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[Ed]

Primary Care Reflective Case Study Series

A typical case of end stage heart failure

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Patient Details

82 year old man with a past history of ischaemic heart disease (myocardial infarctions in 1978 and 1998), hypertension, atrial fibrillation and gout. At presentation he was on warfarin per INR, frusemide 80mg, digoxin 125mcg, isosorbide mononitrate 40mg, amlodipine 10mg, allopurinol 300mg, perindopril 4mg and GTN spray. A married, retired engineer who was an ex-smoker and had an alcohol intake of 8 units weekly. He developed what was felt to be a chest infection and was admitted to hospital where he had two courses of antibiotics. Patient was not investigated by echocardiography whilst in hospital. Seen on discharge by GP who referred him to the one-stop heart failure diagnostic clinic[1]. He was still producing some white sputum which tends to be worse at night and has shortness of breath on exertion corresponding to New York Heart Association class II. Previous ankle oedema had resolved after GP initiated diuretic. He had mild orthopnoea but no paroxysmal nocturnal dyspnoea or angina at initial presentation.

Examination

Blood pressure 110/60, pulse 92 per minute irregularly irregular. JVP raised 2cm, heart sounds normal with loud grade 3 pan-systolic murmur in all areas but maximal at the apex. Auscultation of his chest revealed bi-basal fine crepitations but he had no ankle oedema or organomegaly.

Initial investigations

- Serum biochemistry including Urea and electrolytes, creatinine, blood sugar, cholesterol, digoxin level, TSH, BNP & NT pro-BNP
- Haematology including full blood count
- Electrocardiography
- Chest x-ray
- Echocardiogram
- Spirometry

Differential Diagnosis

Heart Failure due to ischaemic left ventricular systolic dysfunction (LVSD)

Mitral regurgitation

Atrial Fibrillation

Chronic Obstructive pulmonary disease

Results

Serum Biochemistry & Haematology - Urea & electrolytes, creatinine, digoxin level, random blood sugar, cholesterol, full blood count, ESR, TSH all normal.

BNP significantly high at 580 pg/ml and NT-Pro BNP 3284.8 pg/ml – indicating the need for further cardiac assessment[2].

Electrocardiogram showed atrial fibrillation at a rate of around 90/minute with LBBB, ST depression of the lateral leads, anterior Q waves and a mean frontal QRS axis of -45 degrees, QRS duration was approximately 120 ms.

Chest x-ray (figure 1) showed cardiomegaly with pulmonary venous congestion and Kerley B lines suggestive of cardiac failure

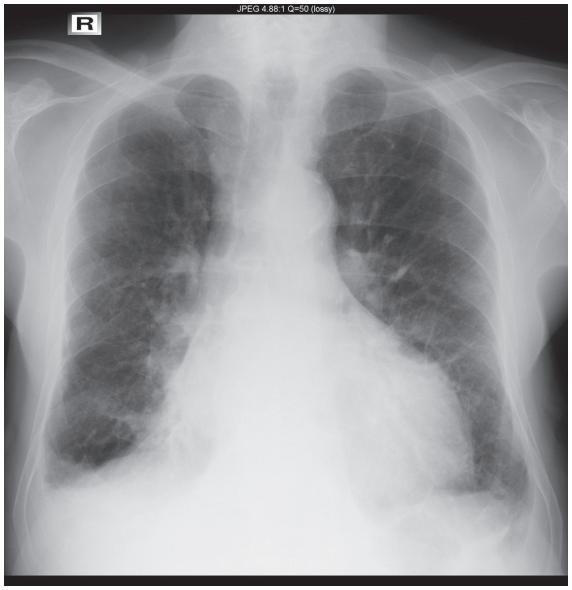

Figure 1.

Echocardiogram showed moderate to severe systolic impairment with wall motion hypokinesis and akinesis. Significant left ventricular dilation, mild aortic regurgitation, severe mitral regurgitation with some dilation of the right ventricle and mild pulmonary hypertension. Ejection fraction (Simpson's) 33%. Left ventricular end diastolic volume (LVIDd) 7.21cms (normal < 5.5). LA diameter 5.45cms (normal < 4.5)[3]. Peak expiratory flow rate was 360 L/minute but he had poor technique for spirometry and an adequate result was not obtained.

Diagnosis

Heart failure due to LVSD

Severe mitral regurgitation

Atrial fibrillation.

Pathophysiology

This man had significant LVSD with mitral regurgitation and atrial fibrillation. A degree of mitral regurgitation frequently accompanies heart failure, even where the valve is structurally normal, due to stretching of the mitral valve annulus. In severe left ventricular dilatation such mitral regurgitation may become significant. It is important though difficult to establish whether the mitral regurgitation is truly functional and whether it is secondary rather than aetiological. While mitral valve replacement may benefit the latter, it will be of little value in the former[4]. It was considered that this man had mitral regurgitation secondary to ischaemic LVSD. Atrial fibrillation is present in up to 10% of patients with mild to moderate LVSD, rising to 50% in severe LVSD and is common in patients with mitral regurgitation[5]. Atrial fibrillation is associated with a worse prognosis compared with sinus rhythm in heart failure[6].

