New Concepts in ECG Interpretation

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Introduction

In the last few decades, there was a clear modification of the patient clinical approach. Echocardiography from the 1970s deeply impacted with our medical practice, and from those times on also other images type of exams did come out as diagnostic supports such as MRI, coronary tomography, scintigraphic methods, and so on.

The neat result is that many different specialists are involved in a single diagnosis, and sometimes they do not communicate with one another. Thus, certainly the diagnostic and therapeutic chances did enlarge, but in the same time, there was a progressive and constant decrease of the possibility that a specific diagnosis is made from a single doctor; the concept of "team" is therefore today leading.

Until the 1970s, one cardiologist was usually taught that he has to consider accurately the patient anamnesis before passing to the semeiotic objective clinical evaluation, then he probably needs just a 12-lead EKG and eventually a chest X-ray in order to straightly reach the final diagnostic response. Therefore, a single cardiologist with just few but important elements was able to reach the correct diagnosis in the majority of cases without other aids. That clinical straight process was full of responsibility for the single medical doctor, meanwhile nowadays other MDs may share them, but could lead to a "special strict relationship" between patient and MD that was and should continue to be the basal instrument not only for the right diagnosis but particularly for a therapeutic final positive success.

EKG interpretation was a clear mainstay of the diagnostic cardiological process, a tool that could help the correct diagnosis not only in sophisticated laboratories but even in very peripheric ambulatories.

Is the correct EKG interpretation still of significant value in the diagnostic process? Are there new insights that may help its correct interpretation that may even enlarge its positive clinical impact? Are there new ways to take advantage of the electrical signals in a different way than the classical 12-lead system?

Those and other will be the questions we are going to answer with this book, where starting from simple but meaning everyday clinical cases, we will reach the way to the correct interpretation sometimes going over the static well-known interpretation by opening new windows and ways of thinking.

After many years of medical practice not only in the electrophysiologic field but also in the clinical cardiologic arena, my personal feeling is that the

correct EKG interpretation is even today a fundamental and necessary aid for the cardiologist in order to interpret correctly any specific pattern, and many times thanks to this we could even save money by preventing unuseful and costly examinations.

My very deep gratitude is going to the memory of Dr. Domenico Montuschi, Prof. Bruno Magnani, and Prof. Ralph Lazzara together to the teacher and friend Prof. Michiel Janse, that highly enlighted my way to the knowledge and greatly contributed to the proudness feeling of being an MD and a cardiologist.

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P-Waves Are the Main Clues for Correct ECG Interpretation

1

Mirko Beltrame, Paolo Compagnucci, and Alessandro Maolo

1.1 Case 1

A 63-year-old male with history of hypertension was admitted to the ER with aphasia and hemiparesis. Blood pressure was 140/85 mmHg. There were no clear heart murmurs or signs of heart failure. CT angiography showed left fronto-insulo-temporal hypodense area related to an acute ischemic lesion. Carotid arteries were normal at echocolordoppler.

The following was his standard 12-lead ECG (Fig. 1.1).

1.1.1 ECG Analysis

Sinus rhytm, heart rate 71 bpm, regular RR intervals.

There is a positive P-wave in leads I, II, III and VF, isoelectric in VL and negative in VR. P axis is +60; PR interval is 180 ms.

P-wave terminal force in lead V1 (PTFV1, the product of the depth of the terminal portion of P-wave in V1 multiplied by its duration) is 50 ms mm (Fig. 1.2).

P-wave duration (PWD) in lead II is 100 ms (Fig. 1.3).

P-wave area (PWA, the product of the duration and amplitude of the P-wave) is also higher than normal.

The QRS is 80 ms, with normal morphology and axis of +15°. Ventricular repolarization is normal with a QT interval of 380 ms and QTc (Bazett's formula) of 413 ms.

Final ECG diagnosis: regular sinus rhythm and bi-atrial enlargement.

A 2D echocardiography and a 7-day-long ECG-Holter monitoring were recorded in order to check for paroxysmal AF episodes:

- At echocardiography: mild dilatation of left and right atria, grade I diastolic dysfunction and moderate mitral regurgitation.
- ECG monitoring did not document any episode of atrial fibrillation, atrial flutter or even atrial tachycardia.

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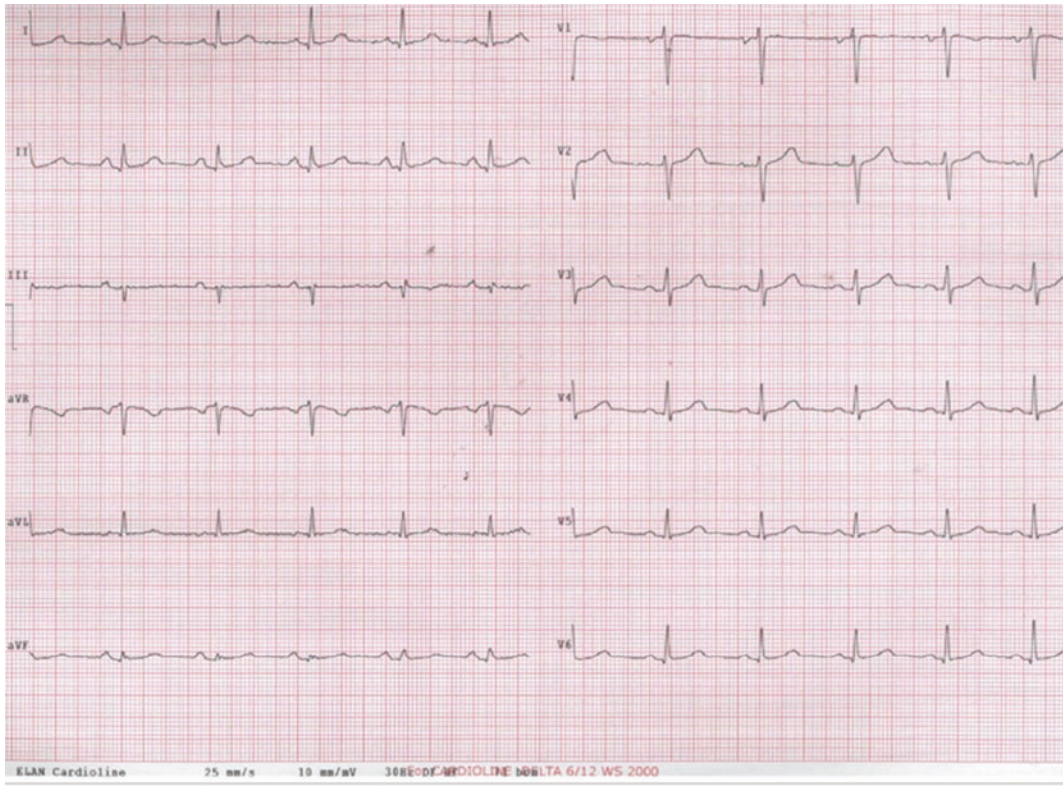

Fig. 1.1 Case 1. 12-lead ECG

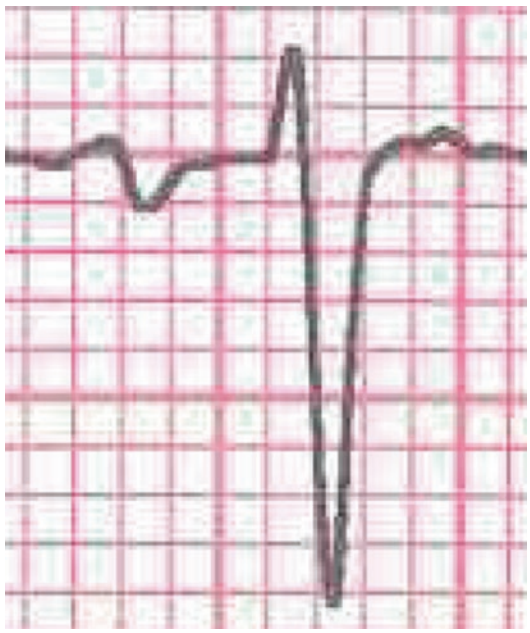

Fig. 1.2 P-wave terminal force in lead V1

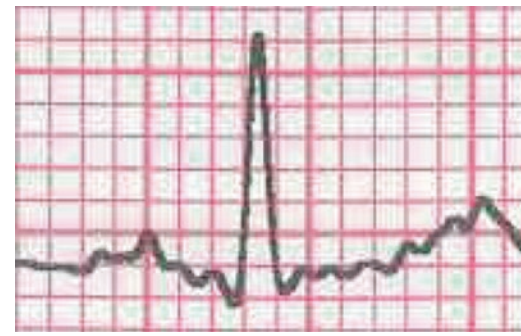

Fig. 1.3 P-wave duration (PWD) in lead II

Therefore, in this case the single 12-lead ECG could suggest an atrial pathology, probably due to end-diastole pressure overload, a likely consequence of undertreated arterial hypertension (Fig. 1.4).

