Drug embolization was believed to be improbable, since Immunex Corporation verified that a case of drug embolization was never identified with both premarketing and postmarketing data. Birefringent crystalline inclusions have been described with noncaseating granulomas, unrelated to IV drug usage or inhalation exposure, but are usually not numerous. Researchers have demonstrated that these inclusions are primarily calcium oxylate crystals. Some investigators have proposed that these crystals play a role in the inflammatory pathway. For our patient, the role and composition of these inclusions remain to be determined, but their existence seems more than coincidental.

The cornerstone of treatment for drug-induced lung injury is drug removal. The indications for prednisone are less clear. For this case, a distinct and rapid improvement was observed after adding prednisone, suggesting a possible role for early prednisone initiation when etanercept-induced lung injury is suspected. This observation also begs the question whether the true incidence of drug-induced lung injury is drug removal. The indications for prednisone are usually not numerous. Researchers have demonstrated that these inclusions are primarily calcium oxylate crystals. Some investigators have proposed that these crystals play a role in the inflammatory pathway. For our patient, the role and composition of these inclusions remain to be determined, but their existence seems more than coincidental.

CONCLUSION

We propose that etanercept-induced lung injury be considered in any patient who acquires respiratory symptoms with interstitial infiltrates while receiving this agent. The diagnosis is one of exclusion. Since this injury appears to be a systemic process, other organs should be evaluated, particularly the skin. Treatment should consist of drug removal, and prednisone should be administered early in clinically compromised individuals.

ADDENDUM

Follow-up chest radiographs and clinical examinations over the following 12 months after manuscript submission showed complete resolution of alveolar and interstitial abnormalities. The Immunex Corporation was contacted early in this patient’s course with continued correspondence, the most recent being in January 2002. As a result of this case, they performed an extensive review of their premarketing and postmarketing data. With this detailed review, they could find no cases of granulomatous inflammation, foreign-body embolization, or lung injury.

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Posterior Myocardial Infarction and Complete Right Bundle-Branch Block*

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We describe two patients with posterior myocardial infarction (PMI) with unusually atypical clinical presentations and cardiac enzymatic profiles, but with the abrupt development of complete AV block in patient 1, and Mobitz II second-degree AV block with paroxysmal phases of higher degrees of AV block in patient 2, and mitral regurgitation leading to symptomatic pulmonary congestion. Also, both patients had complete right bundle-branch block (RBBB) [old in patient 1, new in patient 2], the pattern of which was altered due to the associated PMI. The alteration included tall R waves involving the early part of the QRS complex, and tall T waves, both noted in the right precordial leads. The mechanism of these ECG modulations of the RBBB pattern was believed to be a superimposition of the early depolarization and repolarization consequences of the PMI. The significance of this observation lies in the ECG detection of PMI, frequently underdiagnosed particularly in patients with an atyp-
ical presentation, and with the RBBB adding further to the complexity. Thus, it is gratifying to note the contribution of the ECG to diagnostics, the only modality that provided a pathophysiologic insight in these two patients who appeared to be abruptly deteriorating clinically without an apparent reason.

**Key words:** ECG; myocardial infarction; posterior myocardial infarction; primary T-wave changes; right bundle-branch block; right ventricular hypertrophy; secondary T-wave changes

**Abbreviations:** AMI = acute myocardial infarction; CK = creatine kinase; cTnI = cardiac troponin I; PMI = posterior myocardial infarction; RBBB = right bundle-branch block; RVH = right ventricular hypertrophy

Acute myocardial infarction (AMI) is easier to diagnose in the presence of complete right bundle-branch block (RBBB) than left bundle-branch block. Since the former does not affect the initial 40- to 60-ms QRS vectors, Q waves diagnostic of an AMI are clearly inscribed in the presence of RBBB. However, with the posterior myocardial infarction (PMI) and RBBB combination, the diagnosis becomes problematic, since PMI is not associated with Q waves in the standard ECG, and the tall R waves in leads V1 through V3 (the hallmark of PMI) are also encountered in right ventricular hypertrophy (RVH), type A preexcitation syndrome, RBBB *per se*, and as a normal variant.

