CASE 1

CLINICAL PRESENTATION

A 70-year-old Chinese man was admitted with a one-month history of progressive bilateral lower limb swelling and exertional dyspnoea. His functional status was noted to be New York Heart Association (NYHA) class III. He had a history of multiple myeloma diagnosed three years prior to this current admission, which was complicated by worsening renal disease. He was subsequently diagnosed with amyloid nephropathy based on renal biopsy. On physical examination, his blood pressure was 105/60 mmHg and heart rate was 80 beats per minute (bpm), and the jugular venous pressure was elevated. Both the first and second heart sounds were audible, with a pan-systolic murmur at the apex and lower left sternal edge. There were bilateral crackles heard at the lung bases, as well as bilateral pitting oedema at the ankles. What does the electrocardiogram (ECG) in Fig. 1 show?

![ECG Image](image_url)

Fig. 1 ECG shows low voltages in the QRS complexes, especially in praecordial leads V1 to V6.

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ECGs with small QRS voltages

Ting Ting Low¹, MBBS, MRCP, Voon Shiong Ronnie Tan¹, MBBS, Swee-Guan Teo¹, MBBS, MRCP, Kian-Keong Poh¹,², FRCP, FACC

¹Cardiac Department, National University Heart Centre, ²Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Correspondence: A/Prof Poh Kian Keong, Senior Consultant and Associate Professor, Cardiac Department, National University Heart Centre, 1E Kent Ridge Road, NUHS Tower Block, Level 9, Singapore 119228. kian_keong_poh@nuhs.edu.sg
ECG INTERPRETATION
The ECG in Fig. 1 shows atrial fibrillation. The voltages of the QRS complexes are globally small, especially those in leads V1 to V6, where all the complexes are less than 1 millivolt (10 mm). Prominent Q waves are seen in leads V4–V5.

CLINICAL COURSE
Transthoracic echocardiogram performed revealed an increase in left ventricular wall thickness (Fig. 2). There was severe left ventricular systolic dysfunction. The left ventricular ejection fraction was only 25% (normal range is usually above 55%). Both the atria were dilated. The mitral and aortic valves were thickened, and there was moderately severe mitral and tricuspid regurgitation. The mitral inflow Doppler signals showed a restrictive pattern. The pulmonary artery systolic pressure was quantitated to be 46 mmHg. The echocardiographic findings were consistent with those of amyloid heart disease. Magnetic resonance (MR) imaging of the heart was subsequently performed. There was global gadolinium enhancement of the myocardium, with difficulty in nulling the myocardium and rapid clearance of contrast from the blood pool, consistent with cardiac amyloidosis. The option of an implantable cardioverter-defibrillator device was offered for primary prophylaxis against sudden cardiac death, but the patient declined. His medications for heart failure were optimised, including the use of an angiotensin-converting enzyme inhibitor, spironolactone, digoxin and a diuretic (bumetanide).

CASE 2
CLINICAL PRESENTATION
A 48-year-old female patient was admitted for progressive shortness of breath associated with intermittent chest discomfort over the last three months. On physical examination, sinus tachycardia at 105 bpm and a blood pressure reading of 100/60 mmHg were noted. Both the first and second heart sounds were heard but muffled. There was no pericardial rub. The jugular venous pressure was markedly elevated. What does the ECG in Fig. 3 show?
ECG INTERPRETATION
The ECG in Fig. 3 shows sinus rhythm (heart rate = 107 bpm) and small QRS complexes globally. The QRS complexes in the limb leads averaged 3–4 mm, and those in the precordial leads averaged 6–7 mm. In addition, the voltages of both the T and P waves are also globally reduced. In the clinical context, these ECG findings are highly suggestive of the presence of a large pericardial effusion. There is no evidence of electrical alternans present in this ECG. After pericardiocentesis (Fig. 4), there is a marked increase in the voltages of the QRS complexes, the T waves and P waves in all the 12 leads.