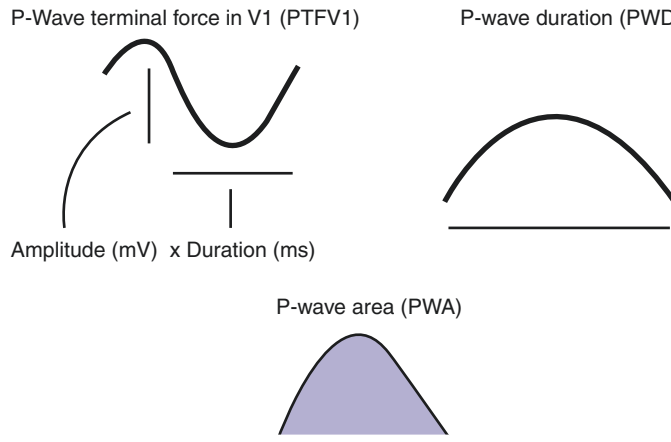

Fig. 1.4 Measurements of P-wave terminal force in V1 (PTFV1), P-wave duration (PWD) and P-wave area (PWA)

1.1.2 From ECG to Pathology

There are many data in literature underlying how, in some patient that may have even QRS and repolarization abnormalities, a normal P-wave may be a quite specific index pointing to the absence of any cardiac dysfunction. On the other end, a P-wave abnormality may unmask a left ventricular hypertrophy [1, 2] or a diastolic dysfunction.

Over the past years, there has been a surge of interest towards a condition called "atrial cardiomyopathy". For the first time, this term was used in a paper dating back in 1972 [3] describing a family whose members developed supraventricular arrhythmias, atrioventricular block and atrial standstill; the authors reported at autopsy how "the right atrium showed diffuse interstitial fibrosis with areas of subtotal muscle loss. There was extensive interstitial fibrosis throughout the wall", thus identifying fibrosis as a key element underlying atrial pathologies. Other experiences were published later [4].

It was only in 1997, however, that the term atrial cardiomyopathy was adopted referring to patients affected by atrial fibrillation. In an editorial Douglas Zipes [5] commented on one of the first studies regarding pulmonary vein isolation as a treatment of atrial fibrillation. More recently, in 2016 [6], the European Heart Rhythm Association (EHRA), Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS) and Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiología (SOLAECE), in cooperation with the American College of Cardiology and the American Heart Association, developed a consensus document on atrial cardiomyopathy, which is now defined as:

> any complex of structural, architectural, contractile or electrophysiological changes affecting the atria with the potential to produce clinically relevant manifestations.

It is well recognized that the atria's fundamental functions are not only to fill the ventricles but also to generate properly the cardiac rhythm and to secrete hormones such as the natriuretic peptides. Therefore, the atria may be involved in a wide spectrum of cardiovascular and systemic disorders, which are classified in a pathological-clinical way in that consensus document, according to whether the cardiomyocyte is mostly involved (Class I, such as in lone atrial fibrillation, diabetes mellitus or genetic cases), the fibroblast is mostly involved (Class II, such as in ageing or cigarette smoking), both cell types are involved (Class III, such as in valvular heart disease or congestive heart failure) or there are non-collagen deposits (Class IV, such as in isolated atrial amyloidosis, granulomatosis, inflammatory infiltrates or glycosphingolipids).

What is most interesting for the clinician is that this atrial cardiomyopathy can be involved in the development of complications, such as atrial fibrillation and stroke. It is well known that the risk of stroke and the consequent need

to prescribe an anticoagulant in patients with atrial fibrillation do not depend on the duration or frequency of the arrhythmia but rather on the presence of clinical risk factors involved in the pathogenesis associated with the atrial cardiomyopathy, such as hypertension, heart failure, diabetes mellitus, a prior stroke or embolic event, age and evidence of atherosclerotic vascular disease, factors that grouped together are the bases of the CHA2DS2-VASc score [7].

One hypothesis is that most cases of cardioembolic stroke could not be a consequence of the blood stasis in the atrial appendages with clot formation, but rather stroke may be explained by the presence of the atrial cardiomyopathy independently of atrial fibrillation. Some clinical data in patients with an implanted cardiac device and thus a continuous rhythm monitoring have shown that there is not a strong time correlation between atrial fibrillation and stroke. In the ASSERT (Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial) study, only 8% of the 51 patients who developed a stroke had an atrial fibrillation episode in 30 days preceding the cerebrovascular accident [8].

Thus, at present there is a belief considering that atrial fibrillation is not a direct cause of stroke but rather an epiphenomenon related to an abnormal atrial substrate (atrial cardiomyopathy) [9]. The atrial fibrosis (an element already recognized in the first paper of 1972), the inflammation state and the endothelial dysfunction may create a pro-thrombotic milieu.

Atrial fibrillation may be considered as one of the clinically relevant markers of an increased stroke risk, and, perhaps more importantly, the clinician should start as soon as possible to look more carefully for other markers that can increase the risk.

The ECG therefore is a fundamental and meaningful tool in this context. Starting in 1954 with the publication of a paper by Puech [10], it was recognized that an interatrial block of conduction is characterized by a wide P-wave in DII. It was early recognized that interatrial block is frequently associated with other conduction disturbances, such as sinus node dysfunction and atrioventricular conduction problems, and also with structural abnormalities of the left atrium, mainly enlargement, which, however, is not always present [11].

Bayés de Luna [12] described the association of interatrial block (defined as a P-wave duration of 120 ms or more with a biphasic morphology in DII, aVF or DII) [13] and supraventricular arrhythmias. The ECG findings could be explained by the sequential cranio-caudal activation of the right atrium followed by the retrograde activation of the left atrium.

More recently, it has been suggested that the Bayés syndrome, as it is now called, is associated with an increased risk of stroke [14, 15].

A recently published meta-analysis [16] has confirmed the association of three left atrial abnormalities easily assessable by means of a surface ECG, namely, increased P-terminal force in the precordial lead V1 (PTFV1) >40 ms mm, prolonged P-wave duration (PWD) >120 ms reflecting interatrial block or greater maximum P-wave area (PWA) not only with an increased risk of atrial fibrillation and other supraventricular arrhythmias but also with an increased risk of stroke.

A careful ECG P-wave analysis may be considered as useful instrument which, together with a clinical evaluation, echocardiogram, biomarkers and cardio-MRI, might help us find those patients who, independently of a known atrial fibrillation, are at risk of developing a cardioembolic stroke with consequent possible benefit coming from an anticoagulant therapy.

P-wave duration analysis can also be more accurate by evaluating the signal-averaged ECG (SAECG). SAECG is a simple noninvasive method, using cardiac electric signals from many surface electrodes, which has been used for years, initially to evaluate ventricular late potentials, and which has been extended to the P-wave to provide a more accurate evaluation of atrial conduction [17].

The values measured with all the leads are averaged to minimize interference and to see even the smallest alterations. A prolonged signal-averaged P-wave duration compared to the standard 12-lead ECG was found to be a more precise marker for the development of atrial fibrillation [18].

Other important findings detectable using SAECG are atrial late potentials. Late potentials are very-low-amplitude electric signals not visible with the standard 12-lead ECG. The QRS late potentials originally were studied to estimate the ventricular arrhythmia risk. Similarly, the P-wave (or atrial) late potential can be useful to stratify the risk for paroxysmal atrial fibrillation. Budeus et al. hypothesized that atrial late potentials found on P-wave SAECG could have a role in the development of paroxysmal atrial fibrillation [19, 20]. However, the predictive value of atrial late potentials has not yet been demonstrated.

In summary, atrial cardiomyopathy is a clinically meaningful concept that after many years of negligence is now under the light again, and its diagnostic correct evaluation could be of practical consequences. The ECG is therefore a simple and yet pivotal instrument that must not be forgotten in an era in which the diagnostic armamentarium is continuously enlarging but with also economic limitations.

1.2 Case 2

This ECG of an asymptomatic and obese (BMI 32) 65-year-old man was recorded on a preoperative visit for an elective noncardiac surgery. The past medical history is unremarkable except for hypertension and dyslipidemia both well managed with medications (Fig. 1.5).

1.2.1 ECG Analysis

Calibration: 0.5 cm/mV.
Speed: 25 mm/s.
RR interval: regular.
HR: 55 bpm.
P-wave duration: 80 ms.
P-wave morphology and amplitude: normal.
P-wave axis: P-wave is positive in leads I, II, VF and VL, isoelectric in lead III and negative in VR lead. Axis is +30°.
PR interval: 200 ms.
QRS duration: 80 ms.

