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Sacubitril/valsartan as first-line therapy in anthracycline-induced cardiotoxicity

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A 69-year-old female patient was admitted to the cardiology department due to a diagnosis of acute heart failure (AHF). She had a history of chemotherapy due to diffuse large B-cell lymphoma. The patient received the total anthracycline dose of 450 mg/m². The last anthracycline chemotherapy was two months ago. The patient had no previous history of cardiovascular diseases. On admission, N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and high-sensitivity troponin I (hsTnI) levels were elevated (NT-proBNP: 5987 pg/ml; reference range <125 pg/ml; hsTnI: 74 pg/ml; reference range <14 pg/ml). Coronary angiography excluded vessel narrowing. Echocardiography showed moderate functional mitral regurgitation and severe left ventricle systolic dysfunction. Left ventricular ejection fraction (LVEF) was 24%, and global longitudinal strain (GLS) was 8.1% (Figure 1A). A preliminary diagnosis of anthracyclines-induced cardiotoxicity was made. The patient was treated initially with intravenous catecholamines and diuretics. After hemodynamic improvement catecholamines were stopped and intravenous diuretics were switched to oral torasemide 40 mg once daily (OD). Sacubitril/Valsartan (S/V) 24/26 mg *bis in die* (BID, twice a day) and

bisoprolol 2.5 mg OD were started. During the next few days, hypotension was observed. Bisoprolol was switched to ivabradine (2×5 mg), and diuretics were reduced. Increased supervision (control of diuresis, creatinine and potassium levels) allowed to maintain the S/V treatment (Table 1). The patient was discharged home with the diagnosis of heart failure with reduced ejection fraction (HFrEF) associated with anthracycline-induced cardiotoxicity. At discharge the patient was in New York Heart Association (NYHA) class III; a 6-minute walk (6MWT) was 192 m.

After one month, patient's status was stable and S/V was increased to 49/51 mg BID. On the third-month follow-up patient was in NYHA class II, 6MWT distance increased to 384 m. The creatinine and potassium levels were stable, NT-proBNP and hsTnI levels decreased to 865 pg/ml and 23 pg/ml, respectively. The left ventricle systolic function improved (LVEF 42%, GLS -10.2% ; Figure 1B), and mitral regurgitation was only mild.

DISCUSSION

Our clinical vignette concerns the problem of anthracycline-induced myocardial injury. Cardiotoxicity due to anthracyclines may be acute, early or late [1]. In our case we observed the early type (i.e. <1 year since the anthracycline chemotherapy). The previous retrospective studies considered both — early and late types of anthracycline-induced cardiotoxicity as irreversible [2]. However, recent studies showed that early detection and adequate, guideline-directed heart failure treatment could stop or even reverse the progression of cardiac dysfunction [3, 4].

Our case demonstrates that S/V can be initiated immediately after achieving the patient's hemodynamic stability. S/V was administered as the first-line therapy in our patient, instead of angiotensin-converting enzyme inhibitors. The essence of our observation is compliant with the PIONEER-HF trial's results, which proved the safety and feasibility of early initiation of S/V therapy in hospitalized patients after the AHF episode [5]. Importantly, our case addresses also the central issue of S/V treatment — hypotension. We demonstrated that it could be effectively managed by reducing diuretics dose and switching from beta-blocker to ivabradine.

We can conclude that S/V could be safely started as the first-line therapy in patients with anthracycline-induced cardiotoxicity.

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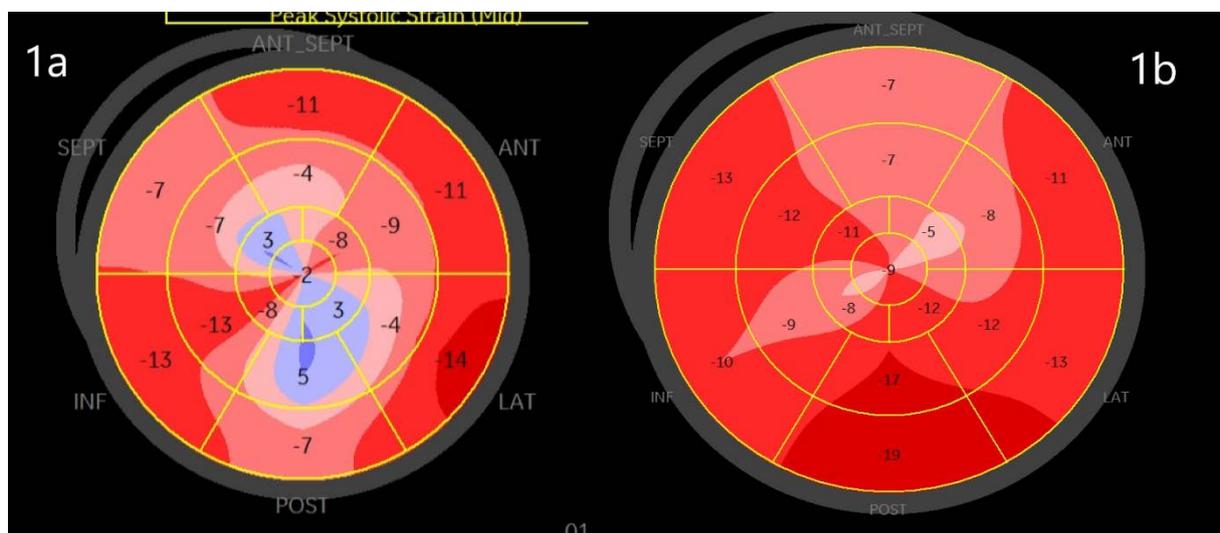


Figure 1. Global longitudinal strain — bull's-eye presentation. **A.** Baseline. **B.** Follow-up

Table 1. Pharmacological treatment, hemodynamics, and laboratory results of the patient during the hospitalization

	Admission	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Discharge
Treatment										
Catecholamines IV	Start			Stop						
Furosemide IV	Start			Stop						
Torasemide 40 mg OD				Start	Reduced (20 mg OD)					
Sacubitril/Valsartan 24/26 mg BID				Start						
Ivabradine 5 mg BID						Start				
Bisoprolol 2.5 mg OD			Start		Stop					
Hemodynamics										
Blood pressure, mm Hg										
Morning	92/78	109/81	111/69	106/73	87/54	93/69	99/67	97/58	101/71	102/61
Evening	102/76	104/78	103/77	97/62	91/62	92/65	92/68	91/52	97/59	
Heart rate, beats/min										
Morning	107	80	85	79	99	79	76	82	60	73
Evening	104	101	88	78	88	89	69	74	72	71
Laboratory results										
Potassium, mmol/l	5.1	4.6	3.9	4.1	4.6		4.3		4.5	
Creatinine, $\mu\text{mol/l}$	97.3	132.6	123.8	123.8	88.4		97.3		88.4	
eGFR, ml/min/1.73m^2	50.2	37.8	39.6	38.4	58.0		50.2		58.0	
Diuresis, ml/24 h		2500	2800	2600	2700	2900	3200	2300		

Abbreviations: BID, twice daily; IV, intravenous; OD, once daily