We are reporting the cases of two patients who, in the presence of RBBB, had a small PMI, which we diagnosed by changes noted in the early part of the QRS complex and the T waves in leads V1 through V3. The resultant ECG pattern featured changes of both underlying pathophysologies.

**CASE REPORTS**

**Case 1**

A 75-year old man with history of hypertension and RBBB was admitted to the hospital with fatigue and lightheadedness. His BP was 142/82 mm Hg, and his heart rate was 43 beats/min. A grade 2/6 holosystolic murmur was heard at the apex, suggestive of mitral regurgitation. The ECG showed complete AV block, with a subsidiary pacemaker revealing his previously present RBBB at a rate of 43 beats/min (Fig 1). Initial creatine kinase (CK) was 84 IU/L (normal range, 26 to 189 IU/L), and cardiac troponin I (cTnI) was <0.1 ng/mL (normal range, 0 to 2 ng/mL). He remained asymptomatic without a temporary pacemaker, and an AMI was ruled out by a peak CK of 180 IU/L, a CK-MB fraction of 2.6% (normal value ≤6%), and a cTnI of 0.2 ng/mL. A few hours later, he complained of chest pain for a few minutes, which

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**Figure 1** Twelve-lead ECG readings of patient 1. The left column shows the tracing recorded at hospital admission, which was not different from the patient's previous ECGs. This revealed RBBB, with inverted and biphasic T waves in leads V1 and V2, corresponding (small arrows), and P waves erratically associated with the QRS complexes in the different leads due to complete AV block. The right column shows the ECG 3 h later. The patient was still in complete AV block, and had now an upright T wave in V1 and peaked T wave in leads V2 and V3, with a tall R wave early in the inscription of the QRS complex in lead V2 (before the R’ wave of simultaneously recorded lead V1) [large arrows].
resolved spontaneously. IV nitroglycerin was administered. An ECG showed conversion of a biphasic T wave to a tall upright T wave in lead V2, increase in the amplitude of T wave in lead V3, and a tall R wave in lead V2 involving the early part of the QRS complex. The frontal axis was unchanged (99° vs 100°) [Fig 1].

A permanent dual chamber pacemaker was implanted. Several hours later, the patient abruptly became dyspneic, and was found to have pulmonary edema. Tracheal intubation, mechanical ventilation, diuresis, morphine, and brief vasopressor support were required for stabilization. Echocardiography revealed inferior/posterior hypokinesis, moderate mitral regurgitation, and overall preserved left ventricular function. On day 2 of hospitalization, peak CK of 214 IU/L, CK-MB fraction of 3.3%, and cTnI of 14.6 ng/mL were consistent with a small AMI. The ECG showed appropriate atrial sensing and ventricular pacing.

Cardiac catheterization on day 3 showed an acute subtotal occlusion of the left circumflex coronary artery, a chronic total occlusion of a dominant right coronary artery that was distally filled by septal collaterals, and nonobstructive disease of the left main and left anterior descending coronary arteries; the AV nodal artery was not visualized. The ventriculogram corroborated the echocardiographic findings.

Percutaneous intervention on the circumflex coronary artery was attempted unsuccessfully, followed by placement of intraaortic balloon, and urgent coronary artery bypass surgery. Unfortunately the patient had a stroke in the postoperative period and died after being in a vegetative state for several weeks.

**Case 2**

A 62-year-old man with history of hypertension, diabetes mellitus, hemodialysis for end-stage renal disease, and hyperlipidemia was admitted to the hospital in the course of the same week as patient 1, after he was found in the outpatient hemodialysis unit to have a new Mobitz II, 2:1 AV block. He complained of intermittent epigastric discomfort without nausea or vomiting. BP was 157/94 mm Hg, and heart rate was 40 beats/min. An apical 2/6 holosystolic murmur, positive hepatojugular reflux, occasional rhonchi in the lungs, and trace peripheral edema were noted. The ECG revealed a new 2:1 AV block and RBBB, with tall upright T waves in leads V2, and V3, and a tall early R wave in lead V2 (Fig 2). The peak CK was 167 IU/L, the CK-MB fraction was 4.2%, and the cTnI was 2.6 ng/mL.

