JACC: CASE REPORTS VOL. 2, NO. 10, 2020

MINI-FOCUS ISSUE: HEART FAILURE

INTERMEDIATE

CASE REPORT: CLINICAL CASE

A Rare Case of Lead-Induced Cardiomyopathy

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ABSTRACT

A 39-year-old man, painter by profession, presented with symptoms of heart failure. His work up was unrevealing except for elevated blood lead levels (BLL). He was started on guideline-directed medical therapy and was referred to occupational therapy. No improvement in his ejection fraction was noted until his BLL decreased. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:1496–500) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

PRESENTATION

A 39-year-old male presented to the emergency room with complaints of shortness of breath on exertion and pedal edema for 1 month. His vital signs were significant for a heart rate of 105 beats/min, blood pressure of 150/95 mm Hg; he was afebrile, and his oxygen saturation was 94% on room air. Physical examination was notable for elevated jugular venous pressure, 2+ pitting pedal edema, and bibasilar crackles on respiratory examination, and S_3 was heard on cardiac auscultation.

LEARNING OBJECTIVES

- To recognize chronic lead exposure as one of the causes of cardiomyopathy and myocarditis.
- To understand that, with early diagnosis and management, there can be a potential improvement in ejection fraction.
- To understand the spectrum of cardiovascular effects of chronic lead exposure.

MEDICAL HISTORY

His medical history was significant for resistant hypertension, which was diagnosed at 35 years of age. He initially required 4 different antihypertensive agents for optimal control of his blood pressure. With lifestyle changes and weight loss, his therapy was reduced to hydrochlorothiazide and metoprolol succinate. He had undergone complete workup for secondary hypertension at the time of diagnosis and was negative. The patient was a painter by profession, was never a smoker, and used alcohol occasionally but not illicit drugs. His family history was significant for diabetes in his mother. A transthoracic echocardiogram performed at the time of diagnosis of his hypertension showed normal left ventricular ejection fraction (LVEF).

INVESTIGATIONS

Electrocardiography revealed sinus tachycardia with left ventricular hypertrophy and secondary ST-T changes. A chest radiograph revealed an enlarged cardiac silhouette and pulmonary vascular congestion.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

Manuscript received March 3, 2020; revised manuscript received April 29, 2020, accepted May 26, 2020.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2020.05.047

Complete blood count and basic metabolic profile were within normal limits, as was his N-terminal pro-B-type natriuretic peptide concentration, and his troponin T peaked at 0.2 ng/ml (normal is <0.03 ng/ml). A transthoracic echocardiogram showed an LVEF of 23%, a mild LV dilation, a severe left ventricular hypertrophy (LVH) (139 g/m^2; normal 50 to 102 g/m^2), a markedly reduced right ventricular (RV) function, a mild to moderate central mitral regurgitation, and global hypokinesis.

DIFFERENTIAL DIAGNOSIS AND WORK-UP

He underwent cardiac catheterization, which showed no angiographically apparent epicardial coronary artery disease and elevated filling pressures with normal cardiac output and index. He had had no viral syndromes in the preceding 6 months, and he tested negative for *Trypanosoma cruzi* infection, HIV, and Lyme disease. His serum and urine protein electrophoreses were normal, as were his serum iron and ferritin levels. He had no history of cocaine or other illicit drug use. He drank 2 to 4 beers/week. He underwent cardiac magnetic resonance (CMR), which revealed diffuse enlargement of all cardiac chambers, with focal areas of subepicardial abnormal delayed enhancement consistent with myocarditis. Diffuse moderate hypokinesis of the left ventricle without the focal area of dyskinesis. Small pericardial effusion and depressed left and right ventricular functions were observed.

TREATMENT AND FOLLOW-UP

He underwent inpatient intravenous diuresis and was discharged on guideline-directed medical therapy for heart failure. During his outpatient follow-up visit, careful scrutiny of his history reveled significant occupational exposure to lead. He had started working as a painter at the age of 25 and had been exposed to lead in paints. He reported that he had not used protective face masks during work. His blood lead level (BLL) was elevated at 41 μg/dl (normal is 0 to 4.9 μg/dl). He was referred to occupational therapy, where it was recommended he change his profession, which he did. The standard recommendation for lead chelation is 80 μg/dl or above, hence, he did not receive any treatment with chelating agents. A decision was made to monitor his BLLs, and if it did not decrease as expected, he would be started on chelation. His BLLs decreased quickly to 15 μg/dl. The echocardiogram was repeated 2 months later which showed improvement in EF to 52%, mild LVH (111 g/m^2), and normal RV dimensions and function (Videos 1, 2, 3, and 4).

