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Case Report

Extensive triple vessel coronary artery disease in a young male with juvenile idiopathic arthritis

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Abstract

The risk of cardiovascular disease in patients with chronic inflammatory joint conditions is substantially increased compared to the general population. We present a case of a 27-year-old male with a chronic history of juvenile idiopathic arthritis (JIA) who presented with denovo acutely decompensated chronic heart failure. He had no traditional risk factors for atherosclerotic cardiovascular disease (ASCVD). However, during his workup for dilated cardiomyopathy, he was found to have extensive triple vessel disease on coronary artery angiography, and this was subsequently thought to be the most likely aetiology for the dilated cardiomyopathy despite being of young age. The chronic JIA was identified as the principal risk factor for the ischaemic cardiomyopathy. Clinicians treating patients with rheumatological conditions should routinely screen for ASCVD, despite the absence of traditional cardiovascular risk factors.

INTRODUCTION

The risk of cardiovascular disease (CVD) in patients with chronic inflammatory joint conditions is substantially increased when compared to the general population [1]. The underlying chronic inflammation may affect the cardiovascular system, resulting in accelerated atherosclerosis, myocarditis or pericarditis [2]. This case report emphasizes the importance of routine screening for atherosclerotic cardiovascular disease (ASCVD) in young patients with chronic inflammatory joint diseases.

CASE REPORT

We present a case of a 27-year-old male with a 1-month history of neck and lower back pain associated with worsening dyspnea on exertion. He had no prior history of angina, syncope, palpitations, flu-like illness, vomiting or diarrhoea. In addition, he had no family history of premature CVD or traditional ASCVD risk factors. Specifically, he reported no history of cigarette smoking or any form of substance abuse.

On clinical examination, he had conjunctival pallor, grade three pedal oedema and abdominal ascites. Examination of the cardiovascular system revealed an elevated jugular venous pressure, a myopathic displaced apex beat with a right parasternal heave and an S3 gallop. He was in New York Heart Association functional class III. His respiratory examination was normal.

The musculoskeletal examination revealed loss of cervical lordosis, tender and swollen joint count of eight, fixed flexion deformity of the elbows, ankylosis of the wrists and the proximal interphalangeal joints of both hands. The clinical disease activity index score was 34, signifying a high rheumatologic disease activity.

All inflammatory markers were elevated (Table 1), and the rheumatologic serological studies were unremarkable (Table 2). The Human immunodeficiency virus ELISA screen was negative. A resting electrocardiogram (ECG) showed a narrow QRS complex sinus tachycardia (Fig. 1). Echocardiography demonstrated four-chamber enlargement with global hypokinesis of the left ventricle and a left ventricular ejection fraction of 20–25% (Fig. 2). The diagnostic coronary angiogram revealed extensive triple vessel disease (Fig. 3), with a syntax score I of 36.5. Furthermore, computed tomography angiography of the neck and brain revealed large vessel vasculitis of the common carotid and middle cerebral arteries. The vasculitis flare was subsequently treated with two cycles of cyclophosphamide at 13 mg/kg, administered 2 weeks apart.

The patients' rheumatic symptoms were treated with pulsed solumedrol 1 g for 3 days, followed by prednisone

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Table 1. Basic laboratory studies

