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

Rafał Dankowski[1*], Wioletta Sacharczuk[1*], Anna Łojko-Dankowska[2], Anna Nowicka[1], Anna Szałek-Goralewska[1], Andrzej Szyszka[1]

[1]2nd Department of Cardiology, Poznan University of Medical Sciences, Poznań, Poland
[2]Department of Hematology and Bone Marrow Transplantation, Poznan University of Medical Sciences, Poznań, Poland
*Both authors equally contributed to the study

Correspondence to:
Rafał Dankowski, MD, PhD, 2nd Department of Cardiology, Poznan University of Medical Sciences, 28 Czerwca 1956 194, 61–485 Poznań, Poland, phone: +48 61 227 41 60, e-mail: rafaldan@ump.edu.pl

Kardiol Pol. 2021; 79 (9): 1040–1041; DOI: 10.33963/KP.a2021.0052

Received: April 25, 2021

Revision accepted: June 28, 2021

Published online: June 30, 2021

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/m^2. The last anthracycline chemotherapy was administered 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 ventricular systolic dysfunction. Left ventricular ejection fraction (LVEF) was 24%, and global longitudinal strain (GLS) was 8.1% (Figure 1A). A preliminary diagnosis of anthracycline-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 twice a day (BID) and bisoprolol 2.5 mg OD were started. During the next few days, hypotension was observed. Bisoprolol was switched to ivabradine 5 mg BID, and diuretics were reduced. Enhanced superveillance including 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 test (6MWT) was 192 m.

After one month, the patient's status was stable and S/V was increased to 49/51 mg BID. At the third-month follow-up the patient was in NYHA class II, and 6MWT distance increased to 384 m. The creatinine and potassium levels were stable, while NT-proBNP and hsTnI levels decreased to 865 pg/ml and 23 pg/ml, respec-

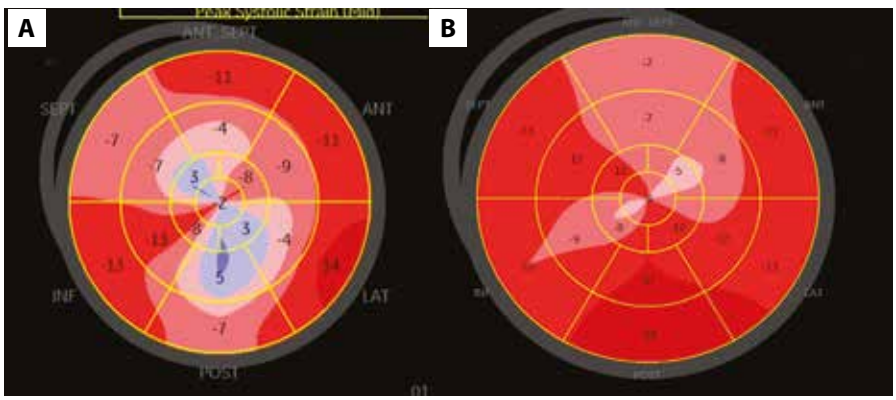

Figure 1. Global longitudinal strain — bull's-eye presentation. **A.** Baseline. **B.** Follow-up

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 investigations										
Potassium, mmol/l	5.1	4.6	3.9	4.1	4.6		4.3		4.5	
Creatinine, µmol/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

tively. The left ventricular systolic function improved (LVEF, 42%, GLS, –10.2%; Figure 1B), and mitral regurgitation was only mild.

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 results of the PIONEER-HF trial , 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.

Article information

Conflict of interest: AS, WS and RD received lecture honoraria from Novartis.

How to cite: Dankowski R, Sacharczuk W, Łojko-Dankowska A, et al. Sacubitril/valsartan as first-line therapy in anthracycline-induced cardiotoxicity. Kardiol Pol. 2021; 79(9): 1040–1041, doi: 10.33963/KP.a2021.0052.

REFERENCES

1. Semeraro GC, Lamantia G, Cipolla CM, et al. How to identify anthracycline-induced cardiotoxicity early and reduce its clinical impact in everyday practice. Kardiol Pol. 2021; 79(2): 114–122, doi: 10.33963/KP.15782, indexed in Pubmed: 33506661.
2. Steinherz LJ, Steinherz PG, Tan CT, et al. Cardiac toxicity 4 to 20 years after completing anthracycline therapy. JAMA. 1991; 266(12): 1672–1677, indexed in Pubmed: 1886191.
3. Cardinale D, Colombo A, Bacchiani G, et al. Early detection of anthracycline cardiotoxicity and improvement with heart failure therapy. Circulation. 2015; 131(22): 1981–1988, doi: 10.1161/CIRCULATIONAHA.114.013777, indexed in Pubmed: 25948538.
4. Słowik A, Jagielski P, Potocki P, et al. Anthracycline-induced cardiotoxicity prevention with angiotensin-converting enzyme inhibitor ramipril in women with low-risk breast cancer: results of a prospective randomized study. Kardiol Pol. 2020; 78(2): 131–137, doi: 10.33963/KP.15163, indexed in Pubmed: 31995035.
5. Velazquez EJ, Morrow DA, DeVore AD, et al. PIONEER-HF Investigators. Angiotensin-neprilysin inhibition in acute decompensated heart failure. N Engl J Med. 2019; 380(6): 539–548, doi: 10.1056/NEJMoa1812851, indexed in Pubmed: 30415601.