CLINICAL COURSE
Transsthoracic echocardiogram revealed the presence of a large pericardial effusion (Fig. 5). The ejection fraction was normal at 68%. Echocardiographic features of increased intra-pericardial pressures were observed. There was collapse of the right atrium and right ventricle during diastole, as well as dilatation and less than 50% reduction in the diameter of the inferior vena cava during inspiration. A pericardiocentesis was performed emergently. Analysis of the pericardial fluid revealed the presence of abnormal blast cells (80%), and flow cytometry confirmed the diagnosis of acute myeloid leukaemia. The patient was commenced on chemotherapy and underwent allogenic stem cell transplantation as part of curative treatment. Follow-up echocardiography 72 hours later showed marked interval reduction in the size of the pericardial effusion. ECG repeated post pericardiocentesis also showed that all QRS voltages had become considerably larger (Fig. 4).

DISCUSSION
The American College of Cardiology/American Heart Association (ACC/AHA) Committee defined the criteria for low voltage QRS complexes on the ECG as amplitude of the QRS complexes less than 5 mm in each standard limb lead, or less than 10 mm in the precordial leads. The differential diagnoses are many, and may include myocardial disease, pericardial disease and metabolic abnormalities (Table I). The ECG complexes may also be attenuated by any condition that increases the distance between the heart and the ECG leads, such as in anasarca, lung disease and morbid obesity. Inappropriate calibration is another common pitfall. The standard ECG should be calibrated to a voltage sensitivity of 10 mm/mV on the vertical axis.

In our first case, the patient has low voltage QRS complexes secondary to cardiac amyloidosis. This is a manifestation of a group of diseases of amyloid production, which is characterised by extracellular amyloid infiltration throughout the heart. Pathologically, the amyloid deposits occur in the atria, ventricles, valves, as well as perivascularly and in the conduction system, resulting in biventricular wall thickening, atrial dilatation and pericardial effusion. Consequently, clinical manifestations may
In our second case, the patient had low voltage QRS complexes due to a large pericardial effusion with impending cardiac tamponade. The causes of pericardial effusion are broad, and may be classified into categories of infections, malignancy, radiation-induced, autoimmune diseases, uraemia, hypothyroidism, post-myocardial infarction and idiopathic. Regardless of the respective underlying cause, the diagnosis is suspected when the ECG reveals suggestive changes of low voltage QRS complexes and electrical alternans. Low voltage QRS complexes may be due to short-circuiting of cardiac potentials by the pericardial fluid surrounding the heart. Electrical alternans, which is uncommonly seen, describes a beat-to-beat variation in the QRS axis and amplitude, which may also involve the P wave and T wave. This alternation occurs in association with a swinging of the heart, due to a very large pericardial effusion. The presence of these changes should increase the index of suspicion for a significant pericardial effusion and prompt further evaluation such as echocardiography.

However, a few studies have shown that clinical correlation and the diagnostic value of the above ECG findings have been poor. In a study of 46 patients who had undergone two temporally separate echocardiographic and ECG examinations, it was concluded that the ECG findings were too few, subtle, insensitive and nonspecific to be useful as indicators of the presence of pericardial effusion. Only a weak correlation \( r = 0.296 \) was noted between QRS voltage and effusion size.\(^{19}\) In another cross-sectional study of 136 patients, the authors concluded that low voltage and PR-segment depression are ECG signs that are suggestive, but not diagnostic, of pericardial effusion and cardiac tamponade.\(^{13}\) Another consecutive case series analysis of 121 patients, however, concluded that in the presence of PR-segment depression, even a small pericardial effusion may cause low voltage in the surface ECG.\(^{14}\)

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**ABSTRACT** The causes of low voltage complexes on the electrocardiogram (ECG) are variable; however, they are not commonly discussed. An ECG with small QRS amplitudes may initially look unremarkable to the unwary, but some of the underlying conditions may be critical. Although imperfect, the ECG is still a useful, noninvasive and readily available tool for the screening of these underlying conditions. We present two cases with low voltage complexes in the ECG. The first case highlights how the findings on ECG and subsequent echocardiogram led to the diagnosis of a rare case of cardiac amyloidosis. In the second case, a screening electrocardiogram alerted the physicians to a life-threatening condition, that of a large pericardial effusion with cardiac tamponade.

Table I. Causes of low voltages on ECG.

