CASE REPORT

A reminder of *Escherichia coli* sepsis-induced reversible cardiomyopathyAung Naing Lin,¹ Atif Shaikh,^{2,3} Sithu Lin,¹ Deepika Misra³

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/bcr-2017-220556>)

¹Department of Internal Medicine, The Brooklyn Hospital Center, Brooklyn, New York, USA

²Department of Cardiology, The Brooklyn Hospital Center, Brooklyn, New York, USA

³Department of Cardiology, Mount Sinai Beth Israel, New York City, New York, USA

Correspondence to

Dr Sithu Lin, dr.sithulin@gmail.com

Accepted 13 June 2017

SUMMARY

Cardiomyopathy is a progressive disease of myocardium causing either mechanical or electrical disturbances. Sepsis-induced cardiomyopathy (SICM) is an entity of cardiomyopathy which is reversible in 1–2 weeks after recovery from sepsis or septic shock. SICM is thought to have unpredictable cumulative mortality towards sepsis but its exact mechanism remains elusive. We report a case of *Escherichia coli* SICM in a 63-year-old woman presented with sudden onset of dyspnoea on exertion and orthopnoea following nausea, vomiting and diarrhoea after consuming Chinese foods. Transthoracic echocardiogram revealed severely reduced global left ventricular ejection fraction (LVEF) of <20% which returned back to normal LVEF of 57% after 10 days. Subsequent cardiac catheterisation showed non-obstructive coronaries. No specific therapy intended for reversal of SICM presents to date despite current sepsis survival guideline available for haemodynamic support. Initiation of beta blockers after recovery from septic shock has been beneficial.

BACKGROUND

Sepsis is a bodily response to infections leading to multiorgans dysfunction, shock and death.^{1,2} Cardiomyopathy, as we have known, is a progressive disease of myocardium causing either mechanical or electrical disturbances. Sepsis-induced cardiomyopathy (SICM) is a subset of dilated cardiomyopathy and is reversible. The exact mechanism of SICM is still elusive despite various hypotheses. Bacteria as well as viral, fungal and parasite infection can cause SICM.^{3–5} Echocardiography is helpful for assessment of ventricular dysfunction. No specific treatment is currently available for the sepsis-induced myocardial dysfunction. In our case of *Escherichia coli* SICM, left ventricular ejection fraction (LVEF) recovered in 10 days with appropriate empirical antibiotics and vasopressors according to sepsis survival guideline; and initiation of heart failure medications, especially beta-blocking agents after recovery from septic shock. It is still questionable about timing to initiate heart failure medications and how long beta blockers should be continued for cardiomyopathy after recovery from sepsis. Therefore, comprehensive understanding and development of a guideline for SICM are warranted as increasing numbers of sepsis or septic shock have been encountered.

CASE PRESENTATION

A 63-year-old woman with hypertension, well-controlled type 2 diabetes mellitus and dyslipidaemia presented with sudden onset of shortness of breath associated with tachypnoea, tightness of chest and orthopnoea. She had experienced fever, nausea, vomiting and watery diarrhoea after consuming Chinese food 3 days prior to presentation. She had known history of penicillin allergy and denied smoking, alcohol drinking or substance abuse. The patient was found in respiratory distress and was confused during the initial assessment. Third heart sound and trace oedema in lower extremities were appreciated. Having experienced temperature of 98.5°F, tachypnoea of 30/min, desaturation at 85% with supplemental oxygen, tachycardia of 125/min and persistent hypotension of 70/30 mm Hg after 2 L bolus normal saline, she was intubated to protect the airway and started empirical antibiotics with intravenous vancomycin, aztreonam and levofloxacin after collecting blood cultures. Subsequently, norepinephrine drip was required to maintain mean arterial pressure above 65 mm Hg.