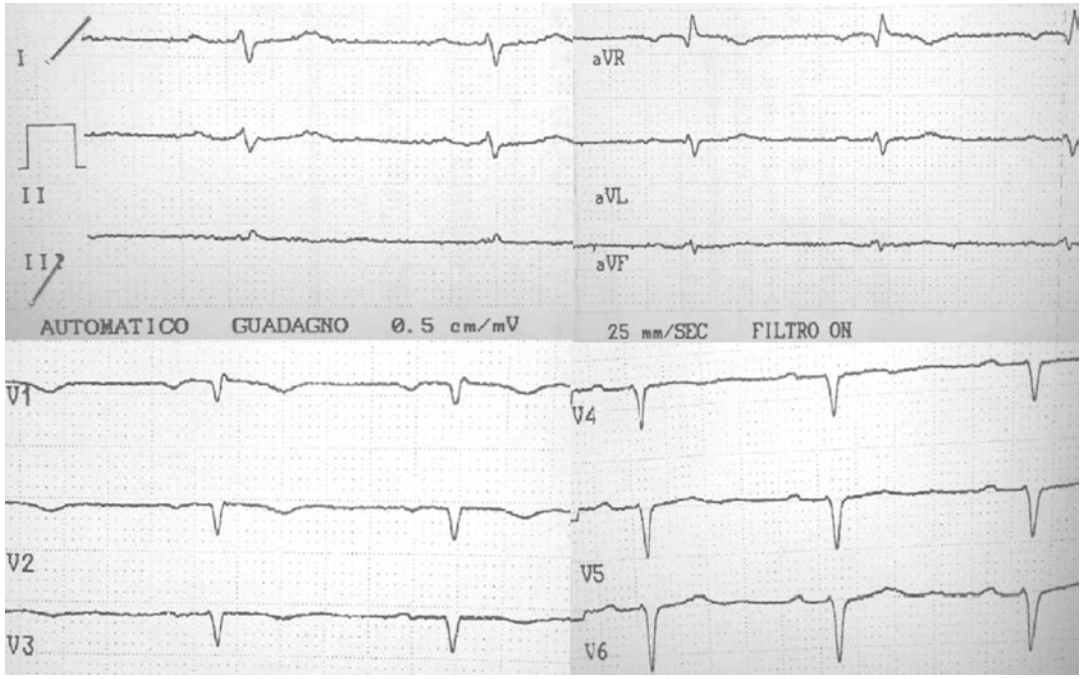

Fig. 1.5 Case 2. 12-lead ECG

QRS morphology and amplitude: at first sight we could say that QRS voltages are small; however, this ECG was recorded with 0.5 cm/mV gain, so actually the maximum amplitude in V6 is 1.5 mV, and in the peripheral lead, the criteria for low voltages are not satisfied. QRS amplitude is thus within normal limits.

In the QRS there is a minor right bundle conduction delay and absent R-wave progression in the precordial leads from V2 to V6. *That pattern may be consistent with a possible previous silent myocardial infarction*.

QRS axis: isoelectric in VF, positive in VR and almost negative in I and II leads. Thus, QRS axis is right deviated with a value of +120°.

ST segments and T waves were normal without any clear sign of acute myocardial ischemia.

QT interval: 440 ms with a QTc of 421 ms (Bazett).

Among the possible differential diagnosis, mostly related to the right axis deviation and the absence of R-wave progression, we should mention:

- Previous silent anterior myocardial infarction
- COPD
- Congenital unknown cardiac abnormalities

In order to exclude major comorbidities, the patient was admitted to the cardiology department for further evaluation.

At echocardiography even with contrast, not any significant abnormalities were noticed. The overall ejection fraction was normal together with the regional wall motion. Thus, the ischemic aetiology was unlikely.

Because of the poor acoustic window, a cardiac MRI scan was afforded to exclude any congenital abnormalities that could have been missed at the transthoracic echocardiography.

The cardiac MRI surprisingly revealed the *absence of the pericardium and of the pericardial fat*.

Going back to ECG, we can notice that the morphology, the axis and the voltages of the P-waves are completely normal. This should have helped us to exclude any major cardiac congenital abnormalities. In fact, those should have led to atrial overload.

The complete congenital absence of the pericardium is a very uncommon finding. Subjects are often asymptomatic, but the first clinical presentation could be a non-exertional chest pain [21, 22]. Describing in detail this condition is not the purpose of this chapter and textbook, though we will focus on the ECG tracing associated to this rare malformation.

The ECG abnormalities consistent with congenital absence of pericardium described in literature are quite unspecific. They include sinus bradycardia, complete or incomplete bundle branch block, poor R-wave progression in the precordial leads secondary to a left displacement of the QRS transitional zone and prominent P-waves in case of a presence of a right atrial overload [21–28].

The ECG we report has two of these features (incomplete RBBB and poor R-wave progression), while P-waves are normal.

P-wave focusing may therefore help not only in the right ECG interpretation but mainly in the correct clinical evaluation.

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Atrial Pathologies

2

Claudio Cupido, Giulia Enea, Alessio Menditto, and Cristina Pierandrei

2.1 Case 1

I.C., a 65-year-old man, went to the hospital for a cardiologic check. His medical history is characterized by Hodgkin lymphoma at 40 years old treated by chemotherapy and radiotherapy. He denied any previous cardiovascular disease and did not take any specific medication. No signs of heart failure at clinical examination, and artery pressure was 110/60 mmHg.

A 12-lead ECG was recorded (Fig. 2.1).

2.1.1 ECG Analysis

There is a regular rhythm. RR interval is constant with 680 ms intervals (heart rate is 88 beats per minute). A P-wave is before any QRS complex with a frontal plane axis of +15° and, thus, compatible with sinus node origin. PR interval is normal (160 ms). QRS complex is wide (160 ms) with rS morphology in right precordial leads and monophasic R morphology in leads I, VL, and left precordial. This is a left bundle branch block (LBBB) morphology. QRS complexes have normal frontal plane axis (+15°) with a transitional zone in V4. In lead VF it is possible to see respiratory morphology variation of the QRS axis. ST segment and T-wave have the typical pattern secondary to the conduction delay (LBBB): ST elevation in right precordial leads and ST depression in the left leads (I, VL, V4–V6). QT interval is 440 ms. In this case QT interval is prolonged because of depolarization delay due to LBBB, and therefore that is not a real long ventricular repolarization pattern [1]. Bogossian H and colleagues developed a new formula to assess QT in patient with LBBB (modified QT, QTm). QTm is QT—50% QRS in this case is 360 ms [1, 2]. By employing the standard Bazett formula QTc is anyway normal (436 ms).

Conclusion: sinus rhythm with LBBB and secondary repolarization patterns.

The question could be, is this ECG just showing a conduction delay or is there something else hidden? How is the P-wave?

The P-wave (normal frontal plane axis) has a sinus origin, but its morphology is not normal. Its length (120 ms in lead II) is at the upper limit, with a notched shape in the limb leads. Peak-to-peak interval is more than 40 ms. P-wave in lead V1 is biphasic (positive-negative) with a terminal negative part prolonged and deeper compared to the first one. This feature is due to prevalence of the posterior atrial vectors (left atrium). These electrocardiography signs are suggestive of left atrial enlargement or left atrial strain.

An echocardiography was evaluated and did show a dilated cardiomyopathy with depress sys-

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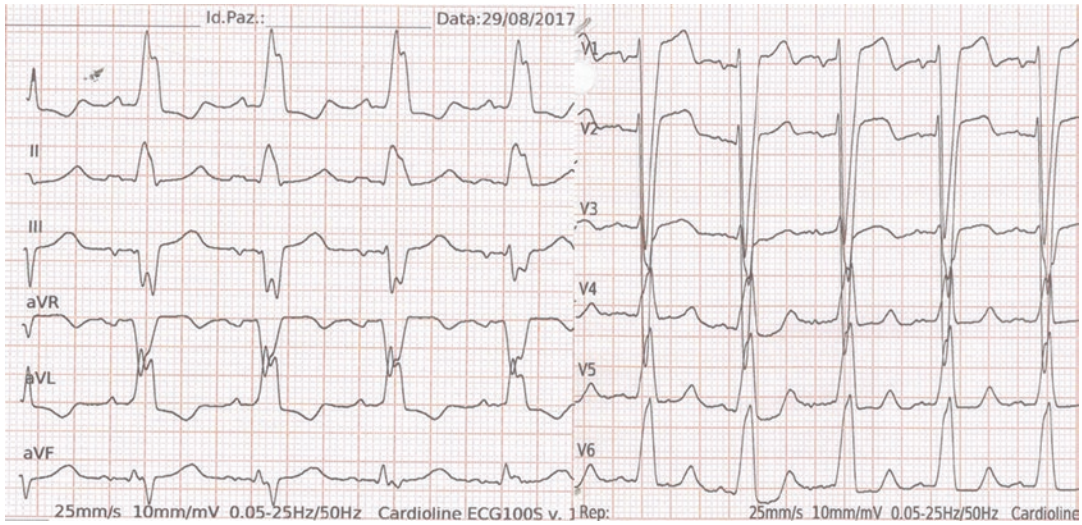

Fig. 2.1 Case 1: 12-lead ECG

tolic function (EF 30%), type II diastolic dysfunction, and a moderately dilated left atrium (index LAV 44 ml/mq).

2.1.2 Left Atrial Enlargement (LAE)

Left atrial dilation, left atrial hypertrophy, and elevated left atrial pressure are structural and functional atrial patterns that can influence ECG P-wave modifications. The left atrium is located posteriorly, and its electrical activation corresponds to the terminal part of the P-wave. LAE causes prolonged and increased amplitude of the P-wave terminal part.

