Energy drink-induced cardiomyopathy

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SUMMARY
We report a case of severe biventricular heart failure potentially related to excessive energy drink consumption in a 21-year-old man. The patient presented with a 4-month history of shortness of breath on exertion, orthopnoea and weight loss. Transthoracic echocardiography demonstrated severely impaired biventricular systolic function and bilateral ventricular thrombi, subsequently confirmed on cardiac magnetic resonance imaging, which found in addition no oedema, inflammation or focal fibrosis. Blood tests, renal ultrasound and subsequent abdominal MRI demonstrated severe renal failure caused by a chronic obstructive uropathy, long-standing and previously undiagnosed. There was no significant past medical, family or social history other than excessive intake of an energy drink. This case report adds to the growing concern in the literature about the potential cardiotoxic effects of energy drinks, which should be considered when assessing young patients presenting with a non-ischaemic dilated cardiomyopathy.

BACKGROUND
Energy drink consumption is growing worldwide,1 however the impact of excessive and chronic use of such products on the cardiovascular system remains poorly understood. Concerns have been raised about a wide range of potential harmful health effects including cardiovascular dysfunction and heart failure,1 2 although most consumers are not aware of this.

The evaluation of patients with unexplained cardiomyopathy should include a careful search for a specific cause, which can be found in approximately half the cases.3 Identifying the underlying aetiology of heart failure has both prognostic and potentially therapeutic importance.4

CASE PRESENTATION
A 21-year-old man initially presented with shortness of breath and abdominal swelling. He was found to be in renal failure with urinary retention and subsequent imaging confirmed severe bilateral hydronephrosis requiring bilateral nephrostomies. He described a 4-month history of progressive shortness of breath on exertion, orthopnoea, weight loss and general malaise. Three months prior to this he had been treated by his general practitioner with a course of oral antibiotics for a productive cough, fevers and shortness of breath. There was no significant past medical history and family history was not suspicious for cardiomyopathy or sudden cardiac death. He was an ex-smoker, having stopped 3 years earlier. Alcohol and illicit drug use were denied, however there was a history of regular ‘Energy drink’ drink consumption, specifically consuming an average of four 500 mL cans per day for approximately 2 years. Each can contains 160 mg of caffeine in addition to taurine and various other ingredients. Retrospectively, the patient recalls occasional symptoms of dyspepsia, tremor and a racing heartbeat but without seeking medical review. In the 3 months prior to admission he was unable to continue his university studies due to his lethargy and feelings of ill health.

Creatinine on presentation was 562 μmol/L, with urea of 47.4 mmol/L. Bilateral nephrostomies were inserted on day 3 of admission, with little subsequent improvement in renal function. He did not require any cardiovascular or respiratory support. On examination he was found to be in decompensated cardiac failure with pitting oedema to his knees and ascites. Clinically, he was not in pulmonary oedema. ECG demonstrated minor non-specific findings (figure 1). A transthoracic echocardiogram showed a dilated left ventricle (LV) with a severely

Figure 1 Admission ECG.
Case report

reduced ejection fraction (EF), biplane EF 11% with no left ventricular hypertrophy (LVH), a dilated right ventricle (RV) with impaired systolic function, bi-atrial dilatation, mild mitral regurgitation, mild tricuspid regurgitation and a small localised pericardial effusion 0.4 cm in size. There were bilateral ventricular thrombi caused by stasis requiring systemic anticoagulation with intravenous unfractionated heparin (video 1).

The patient was then transferred to a tertiary hospital with access to advanced mechanical circulatory support in the event of deterioration. His admission was complicated by subclinical embolic and hypoperfusion-related cerebral infarcts, uraemic encephalopathy requiring emergency haemodialysis and heparin-induced thrombocytopenia. Haemodialysis was initiated on the intensive care unit on day 9, requiring a small amount of norepinephrine vasopressor support initially (0.04 μg/kg/min) but no inotropic agents were required. At the time there was concern that initiation of dialysis might result in cardiovascular collapse, which fortunately did not occur. This suggests that the low cardiac output was likely to have been chronic over a period of months for such haemodynamic compensation to occur. Given his intracardiac thrombi and renal failure, he initially received anticoagulation with intravenous unfractionated heparin. On day 9 of unfractionated heparin treatment his platelet count was noted to be 70×10^9/L following a gradual decline over the previous week (lowest platelet count 26×10^9/L on day 12) (table 1, figures 2 and 3). A positive heparin-induced thrombocytopenia screen resulted in a switch to argatroban.

The patient stabilised on the intensive care unit but remained in cardiac and renal failure requiring regular haemodialysis without improvement in cardiac function and remaining haemodynamically stable off vasopressor support and without any inotrope requirement.