INVESTIGATIONS

Investigations revealed leukocytosis of $18.8 \times 10^9/L$ (normal: $4.8–10.8 \times 10^9/L$), lactic acid of 9.3 (normal: 0.5–1 mmol/L), elevated creatinine, urine white blood cell counts of 20–50/Hpf and elevated brain natriuretic peptide (BNP) of 3157. Serial troponin-I and electrolytes are unremarkable. Chest X-ray was impressed as cardiomegaly and mild pulmonary congestions without evidence of consolidation. Serial ECGs recorded sinus tachycardia at 120/min. Transthoracic echocardiogram (TTE) was performed and showed severely reduced global LVEF less than 20% with restrictive left ventricle (LV) filling, dilated LV and increased left atrial pressure (figures 1 and 2, see online supplementary videos 1 and 2)

She was initially treated for broad differential of acute hypoxic respiratory failure due to suspected septic shock, hypovolaemic shock from gastrointestinal loss and acute congestive heart failure due to cardiomyopathy. Empirical antibiotics coverage was tailored to levofloxacin after day 2 when blood culture and urine culture grew *E. coli*. She was judiciously administered with low-dose carvedilol 3.125 mg titrated to 25 mg every 12 hours and lisinopril 5 mg titrated to 10 mg daily after recovery from septic shock. Clinical improvement from sepsis was obtained after 24 hours of

CrossMark

To cite: Lin AN, Shaikh A, Lin S, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-220556

Figure 1 Parasternal long axis view showing left ventricle dilation.

presentation and return of normal cardiac function was achieved after 10 days of recovery from septic shock. Repeated TTE on day 10 was evidenced as normal LVEF of 55%–60% (figure 3, see online supplementary video 3). The patient underwent coronary angiography which showed non-obstructive coronaries (figure 4A,B). She was continued with lisinopril only for blood pressure control after discharge.

OUTCOME AND FOLLOW-UP

Follow-up visits with cardiology clinic at 3, 6 and 9 months were uneventful.

DISCUSSION

Sepsis and septic shock have been considered potential lethal conditions and are major health burdens in both developed and developing countries. Despite the refinement of sepsis management guidelines over the past decade, mortality from septic shock is estimated at approximately 50%.^{1,2} SICM is a different form of dilated cardiomyopathies evidenced by low ejection fraction and is less responsive to volume resuscitation and

Figure 3 Parasternal long axis view showing reversal of left ventricle dilation and function.

vasopressors. The first case of SICM was described by Parker *et al* in 1984.³ SICM is reversible in 1–2 weeks after recovery from sepsis or septic shock.^{3–5} Although myocardial dysfunction has been thought to be one of the determinants of mortality in septic shock, in a recent Japanese cohort study on 210 patients suffering from sepsis or septic shock by Sato, Ryota *et al* found no significant changes in mortality among patients with SICM.⁵

The incidence of SICM varies among existing studies ranging from as low as 13.8% to as high as 65%.^{6–10} Links between sepsis or septic shock and cardiac dysfunction are still unclear. Bacteria as well as viral, fungal and parasite infection can cause systolic or diastolic dysfunctions. Cappelletti *et al* in 2016 correlated between sepsis and takotsubo cardiomyopathy. Septic shock or sepsis due to bacteria were most common causes of reversible cardiomyopathy, with *E. coli*, *Klebsiella pneumoniae*

Figure 2 Apical four chamber views showing left ventricle dilation.

Figure 4 Coronary angiography depicting non-obstructive coronaries. Left coronary artery and branches (A) and right coronary artery and branches (B).

and *Staphylococcus aureus* being the most common organisms accounted for 57.7% while viral and unidentified infection-related cardiomyopathies were responsible for 7.8% and 26.9%, respectively.^{11 12}