He continued to do well for the next 2 years. He remained compliant with his medications and outpatient follow-up examinations. Thereafter, he presented with congestive heart failure symptoms to his primary care physician again. During his visit, he admitted to going back to his painting profession but has not been wearing masks. Repeat TTE showed a decline in LVEF to 31% and an increase in LV mass (141 g/m^2), and his BLLs had increased to 38.7 μg/dl. He refused to switch jobs, hence, he was extensively counseled on wearing protective gear during work. His BLLs decreased slowly but steadily. TTE was repeated 6 months later, which showed improvement in EF to 46% and regression of LV mass index to 124 g/m^2 (Videos 1 and 2).

ABBREVIATIONS AND ACRONYMS

BLL = blood lead level

CMR = cardiac magnetic resonance

EMB = endomyocardial biopsy

LV = left ventricle

LVEF = left ventricular ejection fraction

LVH = left ventricular hypertrophy

PET = positron emission tomography

RV = right ventricle

RVEF = right ventricular ejection fraction

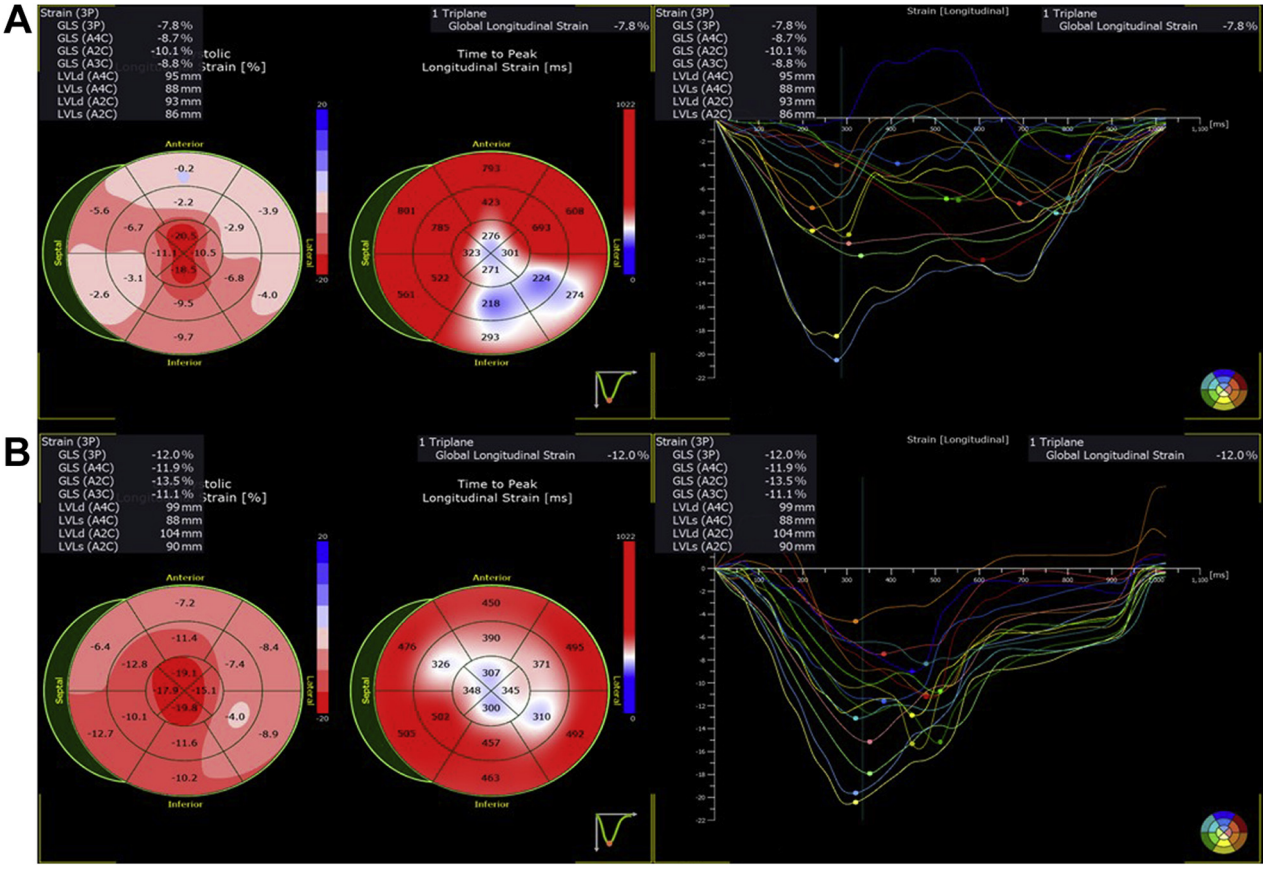
TTE = transthoracic echocardiogram

DISCUSSION

Lead is a common environmental toxin absorbed into the human body through the respiratory system, gastrointestinal tract, and skin. Chronic lead exposure is well known to affect a variety of organ systems. However, little is known about its effect on the cardiovascular system. More recently, the effect of chronic lead exposure has been implicated in resistant hypertension. The exact mechanism is still unclear, but it is believed to be related to