Hong Kong College of Physicians
Case report for Interim Assessment
Specialty Board of Advanced Internal Medicine (AIM)

For AIM Training, case reports should be submitted in the prescribed format together with the application form for Interim Assessment at least EIGHT Weeks before the date of Interim Assessment

Name of candidate (print and sign): Ho Chi Wai
Hospital and Unit: QMH MED Specialty: Haematology and AIM
Name of supervisor (print and sign): Dr. WOO Yu Cho
Date(s) and place (hospital) of patient encounter: 10th Jan 2023
Date of report submission: 10-March-2023

Case report

Note: Failure to follow the prescribed format (including the number of words) results in a FAILURE mark (score between 0 and 4) for the Case Report.

Title: AUTONOMIC NEUROPATHY COMPLICATING A PATIENT WITH ACUTE DECOMPENSATED HEART FAILURE

Case history:

A 92-year-old community-dwelling man with a history of stable coronary artery disease requiring percutaneous coronary intervention in 2019 presented to the emergency department for shortness of breath on exertion, difficulty in breathing upon lying flat and swollen legs on 10th Jan 2023. He has been in his usual state of health until 1 month before admission, when exertional dyspnea and orthopnoea started to develop insidiously. There had not been similar symptoms in the past. He had not been instructed to restrict salt or fluid intake in the past, but had not become more liberal in the consumption of fluid or food either. He has a history of ischaemic heart disease requiring percutaneous coronary intervention in 2019 and sciatica managed non-operatively. His regular medication included aspirin, bisoprolol, atorvastatin, famotidine, pregabalin and glyceryl trinitrate sublingual tablet.

Physical examination upon arrival showed a well-nourished, communicable and coherent elderly man. Blood pressure 118/75 mmHg, heart rate 64 beats per minute. Saturation was 98% on 2 litres of oxygen via nasal prong using pulse oximetry. Pallor, bilateral lower limb oedema and

elevated jugular venous pressure were evident. Auscultation of the chest demonstrated bilateral fine crepitations up to two-thirds from lung bases. First and second heart sounds were normal in intensity and character. The abdomen was soft and not distended. Chest radiograph showed pulmonary venous congestion and cardiomegaly. Electrocardiogram showed sinus rhythm with a known left bundle branch block and low voltages for limb leads. Blood test was remarkable for a new microcytic anaemia (haemoglobin 7.3 grams per deciliter, mean corpuscular volume 73.0 femtolitre). High-sensitive troponin was not elevated (56 nanograms per litre). Creatinine was stable at 159 micromole per litre. Liver function was normal. On further assessment, there is no clinical evidence of active or occult gastrointestinal haemorrhage. He was treated with intravenous frusemide bolus injection 40 miligrams every 12 hours. Oral iron replacement with vitamin C cover was started after blood for iron profile was taken, which later confirmed iron deficiency.

His condition deteriorated despite gentle diuresis. On the 5th day of admission the patient developed hypotension requiring inotropic support. Blood pressure measured 90/53, heart rate 82 beats per minute whilst receiving dopamine infusion at 20 mililitres per hour in a concentration of 2 miligrams per 1 mililitre of normal saline solution. Saturation measured 96% on 3 litres of oxygen via nasal prong. Lucid cognition was maintained so long as there were no severe hypotension. Focused bedside ultrasound demonstrated a heart with normal left ventricular size. Hypokinesia of left anterior descending territory leading to left ventricular ejection fraction (LVEF) 45% was observed. There were no significant valvular lesions. NT-pro-BNP was 5796 nanograms per litre. There was a rise in creatinine to 247 micromole per litre, even though urine output of more than 40 mililitres per hour could be maintained. Diuresis was stopped in view of hypotension and cardio-renal syndrome. Despite cessation of diuretics, the patient continued to require a combination of dopamine and phenylephrine to maintain appropriate blood pressure. The dependence on inotropic and vasopressor support appeared incompatible with the mild impairment of left ventricular ejection fraction and moderately elevated NT-pro-BNP. Meanwhile, with iron replacement, haemoglobin have gradually improved to 8.5 grams per deciliter without requiring blood transfusion. Alternative diagnoses were considered. Culture of peripheral blood and urine were negative. Procalcitonin measured < 0.1 nanograms per millilitre. Bisoprolol was stopped once the patient started to require inotrope, and yet the