Sepsis is a dysregulated, adaptive and protective body response to infection leading to multiorgans damage. Cardiovascular derangements such as increased vascular permeability, reduced vascular resistance and degree of cardiac dysfunction are determinants for the outcomes of sepsis or septic shock. Cardiac dysfunction during sepsis seems to be a myocardial adaption in response to sepsis. Various hypotheses regarding the possible mechanism of myocardial depression in sepsis have been developed over the past four to five decades but none is conclusive. Impaired coronary perfusion or myocardial microischaemic injury was the primitive and obsolete assumption which originated from theory of supply-demand ischaemia due to hypotension and vasodilatation during septic shock. Direct mitochondrial injury from damaged associated molecules such as nitric oxide (NO) and reactive oxygen species is also recognised as one of feasible postulations. In addition, direct myocardial dysfunction by means of myocardial depressant factors such as exotoxin or endotoxin, and cytokines including tumour necrosis factor- α , interleukin 1- β , NO and free radicals has been developed. Similarly, beta-adrenergic receptor downregulation and attenuation of adrenergic signalling that resulted from excessive beta-adrenergic stimulation during sepsis is also acceptable mechanism of SICM. An altered calcium exchange in myocardium in association with mitochondrial injury has also been appreciated in some study. Myocardial cells' apoptosis due to activation of apoptosis enzymes is another proposed mechanism coming out of animal experiments but found to be unreliable by postmortem investigations.^{3–10}

Echocardiogram of various techniques is useful for the assessment of ventricular dysfunctions. Although no specific management recommendations are available, supportive management of sepsis such as aggressive volume resuscitation, vasopressors to maintain mean arterial pressure, empirical antibiotics or surgery to eliminate the source of sepsis and standard heart failure therapy is commonly used. However, excessive adrenergic stimulation by vasopressors and over-volume resuscitation with fluid can have detrimental effects on the myocardium which is already injured by the sepsis. The addition of beta blockers in septic shock management is more effective in reduction of mortality from sepsis proven by various animal models and a few human trials. A recent randomised, controlled study in intensive care unit conducted by Morelli *et al* highlighted the short-term mortality benefit of selective beta blocker, esmolol, during septic shock.¹³ A retrospective study by Schmittinger *et al* provided the feasible effect of metoprolol and milrinone sepsis-induced cardiac dysfunction.¹⁴ More than mortality benefit from septic shock, reduction of heart rate and increasing stroke volume without hampering peripheral organs perfusion, beta blockers are thought to improve left ventricular function and myocardial blood flow; suppress inflammatory mediators and hypermetabolic state during sepsis; correct coagulation derangement; and reduce fluid and vasopressors requirement.^{15 16} Despite known short-term possible mortality benefits in recent studies, outcomes of heart failure medications remain unclear for the long term.^{5 13–19} It is still undetermined about superiority among beta-blocking agents as well. There is also no recommendation for timing to initiate beta blockers and how long heart failure regime should be continued after recovery from cardiomyopathy. Randomised multicentre studies are still needed for proper management for SICM.

In our case, the non-alcoholic woman came for rapid onset of progressive shortness of breath following fever and gastrointestinal symptoms. BNP was significantly high and serial cardiac enzymes were normal. Although no previous history of heart failure or coronary artery disease has been recognised, she was found to have dilated LV and severely reduced LVEF. The LV function returned to normal after 10 days recovering from septic shock. Cardiac catheterisation subsequently ruled out coronary arteries occlusion that can precede cardiac dysfunction. All clinical parameters and investigational findings were consistent with reversible dilated cardiomyopathy due to *E. coli* endotoxin-induced septic shock. She was managed with heart failure regime within 24 hours after recovery from the septic shock and reversal of cardiomyopathy was observed in 10 days. Only lisinopril was continued for blood pressure control in the setting of diabetes after discharge since patient had regained normal cardiac function and non-obstructive coronaries. Moreover, long-term benefit of beta blocking in SICM was unclear. Her haemodynamic and ejection fraction has been stable at 3, 6 and 9 months of follow-ups.

Learning points

- ▶ Sepsis-induced cardiomyopathy (SICM) is an entity of cardiomyopathy with the elucidative pathophysiology but is reversible.
- ▶ Mainly caused by bacterial sepsis but viral, fungal and parasite infection can also lead to SICM.
- ▶ No specific therapy for reversal of SICM has been established but haemodynamic support according to sepsis survival guideline and heart failure regimen after recovery from septic shock, especially beta-blocking agents, are found to be beneficial.

Acknowledgements Special thanks to Dr. Cesar Ayala-Rodriguez, Department of Cardiology, the Brooklyn Hospital Center and Mount Sinai Hospital, NY, USA for the guidance in patient management and educational information.