oxidative stress, nitric oxide dysregulation, and alteration in the renin-angiotensin-aldosterone system (1). Population studies in the United States conducted by National Health and Nutrition Survey has found a direct relationship between lead exposure and elevated blood pressure (2). This patient initially came to medical attention years before the diagnosis of lead toxicity with resistant hypertension, which was likely secondary to his chronic lead exposure. Lead intoxication has also been associated with an increased incidence of coronary artery disease, stroke, peripheral arterial disease, and an increase in non-high-density lipoprotein cholesterol. Potential mechanisms of these agents remains to be studied (3).

The effect of lead exposure on myocardial structure and function has yet to be determined. Small case-controlled and observational studies have reported a decline in LVEF and global longitudinal strain in people chronically exposed to lead (4,5). A similar observation was made in this patient, as well (**Figures 1 and 2**). He had no other causes for his LV dysfunction other than elevated BLLs. His LVEF was at the lowest when his BLLs were at their peaks. As the BLL decreased, his LVEF, and his LV mass

FIGURE 1 Relationship of BLL With LVEF, GLS, and LV Mass



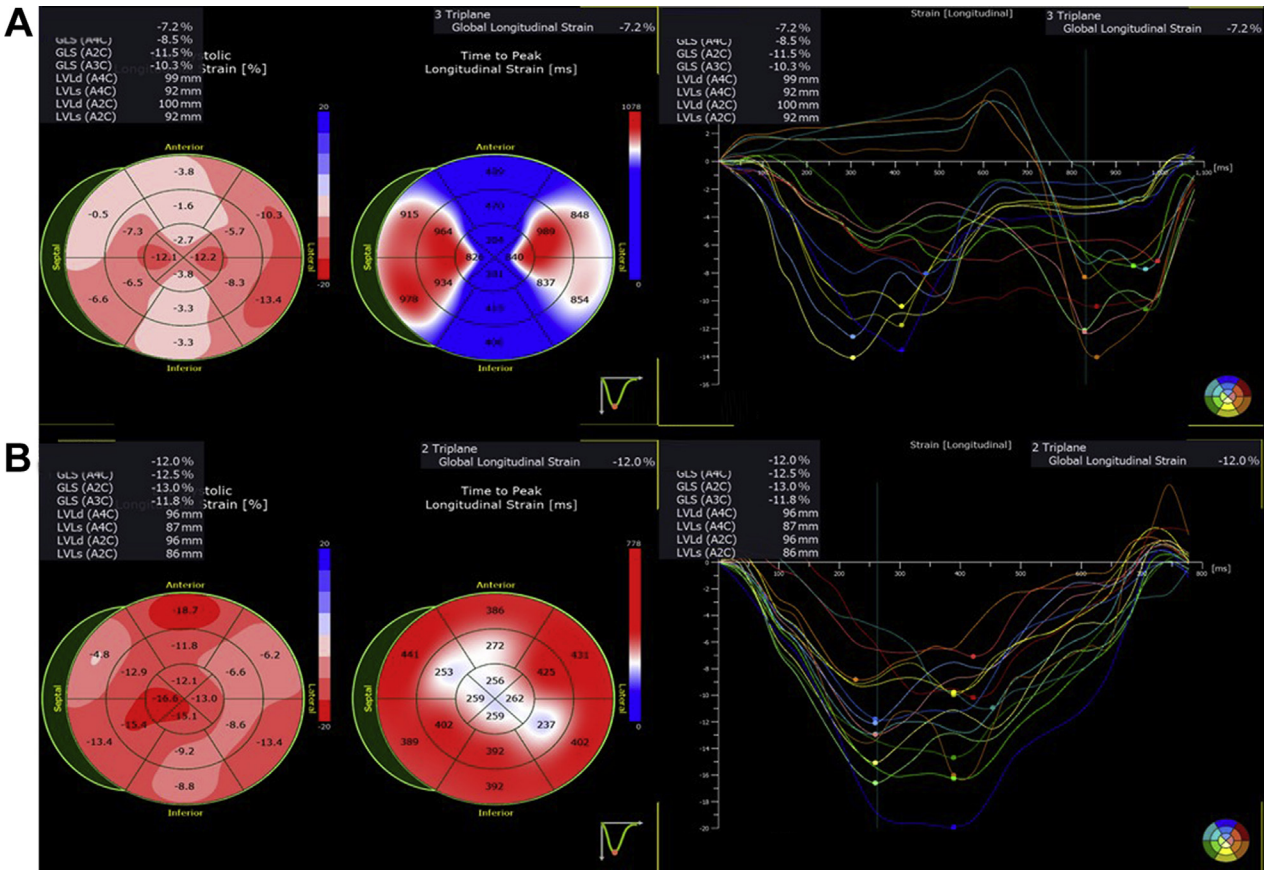
(A) End diastolic global longitudinal strain (GLS) (%) and time-to-peak longitudinal strain (ms) at blood lead level (BLL) of 41 μg/dl. **(B)** End-diastolic GLS and time-to-peak longitudinal strain at BLL of 17 μg/dl. LVEF = left ventricular ejection fraction.