Laboratory study	Value	Reference range
Sodium	138	136–145 mmol/L
Potassium	4.3	3.5–5.1 mmol/L
Urea	7.4	2.1–7.1 mmol/L
Creatinine	77	64–104 μmol/L
Estimated glomerular filtration rate	135.4	>60 mL/min
Calcium	2.25	2.15–2.50 mmol/L
Magnesium	0.78	0.63–1.05 mmol/L
Liver Function Tests		
Total protein	83	60–78 g/L
Aspartate transaminase	144	13–35 U/L
Alanine transaminase	62	7–35 U/L
Alkaline phosphatase	172	42–98 U/L
Gamma-glutamyl transferase	142	<40 U/L
Total bilirubin	6	5–21 μmol/L
Albumin	33	35–52 g/L
Lipid profile		
Total cholesterol	2.83	<4.0 mmol/L
Triglyceride	0.72	<1.7 mmol/L
LDL cholesterol	1.94	<1.8 mmol/L
HDL cholesterol	0.41	>1.0 mmol/L
Full Blood Count		
Haemoglobin	9.3	11.6–16.4 g/dL
Platelets	475	186–454 $\times 10^9$/L
White blood cells	8.42	3.90–12.60 $\times 10^9$/L
Red blood cells	4.16	3.93–5.40 $\times 10^{12}$/L
Mean corpuscular volume	76.2	78.9–98.5 fL
Cardiac enzymes		
Creatine kinase	31	20–180 U/L
CK-MB	1.21	0.00–6.22 μg/L
Inflammatory Markers		
Erythrocyte sedimentation rate	120	0–10 mm/h
C-reactive protein	132	<10 mg/L

CK-MB = creatine kinase-MB, HDL = high-density lipoprotein, LDL = low-density lipoprotein

Table 2. Rheumatologic serologic studies and hypercoagulability studies

Laboratory study	Value	Reference range
Anti-nuclear antibodies	Negative	
Anti-cyclic citrullinated peptide antibody	2.0	<20 U/mL
Thyroglobulin	42.6	3.5–77.0 μg/L
Anti-thyroglobulin antibody	12	<115 U/mL
Anti-proteinase 3 antibody	1.0	0–0.9 U/mL
Anti-myeloperoxidase antibody	1.0	0–0.9 U/mL
Direct Coombs (typing)		
IgG	positive	
C3d	negative	
Coagulation		
INR	1.29	2.0–3.0
Prothrombin time	18.2	14.0 s (control)

Ig = immunoglobulin, INR = international normalized ratio

at 0.5 mg/kg. As part of the heart failure therapy, the patient was acutely initiated on furosemide, low dose carvedilol, an angiotensin-converting enzyme inhibitor and spironolactone, to which he responded well. The patient was also treated with simvastatin, baclofen, chloroquine, methotrexate, folic acid and carbamazepine. The ECG did not show any features suggestive of chloroquine-induced QT prolongation (QTc > 450 ms) as both the QT and corrected QT interval were 308 and 429 ms, respectively.

The differential diagnoses were ischaemic cardiomyopathy secondary to accelerated atherosclerosis and a vasculopathy of the coronary arteries as a sequela of the juvenile idiopathic arthritis (JIA). A differential diagnosis of cyclophosphamide-induced cardiomyopathy was also entertained.

The institutional heart team decided to refer the patient for elective coronary artery bypass graft surgery once the inflammatory markers had settled. Unfortunately, 3 weeks later, the patient experienced a sudden cardiac arrest while at home. The likely cause of death was a lethal arrhythmia such as ventricular tachycardia. An intracardiac defibrillator would have been an ideal therapy to prevent his sudden cardiac death. However, in our local clinical setting, such devices are not readily available due to their high cost.

DISCUSSION

JIA refers to a group of conditions characterized by inflammatory joint disease of unknown aetiology, occurring before the age of 16 years and lasting more than 6 weeks [3]. Patients with JIA have been found to have impaired endothelial dysfunction and elevated levels of pro-inflammatory cytokines, which play a significant role in the development of ASCVD [4, 5].

In our patient, cytokines and chemokines implicated in the pathogenesis of rheumatoid arthritis most likely led to prematurely accelerated atherosclerosis. Furthermore, chronic inflammatory joint pain may have led to physical inactivity, a well-established risk factor for ASCVD. As such, the increased inflammation, corticosteroid use and reduced physical activity may well have had a synergistic effect on advancing ASCVD [6]. Sonographic surrogate markers of early endothelial dysfunction such as carotid intima-media thickness, flow-mediated dilatation and pulse-wave velocity could have played a crucial role in diagnosing ASCVD early [7].