Contributors ANL was involved in conception of the idea, manuscript preparation, assay analysis and interpretation. AS was involved in patient care, conception of the idea and manuscript preparation. SL was involved in manuscript preparation, correlative assays and interpretation. DM was involved in conception of the idea, assay analysis and proofreading. All the authors approved the submitted manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Esper A, Martin GS. Is severe Sepsis increasing in incidence AND severity? *Crit Care Med* 2007;35:1414–5.
- 2 Rangel-Frausto MS, Pittet D, Costigan M, *et al*. The natural history of the systemic inflammatory response syndrome (SIRS): a prospective study. *JAMA* 1995;273:117–23.
- 3 Parker MM, Shelhamer JH, Bacharach SL, *et al*. Profound but reversible myocardial depression in patients with septic shock. *Ann Intern Med* 1984;100:483–90.
- 4 Landesberg G, Gilon D, Meroz Y, *et al*. Diastolic dysfunction and mortality in severe Sepsis and septic shock. *Eur Heart J* 2012;33:895–903.
- 5 Sato R, Kuriyama A, Takada T, *et al*. Prevalence and risk factors of sepsis-induced cardiomyopathy: a retrospective cohort study. *Medicine* 2016;95:e5031.
- 6 Kumar A, Haery C, Parrillo JE. Myocardial dysfunction in septic shock. *Crit Care Clin* 2000;16:251–87.
- 7 Jardin F, Brun-Ney D, Auvert B, *et al*. Sepsis-related cardiogenic shock. *Crit Care Med* 1990;18:1055–60.
- 8 Vieillard-Baron A, Caille V, Charron C, *et al*. Actual incidence of global left ventricular hypokinesia in adult septic shock. *Crit Care Med* 2008;36:1701–6.

- 9 Bouhemad B, Nicolas-Robin A, Arbelot C, *et al.* Acute left ventricular dilatation and shock-induced myocardial dysfunction. *Crit Care Med* 2009;37:441–7.
- 10 Kakiyama Y, Ito T, Nakahara M, *et al.* Sepsis-induced myocardial dysfunction: pathophysiology and management. *J Intensive Care* 2016;4:22.
- 11 Cappelletti S, Ciallella C, Aromatario M, *et al.* Takotsubo cardiomyopathy and Sepsis : a systematic review. *Angiology* 2017;14:288–303.
- 12 Patel N, Shenoy A, Dous G, *et al.* Sepsis-Induced Takotsubo Cardiomyopathy leading to Torsades de Pointes. *Case Rep Cardiol* 2016;2016:1–6.
- 13 Morelli A, Ertmer C, Westphal M, *et al.* Effect of heart rate control with esmolol on hemodynamic and clinical outcomes in patients with septic shock: a randomized clinical trial. *JAMA* 2013;310:1683–91.
- 14 Schmittinger CA, Dünser MW, Haller M, *et al.* Combined milrinone and enteral metoprolol therapy in patients with septic myocardial depression. *Crit Care* 2008;12:R99.
- 15 Suzuki T, Suzuki Y, Okuda J, *et al.* Sepsis-induced cardiac dysfunction and β -adrenergic blockade therapy for Sepsis. *J Intensive Care* 2017;5:22.
- 16 Balik M, Rulisek J, Leden P, *et al.* Concomitant use of beta-1 adrenoreceptor blocker and norepinephrine in patients with septic shock. *Wien Klin Wochenschr* 2012;124(15-16):552–6.
- 17 Antonucci E, Fiaccadori E, Donadello K, *et al.* Myocardial depression in Sepsis: from pathogenesis to clinical manifestations and treatment. *J Crit Care* 2014;29:500–11.
- 18 Hagiwara S, Iwasaka H, Maeda H, *et al.* Landiolol, an ultrashort-acting β 1-adrenoceptor antagonist, has protective effects in an LPS-induced systemic inflammation model. *Shock* 2009;31:515–20.
- 19 Gore DC, Wolfe RR. Hemodynamic and metabolic effects of selective β 1 adrenergic blockade during Sepsis. *Surgery* 2006;139:686–94.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow