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Heart Failure Masked as Pulmonary Embolism in Non-adherent Patient With Atrial Fibrillation: Case Report and Analytical Review of the Literature

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Abstract. *Background/Aim: Atrial fibrillation (AF) and heart failure (HF) commonly co-occur, significantly increasing morbidity and mortality. Poorly controlled AF can contribute to complications like HF and is associated with conditions, such as stroke and pulmonary embolism (PE). This report involves a man with AF who had persistent respiratory symptoms and left-sided chest pain, initially suspected to be PE, but eventually diagnosed as HF. Case Report: A 43-year-old male experienced increasing breathlessness, cough, and fatigue. Initially suspected to have a respiratory infection, his persistent symptoms raised concern for PE. The patient had a history of AF, unsuccessful cardioversion, and long-term non-adherence to beta blockers. Initial assessment revealed persistent respiratory symptoms and elevated levels of C-reactive protein, D-dimer, N-terminal pro-B-type natriuretic peptide, and Troponin T. Chest X-ray showed pulmonary congestion, and echocardiogram confirmed a severely impaired ejection fraction (EF <20%). While the differential diagnosis included community-acquired pneumonia, PE, and HF, the final diagnosis was worsening AF and HF with reduced EF, not PE. Conclusion: PE symptoms can overlap with HF, making careful differential diagnosis essential, particularly in AF patients with elevated D-dimer levels, where false positives necessitate caution. This case underscores the importance of thorough differential diagnosis and clinical judgment before ordering tests to avoid misdiagnosis. Long-term non-adherence to beta blockers exacerbated the patient's symptoms, emphasising the critical role of consistent medication use in managing AF and preventing complications like HF. This case report also highlights the importance of thorough investigations, guideline-based treatments and multidisciplinary care in complex AF-HF cases.*

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Atrial fibrillation (AF), the most common type of arrhythmia, affects approximately 33 million people globally (1). A study involving over 8 million individuals demonstrated that the prevalence of AF is age-dependent, with the average age of patients with AF being 73.1 years; of these patients 55.5% were male (2). AF is characterised by rapid and irregular beating of the atria leading to irregular rapid atrial depolarisations between 300-600 beats/min (1, 3), leading to poor blood flow and an increased risk of thromboembolism and death (4-6). AF is associated with a doubled risk of early death and major cardiovascular complications, such as heart failure (HF), severe stroke and myocardial infarction (1, 4, 5). Symptoms of AF, such as shortness of breath, fatigue, dizziness, and weakness, can overlap with those of pulmonary embolism (PE) or complications arising from poorly controlled AF such as HF (7, 8).

In the UK, 200,000 people are diagnosed with HF annually, with 63,530 acute HF admissions recorded in 2022/2023 (9). Patients with HF often have high levels of comorbidities, and a significant portion of their hospital readmissions - up to two-thirds – are due to non-HF-related issues (10). HF is characterised by the heart's inability to pump blood effectively, resulting in inadequate cardiac output to meet the body's metabolic needs and manage venous return. This leads to clinical manifestations such as breathlessness due to pulmonary congestion and fluid retention due to impaired systemic venous return (11, 12). HF develops due to damage to the myocardium, which can be caused by various factors, such as hypertension, diabetes, ischemic heart disease and less frequently valvular disease (11). While HF can manifest acutely, for example following an acute myocardial infarction (MI), it can develop gradually as a chronic condition where acute decompensation can subsequently develop (12). HF with reduced ejection fraction (HFrEF) accounts for approximately half of all HF diagnoses (13).

Both AF and HF are prevalent and their combination is increasingly common, particularly in an ageing population (14). With an ageing population, AF prevalence is projected to more than double in the next four decades (1). The incidence of HF is also likely to rise, given that it shares many of the same risk factors as AF such as hypertension (3). HF can lead to the development of AF, and AF can also contribute to the progression of HF. AF occurs in about one-third to one-half of patients with HF (3). This co-occurrence is significantly associated with poor long-term outcomes and high morbidity and mortality, making accurate and timely diagnosis essential for effective treatment and management (15-17).

This report details a patient with poorly controlled AF due to sustained non-adherence, presenting with ongoing respiratory symptoms and left-sided chest pain. Though initially suspected of PE, the patient was ultimately diagnosed with HF with reduced ejection fraction (HFrEF). We also describe the epidemiology and pathophysiology of AF and HF and review the literature and relevant treatment guidelines.

Case Report

Patient presentation. A 43-year-old male patient, with a history of drug and alcohol abuse and a failed cardioversion for AF, experienced increasing breathlessness, cough and fatigue. A respiratory tract infection was initially suspected, and Amoxicillin 500 mg three times daily was prescribed. Over the next eight days, the patient's condition deteriorated, with the development of new left-sided chest pain. A PE was suspected. Rivaroxaban 15 mg twice daily was prescribed and the patient was referred to Same Day Emergency Care (SDEC). Upon assessment at SDEC the following day, a twelve-lead electrocardiogram (ECG) confirmed AF, consistent with the patient's history of AF from 10 years prior (Figure 1). The patient reported experiencing orthopnea and a history of three unsuccessful cardioversion attempts over the 10 years since being diagnosed with AF, with the most recent attempt occurring three years ago. The patient also reported that he had stopped taking sotalol 160 mg twice daily at least a year ago and had been taking it inconsistently for a few years before that, mistakenly believing his symptoms had improved. While he was open about this, he could not remember the exact dates when he started or stopped the medication. The patient's social history revealed chronic drug and alcohol abuse, which likely contributed to his non-adherence to AF medication.

Investigations/Differential diagnoses. The patient scored 4/10 on the Borg Rating of Perceived Exertion (RPE) at rest, a scale commonly used to assess perceived exertion, including the respiratory component, as part of overall physical effort (18). The patient exhibited a dry, irritable cough with concurrent left chest pain. Examination revealed an irregular pulse and bilateral basal wheezing. Despite these symptoms, the patient believed it was merely a severe case of the flu.

The differential diagnosis included community-acquired pneumonia (CAP), PE, pleuritis, aortic dissection and pneumothorax. The patient's blood pressure was 154/92, heart rate 126 and oxygen saturation (SpO2) 95%. The patient's laboratory results showed several abnormalities. An elevated C-reactive protein (CRP) level of 10 mg/l (normal ≤5 mg/l) suggested inflammation, and a significantly raised D-dimer level of 993 ng/ml (normal ≤250 ng/ml) indicated a possible thromboembolic event, warranting further investigation to rule out PE. The N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) level of 6,374 ng/l (normal 0-399 ng/l) was highly indicative of HF, and an elevated Troponin T level of 161 ng/l (normal ≤14 ng/l) indicated cardiac injury.

CAP was ruled out based on the lack of consolidation on the chest X-ray (19) and only slightly raised CRP levels (20), making pleurisy due to CAP unlikely as well. The absence of pain triggered by coughing, chest wall movements and sneezing further supported this. Aortic dissection and pneumothorax were also excluded based on clinical examination and investigations. The patient's clinical scoring results indicated a low probability of PE with a low Wells score of less than 2 (21) and negative YEARS algorithm results (22). The patient's lab results indicated significant cardiac stress and potential HF. Chest CT or CT Pulmonary Angiogram (CTPA) are the gold standard for diagnosing PE (23). However, a discussion with the radiologist concluded that neither chest CT nor CTPA was necessary, as the chest x-ray indicated acute pulmonary oedema (Figure 2), strongly suggesting HF. This, along with the clinical presentation, required immediate hospital admission.

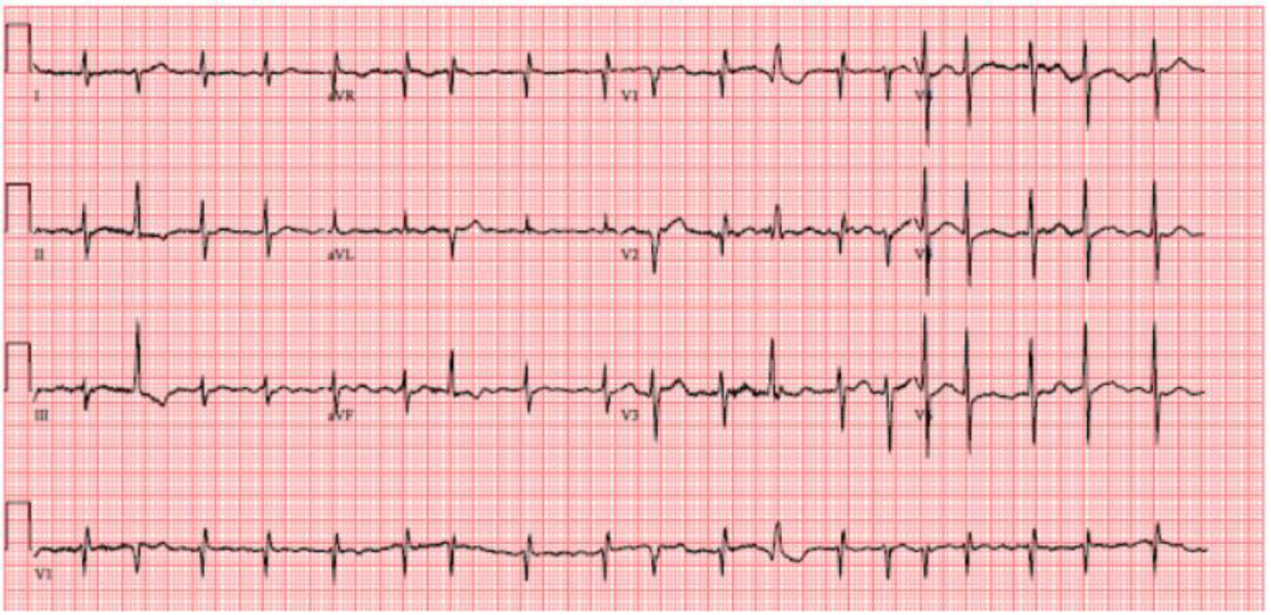

Figure 1. *A twelve-lead electrocardiogram (ECG) confirms atrial fibrillation in the patient.*

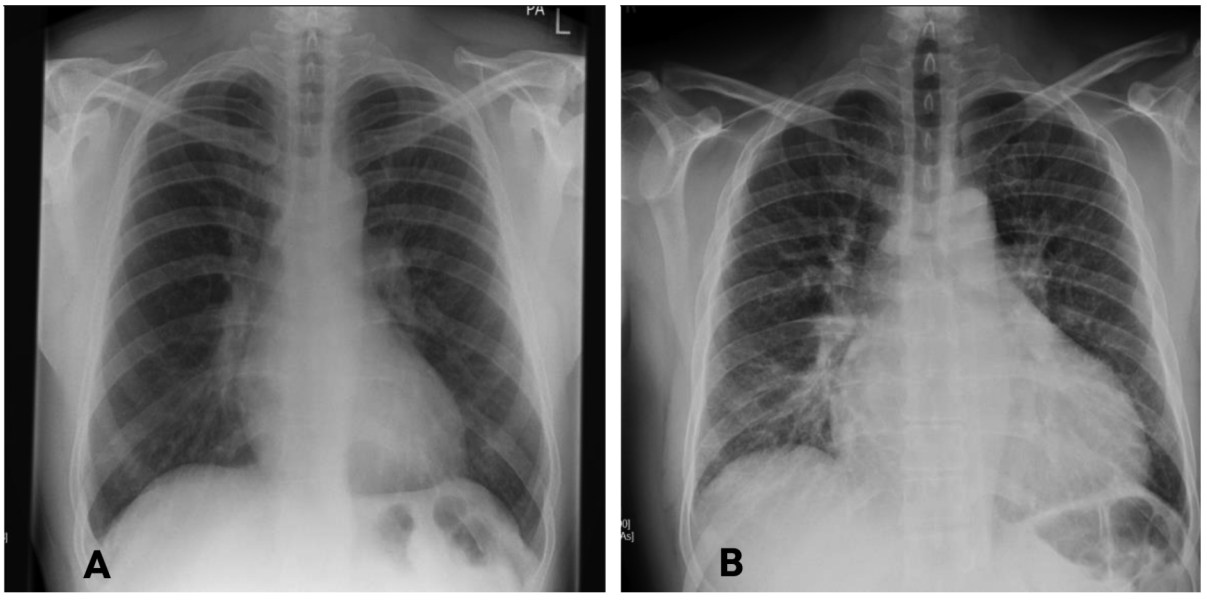

Figure 2. *Chest X-ray findings: A) Five years ago, the X-ray showed normal cardiopulmonary structures. B) The recent X-ray, following referral to Same Day Emergency Care (SDEC), revealed an enlarged heart and prominent pulmonary vasculature, consistent with signs of pulmonary congestion.*

Management plan/Follow-up. The patient was initially transferred to the cardiology team and admitted to the hospital, where he remained as an inpatient for five days. The initial management plan included immediate rate control with a stat dose of Bisoprolol 2.5 mg and sotalol was considered inappropriate due to its lack of efficacy and potential pro-arrhythmic effects and prolongation of cardiac repolarisation (24, 25). To reduce congestion and off-load fluid, the patient received stat doses of intravenous (IV) furosemide 40 mg and oral spironolactone 25 mg (26). An urgent cardiac echo was performed on the second day of admission, confirming HF with an ejection fraction (EF) of less than 35% and a Simpson's method (27) EF of below 20%.

The cardiology team reviewed the need for anticoagulation, considering the patient's ORBIT score of 0, indicating a 2.4% annual risk of bleeding (low risk) (28), and a CHA_2DS_2-VASc score of 1, indicating a 0.6% annual risk of stroke (low to moderate risk) and a 0.9% annual risk of stroke or transient ischaemic attack (TIA) (29). Given these risk levels, anticoagulation was not indicated. Following his hospitalisation, the patient was discharged to the outpatient heart failure clinic (HFC) with a diagnosis of HFrEF.

Upon follow-up with the HFC, the patient was pharmacologically optimised with dapagliflozin 10 mg tablet (oral, once daily), digoxin 125 micrograms (oral, once daily), eplerenone 25 mg tablet (oral, once daily), furosemide 40 mg tablet (oral, once daily), apixaban 2.5 mg tablet (oral, twice daily) and bisoprolol 5 mg tablet (oral, once daily). During his treatment, the patient's clinical progress showed significant improvement with optimised medical management. The patient no longer experienced orthopnoea and his weight decreased from 94 to 86 kg. The patient's blood pressure decreased to 124/65, heart rate to 65, and SpO2 increased to 98%. A follow-up appointment was scheduled to discuss the initiation of angiotensin receptor-neprilysin inhibitors (ARNIs) alongside other therapies. Additionally, the patient participated in shared decision-making regarding medication adherence and received education on self-care for his condition.

The patient was contacted for a telephone follow-up, during which he reported notifying the Driver and Vehicle Licensing Agency (DVLA) about his condition due to his role as a truck driver. As a result, he has been temporarily reassigned to an office job while his health is improving. He also confirmed strict adherence to his medication regimen and reported no side effects.

Discussion

Diagnosing HF in patients with AF is challenging due to overlapping symptoms. AF affects ECG and circulating natriuretic peptide, troponin and D-Dimer levels, complicating the accurate diagnosis of HF (30). Tachycardia-induced cardiomyopathy, rapid heart rates, irregular cardiac output from uneven heartbeat intervals and the loss of atrial contribution to cardiac output in AF all may precipitate or exacerbate HF symptoms (3). Effective treatment of AF is therefore crucial to prevent AF from progressing to HF, with medication adherence being key. In this case, sustained non-adherence and sotalol discontinuation likely contributed to cardiac deterioration and worsening symptoms. Ultimately this resulted in HFrEF, which presented as respiratory symptoms and left-sided chest pain, initially mistaken for PE. The high D-dimer level suggested a thromboembolic event, but the low Wells score, negative YEARS algorithm and elevated NT-pro-BNP and Troponin T levels, indicative of HF and cardiac injury, justified not pursuing further imaging for PE. This highlights the important role of clinical prediction rules such as Wells criteria for PE as part of a thorough clinical assessment, and only using D-Dimer tests when clinical assessment suggests thromboembolism is a likely possibility, not as a general rule for all patients with chest pain or dyspnoea (31).

Over-reliance on blood diagnostic tests without appropriate clinical context can lead to unnecessary investigations, misinterpretation of results, false positives and delays in accurate diagnosis, potentially resulting in mismanagement of patient care and subsequent harm. To avoid the use of a broad "battery of tests", a thorough clinical evaluation should be conducted first, and clinical prediction rules should guide the decision as to which test to order. In this case, the risk of ordering cardiorespiratory blood tests, such as troponin, NT-pro-BNP and D-dimer before a thorough clinical evaluation is the increased likelihood of false positives complicating the diagnostic process. The indiscriminate use of such diagnostic blood tests prior to thorough clinical evaluation can be particularly problematic in cases such as AF, which is known to elevate levels of biomarkers, such as CRP, NT-pro-BNP and D-dimer which complicate the diagnosis (32), due to its association with thrombosis without the presence of thromboembolism (33). This can result in false positives, falsely suggesting PE or other thromboembolic events and can lead to unwarranted investigations such as CTPA. Therefore, it is vital to exercise caution when considering a diagnosis of PE in these patients. In many cases, this patient could have undergone unnecessary CTPA or even coronary angiography, which are not clinically indicated. Both procedures can result in overdiagnosis and carry risks of radiation exposure and potential cardiac injury. Chest CT is still the gold standard for diagnosing PE (23), and PE should always be considered as a potential trigger for acute HF, as patients with HF are often in a hyper-coagulable condition (10, 34).

The patient's pulmonary oedema and raised plasma levels of NT-pro-BNP indicated acute HF (35, 36). Acute HF can result in systemic complications and vital organ damage due to inadequate blood circulation, caused by elevated venous pressure and/or reduced cardiac output (10, 37), thus, making it a medical condition that requires timely diagnosis and intervention to ensure patient survival (10, 34, 35). While acute HF is typically an exacerbation of chronic HF, it can also occur as a first-time episode (*de novo*) often due to primary cardiac dysfunction, uncontrolled hypertension or arrhythmias (10), as was the case with our patient. The patient's SpO2 was monitored due to worsening dyspnoea, but oxygen therapy was withheld since SpO2 was above 90%, avoiding hyperoxia, which can cause vasoconstriction and reduce blood flow to the heart and brain (10).

The primary objective in the new-onset and acute phase of HF is to relieve congestion and manage fluid overload with diuretics. For long-term management of HFrEF, key

medications including MRAs, sodium-glucose cotransporter 2 (SGLT2) inhibitors, beta-blockers and ARNIs are recommended to optimise outcomes in most patients to reduce mortality and hospitalisation (38-40). These medications should be titrated to the maximum tolerated or recommended doses. When compared to treatment with ACE inhibitors alone, the combination of these four key therapies for HFrEF has been found to significantly reduce the risk of cardiovascular mortality and HF-related hospitalisations in patients with HFrEF (41). Additionally, when managing HF patients with AF after stabilisation, the goals are to prevent thromboembolic events, minimise the adverse impact on cardiac function and symptoms by optimising HF treatments and apply AF therapies when indicated (3). Following stabilisation, evidence-based oral therapies were therefore recommended including discontinuation of sotalol and initiation of bisoprolol, digoxin, apixaban, dapagliflozin, eplerenone and transitioning the patient from IV furosemide to oral furosemide; the patient showed significant improvement with resolved orthopnoea and improved blood pressure, heart rate, oxygen saturation and subsequent weight loss.

The initial management plan for our patient included administering IV furosemide alongside oral spironolactone to alleviate congestion and manage fluid overload. In cases of acute HF with pulmonary oedema, first-line therapy typically involves loop diuretics, such as furosemide, to reduce fluid overload and alleviate symptoms (10, 26, 34, 35). Furosemide is rapidly absorbed, reaching peak plasma concentration within 30 min to 2 hours orally (42) and 5 min intravenously (43). About half is excreted unchanged in urine (44). It lowers blood pressure by reducing fluid volume yet it can cause hypotension, necessitating careful monitoring and dose adjustments. HF therapy should be withheld in all patients with severe hypotension until their condition improves. While its exact mechanism in lowering blood pressure is not fully understood (45), renal function is crucial to its antihypertensive effect (46). The DOSE-AHF Study found no significant differences in patient's overall symptom assessment when intravenous furosemide therapy was administered as a bolus *versus* continuous infusion, or at a high dose *versus* a low dose (47). Thus, it is advised to use the lowest possible diuretic dose that achieves adequate symptom relief, adjusting the dosage according to renal function and the patient's previous diuretic dosage, particularly in diuretic naïve patients or *de novo* acute HF as was the case with our patient (10, 34, 35).

Spironolactone, a potassium-sparing diuretic, has proven efficacy in reducing mortality in patients with HF, particularly in combination therapy with furosemide for HF with pulmonary oedema (26). While spironolactone is well-tolerated and safe to add to standard care in patients with acute HF (48, 49), and this combination is more effective, careful monitoring of electrolyte levels and renal function is essential due to the increased risk of hypokalaemia and potential renal impairment associated with spironolactone (50, 51). The COACH study, which included 534 patients with acute HF treated with spironolactone during hospitalisation, found significantly reduced 30-day mortality and fewer HF-related re-hospitalisations, especially in high-risk patients (52). Similarly, in the Medicare-linked OPTIMIZE-HF registry, 8,206 hospitalised older patients with HFrEF (EF≤35%) who had not previously used spironolactone demonstrated that its use was associated with an 8% to 13% reduction in the risk of all-cause mortality and HR-related re-hospitalisations (53). The JCARE-CARD study, involving 946 patients with HFrEF (EF<40%) hospitalised for HF, found that spironolactone use at discharge was significantly associated with improved long-term survival (54). However, other observational studies have produced mixed results regarding the association of MRAs at hospital discharge or in acute HF with 30-day all-cause readmission, mortality or cardiovascular readmission (50, 55).

The clinical efficacy of MRAs in improving prognosis for patients with HFrEF is well-established and consistently demonstrated in the literature (40). Two large randomised controlled trials (RCTs) demonstrated that MRAs significantly reduce hospitalisation rates, morbidity, and mortality in patients with HFrEF (56, 57). The RALES trial, which included 1,663 patients with New York Heart Association (NYHA) Class III or IV heart failure with EF of ≤35%, demonstrated that spironolactone significantly reduced the risk of death and cardiovascular hospitalisations by 30% (56). The EMPHASIS-HF randomised double-blind trial involving 2,737 patients with HFrEF (EF<35%) found that eplerenone significantly reduced the risk of both death and hospitalisation compared to placebo (57). In patients with preserved ejection fraction (HFpEF), a meta-analysis of RCTs showed that spironolactone improves left ventricular diastolic function (58). However, in this population, spironolactone did not significantly reduce all-cause mortality, cardiovascular-related deaths, or hospitalisations (58, 59).

Recent developments in HF therapy have introduced SGLT2 inhibitors, commonly used in the management of type 2 diabetes. The therapeutic effects of SGLT2 inhibitors appear to extend beyond blood sugar control, as these effects were not seen with other anti-diabetic agents that have even stronger glucose-lowering properties (60). Data from RCTs have demonstrated that SGLT2 inhibitors are effective in reducing cardiovascular death and HF hospitalisations in patients with HF, with or without type-2 diabetes (61, 62). A meta-analysis of 15 studies with 20,241 patients found that SGLT2 inhibitors reduced all-cause and cardiovascular mortality by 14%, and HF hospitalisations by 31% (63). SGLT2 inhibitors significantly lowered the composite risk of cardiovascular mortality, HF hospitalisations, and urgent HF visits across all subgroups. While the precise mechanisms are not yet entirely understood (64), various theories have been suggested to explain their direct and indirect

cardioprotective effects. Savage *et al*. (61) provided an excellent summary of these mechanisms: SGLT2 inhibitors can enhance natriuresis secondary to glycosuria (65), lower blood pressure (66), boost ketone and fatty acid use thereby reducing HF remodelling (67), inhibit proinflammatory pathways (68), inhibit myocardial fibrosis (69), enhance autophagy thereby maintaining cardiac homeostasis (70), and positively impact cardiac risk factors by reducing HbA1c, body mass index, blood pressure and serum uric acid (71).

A key element in treating HF and AF is the beta-adrenergic receptor blockade, which controls rapid heart rate in AF and improves survival in patients with HF. Rate control with beta-blocker therapy has demonstrated a 30% reduction in cardiovascular mortality, a 25% reduction in HF (72-75), and a decrease in arrhythmias (76, 77). Discontinuing beta-blockers in patients with HF has been demonstrated to substantially elevate the risk of adverse events (78). While various guidelines recommend rhythm control and urgent electrical cardioversion before rate control when HF is precipitated by AF (79-81), the deviation is justified when restoring sinus rhythm is unlikely to be successful or could be harmful due to the patient's history of failed cardioversion for AF. Research comparing rhythm control to rate control in patients with AF and HF has not indicated any superiority of medication-based rhythm control over rate control in achieving better major clinical outcomes including mortality, thromboembolic events and stroke (82-84). Rate control is also especially beneficial over rhythm control for patients with tachycardia-induced cardiomyopathy (3), as seen in our patient.

Results from the RATE-AF trial indicated no significant difference in 6-month patient-reported quality of life or ventricular rate between patients with AF treated with either bisoprolol or digoxin (85, 86). Digoxin is used in patients with AF to help control rapid ventricular rates (86). However, previous research has yielded inconsistent findings regarding the effects of digoxin on clinical outcomes and quality of life in patients with AF (87). Digoxin has been used for many years to treat HF, effectively alleviating symptoms and reducing hospital readmissions (88). In patients with HFrEF (EF<40%) enrolled in the Swedish HF registry, most digoxin users had a history of AF (89). The study found that among HFrEF patients with AF, digoxin use was associated with lower mortality and morbidity, but in those without AF, it was linked to higher mortality and morbidity. This suggests that digoxin could be considered a first-line treatment for HFrEF patients with AF. Awareness of the risk of digitalis toxicity is essential, so patients with both AF and heart HF should not receive higher doses than those with HF alone.

AF increases stroke risk fivefold, even after adjusting for other factors (4, 14), rendering anti-thrombotic therapy critically important in the management of AF, irrespective of HF (79). For AF patients, long-term anticoagulation therapy is the only treatment proven to decrease mortality (14). The decision to start anticoagulation for our patient was based on the CHA_2DS_2-VASc score and weighed against the patient's ORBIT bleeding risk score. These scores ensure that all patient factors are considered comprehensively in managing AF and preventing thromboembolic events (90). Based on the factors included in the CHA_2DS_2-VASc score, anticoagulation is advised for all patients with AF-HF, provided there are no bleeding risk or contraindications. While warfarin has been the foundation of anticoagulation, direct oral anticoagulants (DOACs) have been introduced into clinical practice, supported by strong evidence from RCTs compared with warfarin (14).

In terms of safety, our previous analysis of real-world prescribing data and adverse drug event reports (91) shows furosemide has fewer serious and fatal adverse effects than bumetanide, bisoprolol has fewer serious and fatal adverse events than sotalol, apixaban is safer than other DOACs, and dapagliflozin is safer than canagliflozin and empagliflozin.

In addition to medications, all patients with HF should receive guidance on adopting a healthy lifestyle, including recommendations to limit daily sodium intake to less than 3 g (and no more than 5 g per day), quit smoking, reduce alcohol consumption and engage in daily exercise, as tolerated (92). Patients should receive self-care education and follow-up care through a multidisciplinary HF service including a nurse team. A randomised trial of 223 patients with HF showed that adding a one-hour teaching session led by a nurse educator at hospital discharge improved clinical outcomes and enhanced adherence to self-care measures as well as lowered care costs (93). Furthermore, since non-adherence is a major factor that often worsens HF, identifying and assessing it, is vital for effective management of HF. Studies show that better medication adherence significantly reduces hospital admissions and improves the quality of life for patients with AF and HF (14). Shared decision-making during consultations has been shown to improve adherence, as patients are more likely to follow treatment plans they helped create (94).

Conclusion

This case highlights the critical importance of medication adherence in managing AF to prevent complications such as HF. The patient's non-adherence with sotalol contributed to symptoms that were initially suspected to be CAP and PE but were ultimately diagnosed as HFrEF. Additionally, the case emphasises the need for thorough clinical evaluation and judgment before ordering diagnostic tests, to avoid misdiagnosis in patients presenting with acute respiratory symptoms. PE symptoms can mimic those of HF, making an accurate differential diagnosis critical, especially in AF patients with elevated D-dimer levels, where false positives are common. While the co-occurrence of AF and HF presents a

therapeutic challenge, it also offers opportunities for optimising treatment. Effective management with bisoprolol, furosemide and spironolactone stabilised the patient, demonstrating the success of guideline-based treatment and multidisciplinary care as such patients usually have multiple comorbidities. Ensuring medication adherence, conducting thorough investigations, regular follow-ups and providing coordinated care are essential in managing such complex cases.

Data Availability

All data relevant to the study are included in the article.

Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this case report.

Authors' Contributions

GJ: Patient management, assessment, data collection and manuscript contribution; KM: Led the drafting of the manuscript, supervised the study and ensured rigorous adherence to ethical and scientific standards of clinical relevance; GJ, KM, RD, KE, UK, MA: All contributed equally to critical discussions and clinical review of the case.

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