CASE STUDY

CONTENTS

Complex mechanism of brugada phenocopy: moderate hyponatremia and right ventricular compression by liver metastatic tumor – case report

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ABSTRACT

Brugada phenocopy (BrP) occurs in various clinical conditions and manifests as a Brugada-like ECG pattern with coved (type 1) or saddle-back (type 2) ST-segment elevation in the right precordial leads. Unlike Brugada syndrome (BrS), which is an inherited channelopathy, BrP is not associated with an increased risk of malignant arrhythmia. BrP has been reported in severe metabolic disturbances (significant hyponatremia, hypokalemia or hyperkalemia), mechanical heart compression, coronary artery disease, pulmonary embolism and myocarditis/pericarditis.

The authors described a case of a 69-year-old female whose Brugada-like ECG was atypically associated with only moderate hyponatremia (127 mmol/l). She was admitted due to a skin and subcutaneous tissue infection of the left shank and coexistent urinary tract infection (without a fever). She had the history of advanced melanoma with multiple liver metastases. Her cardiac history was negative, especially the patient has never suffered from ventricular arrhythmias. ECG on admission showed saddle-back ST-segment elevation in the right precordial leads; however, the patient did not report any chest pain. Troponin I level and left ventricular function in echocardiography were normal while regional longitudinal strain in RV apex was decreased and showed post-systolic shortening. The substernal view revealed compression of the right ventricle (RV) by liver metastatic tumor. ECG changes disappeared quickly during natrium chloride supplementation and did not recur during hospitalization. This case illustrates that even moderate hyponatremia may be a reversible cause of BrP when other predisposing conditions (e.g. heart compression by tumor) coexist.

KEY WORDS: Brugada syndrome, Brugada phenocopy, Brugada-like ECG pattern, hyponatremia, right ventricle compression, longitudinal strain

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INTRODUCTION

Brugada phenocopy (BrP) occurs in various clinical conditions and manifests as a Brugada-like ECG pattern with coved (type 1) or saddle-back (type 2) ST-segment elevation in the right precordial leads [1,2]. Unlike Brugada syndrome (BrS), which is an inherited channelopathy, BrP is not associated with an increased risk of malignant arrhythmia [3,4]. Expert cardiologists suggest that BrP and BrS ECG patterns are visually identical and indistinguishable [5]. BrP has been reported in severe metabolic disturbances (significant hyponatremia, hypokalemia or hyperkalemia), mechanical heart compression, coronary artery disease, pulmonary embolism, and myocarditis/pericarditis [6,7]. Typically, Brugada-like ECG pattern has transient character, but when caused by mechanical heart compression (due to right ventricular outflow tract-RVOT tumor or pectus excavatum), usually persists until the target treatment is applied [7,8].

Differential diagnosis between BrS and BrP includes evaluation of the above-mentioned clinical conditions, history of life-threatening arrhythmias, provocative pharmacological tests with sodium channel blockers and genetic assessment [6]. However, serious health condition, advanced age, coexistence of multiple disorders and lack of arrhythmia symptoms as well as negative family history suggestive of BrS may indicate the omission of such algorithm [9].

AIM

The purpose of this paper is to show that Brugada phenocopy may have a complex mechanism related to underlying coexisting conditions whose expression would not be sufficient independently to provoke Brugada-like ECG.

CASE REPORT

A 69-year-old female was admitted due to a skin and subcutaneous tissue infection of the left shank, coexistent urinary tract infection (with high inflammatory markers levels, but without a fever), and transient renal function deterioration (creatinine concentration 216 µmol/l; normal up to 106 µmol/l) with moderate hyponatremia (sodium concentration 127 mmol/l; normal 135-145