Initial management

Remain on frusemide 80mg daily, commenced on bisoprolol 1.25mg daily with a view to up titration to 10mg, in line with current evidence[7]. Patient was already on evidence-based dose of ACE inhibitor[8], and digoxin according to guideline advice[9]. Digoxin dose was increased to 187.5µg in an attempt to reduce the resting heart rate (92/min). Referred to specialist heart failure nurse for beta-blocker titration, lifestyle advice and patient/carer education. Specialist HF nurses are playing an increasingly important role in monitoring and education of patients, and nurse-led interventions have been shown to reduce hospital admissions and re-admissions[10].

Further management

He rapidly went from class II to class IV heart failure despite treatment with ACE inhibitor, diuretic, beta-blocker, digoxin and nitrates. He developed intractable paroxysmal nocturnal dyspnoea and very poor exercise tolerance

having to stop after a few yards of walking. Spironolactone was introduced but led to hyperkalaemia, lethargy and deterioration of renal function and was withdrawn.

His sleep was greatly affected and trazodone was initially successful at improving sleep pattern. However, he continued to deteriorate and after discussion with cardiologist it was decided to refer to our tertiary centre for consideration of biventricular pacing/cardiac resynchronization therapy (CRT) [11].

Unfortunately CRT was not considered appropriate for this patient. Firstly, the benefit is said to be less in patients with atrial fibrillation than those in sinus rhythm. Furthermore his QRS duration was 120ms and the tertiary care centre protocol required a QRS duration of 150ms or more at that time.

He continued to decline requiring a lot of medical, social and specialist nursing support. He developed increased oedema and ascites despite frusemide 160 mgs daily and needed metolazone 5mg twice a week to control peripheral and pulmonary oedema. He needed morphine sulphate 5mg nocte to reduce nocturnal breathlessness and agitation. Attendance at the local hospice day care centre twice a week gave his wife respite from her exhausting carer role.

Ultimately his wife decided that despite intensive daily support from our Immediate Response Team of nurses, carers and family members she could not cope with him at home. Hospice bed was unavailable and admission was arranged to hospital where he died shortly after.

Learning Points

This case raises some learning points for clinicians:

What are the referral criteria and benefits of cardiac resynchronization therapy in HF?

Cardiac resynchronisation therapy/biventricular pacing has been shown to increase LV ejection fraction, cardiac output, prolong diastole and left ventricular filling time, reduce left ventricular end diastolic and end systolic volumes, increase left ventricular synchrony and pulse pressure, increase peak oxygen uptake, decrease pulmonary capillary wedge pressure and decrease mitral regurgitation[11]. In this instance the QRS duration and presence of atrial fibrillation were felt to reduce the potential success of this procedure. Recent guidelines suggest that patients with highly symptomatic LVSD (NYHA III-IV) of non-reversible cause on optimal therapy and in sinus rhythm should be considered for CRT if they have ventricular dys-synchrony suggested by a QRS > 130ms or induced by right ventricular pacing[11]. Significant mitral regurgitation is also a referral criterion[11]. More recently it has been suggested that patients with QRS of < 120ms may also benefit from CRT[12, 13]. Recently the CARE-HF trial has confirmed that CRT can reduce mortality and is cost effective in appropriately selected patients.

How prevalent are side effects with spironolactone in elderly patients with HF?

The RALES study confirmed the mortality benefits of spironolactone use in patients with NYHA III-IV LVSD (27% RRR, $p<0.0001$)[14]. Furthermore, hospital admissions for all cardiac causes and worsening heart failure by 30% and 35% RRR respectively[14]. Recent guidelines suggest that patients with moderate to severe HF should be considered for treatment with spironolactone if they remain symptomatic on an ACE inhibitor and beta-blocker[9]. However, in practice many elderly patients on ACE inhibitors or angiotensin receptor blockers develop significant hyperkalaemia and renal impairment or failure. Advanced age, dose of

spironolactone > 25mgs, reduced renal function and type 2 diabetes mellitus, LVEF below 20% all seem to be predictors of hyperkalaemia and azotemia[15, 16]. Eplerenone is a newer aldosterone antagonist with potentially fewer side-effects including less gynaecomastia and hyperkalaemia. The recent EPHESUS study demonstrated its efficacy in reducing mortality[17]

What do we know about the use of morphine in intractable HF?

The trajectory of dying from end stage HF is very different to that of cancers[18]. Barriers to good information, communication and understanding for patients are widespread and communication with professionals is poor regarding advance planning for the end of life[19, 20]. Evidence for the use of opioids or benzodiazepines is limited, but they may be safe in heart failure[21] and their palliative use is recommended by NICE[9]. Oral morphine at low dosage has been shown to provide significant symptomatic improvement in refractory dyspnoea in the community setting[22]. Locally we have looked at close liaison between primary, secondary and palliative care and are developing pathways of care and local formularies. These sorts of areas are essential in seamless care of heart failure patients from diagnosis to end of life. Little is known about place of death in heart failure versus cancer care and is in need of further study to identify barriers to choice of place of death for these patients.

What is diuretic resistance and how do we use loop and thiazide diuretics together?

Diuretic resistance is the condition of increasing symptoms of fluid and electrolyte retention in face of increased doses of diuretics[23]. Although high doses of loop diuretics may help[24], intravenous therapy is often needed. An alternative approach is to use a combination of loop and thiazide diuretic – so called 'sequential nephron blockade'[23]. Such strategies may cause unpredictably large diuresis with intravascular dehydration, hypotension and renal failure. Close monitoring of electrolytes and renal function is essential and should only be undertaken by clinicians skilled in the management of end stage heart failure.

These sorts of cases utilise GP skills in problem solving, communication and team working across primary, secondary, tertiary and palliative care. The difficult area of end stage HF management and allowing patients to die in their preferred place of death and with dignity can be challenging at times, but it is ultimately a rich learning and professional experience.

References

1 Fuat A, Murphy JJ, Hungin APS. Designing heart failure services: A primary care perspective? Heart 2003: 89; A11

2 Fuat A, Murphy JJ, Hungin APS, Curry J, Mehrzad A, Hetherington A, Johnston JI, Smellie WSA, Duffy V, Cawley P. The diagnostic accuracy and utility of natriuretic peptides in a community population of patients with suspected heart failure, using near patient and laboratory assay methods. British Journal of General Practice 2006; 56: 327-333

3 Chambers J. Suspected Heart Failure. In Echocardiography in Clinical Practice. Parthenon Publishing 2002; 36-45

4 Murdoch DR. The patient with intractable heart failure: a practical guide to management. In Heart Failure – Diagnosis and Management. Editors Clark AL, McMurray JJV. Martin Dunitz Ltd 2001; 177- 204

5 The CONSENSUS trial study group. Effects of enalapril on mortality in severe congestive heart failure: results of the Cooperative North Scandinavian Survival Study (CONSENSUS). N Engl J Med 1987; 316: 1429-35

6 Middlehauf HR, Stevenson WG, Stevenson LW. Outcome for advanced heart failure patients with atrial fibrillation. Cardiol Board Rev 1992; 9:101-2

7 Avezum A, Tsuyuki RT, Pogue J et al. Beta-blocker therapy for congestive heart failure: a systematic overview and critical appraisal of the published trials. Canadian Journal of Cardiology 1998; 14: 1045-53

8 Flather MD, Yusuf S, Kober L et al. Long-term ACE-inhibitor therapy in patients with heart failure or left ventricular dysfunction: a systematic overview of data from individual patients. Lancet 2000; 355:1575-1581

9 National Institute for Clinical Excellence. Chronic Heart Failure. Clinical Guideline No.5 July 2003-09-17

10 Blue L, Lang E, McMurray JJV et al. Randomised controlled trial of specialist nurse intervention in heart failure. BMJ 2001; 323: 715-8

11 Chow AWC, Lane RE, Cowie MR. New pacing technologies for heart failure. BMJ 2003; 326:1073-7

12 Ghio S, Constantin C, Klersy C et al. Interventricular and intraventricular dyssynchrony are common in heart failure patients, regardless of QRS duration. European Heart Journal 2004; 25: 571-8

13 Breithardt OA, Claus P, Sutherland GR. Do we understand who benefits from resynchronisation therapy? European Heart Journal 2004; 25: 535-6

14 Pitt B, Zannad F, Remme WJ et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomised Aldactone Evaluation Study Investigators. N Eng J Med 1999; 341:709-17

15 Wrenger E, Muller R, Moesenthin M et al. Interaction of spironolactone with Ace inhibitors or angiotensin rceptor blockers: analysis of 44 cases. BMJ 2003; 327: 147-9

16 Svensson M, Gustaffson F, Galatius S et al. Hyperkalaemia and impaired renal function in patients taking spironolactone for congestive heart failure: retrospective study. BMJ 2003; 327: 1141-2

17 Pitt B, Remme W, Zannad F et al. Epleronone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. N Eng J Med 2003 ; 348 : 1309-21

18 Teno JM et al. Dying trajectory in the last year of life: does cancer trajectory fit other diseases? J Palliat Med 2001; 4: 457-64

19 Hanratty B, Hibbert D, Mair F et al. Doctors' perceptions of palliative care for heart failure: focus group study. BMJ 2002; 325: 581-5

20 Rogers AE, Addington-Hall J, Abery A et al Knowledge and communication difficulties for patients with chronic heart failure: qualitative study. BMJ 2000; 321(7261): 605-7

21 Johnson MJ. Morphine for the relief of breathlessness in patients with chronic heart failure – a pilot study. Eur J Heart Failure 2002;4: 753-6

22 Abernethy AP, Currow DC, Frith P et al. Randomised, double blind, placebo controlled crossover trial of sustained release morphine for the management of refractory dyspnoea. BMJ 2003; 327: 523-6

23 Petrie MC. Treatment with diuretics. In Heart Failure – Diagnosis and Management. Editors: Clark AL, McMurray JJV. Martin Dunitz Ltd 2001; 77-89.

24 Gerlag PGG, Vanmeijl JJM. High-dose frusemide in the treatment of refractory congestive heart failure. Arch Int Med 1998; 148: 286-291