<table>
<thead>
<tr>
<th>Infiltrative heart disease</th>
<th>Amyloidosis</th>
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<tbody>
<tr>
<td>Scleroderma</td>
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<td>Haemochromatosis</td>
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<td>Metabolic abnormality</td>
<td>Myxoedema</td>
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<td>Hypothermia</td>
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<td>Neonatal hyperbilirubinaemia</td>
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<td>Pericardial disease</td>
<td>Large pericardial effusion with cardiac tamponade</td>
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<td></td>
<td>Pericardial mesothelioma</td>
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<td>Constrictive pericarditis</td>
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<td>Pericardial tuberculosis</td>
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<td></td>
<td>Chylopericardium (large)</td>
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<tr>
<td>Increased distance</td>
<td>Obesity (massive)</td>
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<td>COPD with hyperinflation (i.e. emphysema)</td>
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<td>Pneumothorax</td>
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<td>Pleural effusion</td>
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<td>Anasarca</td>
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<td>Atherosclerotic disease</td>
<td>Acute myocardial infarction (large infarct with poor LV systolic function)</td>
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<td></td>
<td>Ischaemic cardiomyopathy</td>
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COPD: chronic obstructive pulmonary disease; LV: left ventricle

include the following: (1) heart failure with peripheral oedema and hepatomegaly; (2) typical angina secondary to amyloid deposits in the small vessels of the heart; and (3) syncope and sudden cardiac death. The most common ECG presentation of cardiac amyloidosis is low voltage QRS complexes in the limb leads, occurring in approximately 50% of patients, and is often associated with extreme left- or right-axis deviation.\(^{4,6}\) Other changes on the ECG can include pseudo-infarct patterns, atrial fibrillation and conduction abnormalities such as second- and third-degree atrioventricular heart blocks.\(^{40}\)

Diagnosis is usually best confirmed on histology with endomyocardial biopsy. There are distinctive features of advanced cardiac amyloidosis on echocardiography as well. These include biventricular wall thickening, thickened valves due to infiltration, myocardial reflectivity (also commonly described as “granular sparkling” [Fig. 2]), pericardial effusion and a restrictive pattern in the transmitial Doppler flow. The combination of increased thickness of the left ventricular posterior wall on echocardiogram and interventricular septum with a low voltage ECG pattern is highly specific for cardiac amyloidosis.\(^{49}\) This combination of increased ventricular mass with reduced ECG voltage is unique to infiltrative cardiomyopathy.\(^{46}\) Other conditions resulting in low ECG voltage (e.g. large pericardial effusion with cardiac tamponade, emphysema) are not associated with increased heart mass, while conditions associated with increased cardiac mass (e.g. hypertension, hypertrophy) are usually associated with normal or increased ECG voltages.\(^{48,50}\) A combination of low voltage on ECG and an interventricular septal thickness > 1.98 cm detects amyloidosis, with a sensitivity and specificity of 72% and 91%, respectively.\(^{56}\)
REFERENCES


Question 1. The following ECG criterion for low voltages is true:
(a) The ACC/AHA Committee defines the criteria for low voltage QRS complexes on the ECG as amplitude of the QRS complexes < 5 mm in each standard limb lead.
(b) The ACC/AHA Committee defines the criteria for low voltage QRS complexes on the ECG as amplitude of the QRS complexes < 10 mm in each of the precordial limb leads.
(c) ECG complexes may also be attenuated by any condition that decreases the distance between the heart and the ECG leads.
(d) The standard ECG should be calibrated to a voltage sensitivity of 10 mm/mV on the vertical axis.

Question 2. Pericardial effusion may result in the following ECG changes:
(a) Atrial fibrillation.
(b) Electrical alternans.
(c) Sinus tachycardia.
(d) Low QRS voltages.

Question 3. The following ECG features may be seen in cardiac amyloidosis:
(a) Second-degree atrioventricular block.
(b) Atrial fibrillation.
(c) Q waves.
(d) Left ventricular hypertrophy with strain pattern.

Question 4. Causes of low voltage ECG include:
(a) Aortic stenosis.
(b) Pleural effusion.
(c) Cardiac haemochromatosis.
(d) Chronic obstructive pulmonary disease with emphysema.

Question 5. The following features assist in the diagnosis of cardiac amyloidosis:
(a) “Granular sparkling” on echocardiogram.
(b) Small QRS voltages on ECG despite a thickened left ventricle on echocardiogram.
(c) ECG findings similar to those in hypertrophic cardiomyopathy.
(d) Cardiac MR imaging with global gadolinium enhancement of the myocardium.