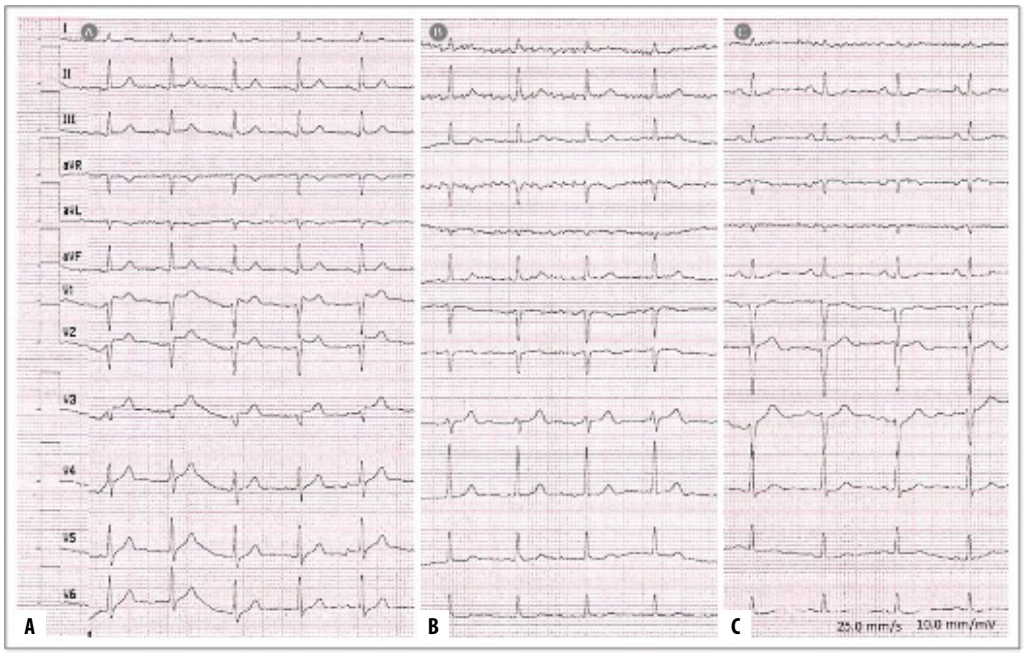

Fig.1. ECG: saddle-back ST-segment elevation in V1-3 on admission (A), disappearance of changes during sodium chloride supplementation (B), normal ST-segment in V1-3 from day 2 (C).

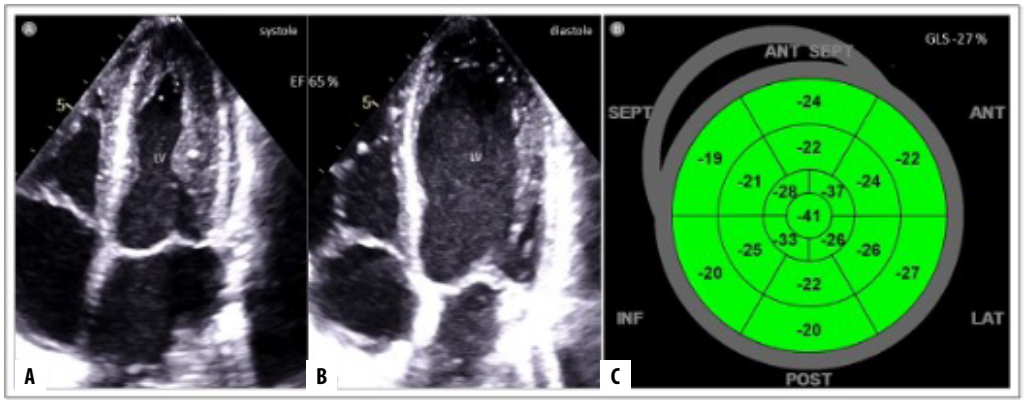

Fig.2. Two-dimensional echocardiography in apical four-chambers view: normal left ventricular function with ejection fraction (EF) 65% (A) and global longitudinal strain (GLS) -27% (B); see high regional LS in apical segments (C).

mmol/l). Potassium and phosphates were within the normal range. Patient's clinical status was determined by multi-morbidity, including advanced melanoma with multiple liver metastases and ovarian cancer. She was disqualified from chemotherapy. Her cardiac history was negative, especially she has never suffered from ventricular arrhythmias. Also, family history of cardiac arrhythmias, including sudden cardiac death, was negative.

ECG on admission showed saddle-back ST-segment elevation in the right precordial leads (fig.1A); however, the patient did not report any chest pain. Troponin I level and left ventricular function in echocardiography, evaluated by ejection fraction (EF) and global and regional longitudinal strain (GLS and RLS), were normal (fig.2A-B). Regional longitudinal strain of RV apex was decreased and showed post-systolic shortening, whereas in basal and midventricular segments RLS was hypernormal (fig.3). The substernal view revealed compression of the RV by liver metastases (fig.4), which was not visible in previously done abdominal computed tomography. ECG changes quickly disappeared during natrium chloride supplementation and did not recur during hospitalization (fig.1B-C). 24-hour ECG monitoring did not show any ventricular arrhythmia. After a few days, the patient was transferred to palliative care; she was discharged with normal renal function and normal inflammatory markers after appropriate treatment with antibiotics.

DISCUSSION

The main groups of BrP reported in the literature include: severe metabolic disturbances (significant hyponatremia, hypokalemia or hyperkalemia), mechanical heart compression, coronary artery disease, myocarditis/pericarditis and pulmonary embolism [7-10]. It is unclear why some patients present with BrP and some do not under the same environmental conditions [6].

Generally, metabolic disturbances, especially electrolyte abnormalities, account for approximately half of BrP cases reported in the literature (a hundred and so patients). On the other hand, BrP is diagnosed only in a

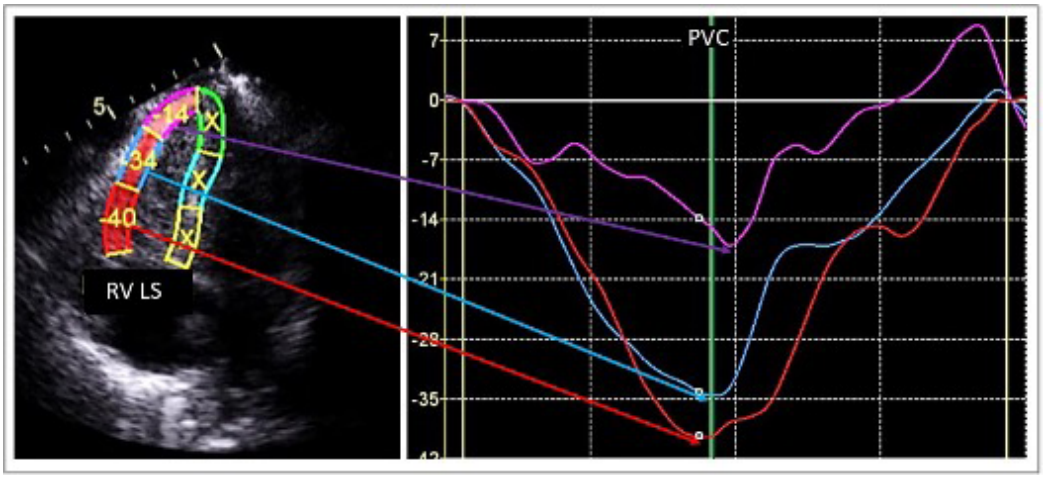

Fig.3. Regional longitudinal strain of the RV free wall: see decreased strain and post systolic shortening (in strain curves presentation) of the apical RV segment as well as hypernormal strain of basal and midventricular RV segments; RV - right ventricle, LS - longitudinal strain, PVC – pulmonary valve closure.