He was referred and subsequently transferred for consideration of combined cardiac and renal transplantation. While urological investigations were being carried out to assess the suitability for kidney transplantation, his urine output via nephrostomies and urinary bladder improved with stable renal chemistry and fluid status, allowing a break from dialysis. Invasive assessment of his cardiac output with right heart catheterisation indicated that this was adequate, so imminent cardiac transplantation or mechanical circulatory support was not required at the time (table 2).

Fifty-eight days after his initial presentation he was discharged home from hospital with ongoing cardiology, renal and urology follow-up with a creatinine of 383 μmol/L. His repeat outpatient cardiac magnetic resonance (CMR) scan after 2 months showed improvement in LVEF to 18% and repeat transthoracic echocardiogram at 9 months post discharge showed further improvement of LVEF to 51% with normal right ventricular function.

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**Table 1 Blood results during admission and 14 days after discharge**

<table>
<thead>
<tr>
<th></th>
<th>Day 0</th>
<th>Day 7</th>
<th>Day 14</th>
<th>Day 21</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (x10^9)</td>
<td>13.8</td>
<td>13.2</td>
<td>8.4</td>
<td>6.6</td>
</tr>
<tr>
<td>Hb (g/L)</td>
<td>81</td>
<td>83</td>
<td>77</td>
<td>126</td>
</tr>
<tr>
<td>MCV (fl)</td>
<td>59</td>
<td>63</td>
<td>69</td>
<td>81</td>
</tr>
<tr>
<td>PLT (x10^9/L)</td>
<td>450</td>
<td>100</td>
<td>67</td>
<td>371</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>9.7</td>
<td>10.6</td>
<td>5.9</td>
<td>4.2</td>
</tr>
<tr>
<td>Iron level (μmol/L)</td>
<td>2.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total iron binding capacity (μmol/L)</td>
<td>53</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Transferrin saturation (%)</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferritin (μg/l)</td>
<td>41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Folate (μg/l)</td>
<td>6.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troponin T (ng/L)</td>
<td>398</td>
<td>760</td>
<td>2758</td>
<td>536</td>
</tr>
<tr>
<td>NT-proBNP (ng/L)</td>
<td>34 810</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium level (mmol/L)</td>
<td>134</td>
<td>133</td>
<td>142</td>
<td>140</td>
</tr>
<tr>
<td>Potassium level (mmol/L)</td>
<td>5.1</td>
<td>5.0</td>
<td>4.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Creatinine level (μmol/L)</td>
<td>580</td>
<td>508</td>
<td>224</td>
<td>366</td>
</tr>
<tr>
<td>eGFR (mL/min)</td>
<td>11</td>
<td>13</td>
<td>32</td>
<td>18</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>211</td>
<td>64</td>
<td>78</td>
<td>40</td>
</tr>
<tr>
<td>ESR (mm/hour)</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Day 0 relates to the day of transfer to our hospital.
CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; Hb, haemoglobin; MCV, mean corpuscular volume; NT-proBNP, N-terminal prohormone of B-type natriuretic peptide; PLT, platelets; WBC, white blood cells.
His CMR indicated that there was no scar, inflammation or oedema (figure 4 and video 2).

INVESTIGATIONS
▶ Admission ECG (figure 1) showed sinus tachycardia with a ventricular rate of 135 bpm, QRS duration of 110 ms and a normal PR interval. There was T-wave inversion in leads I and aVL and left axis deviation.
▶ Blood tests.
▶ Plain film chest radiograph (5/12/19, day 3 of admission) showed cardiomegaly, no pleural effusions and no pulmonary oedema (figure 5).
▶ Transthoracic echocardiogram (1) (5/12/19) showed a dilated LV (LV diameter 7.2 cm) with severely reduced EF (11%). No LVH. Laminated thrombus in LV mid anteroseptal wall extending to apex, dilated left atrium (30 cm²), dilated RV (6.3 cm base) with impaired systolic function. Tricuspid annular plane systolic excursion 14 mm. RV S' 0.09 m/s, dilated right atrium (24 cm²), small pericardial effusion 0.4 cm atrial side, mild tricuspid regurgitation, RV systolic pressure 32 mmHg+right atrial pressure, mild mitral regurgitation, other valves were normal (video 1).
▶ CMR imaging (1) (11/12/19): CMR imaging showed a non-ischaemic cardiomyopathy with globally severely impaired LV and RV systolic function, with LVEF of 9% and RVEF of 16%, severe bi-atrial dilatation with multiple LV and RV thrombi noted. No myocardial fibrosis, infiltration or infarction (video 2).
▶ CMR imaging (2) (14/2/20): CMR imaging showed improving but still severely impaired global LV systolic function (LVEF 18%). The mid inferior lateral wall is relatively more hypokinetic and there is improvement in RV function (RVEF 33%). No myocardial oedema and no obvious thrombi although gadolinium was not used on this occasion.
▶ Transthoracic echocardiogram (2) (10/6/20) showed a normal LV cavity size (LV diameter 5.7 cm) with global moderate impairment of systolic function (LVEF 38%). Normal RV size and function, normal bi-atrial sizes.

