CASE REPORT

Discordant U waves in the setting of hyperkalaemia

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SUMMARY

Physiological U wave genesis occurs likely secondary to either late repolarisation of Purkinje fibres, or late repolarisation of some myocardial cells and/or delayed after depolarisation of the ventricular wall occurring during ventricular filling. Hypokalaemia has a well-known association with pathological 'U wave' which actually combines with the T wave (TU complex) and results from slowing of phase 3 of the action potential with resultant electrical interaction between the three myocardial layers. U waves usually tend to disappear in the setting of hyperkalaemia. We report an unusual case where hyperkalaemia and discordant U waves coexisted. We believe that this may have occurred as a result of partial clinical adaptation of cardiac myocytes to the long-standing effects of hyperkalaemia as the patient had underlying history of chronic kidney disease. We also discuss the possible mechanisms of the U wave genesis and the importance of different U wave morphologies encountered in the real clinical practice.

BACKGROUND

Electrophysiological basis for the genesis of the U wave has been a topic of debate for over a century since Einthoven first defined it in 1903. Three main hypothesis regarding physiological U wave genesis have been proposed which include late repolarisation of Purkinje fibres, late repolarisation of some myocardial cells (M-cell hypothesis) and delayed after depolarisation of the ventricular wall occurring during ventricular filling (electrical diastole) (mechanoelectrical hypothesis). Hypokalaemia has a well-known association with pathological 'U wave' which actually combines with the T wave (TU complex) and results from slowing of phase 3 of the action potential with resultant electrical interaction between the three myocardial layers. Herewith, we report an unusual ECG of biphasic U waves with predominant negative discordance which were noted in association with large amplitude peaked T waves in the setting of hyperkalaemia. We also describe a short review of the possible mechanisms of the U wave genesis and its importance in different clinical settings.

CASE PRESENTATION

An 81-year-old woman with home oxygen-dependent severe emphysema and end-stage renal disease (on haemodialysis thrice weekly) presented to the hospital with symptoms of shortness of breath, chronic cough with increased clear expectoration, anorexia and generalised weakness. Her current symptoms started 2 days previously and were preceded by a viral prodrome. Vital signs were stable but pulse oximetry revealed oxygen

saturations of 93% on 4 L oxygen by nasal cannula. Physical examination was remarkable for dry mucous membranes, wheezing and mildly rhonchorous breath sounds bilaterally. The patient showed moderate clinical improvement with intravenous steroids, nebulisations and intravenous hydration in the emergency room and was subsequently hospitalised on optimal medical management for emphysema exacerbation. Her initial ECG revealed normal sinus rhythm, vertical frontal P-vector, large-amplitude peaked T waves and biphasic U waves (with predominant negative discordance in relation to T wave)¹ most prominently seen in the precordial leads (figure 1).

INVESTIGATIONS

Laboratory data including haemogram and basic metabolic panel did not reveal any significant acute derangements except serum potassium level of 6.1 mEq/L consistent with mild hyperkalaemia. Cardiac biomarkers were negative.

DIFFERENTIAL DIAGNOSIS

- ▶ Physiological U waves
- ▶ Electrolyte disturbance (hypo/hyperkalaemia)
- ▶ Stable multivessel coronary artery disease
- ▶ Acute coronary syndrome
- ▶ Left ventricular hypertrophy
- ▶ Bradycardia causing U waves

TREATMENT

Patient received intravenous hydration and a dose of sodium polystyrene sulfonate (kayexalate) which resulted in normalisation of subsequent serum potassium levels.

OUTCOME AND FOLLOW-UP

A follow-up ECG showed normalisation of T wave amplitude and presence of small upright concordant U waves (figure 2). The rest of the clinical course was uneventful and patient was subsequently discharged on oral prednisone taper for her emphysema exacerbation.

DISCUSSION

The origin and clinical significance of U waves has remained an area of controversy.^{2–11} Identification of U waves and their clinical significance has been often underutilised in clinical practice by most physicians. The majority of clinicians believe that U waves only occur in association with hypokalaemia although that is untrue. A 'physiological' U wave is usually a small positive deflection and is concordant with its preceding T wave that occurs in the setting of normal serum potassium and an absence of cardiac pathology. It can be present in up to 90%

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Figure 1 Initial ECG revealed normal sinus rhythm, heart rate=45/min, vertical frontal P-vector, large-amplitude peaked T waves and biphasic U waves (with predominant negative discordance in relation to T wave) most prominently seen in the precordial leads V2–V5. Patient had a potassium level of 6.1 mEq/L.

of ECGs with heart rates, 65 bpm or lower, though the U wave is often hard to appreciate in the presence of tachycardia especially if the T wave abuts the P wave.^{3 12} Despite such a high common prevalence, clinicians often miss U waves in practice primarily due to their low amplitude, less familiarity with it and probable belief in its negligible clinical significance. Normal U wave amplitude rarely exceeds 0.2 mV,^{3 11} though there are a few reports of amplitudes exceeding 1.0 mV in normal individuals.² The largest U waves are usually seen in the precordial leads. The genesis of U waves is still not entirely clear, despite their having been described in the literature for over a century. Proposed theories for U wave genesis include repolarisation of

Purkinje fibres which have a prolonged action potential,⁶ functional derangement (ischaemia or 'strain') of the papillary muscles,¹³ delayed after depolarisation of the ventricular wall occurring during ventricular filling/electrical diastole (mechanoelectrical hypothesis)^{3 11} and variations in the current flow across the wall due to shifting voltage gradients between epicardium and M cells and endocardium and M cells (M-cell hypothesis).⁷ The most recent literature supports the mechanoelectrical hypothesis for U wave genesis. Schimpf *et al*¹¹ suggested that stretch-induced delayed after depolarisations occurring during ventricular relaxation are the likely cause of U waves under normal physiological conditions. Antzelevitch reported that

Figure 2 Follow-up ECG shows normal sinus rhythm with heart rate of 65/min, normalisation of T wave amplitude and presence of small upright concordant U waves, most prominent in V2–V5. Patient had a potassium level of 3.6 mEq/L.

under certain pathophysiological conditions, prolongation of the M-cell response, particularly in the setting of bradycardia, leads to amplification of a second component of the T wave which may be confused with a true U wave.¹⁴

The clinical significance of U-waves is well related to certain medical conditions. Hypokalaemia is associated with flattening of the T waves and the appearance of prominent pathological U waves which are different from the physiological U waves. U waves in hypokalaemia are actually a part of the T wave and result from slowing of phase three of the action potential with resultant electrical interaction between the three myocardial layers.¹⁵ The apparent 'T-U' complex in hypokalaemia is the result of interruption of the descending limb of T wave due to the interplay of opposing voltage gradients between epicardial, endocardial and M cells. Spodick and colleagues were the first to study clinical significance of U waves in relation to the T waves.¹⁶ They divided patients into three groups: negative T-U concordance (both T and U waves negative), type 1 T-U discordance (negative T waves and positive U waves) and type 2 T-U discordance (positive T waves and negative U waves). Patients with negative T-U concordance had highest incidence of coronary artery disease (CAD) (88%) followed by type-1 and type-2 discordance (64% and 46%, respectively). The incidence of left ventricular hypertrophy was however higher in type-2 discordance than type-1 discordance (58% vs 49%, respectively). Negative U waves usually appear when a large myocardial territory is involved and can help locate the coronary artery involved. Sometimes, negative U waves may be the only early ECG sign of ischaemia. A previous study reported that negative U waves may sometimes be the only ECG sign of ischaemia and they may also serve to be an important sign of extensive myocardial infarction (MI) involving the apex, with global ejection fraction of less than 50%.¹⁷ In another similar study involving patients with prior inferior MI, those with negative U waves in V4-V6 were more likely to have multivessel CAD, significant left anterior descending CAD (70% stenosis) or poor global ejection fraction.^{17 18} In addition to these medical conditions, there has been a described entity known as exercise-induced U waves which have somewhat different clinical significance. Exercise-induced U wave alterations (especially negative U waves) may serve as a useful marker of high-grade coronary narrowing and also help in localising the coronary artery involved.¹⁹ It has also been noted that patients with exercise-induced U waves (positive or negative) often have less angina and ischaemic changes during balloon coronary occlusion, due to well-developed collateral vessels. The recognition of U waves can often be difficult from T wave especially in conditions like an abnormal T:U ratio (eg, in left ventricular hypertrophy, active myocardial ischaemia or severe electrolyte abnormalities) and inverted or biphasic U waves like in our case.⁵ In these conditions, the U wave may often be confused with the second peak of a bifid T wave. This can be easily avoided by measuring the QaU distance in V2 or any other lead with an upright U wave and reporting it to the lead in question; alternately if the position of U is doubtful in all leads, the Q-T distance should be determined; the addition of 0.10 s to this will show the approximate position of aU (if the rate is between 60 and 80/min).⁵

Our case describes a rarity because the patient's ECG demonstrated findings of both hyperkalaemia and discordant U waves, the simultaneous occurrence of both of which is quite unusual and probably not well described previously. Normally, U waves are prominent in hypokalaemia and tend to disappear when patient has hyperkalaemia. The possible cause of U waves in our case despite the presence of hyperkalaemia could be the patient's underlying history of CKD/end-stage renal disease

(CKD/ESRD). Patients with CKD usually develop hyperkalaemia and thus may develop a partial clinical adaptation to the long-standing effects of hyperkalaemia in CKD, that is, ECG changes may be less pronounced in patients with CKD as compared with the normal population with the same degree of hyperkalaemia. Thus, if CKD patients have a pronounced physiological U wave on their baseline surface ECG, that may still be noticed when they have mild hyperkalaemia. In addition, our patient was relatively bradycardic during the first ECG recording, which may be another contributing factor as U waves often may be more prominent at slower heart rates. The reason for biphasic U waves with predominant negative discordance in the first ECG, however, largely remains unclear because the patient did not have known history of CAD, though it is not unlikely to have asymptomatic CAD in the elderly and thus cannot be definitely excluded in our patient. We suspect that possible demand ischaemia secondary to hypoxia and dehydration in the setting of possible underlying asymptomatic CAD could have resulted in predominant discordance of the U waves on presentation when patient also had hyperkalaemia. Though these appear to be the most likely explanations, this observation raises a question whether there is also another possible mechanism apart from the mechano-electrical factors (most acceptable current hypothesis) which plays a role in the morphogenesis of U waves.

Learning points

- ▶ U waves are often underappreciated in common clinical practice and their significance has often been underutilised by most physicians.
- ▶ The morphology of U waves in relation to the T waves can be helpful in raising suspicion for some common clinical conditions.
- ▶ U waves are often commonly appreciated in hypokalaemia; however, may be appreciated in the presence of hyperkalaemia (as in our patient), if the patients probably have underlying history of chronic kidney disease/end stage renal disease where they may possibly develop a partial clinical adaptation to the long-standing effects of hyperkalaemia and physiological U waves can still be apparent on the ECG.

Contributors All authors have significantly contributed in writing the manuscript and in performing the review of the literature.

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