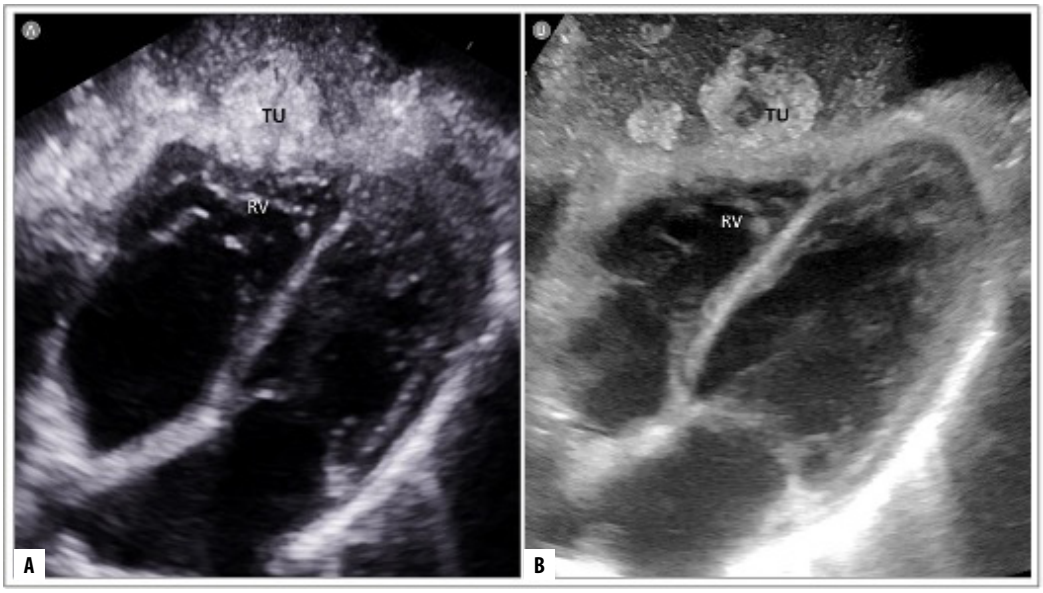

Fig.4. Right ventricle compression by liver metastatic tumor (Tu) - substernal echocardiographic view using cardiac sector probe (A) and convex probe (B).

fraction of population presenting with such abnormalities. Hyponatremia (sodium concentration of less than 135 mmol/l) is the most common electrolyte abnormality and is defined as mild (130-134 mmol/l), moderate (120-129 mmol/l) or severe (<120 mmol/l) [11,12]. The pathophysiology of Brugada-like ECG pattern may be explained by reduced inward sodium current in the RVOT epicardium and/or conduction delay which produce transmural gradient. Using longitudinal strain evaluation in the presented case, we demonstrated significant differences between reduced apical and increased basal RV RLS as well as strain dispersion related to post-systolic shortening in the RV apex. All cases of BrP and hyponatremia described so far were associated with severe sodium concentration decrease (sodium values close to 100-110 mmol/l**)** and presented with type 1 Brugada ECG pattern in most patients [10,13-15] Interestingly, in coexistent hyperkalemia, unique ECG with type 1 Brugada pattern in V1 and type 2 in V2 could be observed [16,17]. Hyponatremia, regardless of its etiology, may contribute to the development of Brugada-like ECG pattern; e.g. in: kidney injury [15], excessive fluids intake [10,13], dehydration during diuretics and antihypertensive drug use [14], dehydration caused by diarrhea and vomiting [13], syndrome of inappropriate antidiuretic hormone secretion (SIADH) [18], adrenal crisis [19], ketoacidosis [20,21]. In the last three examples other than hyponatremia, metabolic/endocrine factors were involved in modulating ECG pattern. It should be remembered, that hyponatremia can reveal BrS [22].

A review of 11 published cases of BP caused by tumor compression of the heart showed that 10 patients represented a type 1 Brugada ECG pattern and only one type 2 Brugada ECG pattern [8,23]. In all these patients, heart compression was associated with RVOT involvement, either by neoplastic (benign or malignant) tumor [23,24] or non-neoplastic (e.g. inflammatory or being hematoma) tumor [25,26] located in the anterior mediastinum, in the RV cavity or in the pericardium [8,24-26]. After appropriate treatment (surgery, radiotherapy, chemotherapy), clinical improvement was accompanied by ECG normalization [23,27]. Contrary to

above cases, in the presented one, echocardiography revealed RV apex compression by liver metastatic tumor. However, it should not be excluded that RVOT was infiltrated by cancer cells. The clinical course indicated that sole RV apex compression was not sufficient to generate Brugada-like ECG, whereas when only moderate hyponatremia additionally occurred, typical BrP could be observed.

CONCLUSIONS

This case illustrates that even moderate hyponatremia may be a reversible cause of BrP when other predisposing conditions (e.g. heart compression by tumor) coexist. The concomitance of underlying conditions in a patient with BrP should always be taken into account because different pathologies may have combined effect on ECG morphology.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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