### Video 2
Cardiac magnetic resonance 11/12/19. (A) Four-chamber view. (B) Two-chamber view. (C) Three-chamber view. (D) Late gadolinium enhancement images in short axis stack.

### Figure 4
Cardiac magnetic resonance 11/12/19 (A) Mid-short axis T1 map: normal homogenous values throughout the myocardium imaged. (B) Late gadolinium four-chamber view. (C) Late gadolinium two-chamber view. (D) Late gadolinium three-chamber view.

### Figure 5
Admission chest X-ray showing an enlarged heart size, no focus of consolidation, collapse, sizeable pleural effusion or pulmonary congestion.

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**Table 2** Right heart catheterisation results

<table>
<thead>
<tr>
<th></th>
<th>Dec 2019</th>
<th>Jan 2020</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA (mmHg)</td>
<td>15</td>
<td>6</td>
<td>0–5</td>
</tr>
<tr>
<td>RV (mmHg)</td>
<td>54/12</td>
<td>39/2</td>
<td>15-25/0-10</td>
</tr>
<tr>
<td>PA, S/D/mean (mmHg)</td>
<td>55/32/42</td>
<td>42/22/30</td>
<td>15-25/6-12/8-20</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>30</td>
<td>20</td>
<td>4–12</td>
</tr>
<tr>
<td>TPG (mmHg)</td>
<td>12</td>
<td>10</td>
<td>≤12</td>
</tr>
<tr>
<td>CO (Fick l/min)</td>
<td>4.1</td>
<td>4.7</td>
<td>4–8</td>
</tr>
<tr>
<td>CI (l/min/m²)</td>
<td>1.93</td>
<td>2.48</td>
<td>2.5–4.0</td>
</tr>
<tr>
<td>PVR (WU)</td>
<td>2.4</td>
<td>2.1</td>
<td>1–2</td>
</tr>
</tbody>
</table>

PVR, pulmonary vascular resistance; CI, cardiac index; CO, cardiac output; D, diastolic; RV EDP, right ventricular end diastolic pressure; PA, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; RA, right atrial pressure; S, systolic; TPG, transpulmonary pressure gradient.
Urodynamic studies (1/7/20): Bladder capacity 400 mL.

Ultrasound abdomen (6/12/19): Enlarged kidneys with...

MRI brain/spinal cord/lumbar spine (17/12/19): Combination of cardioembolic and hypoperfusion acute infarcts. The extensive bilateral subcortical acute infarcts as described favour a cardioembolic aetiology whereas the bilateral internal border zone acute infarcts suggest a hypoperfusion aetiology. No cauda equina/spinal cord compression, normal spinal cord and lumbar spine.

Ultrasound abdomen (6/12/19): Enlarged kidneys with severe hydronephrosis and ureteric dilatation seen bilaterally. Increased echogenicity of the renal cortex and diffuse cortical thinning, appearance suggestive of chronic/long-standing obstruction. The liver is moderately enlarged with mild increased echogenicity of the parenchyma. The IVC in hepatic veins are prominent in size, likely in keeping with cardiac history.

Urodynamic studies (1/7/20): Bladder capacity 400 mL. Reflux to upper tracts increasing volume and lowering pressure. Bladder outline highly trabeculated with closed bladder neck. No loss of compliance measured (upper tracts compensating for this).

Bladder biopsy (20/08/20): Bladder mucosa shows stromal oedema, moderate chronic inflammation and stromal haemorrhage. No malignancy and no smooth muscle in biopsy samples.

DIFFERENTIAL DIAGNOSIS

This was a case of severe biventricular failure with biventricular thrombi of uncertain aetiology. A number of differential diagnoses were considered.

First, a stress-induced or ‘Takotsubo’ cardiomyopathy was felt to be less likely in this case given an absence of a preceding emotional or physical stressor, although these stressors may not be present in up to one-third of patients with Takotsubo syndrome. The insidious onset, over months prior to admission, was also not typical for Takotsubo syndrome, which classically presents more acutely and left ventricular function often recovers more quickly (usually within 21 days of onset). Furthermore, our patient did not fulfil the revised Mayo Clinic criteria or the international Takotsubo diagnostic criteria, and transthoracic echocardiography did not show any of the characteristic features (transient hypokinesis, akinesia or dyskinesia of the left ventricular mid-segments with or without apical involvement or any regional wall motion abnormalities extending beyond a single epicardial vascular distribution). Finally, Takotsubo syndrome predominantly affects postmenopausal women, although there have been case reports of younger male patients.