Typical LAE signs are P-wave duration longer than 120 ms, notching of P especially in lead II (with notching interval more than 40 ms), prolonged duration and depth of the terminal negative part of P-wave in lead V1, and finally left deviation of the P-wave axis [3, 4].

Imaging—ECG correlation studies showed a high sensitivity (71–84%) and a low specificity (35–55%) for P-wave more than 120 ms length and a low sensitivity for P-wave notching (8–19%) and for the negative terminal part of P-wave (37–49%) that had, however, a high specificity (respectively, 85–99% and 54–88%) [4].

2.2 Case 2

A 77-year-old man was admitted to the emergency department for worsening of dyspnea, leg edema, and rapid weight gain starting in the previous week. His medical history was characterized by systemic arterial hypertension and previous right inferior lobectomy for lung cancer 2 years earlier. A 12-lead ECG was recorded (Fig. 2.2).

2.2.1 ECG Analysis

The ECG shows a regular RR interval with 75 bpm HR (RR 800 ms). Each QRS is preceded by a P-wave. P-waves are negative in VR, positive in the inferior leads, and biphasic in VL; the P-wave axis is therefore +60°. It is a sinus rhythm. The maximum P-wave amplitude is 0.25 mV in lead II. The initial positive deflection in V1 is 0.15 mV. P-wave length is 80 ms. PQ interval is 180 ms. QRS complex has normal morphology (100 ms). In V1 there is a rSr' complex.

QRS axis is −60° (aVR is the isodiphasic leads) with a definite left axis deviation. In the precordial leads, there are asymmetrical T-negative waves. QT interval is 400 ms and QTc 447 ms.

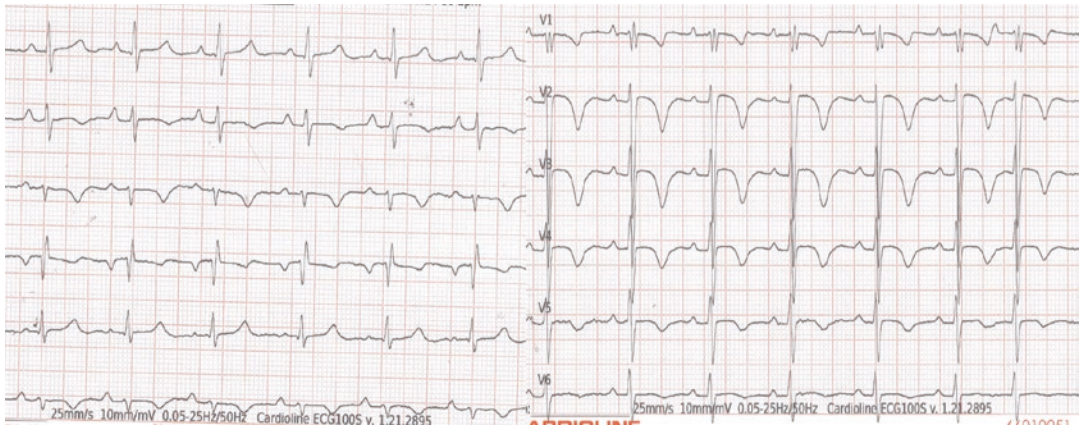

Fig. 2.2 Case 2: 12-lead ECG

There are therefore signs of right atrial enlargement (RAE). P-wave is taller and peaked in the inferior leads with a positive first deflection larger than negative in V1 without affecting P-wave duration. AV conduction is normal. The left QRS axis deviation and the QRS amplitude exclude a RV hypertrophy, but there is an incomplete RBBB that could be consequent of a RV overload.

The asymmetrically inverted T waves seen extensively in the precordial leads are not usually just dependent on RBBB; they could instead be a sign of a true myocardial ischemia or due to left ventricular pressure overload.

In this patient with heart failure signs (dyspnea, peripheral edema, and weight gain), the "pathological" ECG abnormalities suggest the presence of a heart disease.

The echocardiographic evaluation demonstrated concentric left ventricular hypertrophy with normal systolic function (EF 50%) and flattening of the interventricular septum (D-shaped left ventricle). There were right ventricular dilation (RVD1 52 mm) with systolic dysfunction (TAPSE 12 mm), severe right atrial enlargement (index RAV 65 ml/mq) without left atrial dilatation, and mild tricuspid regurgitation with estimated PAPS of 60 mmHg. A right heart catheterization was performed and showed precapillary pulmonary hypertension.

Thus, the pulmonary hypertension due to a pulmonary disease explains the RAE and the incomplete RBBB.

2.2.2 Right Atrial Enlargement (RAE)

The forces generated by right atrial depolarizations are directed anteriorly and inferiorly and produce the early part of the P-wave.

In case of right atrial hypertrophy or dilation, the right atrial depolarization lasts longer than normal, and its waveform extends to the end of the left atrial potentials, and the peak of the right atrial depolarization falls on the top of the left activity. The result is a P-wave that is taller than 2.5 mV and peaked without affecting the overall P-wave duration (<120 ms) in the inferior leads (especially in lead II) and the higher initial positive deflection in V1 (>1.5 mV or 0.20 mV less specific but more sensitive). Sometimes, we can also observe a P right axis with the tallest P appearing in lead III or AVF rather than in lead II. P-wave axis deviation over 70° is frequently observed in patients with severe COPD due to the hyperinflation of lungs, also without morphological changes of the P-waves [3, 5].

Right atrial enlargement is associated with several conditions:

- Chronic obstructive pulmonary disease
- Pulmonary hypertension (acute or chronic)
- Congenital or acquired right valvular disease (tricuspid stenosis, pulmonary stenosis)
- Congenital heart disease such as Fallot's tetralogy, interatrial and interventricular septal

defects especially in the presence of an Eisenmenger syndrome

As in our ECG, a right atrial enlargement is usually associated with electrocardiographic signs of right ventricular hypertrophy. In case of tricuspid stenosis, instead the right atrial enlargement does not coexist with any right ventricular hypertrophy.

A transitory "P pulmonale" may appear in case of acute pulmonary embolism due to acute right atrial strain.

Despite all, the P pulmonale pattern is not strictly and necessarily correlated with a right atrial volume enlargement, but it can be evident even in healthy subjects. In these cases, usually a sympathetic stimulation, resulting in a stronger and synchronous atrial contraction, or the vertical position of the heart can explain this pseudo-"P pulmonale" pattern [6].

2.3 Biatrial Enlargement

Criteria for both right and left atrial enlargements must be satisfied in the same ECG. Biatrial enlargement can be diagnosed if there is one or more of the following [5]:

- P-wave duration ≥120 ms associated with an amplitude ≥2.5 mV
- Biphasic P-wave (positive-negative) in lead V1 with the first deflection ≥1.5 mV and the terminal component with duration ≥40 ms and amplitude ≥1 mV
- Bifid P-wave with amplitude ≥2.5 mV and duration ≥120 ms in lead II
- P-wave with positive deflection ≥1.5 mV in lead V1 or V2 and a notched P-wave with duration ≥120 ms in limb leads, V5 or V6

2.4 Case 3

F.A.B., a 30-year-old female, is 36 weeks pregnant. On a routine examination, a 12-lead ECG was recorded (Fig. 2.3).

2.4.1 ECG Analysis

The ECG shows an ectopic atrial rhythm. The heart rate is 98 beats/min. It is possible to recognize a negative P-wave in DII, DIII, VF, and V3–V6 and positive in VL and VR. Its duration is 40 ms. PR interval is short (approximately 60 ms). QRS complex is narrow with normally orientated axis in frontal plane (about 90°). Ventricular repolarization and QTc interval (409 ms) are normal.

P-wave axis suggests that the atrial activation is spreading from below to upward. We could hypothesize a focus either in the low atrium or at high AV junction. A mid-junctional rhythm should not have any visible P-waves since they will be within the QRS due to a simultaneous activation of atria and ventricles. In low junctional rhythm, the P-wave usually appears after the QRS within the ST segment and is negative in the inferior leads.

2.4.2 Ectopic P-Waves

An ectopic atrial rhythm occurs when the atrial activations ensue from a focus other than the sinus node but localized within the atria. A 12-lead ECG can help in identifying specific sites or regions where the ectopic atrial excitation is starting from.

Sinus P-wave is typically characterized by a duration <120 ms, an amplitude <0.25 mV, and an axis included between 0° and +90° [5, 7].

To identify the origin of an ectopic atrial beat, it is necessary to examine first the P-wave axis.

P-wave direction in leads I and V1 should be used in discriminating right atrial from left atrial foci.