haemodynamics did not improve after more than 72 hours of drug cessation. Furthermore, the patient was noted to have recurrent postprandial hypotension and syncope after lunch and dinner. Observation at bedside and assessment by speech therapist excluded the possibility of aspiration. A suspicion of autonomic dysfunction was raised.

The patient was started on midodrine 2.5mg three times a day per oral route. He was also empirically started on stress dose steroid after blood for morning cortisol, adrenocorticotropic hormone (ACTH) were taken. Subsequent short synacthen test showed sufficient response, and cortisol was taken off. He demonstrated marked improvement afterwards and weaned both dopamine and phenylephrine within 5 days. Notwithstanding being bed-ridden for more than two weeks, he could still walk unaided with 1 standby assistance. No further episode of post-prandial hypotension was noted. In view of advanced age and limited family support, it was decided he would not undergo further investigation for the cause of autonomic failure and iron deficiency anaemia.

Discussion and literature review

Acute decompensated heart failure is a common problem worldwide[1]. The Global Burden of Disease Study estimated more than 37 million cases of heart failure per annum in the year 2010. Data from the Hong Kong Heart Failure registry[2] indicates over a period of 7 years, the annual incidence rate of new-onset heart failure requiring hospitalization reaches 0.59 per 1000 population. Co-morbidities in these patients are most commonly hypertension (69.8%), diabetes (35.9%) and coronary artery disease (29.3%). The mainstay of treatment if decongestion, achieved by using diuretics to eliminate excessive fluid. Where there is evidence of excessive vasoconstriction, vasodilators such as intravenous nitrate can also be considered. Precipitating factors of an acute decompensation should be identified and corrected, the commonly encountered ones of which are arrhythmia, infection, myocardial ischaemia and anaemia. In our patient, the precipitating insult was thought to be a new onset microcytic anaemia. To avoid precipitating further circulatory overload, iron replacement via oral route was chosen in favour of parenteral iron injection and blood transfusion.

Iron deficiency has an intricate relationship with acute decompensated heart failure. Van Dalen and colleagues investigated the prevalence of iron deficiency in all patients admitted to hospital for acute heart failure[3]. These

patients are further classified as having absolute iron deficiency (serum ferritin < 100 micrograms per liter) or functional iron deficiency (serum ferritin 100-300 micrograms per liter, and transferrin saturation < 20%). In their experience, 44.1% of all patients had absolute iron deficiency, whereas another 27.7% had functional iron deficiency. A total of 71.8% of all patients, taken together, had some level of iron deficiency upon admission. They also investigated the evolution of iron profile over time and noted that functional iron deficiency may resolve while the patient is treated for acute heart failure without iron supplementation, whereas absolute iron deficiency would persist. The prevalence of iron deficiency notwithstanding, the role of iron replacement in acute decompensated heart failure remains under investigation. The AFFIRM-AHF trial was a randomized, double-blinded, placebo-controlled trial on the use of intravenous ferric carboxymaltose on hospitalization and mortality in iron-deficient patients admitted for acute heart failure[4]. The drug was given after stabilization and decongestion. The primary endpoint of total heart failure hospitalization and cardiovascular death within 52 weeks was reached by 52.5% of patients in treatment arm, and 67.6% in placebo arm ($p = 0.059$), which means there is a numerical, but statistically insignificant improvement. The safety endpoints are comparable across two arms. Applied on our current patient, the data from AFFIRM-AHF trial would support considering Fe replacement via intravenous route after stabilization, but this is not an urgent therapeutic intervention to consider.

