BRIEF REPORT

QT Interval Prolongation with Global T-Wave Inversion: A Novel ECG Finding in Acute Pulmonary Embolism

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Objective: The purpose of this study was to report a novel electrocardiographic (ECG) phenomenon in acute pulmonary embolism characterized by QT interval prolongation with global T-wave inversion.

Methods: Among a total of 140 study patients with a confirmed diagnosis of acute pulmonary embolism, patients who fulfilled the inclusion criteria for QT interval prolongation with global T-wave inversion were examined. Each of these patients had undergone a detailed clinical evaluation including testing for myocardial injury and echocardiography.

Results: QT interval prolongation with global T-wave inversion was found in five patients (age 51–68 years) with acute pulmonary embolism. Four were women. Acute pulmonary embolism was diagnosed by ventilation-perfusion scan in three patients and by spiral computed tomography in other two patients. None of the patients had any right or left ventricular regional wall motion abnormalities on echocardiography. All patients had changes characteristic of hemodynamically significant pulmonary embolism, including right ventricular stunning or hypokinesis and dilatation in five patients with paradoxical septal motion in four. Acute coronary syndrome was ruled out in each patient by clinical evaluation, serial ECGs and cardiac markers, and lack of regional wall motion abnormalities on echocardiography. Prolongation of QT intervals (QTc 456–521 ms) with global T-wave inversion was noted on presentation. The ECG changes gradually resolved in 1 week in all patients with appropriate treatment of acute pulmonary embolism. One patient died. None of the patients developed torsade de pointes.

Conclusions: Acute pulmonary embolism may occasionally result in reversible QT interval prolongation with deep T-wave inversion, and, thus should be considered among the acquired causes of the long QT syndrome.

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pulmonary embolism; long QT syndrome; global T-wave inversion; electrocardiography

Various coronary and noncoronary events are known to be associated with marked QT prolongation and global T-wave inversion.^{1–10} Acute pulmonary embolism is well known to cause numerous electrocardiographic (ECG) changes but prolonged QT interval with global T-wave inversion has been described in an isolated case report only.¹¹ The purpose of this study was to identify those patients with acute pulmonary embolism who developed this ECG pattern and depict their clinical and relevant ECG findings.

METHODS

From January 1999 to January 2002, among a total of 140 patients with a confirmed diagnosis of acute pulmonary embolism admitted in Long Island College Hospital, five cases satisfied the inclusion criteria, which were: (1) confirmed acute pulmonary embolism; (2) ruled out for acute coronary syndrome; (3) serum electrolytes and cardiac markers creatine kinase (CK), CK-MB, and cardiac troponin-I measured; (4) had transthoracic

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Table 1. Clinical Characteristics and Test Results of Study Population

Patient No.	Age (years)	Sex	Thromboembolic Risk Factors	Clinical Presentation	Transthoracic Echo	VQ Scan of Chest	Spiral CT	Venous Duplex
1	51	F	Recent surgery	Shortness of breath, Pleuritic chest pain	RV stunning RV dilatation Paradoxical septal motion No RWMA SPAP = 38	High probability	Not done	Negative
2	54	F	Morbid Obesity	Shortness of breath, Pleuritic chest pain, Hemoptysis	RV stunning RV dilatation Paradoxical septal motion No RWMA SPAP = 55	Not done	Pulmonary emboli in all the major branches of the right pulmonary artery and a left lobar artery	Negative
3	68	F	Morbid Obesity, Harmon replacement therapy	Shortness of breath, Pleuritic chest pain, Palpitation	RV stunning RV dilatation Paradoxical Septal motion No RWMA	Not done	Embolus in the right main pulmonary artery and left lower lobar artery	Not done
4	58	F	None	Shortness of breath	RV stunning RV dilatation Paradoxical Septal motion No RWMA	High probability	Not done	Negative
5	59	M	Immobility	Hypertension Dyslipidemia	RV hypokinesia RV dilatation No RWMA SPAP = 70	High probability	Not done	Negative

CT = computed tomography; RA = right atrium; RV = right ventricle; RWMA = regional wall motion abnormality; SPAP = systolic pulmonary artery pressure; VQ = ventilation perfusion.

echocardiography performed; (5) 12-lead ECG at presentation had QTc interval > 440 ms with global T-wave inversion, which was defined as T-wave inversion in eight or more leads including four or more chest leads. All five patients had ventilation-perfusion scan or spiral computer tomography of chest performed. The admission and day -1 to discharge ECGs were analyzed using standard criteria for measurements of QT interval. Rate correction for the QT intervals was performed using Bazett's formula.¹²

RESULTS

Among study population of five patients, four were women. Ages ranged from 51 to 68 years. Pertinent clinical characteristics and test results of the study population are summarized in Table 1. Acute pulmonary embolism was diagnosed by ventilation-perfusion scan in three patients and by spiral computed tomography in other two patients. None of the patients had any right or left ventricular regional wall motion abnormalities on echocardiography. All patients had echocardiographic changes

characteristic of hemodynamically significant pulmonary embolism, including right ventricular stunning or hypokinesia and dilatation in five patients with paradoxical septal motion in four. The pulmonary artery pressure (systolic) was reported in three cases and was 38, 55, and 70 mmHg. Acute coronary syndrome was ruled out in each patient by clinical evaluation, serial ECGs and cardiac markers, and lack of regional wall motion abnormalities on echocardiography. An apparent prolongation of the QT intervals (QTc 456–521 ms) with global T-wave inversion was noted on presentation, the ECG changes are reported in Table 2. None of the patient

Table 2. Electrocardiographic Findings

Patient No.	Rhythm	Rate (bpm)	QT (ms)	QT _c (ms)	Other Changes
1	Sinus	85	411	489	None
2	Sinus	87	471	521	None
3	Sinus	78	426	485	S1Q3T3
4	Sinus	99	355	456	None
5	Atrial	47	524	463	None

bpm = beats per minute.