A negative or biphasic P-wave in leads I and aVL and positive in V1 suggest a *left* atrial origin (pulmonary veins). The inferior leads have to be evaluated to distinguish a superior from an inferior left atrial focus. A negative P-wave in leads II, III, and aVF indicates an inferior left atrial focus. A positive P-wave in the inferior leads suggests instead a superior focus position; a negative or biphasic P-wave in VL indicates a left superior

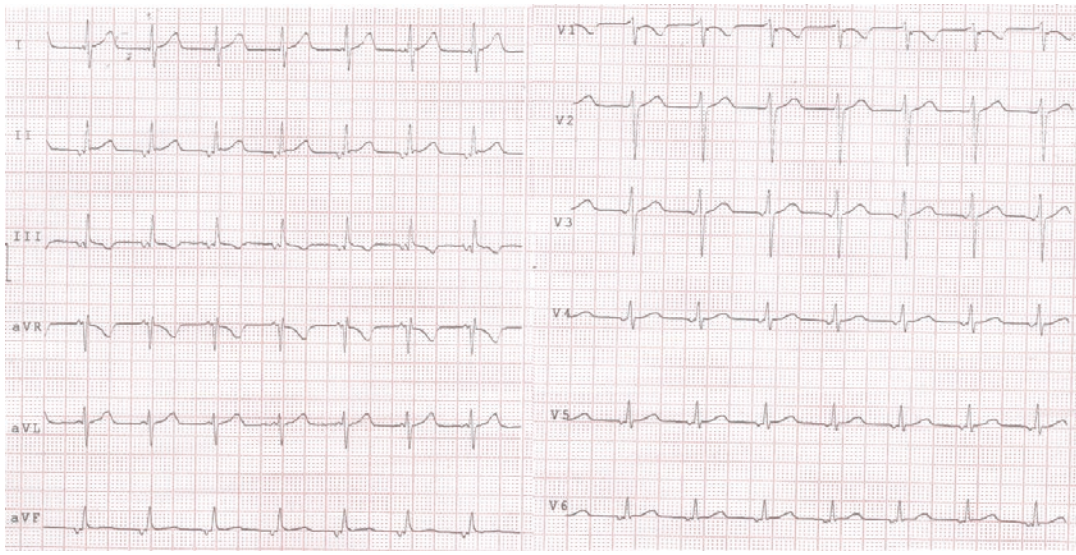

Fig. 2.3 Case 3: 12-lead ECG

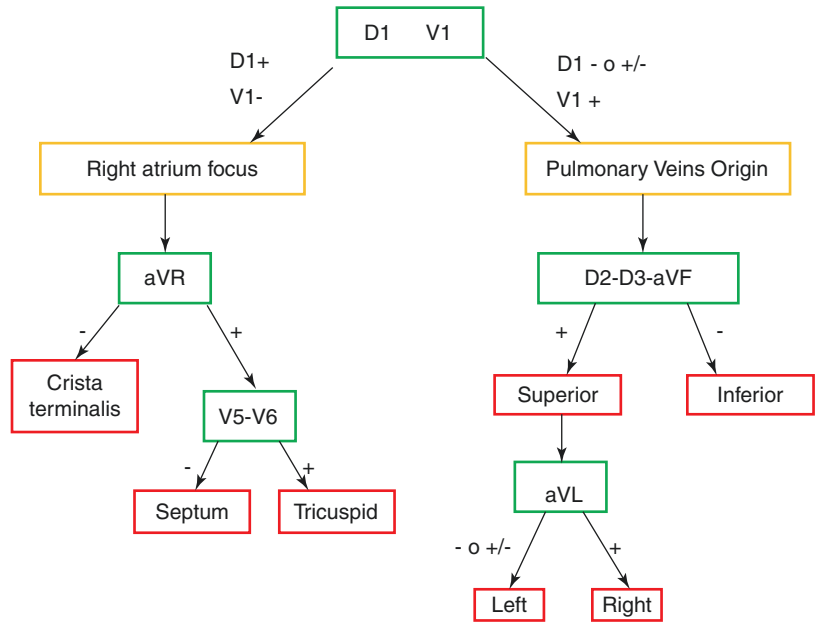

Fig. 2.4 Algorithm for the identification of ectopic atrial beat origin

site of origin, while a positive P-wave in the same lead has a right superior origin.

A positive P-wave in lead I and negative in V1 suggest a *right* atrial origin.

Thus, P-wave configuration in VR has to be examined first. If negative, the atrial activation begins close to crista terminalis; when positive then also leads V5 and V6 should be assessed; a positive P-wave in those leads is typical of a tricuspid site of origin, while a negative P-wave suggests a septal origin [7] (Fig. 2.4).

2.5 Retrograde P-Wave and Junctional Rhythm

In retrograde atrial activation, the atria are depolarized by a focus that origins in distal structures such as the atrioventricular junction or even the ventricles. This activation is characterized by a concentric down-up direction. P-wave shows thus an axis vertically orientated in the frontal plane (approximately −90°); the P is usually negative in the inferior leads and positive in VR, VL, and V1 (the latter is often tall and peaked). There is simultaneous depolarization of the atria that lead to a P shorter than the sinus. This differs from the low atrial activation where there is an eccentric depolarization, with an atrium activated before the other.

During a junctional rhythm, the relation between P-wave and QRS complex is variable, depending on the anterograde or retrograde conduction and on the location of the pulse source; hence, a P can precede, follow, or be simultaneous to QRS.

2.6 Wandering Pacemaker

The wandering pacemaker is a condition characterized by a progressive changing of P-wave morphology (until a maximum of three morphologies) and by a slight different PP interval on the surface ECG.

This phenomenon is due to a progressive migration of the site of atrial activation from an anatomic site to another. In the past, this finding was attributed to a progressive migration of the P-wave from the sinus node to the AV junction; actually, this condition seems more likely due to fusion between two activation fronts, one starting from sinus node and the other from AV junction, coronary sinus, or tricuspid valve [7]. Typically, the P morphologies pass from positive to negative in lead II and also to intermediate morphologies, usually being positive in lead I.

This condition is usually found in young people, especially with a vagal hypertonia, which is responsible for the physically slowing of sinus rhythm, allowing an ectopic rhythm to emerge.

2.7 Paced P-Wave

In the presence of a paced rhythm, the atrial depolarization, which begins after a definite delay from the atrial stimulus, could not be visible on a surface ECG, especially if there are atrial conduction delays that make the atrial activation vectors of low amplitude and/or coincident with the following ventricular activities. Polarity and morphology of P-waves vary according to the pacing site [7]:

- The conventional site for atrial pacing is the *right atrial appendage*: the atrial activation vector is oriented downward to the left, and paced P-wave assumes a morphology similar to sinus P-wave (positive in I, II, III, and VF; positive or biphasic in VL; negative in VR).
- Pacing of *Bachmann bundle*, which is located at the upper atrial septum at the roof of the right atrium, leads to a positive P-wave in the inferior limb leads and a small negative deflection in lead V1 (where normally left- versus right-sided atrium activity is distinguished), since the left atrium gets stimulated little earlier or simultaneously with the right atrium.
- With *coronary sinus* pacing, the atrial activation starts at the lower zone of the left atrium; thus, the activation vector is oriented upward to the right (P-wave negative in I, VL, II, III, and VF and positive in VR).
- Low septal or *coronary sinus ostium* pacing produces an activation vector less deviated to the right (about −90°, retrograde concentric activation of the atria); thus, P-wave is negative in the inferior leads, isodiphasic in I, and positive in VL.

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PR Segment: Cardiac Implications

3

Silvia Cesini, Simone D'Agostino,
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3.1 Case 1

A 66-year-old man coming as out-hospital control reported a progressive exercise dyspnea starting few weeks earlier. He had a history of arterial hypertension (treated with ACE-I) and was obese. A 12-lead ECG was recorded (Fig. 3.1).

3.1.1 ECG Analysis

Figure 3.1 shows an irregular rhythm, with wide QRS complexes and an average heart rate of 70 bpm. QRS have a right bundle branch block morphology, 130 ms width. QRS axis is indeterminate. P waves are not clearly visible. There are negative T-waves from V1 to V4, possibly secondary to the complete RBBB.

Diagnosis was atrial fibrillation with a mean ventricular response, associated with a complete right bundle branch block. Because of the systemic cardioembolic risk (CHA_2DS_2-VASc score 2), the patient started oral anticoagulation therapy, and an electrical cardioversion was programmed 1 month later.

Figure 3.2 shows the ECG after cardioversion. P waves are positive in inferior leads and negative in aVR: there is a sinus rhythm. Heart rate is 55 bpm. QRS complexes are wide and have the same morphology and axis of the ECG before cardioversion. The P/QRS ratio is 1:1, and PR interval is prolonged (220 ms). The patient didn't take any antiarrhythmic drugs by that time.

Some previous ECGs (recorded 2 years before) also showed a first-degree AV block, with the same PR duration. One week after the electrical cardioversion, the patient had an early AF recurrence.