Although our patient did not report a history of flu-like symptoms on index presentation, a possible missed diagnosis of viral myocarditis was considered. Furthermore, a diagnosis of coronary artery disease superimposed on genetic dilated cardiomyopathy cannot be excluded with certainty. We did not screen first-degree relatives for dilated cardiomyopathy nor perform genetic analysis to identify a possible genetic cause for the heart failure [8]. Cardiomyopathy genetic tests are not readily available in state funded hospitals in South Africa.

Cyclophosphamide-induced cardiomyopathy was also considered as part of the differential diagnosis. However, our patient only received a low cyclophosphamide dose of 13 mg/kg per cycle, making this diagnosis unlikely. Cyclophosphamide-induced cardiotoxicity is dose-dependent, and the total dose of

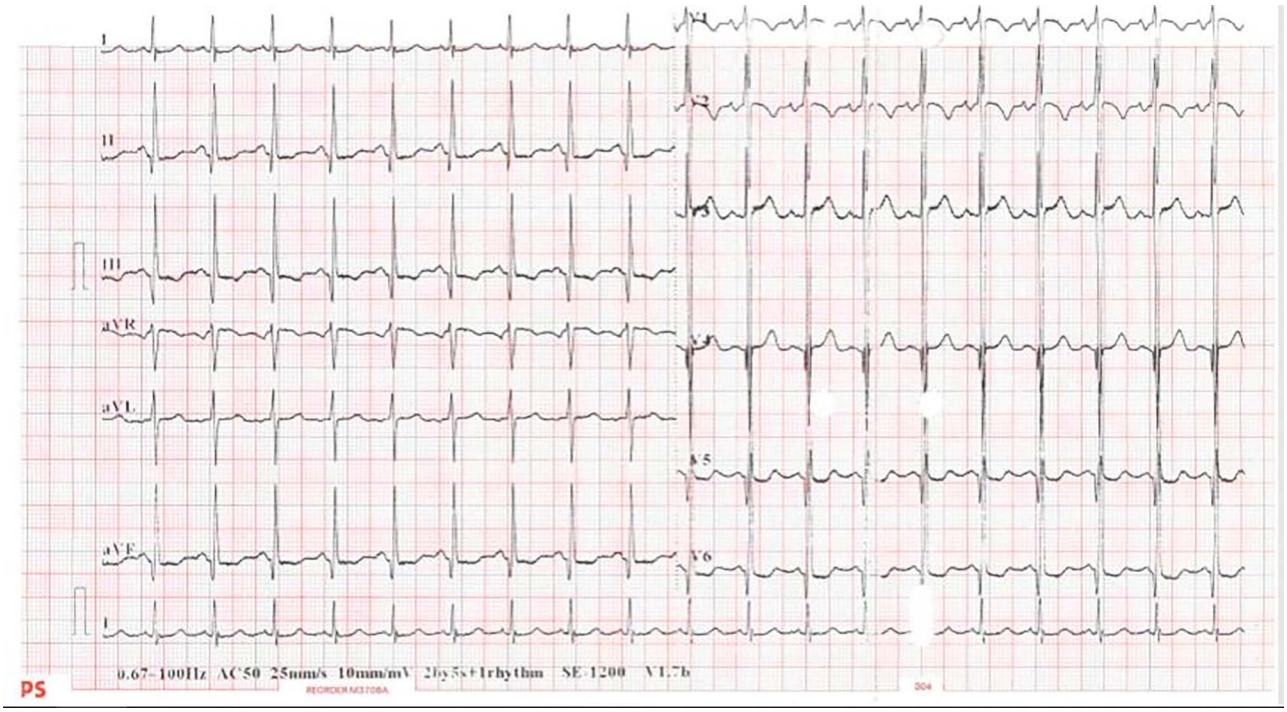

Figure 1. A resting electrocardiogram showing a sinus tachycardia and non-pathological Q waves in the inferior and lateral leads.

