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DIABETIC HEART FAILURE IN A FIT MIDDLE-AGED GENTLE-MAN

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ABSTRACT

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The prevalence of type 2 diabetes mellitus in Malaysia has escalated exponentially in young adults. The burden of managing diabetes mellitus affects all levels from the preventive steps up to the tertiary health care providers. Heart failure is an established complication of diabetes mellitus which carries poor quality of life and outcome. Here we present a case of a fit 44-yearold gentleman with diabetic cardiomyopathy.

Keywords: Diabetic cardiomyopathy, Heart failure, Diastolic, Systolic, Dysfunction, Systolic.

INTRODUCTION

Diabetes Mellitus (DM) is a major global health issue that causes a significant increase in cardiovascular morbidity and mortality amongst other systemic complications. 1,4 One such cardiovascular complication is Diabetic Cardiomyopathy (DCM), a clinical condition of ventricular dysfunction that occurs in the absence of coronary atherosclerosis and hypertension in patients with diabetes.^{2,3} DCM is increasingly common in the face of increasing rates of Diabetes Mellitus in the Malaysian population.⁵ As mortality from cardiac failure is significantly higher in diabetics, it is vital that DCM is anticipated and diagnosed early especially in dia-

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betics with poor glycaemic control. We present a case of a fit young adult with systolic and diastolic heart failure as a result of uncontrolled Type 2 DM. The objective of this case report is to highlight the importance of identifying DCM even in young and fit diabetics and how strict glycaemic control is paramount in its management.

CASE REPORT

A fit 44-year-old sportsman presented to the Emergency Department complaining of occasional central chest tightness on exertion. He is a known diabetic diagnosed in 2014 on oral anti-diabetic therapy and an active chronic smoker. He does not consume alcohol nor illicit drugs. There is no significant family history of cardiovascular disease.

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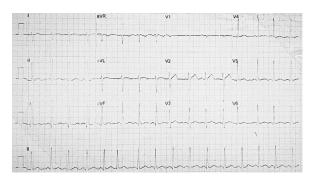


Figure 1: Patient's 12-lead electrocardiogram showing sinus rhythm with no ischaemic changes.

On assessment, he was comfortable at rest, had warm peripheries with normal blood pressure and heart rate of 96 beats per minute. He measured 175cm in height and weighed 70kg, giving a body mass index (BMI) of 23 kg/m2. There were no clinical features of heart failure and cardiac auscultation was unremarkable. Electrocardiogram (ECG) revealed increased R wave amplitude on left-sided leads (V4-V6) and deep S waves in lead V2 fulfilling Sokolow-Lyon criteria of left ventricular hypertrophy (LVH) with no evidence of ischemia (Figure 1). Laboratory examinations showed poor glycaemic control and transaminitis due to liver congestion. High-sensitivity Troponin T, blood counts and renal function were within reference range (Table I).

Transthoracic Echocardiography (TTE) revealed global hypokinesia of the left ventricle (IVSd: 1.19cm, LVIDd: 6.03cm, LVPWd: 0.68cm, IVSs: 1.27cm, LVIDs: 4.67cm: LVPWs: 1.32cm, LV mass index: 124g/m2, relative wall thickness: 0.23) with an ejection fraction of 30% determined by Biplane Simpson's method, impaired relaxation pattern of diastolic dysfunction and dilated cardiomyopathy (Figure 2). Mild functional regurgitation of the mitral, pulmonary and tricuspid valves as well as trivial aortic regurgitation were also seen. There were no features suggestive of congenital heart disease seen on TTE. Both left and right coronary arteries showed mild disease on angiogram (Figure 3) and Cardiac MRI (CMR) reported left ventricular end-

Table I: Patient's laboratory parameters.