Aspirin and heparin were administered, and he remained asymptomatic until the following morning when he showed transiently higher degrees of AV block, without a hemodynamic compromise for which, nevertheless, a temporary transvenous pacemaker was inserted. An echocardiogram revealed normal left ventricular systolic function, moderate mitral and tricuspid regurgitation, and posterior hypokinesis. A chest radiograph disclosed moderate pulmonary congestion. Later that day, the patient underwent hemodialysis and subsequently cardiac catheterization, which revealed a 50% stenosis of the left main coronary artery, an 80% stenosis of both the left anterior descending and left circumflex coronary arteries, and a 50 to 60% stenosis of the right coronary artery, with a long radiolucent-producing plaque, but without features of an acutely destabilized lesion. The distal circumflex and its branches showed diffuse disease. The AV nodal branch could be seen emanating from the right dominant coronary artery, and it was involved with diffuse disease. The patient remained asymptomatic for the next 24 h, had a permanent pacemaker implanted, and underwent coronary artery bypass surgery, uneventfully. He is currently being followed up in our cardiology and pacemaker clinics.
DISCUSSION

Excluding the type A preexcitation syndrome, which can be easily diagnosed by its Δ wave and the short PR interval, there are three clinical conditions that can occasionally be diagnostically confused due to partially similar ECG presentation1–8.

(1) RVH can present with a variety of QRS patterns in leads V1 through V3 and ST segments and T waves opposite to the QRS complexes in orientation.4,5,6,9 Ten common diagnostic criteria for RVH are mentioned,2 but a prominent R wave of ≥ 40 ms in one or more of leads V1 through V3 is the feature often registered.1,3,5 Although such an ECG finding can mimic RBBB,3,4,5,8 RVH or right ventricular dilatation can occasionally cause a real RBBB.1,4,5 Mechanistically, the RVH ECG changes are attributed to an increase in right heart mass and alterations in the anatomic position of the heart.6

(2) RBBB results in a normal initial phase of left ventricular depolarization, as can be documented in both the ECG potentials and the corresponding vectors.4,5 In contrast, late vectors of right septal and free right ventricular activation are abnormally dominant because they are no longer counterbalanced by left ventricular activation.1,4 Thus, in RBBB, the initial part of the QRS complex is minimally if at all affected, while major alterations of the late part of the QRS complex occur due to the late excitation of the right ventricle via the musculature, not the conduction system.1,3 This results in a wide QRS complex in leads V1 through V3, affecting mainly its latter part, with ST-segment depression, and T-wave changes opposite in direction to the terminal part of the QRS complex, and wide S waves in lead V1 and left precordial leads (Figs 1, 2).1,2,4,5,7,8 The secondary T-wave changes in leads V1 through V3 simulate primary ischemic ones, and they are of similar nature to the T-wave inversions noted in the left precordial leads in left bundle-branch block.6–8

(3) PMI is mostly due to left circumflex occlusion and is characterized by an R wave in lead V1 of ≥ 40 ms, R/S wave in leads V1 ≥ 1, R/S wave in V2 ≥ 1.5, and tall T waves in leads V1 through V3.1,3,6,7,9 All of the above constitute changes collectively referred as “the reciprocal sign.”9 Specificity of these criteria is > 95%, but sensitivities are not > 35%.2 Angiographic correlations have reported sensitivities of up to 60% for detecting corresponding asynchrony.10 In addition to leads V1 through V3, these changes are recorded in lead V5, R, and posterior ECG leads.9,11,12