Figure 1. Serial ECGs of patient no. 2: (A) The ECG at presentation demonstrates QT interval of 471 ms with QTc interval of 521 ms and global T-wave inversion; (B) next day, the QT interval has decreased to 369 ms and QTc interval to 483 ms; (C) in a week, both the QT (378 ms) and QTc (393 ms) intervals have become normal and the T-wave inversion has been resolved.

Table 3. Maximal Serum Levels of Cardiac Markers

Patient No.	CK (IU/L)	CK-MB (ng/mL)	Cardiac Troponin-I (ng/mL)
1	152	2.3	2.8
2	84	1.0	<0.4
3	108	2.0	<0.4
4	247	2.6	<0.4
5	136	2.5	2.3

CK = creatine kinase; CK-MB = creatine kinase muscle-brain.

was using QT interval prolonging drugs and electrolytes were within normal ranges in all patients. The ECG changes gradually resolved in 1 week in all patients with appropriate treatment of acute pulmonary embolism (Fig. 1). The data on cardiac markers are reported in Table 3 and that on treatment and outcome in Table 4. Two patients had elevated serum level of cardiac troponin-I: one of these two patients (patient no. 5) underwent coronary angiography and had normal coronary arteries. One patient died due to shock. None of the patients developed torsade de pointes.

DISCUSSION

In this paper we have reported five cases of acute pulmonary embolism where QT interval was prolonged with global T-wave inversion. The ECG changes were most likely due to acute pulmonary embolism as none of these patients had any other clinical condition that could have caused such changes, and these changes resolved with the treatment of pulmonary embolism. Several other diseases causing global T-wave inversions with QT interval prolongation have been reported: the most common being acute myocardial infarction (partic-

ularly subendocardial infarction) and cerebral injury (including subarachnoid hemorrhage).¹⁻³ In the latter, it has been explained by the actions of intermediate mediators of the autonomic nervous system. Other reported causes of global T-wave inversions with QT interval prolongation include cardiac metastasis, apical hypertrophic cardiomyopathy, pheochromocytoma, and cocaine abuse.^{4-6,13-15}

Various ECG patterns associated with acute pulmonary embolism have been studied extensively.¹⁶ Historically, the T-wave changes during pulmonary embolism were first reported in 1938, and the subsequent studies specified association of T-wave inversion in the right precordial leads with pulmonary embolism.¹⁷⁻²⁰ However, global T-wave inversion with QT interval prolongation associated with acute pulmonary embolism has been described in an isolated case report.¹¹ The mechanism of this observed finding is not clear but there could be two postulated mechanisms; the first being coronary insufficiency and the second catecholamine mediated. It has been suggested that coronary insufficiency occurs in patients with pulmonary embolism especially, since right ventricular infarction has been described during the acute phase of massive pulmonary embolism, with angiographically normal epicardial coronary arteries.²¹⁻²³ Conversely, in a study by Stein et al.²⁴ coronary blood flow was rather high in pulmonary embolism with a drop only in the final stages. In another series of 12 patients with massive pulmonary embolism and an ECG appearance suggestive of subepicardial ischemia, a very early myocardial scintigraphy with MIBI did not demonstrate any perfusion defect suggestive of ischemia.²⁵ Coronary insufficiency as the sole mechanism for these reported ECG changes in acute pulmonary embolism is still unclear. Another explanation for these ECG changes in acute pulmonary embolism could be via a catecholamine mediated phenomenon as it occurs in patients with central nervous system disorders and pheochromocytoma.¹⁰ Furthermore, there is an increased platelet activation in acute pulmonary embolism with release of humoral mediators including serotonin that could lead to increased pulmonary artery pressure with resultant right ventricular dysfunction and ensuing ECG abnormalities.

Only a large prospective study evaluating all patients who present with acute pulmonary embolism with serial ECGs would give a clear indication about the prevalence of the described ECG phenomenon, and whether the observed QT interval

Table 4. Treatment and Outcome

Patient No.	Anticoagulation	Thrombolytic Therapy	Outcome
1	LMWH	No	Survived
2	UFH	No	Survived
3	UFH	t-PA	Died
4	UFH	No	Survived
5	UFH	No	Survived

UFH = unfractionated heparin; LMWH = low molecular weight heparin; t-PA = tissue plasminogen activator.

T-wave changes carry a prognostic significance. Although none of our patients developed torsade de pointes, small number of patients limits the exclusion of occurrence of such an event.

CONCLUSION

Patients with acute pulmonary embolism may develop reversible QT interval prolongation with global T-wave inversions, and, thus acute pulmonary embolism should be considered among the acquired causes of the long QT syndrome. The electrophysiological mechanisms and long-term prognostic significance of these findings in patients with acute pulmonary embolism are unclear, and warrant larger studies.

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