3.1.2 First-Degree Atrioventricular Block and Atrial Fibrillation

PR interval reflects the time needed for an electrical impulse to be transmitted from the sinus node to the ventricles, therefore representing an integration of informations about different sites of the conduction system of the heart, such as the atria, the atrioventricular node, and the His bundle. On the surface ECG, PR segment is defined as the interval measured from P-wave onset (junction between the T-P isoelectric line and the beginning of the P-wave deflection) to the beginning of the QRS complex [1]. PR interval usually shows a circadian and heart rate-dependent variation in healthy subjects (i.e., longer PR interval at night) and may change over time [2]. We use to

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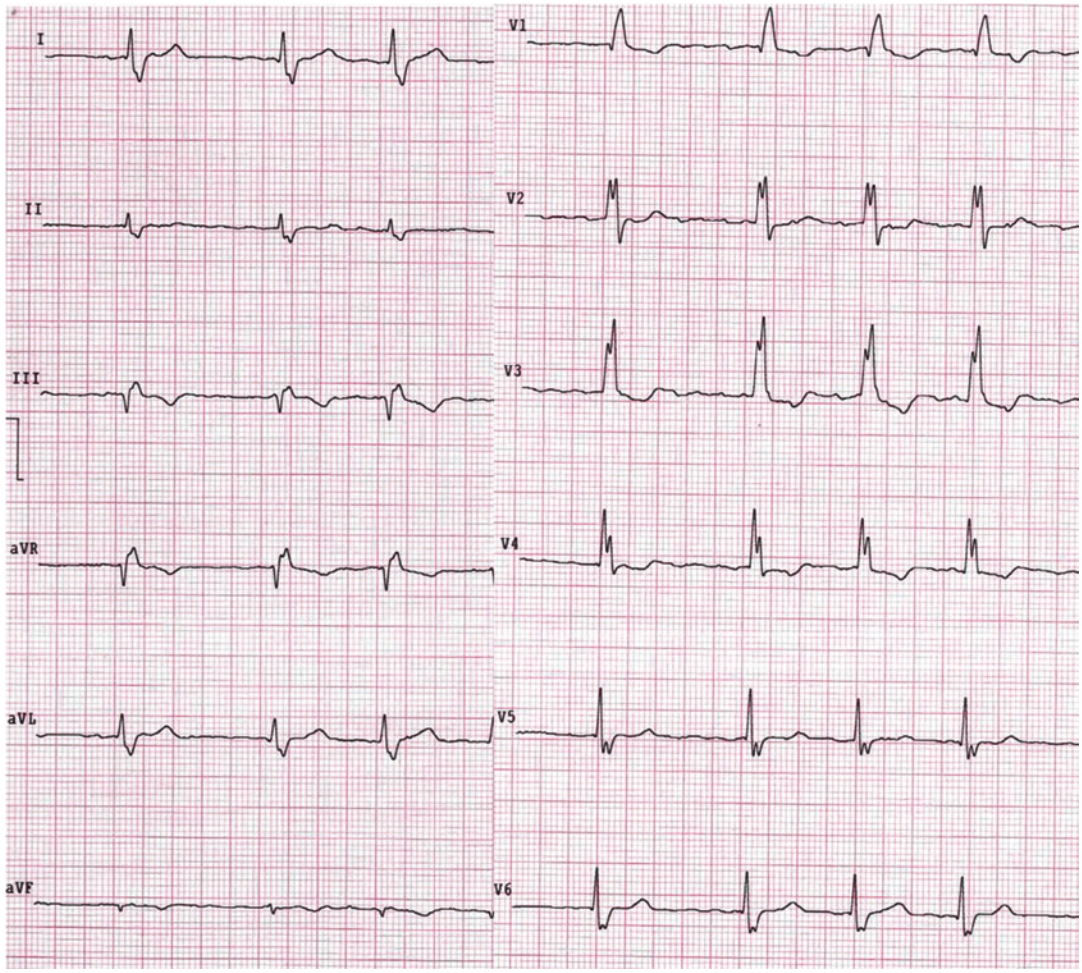

Fig. 3.1 Case 1, 12-lead ECG

define a long PR when it is longer than 200 ms or a short PR when it is shorter than 120 ms.

A first-degree AV block is more common in subjects ≥60 years old (prevalence of 6%), while it is relatively rare among the younger population.

Case 1 is an example of first-degree atrioventricular block associated with atrial fibrillation.

Atrial fibrillation and its adverse outcomes as stroke, heart failure, and dementia might be associated to abnormal atrioventricular conduction. A recent meta-analysis by Kwok et al. has proposed the PR duration as a prognostic predictor for AF incidence/risk [3]. Some researchers demonstrate that prolonged PR interval >200 ms is linked to higher AF incidence [4, 5].

Fibrotic changes and structural remodeling of atrial myocardium are associated with AF onset [6]. The same remodeling processes could also decrease the atrioventricular conduction velocity, thus causing PR prolongation. So "advanced physiological age" (e.g., fibrosis and calcification) could be the pathological substrate of both PR prolongation and AF.

PR interval prolongation has been also proposed as a new element for improving the predictive power of CHADS2 and CHA2DS2-VASc scores in order to foresee new onset of

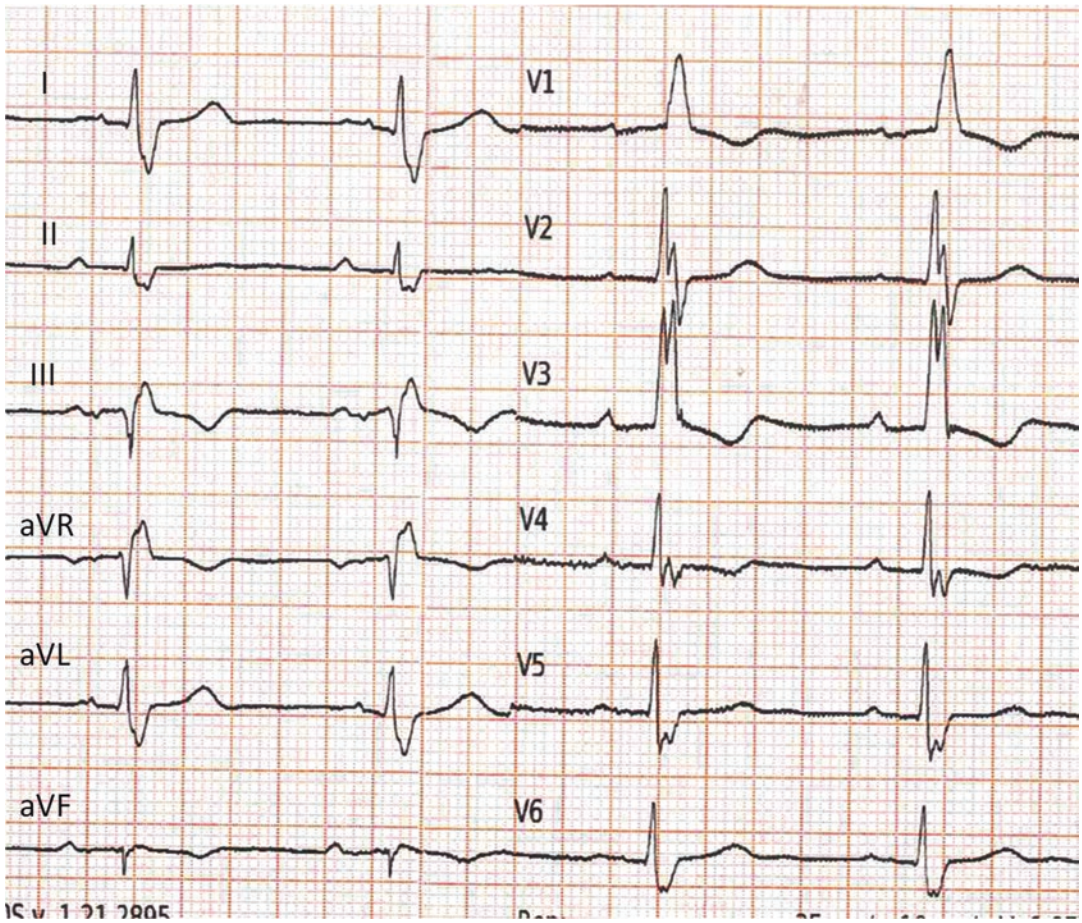

Fig. 3.2 Case 1, 12-lead ECG after electrical cardioversion

cardiovascular events in high-risk patients without clinical AF [7]; however more study information are mandatory to clarify this last issue.

The matter is controversial since some researcher did not find any association between prolonged PR interval and increased mortality or hospitalization secondary to AF, stroke, or heart failure [8]. From these last studies emerges that only the P length—and not the PR interval prolongation—is associated with AF adverse events.

Paradoxically, also short PR interval (<120 ms) was identified in some studies as predictor for AF [5]. The association between a short PR interval and AF is not intuitively explained. A possible explanation is based again on P-wave duration that could be the most relevant part in the PR interval and may actually be linked to adverse outcomes.

Another important ECG parameter in predicting AF onset is "P-wave dispersion," defined by subtracting minimum P-wave duration from the maximum in any of the 12 ECG leads (considered increased at a value close to 40 ms). It is also a marker of atrial remodeling [9, 10].

Both mechanisms explained above reflect prolongation of intra-atrial and interatrial conduction, leading to higher risk of arrhythmias.

By the end it is likely that the association between PR interval and the risk of developing atrial fibrillation could develop as a U-shaped curve, with higher risk in patients with long and short PR intervals [5, 11] (see also Sect. 3.4).

3.2 Case 2

A 75-year-old man was admitted at the emergency department after a sudden loss of consciousness while he was resting at home. He was not on medical treatment and this was his first syncopal episode (Fig. 3.3).