Our patient's subsequent clinical course deviated from usual patients with acute heart failure and unveiled underlying autonomic failure. In particular, it was the observation of postprandial hypotension that allowed clinicians to pinpoint the diagnosis. Postprandial hypotension is a common problem in geriatric patient, and an under-recognized cause of syncope[5]. Among institutionalized elders, postprandial hypotension is present in more than 1 out of 4 persons[5]. Risk factors of post-prandial hypotension can be categorized into disease factor, medication factor and meal factor. Patients with diabetes, Parkinson's disease and end stage kidney disease are at higher risk. The use of diuretics or polypharmacy proved to be risk factors of postprandial hypotension. Taking a carbohydrate-rich or hot meal would also increase the chance of attack in susceptible individual. Our patient had a much more severe autonomic neuropathy as evidenced by the persistent hypotension throughout the day, indicating a general insufficiency of vasomotor tone requiring pharmacological support.

Midodrine is a drug of choice for treating hypotension related to autonomic failure[6]. It is a sympathomimetic prodrug, which leads to vasoconstriction and increases arterial resistance. While midodrine can correct the patient's main physiological disturbance, care was exercised to initiate the drug at the lowest possible dose and keep the drug at the minimal level required, so as the avoid precipitating acute decompensated heart failure. Indeed, acute decompensated heart failure and autonomic hypotension are driven by opposing pathophysiological process. A delicate balance needs to be achieved in the treatment of our patient, who fortunately turned out to respond well to a low dose midodrine and maintained a substantial level of pre-morbid functioning.

All in all, this patient presented with a common medical problem of acute decompensated heart failure. His clinical course took an unexpected turn, with high dependence on inotropic and vasopressor support. Clinical recognition of postprandial hypotension was pivotal to an accurate diagnosis of autonomic failure, for which simple pharmacological treatment with low dose midodrine proved effective. This case illustrates the importance thorough and meticulous clinical assessment in daily practice.

Tables and figures (where applicable) (no more than two figures)

Reference (not more than 10)

1. Arrigo M, Jessup M, Mullens W, et al. Acute heart failure. *Nat Rev Dis Primers* 2020; **6**(1): 16.

2. Hai JJ, Chan PH, Huang D, et al. Clinical Characteristics, Management, and Outcomes of Hospitalized Heart Failure in a Chinese Population-The Hong Kong Heart Failure Registry. *J Card Fail* 2016; **22**(8): 600-8.

3. van Dalen DH, Kragten JA, Emans ME, et al. Acute heart failure and iron deficiency: a prospective, multicentre, observational study. *ESC Heart Fail* 2022; **9**(1): 398-407.

4. Ponikowski P, Kirwan BA, Anker SD, et al. Ferric carboxymaltose for iron deficiency at discharge after acute heart failure: a multicentre, double-blind, randomised, controlled trial. *Lancet* 2020; **396**(10266): 1895-904.

5. Luciano GL, Brennan MJ, Rothberg MB. Postprandial hypotension. *Am J Med* 2010; **123**(3): 281.e1-6.

6. Gilani A, Juraschek SP, Belanger MJ, Vowles JE, Wannamethee SG. Postural hypotension. *Bmj* 2021; **373**: n922.

No of words in Case History and Discussion (excluding references):_____1495_____

(should be between 1000-2000)

Declaration

I hereby declare that the case report submitted represents my own work and adheres to the prescribed format. I have been in clinical contact with the case selected. The case report has not been submitted to any assessment board or publication and it is NOT related to my second specialty(ies), if any. My consent is hereby given to the College to keep a copy of my case report, in written and/or electronic, at the College Secretariat and allow the public to have free access to the work for reference.

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(signature of Trainee)

Endorsed by Supervisor *

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(signature of Supervisor)

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