Myocardial calcification may be localized or diffuse. Localized myocardial calcification is commonly seen after myocardial infarction, cardiac surgery, rheumatic fever, or after myocarditis. Diffuse calcification, however, is a rare phenomenon and a life-threatening condition that can be seen in a setting of generalized sepsis.1–3

Two pathophysiological mechanisms leading to calcium accumulation in cardiomyocytes have been described: metastatic calcification and dystrophic calcification. The first occurs in viable myocardium in the context of abnormal calcium homeostasis, most commonly in chronic renal failure and secondary hyperparathyroidism; the latter takes place in areas of damaged myocardium (e.g. myocardial infarction) in a patient with normal calcium homeostasis.1

Sepsis-related myocardial injury is a complex process. It usually occurs within 24 h and manifests as left ventricular dysfunction associated with high serum levels of myocardial necrosis markers. In patients who survive, myocardial dysfunction usually reverses within 7–10 days.4–6

Myocardial dysfunction is thought to be a consequence of the intense inflammatory response observed in sepsis rather than a reaction to pathogenic organisms or endotoxins.7 Specifically, the increase of inflammatory mediators, such as TNF-alpha, IL-1 beta, and IL-6, have been shown to depress myocardial function and reduce contractility.4 The inflammation causes cellular edema, which impairs microvascular flow and may generate cytopathic hypoxia. Ischemia and oxidative stress disrupt the mitochondrial membrane and damage other mitochondrial structures.8 This triggers apoptotic and autophagic pathways with subsequent possible dystrophic calcifications.9 Genetic factors are also likely to have a contextual role in the genesis of this disorder.3 In particular, Rossi and Santos2 speculate on the possibility of a genetic predisposition to necrotic cell calcification. This would explain the rarity of the myocardial calcification event during septic states.

Myocardial calcification that develops due to septicaemia remains a rare but established sequela of sepsis-related myocardial injury. This is often detected at autopsy and rarely at chest radiography or CT imaging.1

We present the case of a 38-year-old woman with Wolfram Syndrome who developed diffuse myocardial calcification during an episode of generalized sepsis.
abscess, and acute respiratory distress. Non-contrast chest computed tomography (CT) scan that demonstrated characteristic CT signs of pulmonary edema: ground-glass opacification, bronchovascular bundle thickening, interlobular septal thickening, and pleural effusion (Figure 1).

Interestingly, the myocardium of the left ventricle showed hyperdensity (average HU values of approximately 80 HU) (Figure 2(a)) which was not present in a previous non-contrast CT scan done 4 months before (Figure 2(b)).

Blood tests showed positive high sensitive troponin I with a peak of 8384 ng/L, creatinine 2.74 mg/dL, leukocytosis (15,000/mm³), and neutrophilia (83.4%), C-reactive protein 5.49 mg/dL, and lactate dehydrogenase 1079 U/L. Other tests were unremarkable, including serum calcium levels. Hemocultures were negative.

Several days later, the patient underwent a cardiac magnetic resonance (CMR) showing left ventricular (LV) systolic dysfunction (ejection fraction: 44%), hypokinesis of the LV mid-apical segments of the anterior wall, and anterior interventricular septum, with signal hyperintensity in STIR images (Figure 3(a)), an increase of myocardial native T1 (Figure 3(b)) and middle-wall late gadolinium enhancement in the same segments (Figure 3(c)).

After starting a course of empirical antibiotics, the patients’ general conditions rapidly improved. No further diagnostics tests were performed as the patient asked to be discharged against medical advice.

Wolfram Syndrome is a rare autosomal recessive disorder characterized by juvenile-onset diabetes mellitus, diabetes insipidus, optic nerve atrophy, hearing loss, and neurodegeneration.

The prognosis of this syndrome is poor, and many patients die prematurely with severe neurological disabilities.10

Considering the septic state and signs of active myocarditis at CMR, we attributed the diffuse left ventricular myocardial hyperdensity in non-contrast CT scan to myocardial calcium accumulation.

Acute diffuse myocardial calcification sepsis-related has not been previously described in patients with Wolfram Syndrome before. Although not biopsy proved, the
Siani et al.

described CT findings in a patient with septic state condition, ventricular dysfunction, and normal calcium levels are highly suggestive of myocardial calcifications according to data in the literature.

**Declaration of conflicting interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding**

The author(s) received no financial support for the research, authorship, and/or publication of this article.

**References**

1. Simonson S, Miller WT, Jr, Perl A, et al. Diffuse left ventricular myocardial calcification in the setting of sepsis on CT imaging. *J Thorac Imaging* 2007; 22(4): 343–345.
2. Rossi MA and Santos CS. Sepsis-related microvascular myocardial damage with giant cell inflammation and calcification. *Virchows Arch* 2003; 443(1): 87–92.
3. Wong ML, O’Kirwan F, Khan N, et al. Identification, characterization, and gene expression profiling of endotoxin-induced myocarditis. *Proc Natl Acad Sci USA* 2003; 100(24): 14241–14246.
4. Sato R and Nasu M. A review of sepsis-induced cardiomyopathy. *J Intensive Care* 2015; 3: 48.
5. Parker MM, Shellhammer JH, Bacharach SL, et al. Profound but reversible myocardial depression in patients with septic shock. *Ann Intern Med* 1984; 100(4): 483–490.
6. Guest TM, Ramanathan AV, Tuteur PG, et al. Myocardial injury in critically ill patients. A frequently unrecognized complication. *JAMA* 1995; 273(24): 1945–1949.
7. Romero-Bermejo FJ, Ruiz-Bailen M, Gil-Cebrian J, et al. Sepsis-induced cardiomyopathy. *Curr Cardiol Rev* 2011; 7(3): 163–183.
8. Zang Q, Maass DL, Tsai SJ, et al. Cardiac mitochondrial damage and inflammation responses in sepsis. *Surg Infect (Larchmt)* 2007; 8(1): 41–54.
9. Smeding L, Plotz FB, Groeneveld AB, et al. Structural changes of the heart during severe sepsis or septic shock. *Shock* 2012; 37(5): 449–456.
10. Urano F. Wolfram syndrome: diagnosis, management, and treatment. *Curr Diab Rep* 2016; 16(1): 6.