3.2.1 ECG Analysis

The ECG (Fig. 3.3) showed a sinus rhythm of 80 bpm. PR segment is prolonged (280 ms). Every P wave is followed by wide QRS complexes with right bundle branch and left anterior fascicular block morphology, with a duration of 130 ms (bifascicular block). There are also specific repolarization abnormalities.

During the ECG continuous monitoring, he developed a paroxysmal complete AV block, symptomatic for pre-syncope. An electrophysiological study performed before implanting a permanent PM confirmed both nodal and infranodal conduction delays. A bicameral pacemaker was then implanted.

3.2.2 Different Localizations of the First Atrioventricular Block and Prognostic Implications

In first-degree atrioventricular block, there are different possible sites of conduction delay; those specific sites may be guessed looking at the surface ECG especially the amount of PR prolongation and QRS duration length [12]. In particular, the presence of a very long (>300 ms) or highly variable PR interval—associated with a narrow QRS—suggests mainly that the site of delay is the atrioventricular node (AVN; 87% of the patients with a narrow QRS complex and more

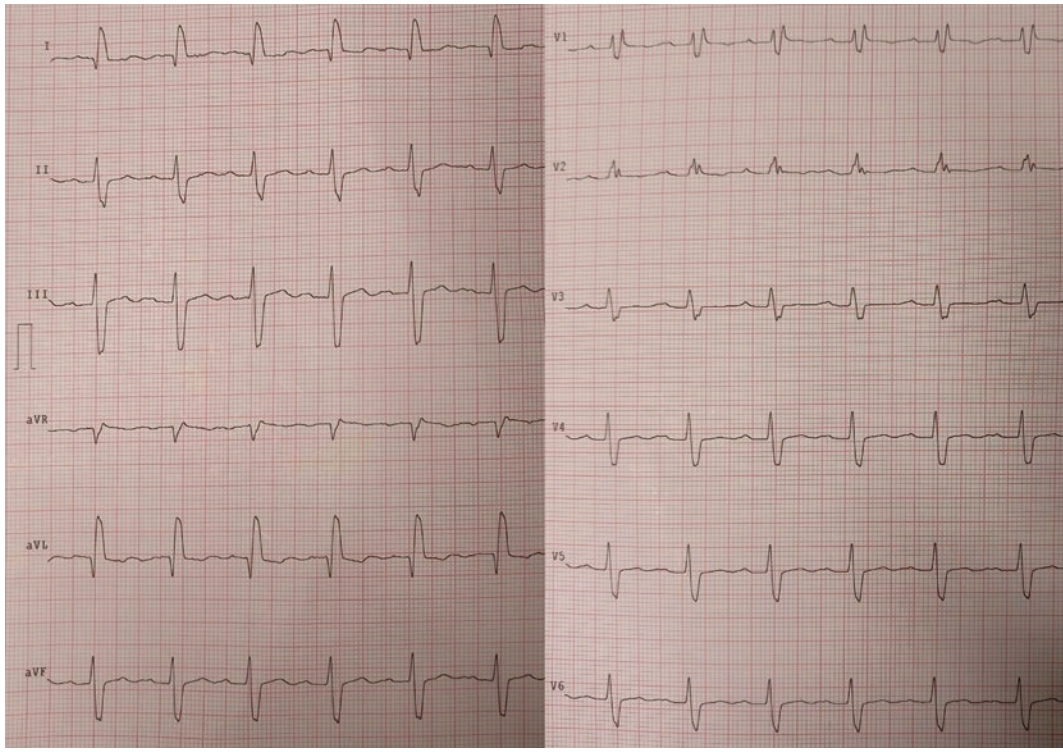

Fig. 3.3 Case 2, 12-lead ECG

than 90% of the patients with a PR interval longer than 300 ms have AVN significant conduction delay) [12, 13]. However a first-degree AV block can be also related to intra-Hisian or His-Purkinje system (HPS) disease; in the presence of a wide QRS, first-degree AV block is due to an infranodal conduction delay in 45% of the cases [12]. Infranodal first-degree AV block has obviously a worse prognosis and, if occurs together with a bundle block (especially with right bundle block and left anterior fascicular block) and with symptoms of syncope, usually requires an electrophysiological study and eventually a pacemaker implant (as in case 2). Finally we have to remember that a first-degree AV block can also be caused by an intra-atrial or interatrial conduction delay that is visible on the surface ECG as a prolonged P wave rather than a PR lengthening.

Cheng et al. suggest that those individuals with PR interval prolongation have a threefold risk of future pacemaker implantation, despite adjustment for cardiovascular risk factors, age, or QRS duration [1]. Also progression of the PR interval delay may be related to primary or secondary diseases. The first situation deals with idiopathic causes, which are generally referred to fibrosis that actually is a dynamic process that can grow over time through repeated pathological insults [3, 14]. Other very common conditions are coronary heart disease, inflammation, calcification, neuromuscular disorders, and infiltrative diseases. Finally a first-degree AV block may also be caused by an enhanced vagal tone that is usually typical of young people, especially athletes, and may disappear at follow-up or after detraining (see also Chap. 8).

3.3 Case 3

A 61-year-old man with a history of coronary heart disease (previously anterolateral STEMI treated with PCI and stent on LAD2), arterial hypertension, dyslipidemia, and end-stage chronic kidney disease went to the emergency department for class III dyspnea and orthopnea. The ECG is shown in Fig. 3.4.

3.3.1 ECG Analysis

This ECG shows sinus tachycardia, with a heart rate of 105 bpm. P waves are positive in inferior leads, with a 50 ms duration, while are biphasic in V1 with deepening of the terminal negative portion (left atrial enlargement; see Chap. 2). PR interval is short (100 ms) and the P/QRS ratio is 1:1. QRS axis is −15°. There are q waves in the anterolateral

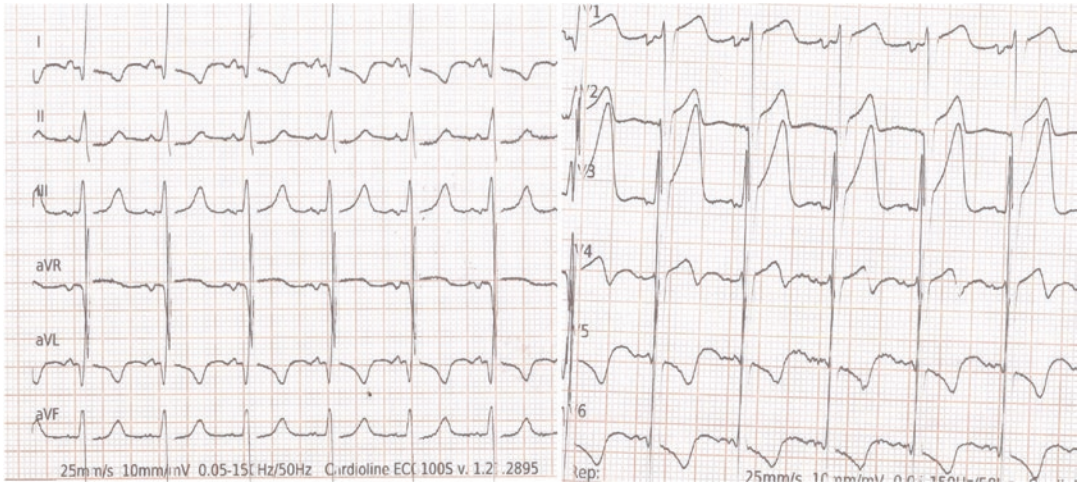

Fig. 3.4 Case 3, 12-lead ECG

leads (I, aVL, V5–V6) with the QRS duration of 110 ms. Repolarization is abnormal, with ST elevation in lead V1 (2 mV), V2 (4 mV), and V3 (6 mV), ST depression with negative T-waves in the lateral leads (I, aVL, V5–V6), diphasic T-waves in V4, and hyperacute T-waves in V2–V3. There are also signs of left ventricular hypertrophy (R in aVL >11 mV and S in V1+R in V5 >35 mm).

In the laboratory tests, elevation of cardiac troponins and BNP was reported. The echocardiogram showed an eccentric hypertrophy with a moderate systolic dysfunction (LVEF = 35–40%); there were apex akinesia and hypokinesia of the inferior interventricular septum and of the lateral and inferior walls at the medium-basal segments.

The patient was admitted to the cardiology department with a diagnosis of acute coronary syndrome without ST elevation and underwent percutaneous revascularization with implant of three DES on LAD1, LAD1–LAD2, and CX.

The ECG of the Fig. 3.5 was recorded after 7 days from the acute coronary syndrome. It shows a regular sinus rhythm, with an average heart rate of 85 bpm. PR interval is 120 ms (at the lower limit of the normal value). After the fifth QRS complex, there is a premature atrial beat not conducted to the ventricles that is visible on the apex of the T-wave (P on T phenomenon). QRS and repolarization patterns are similar to the previous ECG (see Fig. 3.4).

