

Selenium and Chronic Heart Failure

To the Editor:

We read with interest the article by Inoko et al about selenium deficiency,¹ but we do not agree with the interpretation of the data.

Selenium deficiency was identified as a factor in the etiology of heart failure syndromes in areas of very low selenium intakes, such as China, where an endemic selenium-responsive cardiomyopathy is called Keshan disease.² Similar cases of cardiomyopathy were reported in HIV-infected patients³ and in subjects on parenteral nutrition.⁴ The patient with Crohn's disease described by Inoko et al falls into the latter category. When the patient developed his first episode of heart failure, the serum selenium level was not very low (62 µg/L). Low selenium was unlikely the single cause of heart failure, although it certainly contributed. Supplementation "improved the condition of the patient but did not normalize the left ventricular dysfunction," and "despite selenium supplementation for 11 years, the echocardiographic findings gradually deteriorated."¹ The patient "was free from symptoms of heart failure for 11 years" and died suddenly.¹

This discrepancy between the symptoms of heart failure and left ventricular dysfunction emphasizes that the pathophysiology underlying the symptoms of chronic heart failure is complex and poorly understood.⁵ There is no single cause of the main symptoms of heart failure (dyspnea and muscle fatigue), and treatments that correct the hemodynamics of heart failure do not reliably increase exercise tolerance or reduce the severity of dyspnea.⁵

The case described by Inoko et al suggests that selenium may have a role in the symptoms of heart failure rather than in the development of left ventricular dysfunction. Yet, selenium deficiency is not the only cause of Keshan disease, and it coincides with the clinical severity rather than the prevalence of the cardiomyopathy as assessed by echocardiography.² Possible causes of Keshan disease are viral infection and nutritional factors (insufficient zinc or molybdenum, excessive barium or lead). However, when serum selenium levels of residents of an endemic area were raised to the levels found in nonendemic areas, mortality from Keshan disease dramatically decreased, but clinically latent cases were still found, and the echocardiographic prevalence of the disease remained high.² Therefore, selenium deficiency seems to be a predisposing factor rather than a specific cause of Keshan disease.² Finally, although the exact cause of Keshan disease remains unknown, numerous agents probably work synergistically.

Thus, if selenium supplementation did improve the condition of the patient described by Inoko et al, the primary cause of his cardiomyopathy remains unknown.¹ The hypothesis that "once fully developed, the left ventricular dysfunction may be irreversible even after use of selenium supplements"¹ is not supported by either their own case or the relevant literature.

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1. Inoko M, Konishi T, Matsusue S, Kobashi Y. Midmural fibrosis of left ventricle due to selenium deficiency. *Circulation*. 1998;98:2638–2639.
2. Ge K, Yang G. The epidemiology of selenium deficiency in the etiological study of endemic diseases in China. *Am J Clin Nutr (Suppl)*. 1993;57:259S–263S.
3. Lipshultz SE. Dilated cardiomyopathy in HIV-infected patients. *N Engl J Med*. 1998;339:1153–1155.
4. Huttunen JK. Selenium and cardiovascular diseases: an update. *Biomed Environ Sci*. 1997;10:220–226.

5. Coats AJ. Origins of symptoms in heart failure. *Cardiovasc Drugs Ther*. 1997;11(suppl 1):265–272.

Response

We thank Dr Lorgeril and colleagues for their interest in our article.¹ The patient we reported in *Circulation* could take no food and almost no water for a long period of time, so he consequently experienced zinc deficiency in the first 1 month and biotin deficiency in the first 9 months after the beginning of total parenteral nutrition and recovered by the supplementation of each element.² When he had been experiencing progressive heart failure, his serum selenium (Se) level and his erythrocyte glutathione peroxidase activity (GSHPx) were low. After the supplementation of Se, these levels recovered (serum Se 96 µg/L, erythrocyte Se 136 µg/L, erythrocyte GSHPx 23.5U/g hemoglobin), and the deterioration of heart failure was stopped.³ His clinical course suggests that the etiology of his heart failure was Se deficiency. We agree with Dr Lorgeril and colleagues that the cause of Keshan disease may be multifactorial, but it is plausible that Se deficiency can cause cardiomyopathy that is accompanied by myocardial loss and fibrous replacement in the left ventricle.^{4,5} It is well known that dilatation and systolic dysfunction of the left ventricle gradually proceed by remodeling and overload of the residual myocardium, once myocardial loss has occurred. We regard the first episode of heart failure as having been caused by rapidly developing myocardial damage due to Se deficiency, which was terminated by the supplementation of Se, and the second episode of heart failure as having been the terminal feature of cardiomyopathy.

Dr Lorgeril and colleagues pointed out that serum Se was not very low when the patient developed heart failure and that it was unlikely that low Se was the single cause of heart failure. The previous reports about either Keshan disease or Se deficiency in parenteral nutrition revealed that there is no definite relationship between serum and erythrocyte Se concentration and erythrocyte GSHPx.³ Certainly, the serum Se level was not remarkably low in our patient, but the erythrocyte GSHPx level was very low, and the condition of heart failure was improved along with the elevation of erythrocyte GSHPx level after Se supplementation. This clinical course suggests his heart failure was a result of Se deficiency. So, we consider our patient to have demonstrated clinical features caused only by Se deficiency, and this is the first case of Se deficiency that was observed for a long period after supplementation of Se and with subsequent autopsy.

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1. Inoko M, Konishi T, Matsusue S, Kobashi Y. Midmural fibrosis of left ventricle due to selenium deficiency. *Circulation*. 1998;98:2638–2639.
2. Matsusue S, Kashihara S, Takeda H, Koizumi S. Biotin deficiency during total parenteral nutrition: its clinical manifestations and plasma nonesterified fatty acid level. *JPEN J Parenter Enteral Nutr*. 1985;9:760–763.
3. Matsusue S, Kashihara S, Tomonaga G. Selenium deficiency and cardiomyopathy in a patient on long-term parenteral nutrition. *Nippon Geka Gakkai Zasshi*. 1987;88:483–488.
4. Johnson RA, Baker SS, Fallon JT, Maynard EP III, Ruskin JN, Wen Z, Ge K, Cohen HJ. An accidental case of cardiomyopathy and selenium deficiency. *N Engl J Med*. 1981;304:1210–1212.
5. Fleming CR, Lie JT, McCall JT, O'Brien JF, Baillie EE, Thistle JL. Selenium deficiency and fatal cardiomyopathy in a patient on home parenteral nutrition. *Gastroenterology*. 1982;83:689–693.