regressed. When he started painting again, his BLLs increased, LVEF dropped, and LV mass increased. This temporal association strongly suggested the possibility of direct lead toxicity as the cause of a drop in his cardiac contractility. The exact association between LVEF and lead is unknown. Animal experiments have indicated that the cardiotoxic effects of lead are likely related to its interference with calcium-dependent cellular processes (6). There is also a suggestion that depressed myocardial contractility may be due to impaired phosphorylation of the myocardial contractile proteins (7). These findings have yet to be confirmed.

Finally, BLL is reported to significantly affect LV mass, LV end-diastolic dimension, and relative wall thickness. In a study conducted in Poland, Kasperczyk et al. (4) compared a group of individuals exposed to lead in lead factories with a control group of administrative workers, who were not exposed to lead and found that the LV end-diastolic dimension was 6% higher and there was an 11% increase in LV mass index in the group with lead exposure (4). That study did not eliminate the confounding factor of blood pressure. A study by Schwartz (8) in 1991 showed a similar finding after controlling for blood pressure. The present patient had evidence of concentric LVH with LV mass index of 140 g/m^2, an LV end-diastolic dimension of 59 cm, and a relative wall thickness of 0.44. Because hypertension is an independent risk factor for LVH, it became a confounder in interpreting these data in the present patient.

His initial presentation was consistent with myocarditis with elevated troponin levels, depressed RV and LVEF, and CMR results suggestive of myocarditis with marked thinning of the myocardium. This

FIGURE 2 End Diastolic GLS and Time-to-Peak Longitudinal Strain



(A) End-diastolic GLS (%) and time-to-peak longitudinal strain (ms) at BLL of 39 μg/dl. **(B)** End-diastolic GLS and time-to-peak longitudinal strain BLL of 30 μg/dl. Abbreviations as in Figure 1.

patient had a complete workup for myocarditis, short of endomyocardial biopsy (EMB). CMR is the imaging mode of choice for the workup of myocarditis. Fluorodeoxyglucose-labeled positron emission tomography is a good alternative when cardiac CMR cannot be performed. Despite its limited sensitivity and specificity, EMB remains the gold standard for the diagnosis of myocarditis. However, given the rarity of lead cardiomyopathy, there are no defined guidelines or findings to diagnose myocarditis caused by lead by EMB definitively. Histopathological examinations of heart specimens of rats intoxicated with lead showed degenerative changes in myocardial fibers, loss of muscle structure, and focal fibrosis (9). However, the exact mechanism of myocardial damage by lead is largely unknown. Some of the postulated mechanisms include a direct irritant effect on the myocardium, inhibition of cardiometabolic enzymes, and selective disturbance of coronary circulation. None of the above-mentioned hypotheses has been proven (10,11).

Myocarditis due to lead toxicity is a rare condition. It is a very challenging to diagnose because the possibility of coincidental viral myocarditis cannot be ruled out. Nevertheless, the diagnosis of lead cardiomyopathy was more likely in this patient with no viral prodromes in preceding months, and the temporal association of his BLL with his LV function and LV mass. In a review of the medical literature, 3 other cases of myocarditis due to chronic lead exposure in adults (9,12,13) were found. To the best of these authors' knowledge, this case is the fourth reported case of lead myocarditis and second reported case in an adult male.

CONCLUSIONS

The development of cardiomyopathy due to chronic lead exposure is most likely secondary to its direct toxic effect on the myocardium. More experimental

studies are required to establish the cardiotoxic mechanisms of lead. Meanwhile, cardiovascular ill effects of chronic lead exposure should be brought to the awareness of our health care providers for early diagnosis and management of these patients.

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KEY WORDS cardiomyopathy, global longitudinal strain, lead toxicity, myocarditis

APPENDIX For supplemental videos, please see the online version of this paper.