 122/87 mm Hg, a heart rate of 122 beats per minute, and tachypnea without hypoxemia. Cardiac auscultation revealed an S3 and an apical holosystolic 2/6 murmur. An electrocardiogram showed a left bundle branch block with a QRS length of 148 ms, with no previous electrocardiogram for comparison. A chest radiograph confirmed the hypothesis of pulmonary edema.

Blood tests revealed a slightly elevated white blood cell count, with neutrophils at  $9.5 \times 10^9/L$  (upper limits of normal:  $7.00 \times 10^9/L$ ) and slightly elevated creatinine at 92  $\mu\text{mol/L}$  with normal C-reactive protein level. The first N-terminal pro-brain natriuretic peptide (NT-proBNP) titer was at 10,059 ng/L (normal:  $< 300 \text{ ng/L}$ ). The first high-sensitivity troponin I level was mildly elevated, at 14.4 ng/L, and it increased to a maximum level of 52.8 ng/L (normal:  $\leq 12 \text{ ng/L}$ ).

A transthoracic echocardiogram showed a left ventricular ejection fraction of 13%, with a severely dilated and globally hypokinetic left ventricle and moderate-to-severe mitral

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<sup>†</sup>Co-first authors who contributed equally.

Corresponding author: Dr Gabrielle Denault, University of Montreal, 2900 Édouard-Montpetit, Montréal, Québec H3T 1J4, Canada.

E-mail: [gabrielle.denault@umontreal.ca](mailto:gabrielle.denault@umontreal.ca)

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### Novel Teaching Points

- Toluene may be associated with heart disease.
- Cases of cardiomyopathy have been associated with exposure to toluene.
- Clinicians should be careful to investigate the patient's occupational history. Public health assessments can help identify potential toxic agents in the workplace, particularly to aid vulnerable workers who are unaware of the health risks of these products and the importance of wearing appropriate protective equipment.

regurgitation, mild tricuspid regurgitation, and normal pulmonary artery pressure.

The patient was admitted to the internal medicine ward. Cardiac magnetic resonance imaging revealed no myocardial edema in favor of infectious myocarditis and no evidence in favour of Takotsubo, infiltrative, arrhythmogenic, or hypertrophic cardiomyopathy. A mild-to-moderate right ventricular systolic dysfunction was also present. The radiologists' differential diagnoses included toxic, alcohol-related, endocrine-related, auto-immune-related, metabolic, nutritional, and genetic cardiomyopathy. A coronary angiogram was requested and showed minimal atherosclerosis.

Given the cardiac magnetic resonance imaging findings, additional blood tests were ordered. Creatinine kinase, electrolytes including calcium, thyroid stimulating hormone, liver enzymes, ferritin, antinuclear antibody, extractable nuclear antigen (ENA) panel, and an antineutrophil cytoplasmic antibodies test, with both cytoplasmic and perinuclear staining (C/P-ANCA), were all normal. A blood protein electrophoresis only reported a nonspecific mildly increased IgA titer. HIV, *Borrelia burgdorferi*, and *Trypanosoma Cruzi* blood titers were negative.

The patient was thus diagnosed with idiopathic dilated cardiomyopathy and treated with intravenous diuretics and introduction of a beta-blocker, an angiotensin-converting enzyme inhibitor, and a mineralocorticoid receptor antagonist. A cardiomyopathy genetic panel was ordered and was revealed to be negative except for a mutation of unknown significance of the *MYH6* gene.

A myocardial biopsy was considered but was not performed, because the result would not modify the treatment, and the risk of complications did not justify any benefit.

The patient reported working for the preceding 34 years in a plastic cases factory. Given her unusual work, she was referred to occupational medicine to eliminate a toxic cause for her cardiomyopathy. History showed that she was exposed daily to numerous industrial solvents, including glue and glue vapors containing toluene, without personal protective equipment. An investigation from the occupational health team of the regional public health department was therefore requested. A workplace evaluation was done with workers from the same factory. The environmental assessment, evaluated with photoionization, revealed no limit-exceeding volatile organic compounds in the workplace's air. For biological monitoring, urine samples were taken from workers at the end

of the work shift and showed that half of the workers had urinary ortho-cresol levels between 0.33 and 1.5  $\mu\text{mol}/\text{mmol}$  of creatinine, exceeding the index biological exposure level recommended by the American Conference of Governmental Industrial Hygienists (ACGIH) of 0.3  $\mu\text{mol}/\text{mmol}$  of creatinine.<sup>1</sup> Thus, skin and digestive toluene absorption were suspected among workers, given the absence of both adequate skin protection equipment and handwashing at breaks and lunch. To our knowledge, no other case of cardiomyopathy among the other employees was described. Due to its short half-life, our patient's ortho-cresol level was not measured, because she had already been removed from her workplace prior to the public health investigation.

A control transthoracic echocardiogram performed at 9 and 11 months did not show an improvement in the left ventricle ejection fraction.

### Discussion

Toluene ( $\text{C}_6\text{H}_5\text{CH}_3$ ) is an aromatic hydrocarbon. It is colorless, flammable, and insoluble in water. In industry, toluene is used as a solvent for paints, glues, varnishes, and printing inks, and it is found in mixtures of certain petroleum products. Toluene is also used as a recreational inhalant (ie, in glue sniffing).<sup>2</sup>

Toluene is absorbed through the respiratory, gastrointestinal, and dermal tracts. Toluene elimination follows a nonlinear curve, with 3 phases having a half-life of 2 minutes, 30 minutes, and 3.5 hours. For individuals exposed to high concentrations, a fourth phase covers a half-life of 20 to 90 hours. Therefore, a risk of accumulation is present during a workweek.<sup>2</sup>

Experimental studies have shown that toluene could have a direct cardiotoxic effect on the myocardium and induce vasospasms and cardiac conduction system abnormalities.<sup>3</sup> Case reports and series have also reported cases of acute heart failure, arrhythmias, coronary vasospasm, and cardiomyopathy.<sup>4,5</sup> In most cases, the effect of toluene is described as being short-term and reversible, but case reports have also reported cases of chronic heart failure.<sup>6</sup>

### Conclusion

This article highlights a case of dilated cardiomyopathy associated with chronic exposure to toluene. The patient's family history and the mutation of unknown significance of the *MYH6* gene cannot allow us to completely exclude a genetic etiology, but chronic exposure to toluene could constitute a risk factor for heart disease. More studies are needed to better understand the impact of toluene on the heart. Given that patients are rarely asked about their exposure to toluene at work,<sup>7</sup> this article emphasizes the importance of investigating the occupational history of patients. Through better understanding of potential risk factors associated with heart disease, this approach could lead to the strengthening of preventive measures in workplaces.

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