Laboratory analysis	Result	Reference range
HbA1c, %	12.2	<6.5
ALT, IU/L	67.5	29-35
GGT, IU/L	368	8-38
ALP, IU/L	229	44-147
hs-Troponin T, ng/L	9	<14
Haemoglobin, g/dL	13	13-17
White blood cells, $\times 10^9/L$	9.9	4-11
Platelets, $\times 10^9/L$	361	150-400
Sodium, mmol/L	137	135-145
Potassium, mmol/L	4.4	3.7-5.1
Creatinine, µmol/L	79	62-106

ALT - Alanine aminotransferase GGT - Gamma-glutamyl transferase

ALP - Alkaline phosphátase

systolic and end-diastolic volumes of 114 ml (62 ml/m2) [normal: 17-69 ml (10-34 ml/ m2)] and 148 ml (81 ml/m2) [normal:99-199 ml (53-97 ml/m2)] respectively, indicating reduced systolic function with poor ejection fraction of 23%. There was no enhancement in the late gadolinium study to suggest ischemic cardiomyopathy and no features of infiltrative cardiomyopathy were apparent. He fulfilled the diagnostic definition of diabetic cardiomyopathy and was managed with guideline-directed medical therapy i.e., bisoprolol, empagliflozin, aspirin, metformin plus insulin therapy. He was subsequently followed up with multiple disciplines as an outpatient for glycaemic control, having successfully achieved which he was last seen well with New York Heart Association (NYHA) heart failure class 1. He is due for a follow-up echocardiogram at the point of writing.

DISCUSSION

Diabetes Mellitus is a global health concern and a significant cause of cardiovascular disease. Diabetics are at an increased risk of developing heart failure in comparison to non-diabetics where up to a quarter of diabetics suffer from heart failure and mortality from heart failure increases in parallel with increasing HbA1c levels.1,3 Diabetic cardiomy-

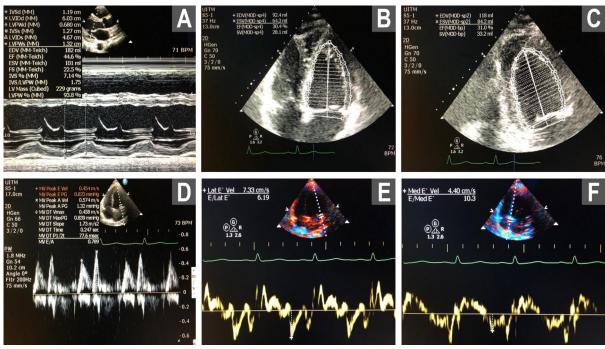


Figure 2: Transthoracic echocardiogram showing systolic (A-C) and diastolic (D-F) heart failure.

opathy (DCM) is the abnormal myocardial structure, function and performance caused by diabetes in the absence of other risk factors such as hypertension, coronary artery disease, valvular or congenital heart disease. ^{2,3,4} In-keeping with the staggering 22.9% prevalence rate of Diabetes Mellitus in Malaysia, more local cases of DCM are expected to be diagnosed. ⁵

In DCM, left ventricular ejection fraction may be preserved (heart failure with preserved ejection fraction, HFpEF) or reduced (heart failure with reduced ejection fraction, HFrEF). In the former, diastolic phase is impaired but with preserved left ventricular ejection fraction. In the latter, ejection fraction is reduced due to systolic dysfunction. Diastolic dysfunction may also ensue from systolic dysfunction in HFrEF. In this case, HFrEF with impairment in both systolic and diastolic phases were found in a relatively young, athletic man. The pathological mechanism of DCM is complex and differs between restrictive/HFpEF and dilated/HFrEF phenotypes. Restrictive/HFpEF is mainly a consequence of hyperglycaemia,

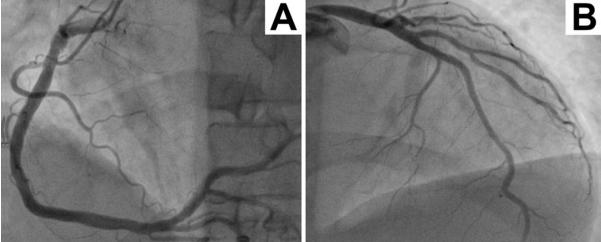


Figure 3: Coronary angiography showing no significant stenosis of the epicardial arteries in both right (A) and left (B) coronary arteries.

hyperinsulinemia and lipotoxicity whereas coronary microvascular rarefaction (reduced myocardial capillary density) and advanced glycation end products (AGEs) contribute to the manifestation of both phenotypes. At the cellular level, glucotoxicity, fibrosis, apoptosis, mitochondrial dysfunction and abnormal signalling pathways result in myocardial dysfunction.^{6,7} Ultimately, hyperglycaemia is implicated in the pathophysiology of both phenotypes, thus emphasising the importance of glycaemic control in managing DCM.