It is generally stated that the recognition of a myocardial infarction in the presence of RBBB is feasible, since the former forms the initial part of QRS, and the latter alters only the late part of the QRS.2,3,6,9 Thus, Q waves in inferior leads suggest an inferior myocardial infarction, while Q waves in precordial and lateral leads are due to myocardial infarctions in these two territories.7 PMI is cited as the single exception, since it is thought to affect the terminal part of the QRS complex and thus it is masked by RBBB.3 Normally the posterior/basal myocardial region is the last to be depolarized, and consequently the PMI is expected to deform the late part of QRS, rather than to generate early QRS abnormalities.2 PMI, RVH, and RBBB all produce prominent anterior positive forces, and thus may lead to diagnostic dilemmas.2 Employment of posterior thoracic ECG leads can detect Q waves diagnostic of PMI with a higher sensitivity than the one based on the standard ECG.2,12

Why was the ECG pattern described herein due to a PMI? (1) No clinical evidence of pulmonary pathology and stable ECG pattern for RVH was evident in our patients, save for a frontal axis > 90° in patient 1. (2) In contrast, our patients revealed changing ECGs over the course of their illness, in association with definite, albeit mild, enzymatic release and abrupt clinical deterioration suggestive of AMI. (3) RBBB was unequivocally present in the patients at the time that the diagnosis of AMI was contemplated (Figs 1, 2).1,4 (4) The alterations that were superimposed on the RBBB pattern were the tall R waves in the early part of QRS, and the peaked T waves, both considered primary changes due to the PMI. The diagnostic certainty would be improved had we recorded posterior chest wall leads (i.e., V7 through V9) for confirmation of the posterior localization of the PMI in these two patients.12

Why did the tall R waves attributed to the PMI affect the early part of QRS contrary to the common belief that an AMI in this territory should have been masked by RBBB, as explained above? It is conceivable that PMI may affect a range of extent and localization of the posterior wall (basal, medial, apical) and lateral (basal, medial, apical), resulting in changes inscribed at different parts of the QRS complex. However, since the depolarization of the left ventricle in the presence of RBBB is completed normally prior to the late activation of the right ventricle, a PMI is expected to produce an early R wave (mirror image of the Q wave recorded in the posterior thorax) that precedes the late R wave due to the intraventricular block as in the two cases reported herein. Thus, there is no any contradiction here: the tall R waves of PMI can affect any portion of the early QRS complex and, because of the explanation provided above, cannot be obscured by the late part of QRS complex.

The encounter of these two cases observed by us over the course of the same week was very stimulating. We pondered regarding the frequency of the occurrence of PMI in association with RBBB, and the feasibility of its diagnosis using the ECG features described herein. However, we have not seen any other similar cases in the acute setting in the past 16 months, since we understood the significance of these ECG features. Nevertheless, during the same period we have repeatedly come across ECGs showing stable features, similar to the ones described in these two cases; it is not clear whether such patients had sustained a PMI in the past, although this is a possibility, particularly for some of them with echocardiographic evidence of posterior wall regional contraction abnormalities. The last point, ie, of diagnosis of chronic PMI in the presence of RBBB, can only be confirmed by a systematic study based on history of an old myocardial infarction, ECG features similar to the ones described here, and non-ECG proof of PMI.

A lot of evidence has accumulated pertaining to the influence of RBBB in the setting of AMI.13–20 Thus, the literature refers to the clinical characteristics, incidence, new vs old RBBB, persisting vs transient RBBB, its association with inferior vs anterior AMI, and short-term vs long-term
mortality of patients in the current thrombolytic era. PMI is often inappropriately managed, even when uncomplicated by bundle-branch block, by failing to provide thrombolysis, due to the preoccupation in practice and design of trials in administering such therapy to patients with AMI and ST-segment elevations in the ECG. In this context, it is even more imperative to diagnose PMI, an AMI often missed when it occurs in association with RBBB. Consequently scrutiny of the ECG for new, early, tall R waves preceding the late R wave due to RBBB will clinch the diagnosis in such problematic cases. Finally, what was striking about these two cases was the contribution of the ECG, which solely provided a diagnostic insight in these two patients, who appeared to be abruptly deteriorating clinically without an apparent reason.

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