Heart failure secondary to myocarditis was also considered, however again the insidious clinical course was not typical for acute fulminant myocarditis and the CMR scan did not show the typical myocardial inflammation or fibrosis associated with this condition. Heart failure secondary to metabolic disturbances resulting from chronic renal failure was also considered as a potential differential diagnosis.

A tachycardia-related cardiomyopathy was excluded as there was no evidence of arrhythmia throughout the admission, during which the patient remained on cardiac monitoring. Given the history of chronic energy drink consumption, lack of significant past medical or family history, cardiac imaging findings and improvement with cessation intake, energy drink-induced cardiotoxicity was felt to be the most likely cause.

TREATMENT

Initial medical treatment was with intravenous furosemide and antibiotics for a suspected community acquired pneumonia. The patient was anticoagulated with unfractionated heparin, later switched to argatroban and then warfarin due to heparin-induced thrombocytopenia.

Bilateral nephrostomies were inserted 3 days after admission, with little subsequent improvement in renal function. He later required temporary haemodialysis and now remains a low clearance patient under renal and urology follow-up with bilateral nephrostomies and ureteric stents.

After stabilisation he was discharged on the following medications: warfarin once daily, carvedilol 3.125 mg twice daily, furosemide 20 mg once daily, isosorbide dinitrate 20 mg twice daily, hydralazine 25 mg three times a day, lansoprazole and oral nutritional supplements. Persisting severe renal impairment prevented the introduction of ACE inhibitor or mineralocorticoid receptor antagonist.

OUTCOME AND FOLLOW-UP

Post discharge, the patient had a considerable increase in exercise tolerance without any symptoms of heart failure or palpitations (NYHA class I). The patient had maintained euolaemia and haemodynamic stability. Renal function remained severely impaired (estimated glomerular filtration rate 18 mL/min), and we were able to uptitrate carvedilol to 6.25 mg twice daily during the follow-up period in addition to his other medications. At 9 months post-discharge, a repeat echocardiogram showed that the left ventricular size had normalised with mildly impaired systolic function (LVEF 51%). There was no evidence of the previous intracardiac thrombus.

As mentioned previously, poor renal function has largely inhibited the use of best medical therapy for heart failure. However, despite this, the patient has continued to improve and recover ventricular function. This is likely to be due to avoidance of energy drinks. He is no longer under follow-up from the cardiac transplantation team due to his improvement. However, it is difficult to predict the clinical progress of his heart failure and renal function going forward.
course of recovery or potential for relapse. It is likely that the patient will at some point require renal transplantation. He has undergone urodynamic studies and bladder biopsies, which have not conclusively identified the cause of obstructive uropathy but do indicate that future bladder reconstruction is likely to be required to protect a future renal graft.

**DISCUSSION**

Several case reports and review articles have highlighted the growing concern of the potential toxic effects of energy drinks on the cardiovascular system, where individuals may possess unknown susceptibility. Kaukis and colleagues reported a reverse pattern stress or Takotsubo cardiomyopathy (with a hyperdynamic apex and akinesis of the base of the LV, in contrast to the typical apical ballooning seen in typical Takotsubo cardiomyopathy), resulting in decompensated heart failure requiring intubation and ventilation in a young previously healthy 24-year-old with a history of excessive energy drink consumption. Belzile and colleagues reported a case of a 26-year-old woman who presented with inotrope-dependent severe dilated cardiomyopathy requiring mechanical support with a left ventricular assist device (LVAD) for 10 months following chronic ingestion of energy drinks with subsequent full ventricular recovery and LVAD explantation. The underlying mechanism of energy drink-induced heart failure remains unclear. Caffeine, found in high concentrations in energy drinks, has positive chronotropic and inotropic properties, largely through its action as a competitive antagonist of myocardial adenosine receptors, and on central catecholamine release. Stress cardiomyopathy has been associated with conditions such as pheochromocytomas and subarachnoid haemorrhage, which lead to a surge in catecholamines. Chronic sympathetic overstimulation through exogenous caffeine consumption may also precipitate a stress cardiomyopathy. Energy drinks are also known to increase blood pressure, and can precipitate a number of arrhythmias such as atrial fibrillation and supraventricular and ventricular ectopy. These chronic effects could also lead to heart failure.

This case highlights the importance of carefully searching for a specific cause in patients with unexplained cardiomyopathy, which begins with a thorough history and should include energy drink consumption. In cases of sudden arrhythmic death syndrome, information regarding energy drink consumption should be sought and perhaps included in post mortem reports. Future human and animal studies should seek to investigate factors which may predispose to severe heart failure or arrhythmias on exposure to energy drinks, with the objective of identifying those at risk and counsel them to avoid consumption. Further research is needed to identify susceptibility factors, the safe amount of energy drink consumption and underlying mechanisms of toxicity.

**Correction notice** This article has been corrected since it was published Online. The videos has been corrected.

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**REFERENCES**


Case report