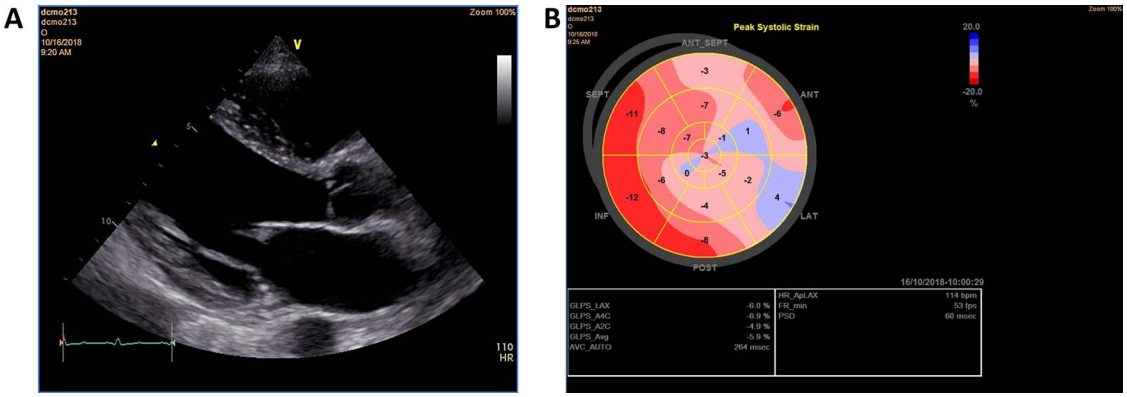

Figure 2. A: Echocardiography in a parasternal long axis view showing a dilated left ventricle and left atrium. B: Summary of the left ventricular global longitudinal strain pattern.

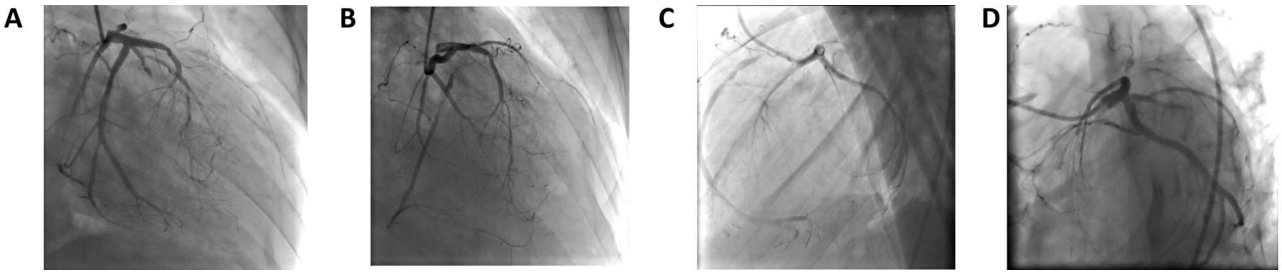

Figure 3. Left coronary angiogram still images in different projections. A: Chronic total occlusion of the proximal LAD; B and C: Retrograde filling of the distal to mid RCA (RCA ostial chronic total occlusion); D: Spider view showing chronic total occlusion of the proximal LAD and proximal ramus. LAD = left anterior descending artery, RCA = right coronary artery.

cyclophosphamide therapy associated with cardiotoxicity is usually 150 mg/kg and above [9, 10].

In conclusion, we recommend optimal treatment of the primary rheumatological condition and active screening for ASCVD despite the absence of traditional cardiovascular risk factors. The clinical use of vascular biomarkers of early atherosclerosis may also be considered.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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ETHICAL APPROVAL

Approval to conduct the study was granted by the University of the Witwatersrand Human Research Ethics Committee (M150467).

CONSENT

Permission to publish the case report was obtained from the patients' mother, as the patient had already demised.

GUARANTOR

Dr Nqoba Tsabedze.

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