The diagnosis of DCM is made based on the presence of myocardial dysfunction after ruling out other causes of heart failure such as coronary artery disease, hypertension, valvular dysfunction, congenital heart disease, infections and cardiac infiltrative conditions. Thorough clinical assessment and relevant investigations such as biochemical tests, diagnostic imaging and coronary angiogram should be considered to obtain diagnosis. Transthoracic echocardiogram (TTE) is easily available and cheap, however the inability to detect the subtle features of myocardial dysfunction is a limitation. Speckle tracking, contrast and three-dimensional (3D) echocardiography has improved the quantitative assessment altogether the accuracy of test readings. Cardiac MRI (CMR) is a useful imaging tool for evaluation of structural, functional myocardium disorders, myocardial perfusion and infarction. Late gadolinium enhancement CMR provides the key to distinguishing the different types of cardiomyopathies. It has been useful in predicting major adverse cardiac events in diabetic patients with no prior history of coronary artery disease.8

Single-photon emission computerised tomography (SPECT) is a useful modality in assessing flow limitation and sarcolemmal membrane integrity. Positron emission tomography (PET) scan assesses myocardial blood flow by radiotrace kinetics.

Two recent cardiovascular outcome trials have shown good clinical outcome in patients with HFREF who were on sodium-glucose co-transporter 2 (SGLT2) inhibitors, Dapagliflozin or Empagliflozin compared to placebo regardless of diabetic status. Both clinical trials also demonstrated reduced risk of cardiovascular death and heart failure hospitalization in the treatment arm. 9,10

CONCLUSION

The diagnosis of DCM should be considered in every diabetic with cardiovascular dysfunction upon ruling out other causes of cardiomyopathy. The pathophysiology of DCM is complex but important in helping physicians devise a therapeutic plan. Prompt glycaemic control has been shown to hamper disease progression therefore regular surveillance and adequate anti-diabetic treatment are key.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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INFORMED CONSENT

Consent has been obtained from the patient.

REFERENCES

- Raghavan S, Vassy JL, Ho YL, Song RJ, Gagnon DR, Cho K, et al. Diabetes Mellitus-Related All-Cause and Cardiovascular Mortality in a National Cohort of Adults. J Am Heart Assoc. 2019;8(4):e011295.
- 2: Umut Kocabaş, Özgür Yılmaz, Volkan Kurtoğlu, Diabetic cardiomyopathy: acute and reversible left ventricular systolic dysfunction due to cardiotoxicity of hyperglycaemic hyperosmolar

- state—a case report, European Heart Journal Case Reports. 2019;3(2):
- 3: Jia, G., M.A. Hill, and J.R. Sowers, Diabetic Cardiomyopathy: An Update of Mechanisms Contributing to This Clinical Entity. Circ Res. 2018;122(4):624-638.
- 4: Gulsin, G.S., L. Athithan, and G.P. McCann, Diabetic cardiomyopathy: prevalence, determinants and potential treatments. Ther Adv Endocrinol Metab. 2019;10: 2042018819834869.
- 5: Wan Nazaimoon, W.M., et al., Prevalence of diabetes in Malaysia and usefulness of HbA1c as a diagnostic criterion. Diabet Med. 2013;30 (7):825-8.
- 6: Mochizuki, Y., et al., Clinical features of subclinical left ventricular systolic dysfunction in patients with diabetes mellitus. Cardiovasc Diabetol. 2015;14:37.
- 7: Matshela MR. Second in a series on diabetes and the heart: diabetic cardiomyopathy mechanisms and mode of diagnosis. E-Journal of Cardiology Practice 2016;14.
- 8: Yoon, Y.E., Kitagawa, K., Kato, S. et al. Prognostic value of unrecognised myocardial infarction detected by late gadolinium-enhanced MRI in diabetic patients with normal global and regional left ventricular systolic function. Eur Radiol 23, 2101–2108 (2013). https://doi.org/10.1007/s00330-013-2817-y
- McMurray JJV, Solomon SD, Inzucchi SE, Kober L, Kosiborod MN, Martinez FA, et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med. 2019;381(21):1995-2008.
- Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. N Engl J Med. 2020;383(15):1413-24.