3.3.2 Short PR and Coronary Artery Disease (CAD)

A short PR interval is generally associated with signs of ventricular pre-excitation (Wolff–Parkinson–White syndrome) or, less frequently, to Lown–Ganong–Levine syndrome or "syndrome of enhanced atrioventricular nodal conduction." However, several individuals can have short isolated PR interval as an expression of normal atrioventricular nodal physiology. The clinical implications of a short PR interval in the absence of a ventricular pre-excitation are still debated.

In 2013 the first results from the Copenhagen ECG study demonstrated the correlation between short PR interval and recurrent atrial fibrillation in women [5].

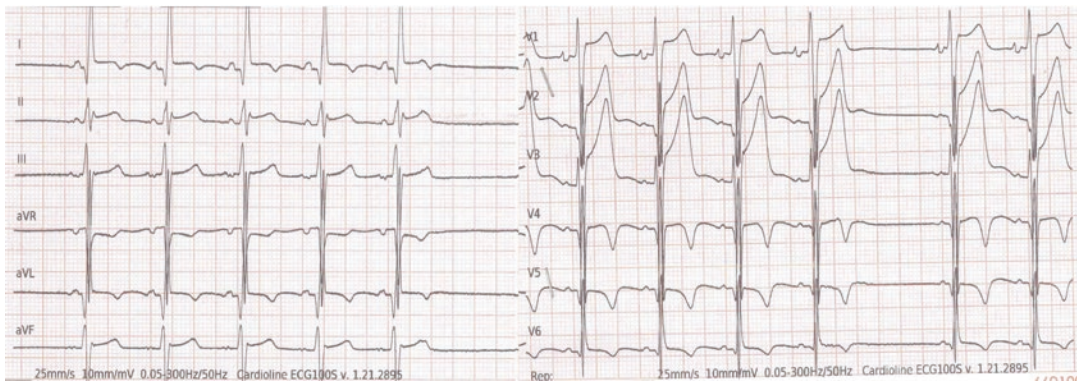

Fig. 3.5 Case 3, 12-lead ECG, 7 days later

Holmqvist et al. reported data from the Duke Databank for cardiovascular disease. A total of 9637 patients, with significant stenosis (>50%) in at least one native coronary artery, were included. They were stratified into three groups based on PR interval length (short, PR <120 ms; normal, PR between 120 and 200 ms; long, PR >200 ms). It was demonstrated that patients with short PR had the highest risk of all-cause mortality, death or stroke, and cardiovascular death or cardiovascular rehospitalization; there was a U-shaped relation between the risk of these endpoints and PR interval length. There were no differences in relation to sudden cardiac death. This relationship was also confirmed after adjustment for relevant covariates; an increased risk of cardiovascular events was associated to 10 ms PR decrements only for PR intervals <162 ms (all-cause mortality, HR 1.057, 95% CI 1.019–1.096, $p < 0.0030$; composite of death or stroke, HR 1.047, 95% CI 1.011–1.085, $p < 0.0095$; and composite of cardiovascular death or cardiovascular rehospitalization, HR 1.032, 95% CI 1.002–1.063, $p < 0.0387$) [11].

In 2017 a new extended Copenhagen ECG study published similar data in a larger population of 293.111 individuals; those were divided into seven groups based on PR interval distribution (cutoff at the 5th, 20th, 40th, 60th, 80th, and 95th percentiles). A short PR interval (<125 ms; hazard ratio [HR], 1.23; 95% confidence interval [CI], 1.08–1.41; $P = 0.001$) as well as a long PR interval (>200 ms; HR, 1.23; 95% CI, 1.14–1.32; $P < 0.001$) was associated with a higher risk of cardiovascular death after multivariable adjustment. In particular long PR intervals were associated with increasing risks of heart failure (>200 ms; HR 1.31; 95% CI, 1.22–1.42, $p < 0.001$) and pacemaker implantation (>200 ms; HR 3.49; 95% CI, 2.96–4.11, $p < 0.001$) [15].

Conclusion

PR lengths out of normal limits are not always a benign condition as previously believed.

Several studies demonstrated a strict linkage between PR prolongation and risks of atrial fibrillation; this may be expression of an underlying atrial high fibrosis level and a generalized remodeling.

Furthermore in heart failure, a long PR interval is likely to reflect widespread electrophysiological abnormalities, including atrial enlargement. Long PR may also contribute in reducing cardiac output, since a long delay between atrial and ventricular systoles may favor in diastolic AV regurgitation.

PR prolongation may underlie a major conduction disturbance such as more advanced types of AV blocks or bundle blocks, with consequent pacemaker implant.

A short PR interval instead has been shown to be a predictor of AF and be linked to an increased incidence of ischemic heart disease.

In Table 3.1, we summarized the main studies relating PR intervals to possible adverse outcomes.

In conclusion PR is an important clue for prognostic implications, and therefore a first-degree heart block shouldn't automatically be marked as a benign condition. On the contrary a closer follow-up and monitoring of those patients might be advisable, in order to avoid future negative events.

Table 3.1 Main studies relating PR interval to adverse outcomes

Study ID	Study design; years; country	Partecipants (*n*)	Age (avg)	Partecipants inclusion criteria	PR duration	Outcome
Framingham Heart Study [16]	Prospective cohort study; 1968–2007; USA	7.575	47	Community based individuals	PR >200 ms	AF, pacemaker implantation, and all-cause mortality
Heart and Soul Study [17]	Prospective cohort study; 2000–2002; USA	938	66	Patients with stable coronary heart disease	PR ≥220 ms	HF and death
Health, Aging and Body Composition Study [18]	Prospective cohort study; 1997–2011; USA	2.722	74	Random sampling of community patients	PR >200 ms	Heart failure and AF in older adults
Copenaghen ECG Study [5]	Prospective cohort study; 2001–2010; Denmark	288.181	54	Patients from primary care who had ≥1 ECG recorded	–PR ≥95th percentile (≥196 ms for women, ≥204 ms for men) –PR <5th percentile (≤121 ms for women, ≤129 ms for men)	– AF in women and men – AF in women
Busselton Health Study [19]	Prospective cohort study; 1994–2010;	4.267	52	Community-based adults	Short PR (length not clearly defined)	Incident atrial fibrillation
Kobayashi et al., Circulation 2014 [20]	Prospective cohort study; 1989–1994; Japan	5.425	56.5	Japanese urban adults without prior cardiovascular disease	PR >220 ms	All cardiovascular disease, CHD, stroke, cerebral infarction
Uhm et al., J Hypertension 2014 [21]	Retrospective cohort study; unclear; Korea	3.816	61	Adults with hypertension and sinus rhythm on first ECG	PR >200 ms	Advanced AV block, sick sinus syndrome, atrial fibrillation, LV dysfunctions
Duke Databank for CV disease [11]	Prospective cohort study; 1989–2010	9.637	63	Patients with CAD	PR <162 ms	All-cause mortality

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The Difficult Extra Beats Cases

4

Erika Baiocco, Laura Cipolletta, and Daniele Contadini

4.1 Case

A 36-year-old man was referred to our hospital because of a progressive onset of dyspnea during mild exercises (NYHA class III); symptoms started in the previous 2 months. He also reported sometime palpitations for just few seconds. He was a smoker (ten cigarettes/day) and had a familiar story of ischemic heart disease (father suffered from two myocardial infarctions at age of 48).

A surface ECG was recorded and reported in Fig. 4.1.

4.1.1 ECG Analysis

Sinus rhythm, heart rate 70 bpm, normal atrioventricular conduction (PQ 120 ms), cardiac electrical axis +30°, normal interventricular conduction (QRS width 80 ms), normal repolarization, QTc 430 ms. The sinus rhythm was interrupted by isolated and monomorphic premature ventricular complexes (PVCs) with an electrical QRS axis of +100° and a PVC-QRS width of 140 ms; the PVC-QRS morphology was of a left bundle branch block (LBBB) with a precordial lead PVC-QRS transition in V4.

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The relatively narrow PVC-QRS (140 ms) and the absence of notch and slurring of the QRS could lead to hypothesize a non-epicardial PVC focus. The LBBB-PVC-QRS morphology suggests a right ventricular starting site, while the inferior axis suggests an outflow tract of origin [1, 2]. A precordial lead transition in V4 is usually associated with a right ventricular outflow tract origin (RVOT). The relatively narrow pvc-QRs duration suggest an origin from septal portion of RVOT. The proximity of this region to the His bundle justifies the relatively narrow PVC-QRS.

The final ECG diagnosis was *sinus rhythm with normal atrioventricular and intraventricular conduction and normal repolarization interrupted by PVC originating from the posterior portion of RVOT.*

Ten days before the hospitalization, the patient was studied with an ECG 24-h Holter because of palpitations. The exam showed a persistent sinus rhythm frequently interrupted by premature ventricular complexes (PVCs). The number of PVCs was 31,640 in 24 h with a PVC burden of 34%. The PVCs were monomorphic and isolated or coupled, rarely in triplet. On the ECG monitoring during the hospitalization, the same PVC number was documented (Fig. 4.2).

Transthoracic echocardiography (TTE) showed a diffuse hypokinesia in all the segments of left ventricular wall with a left ventricle

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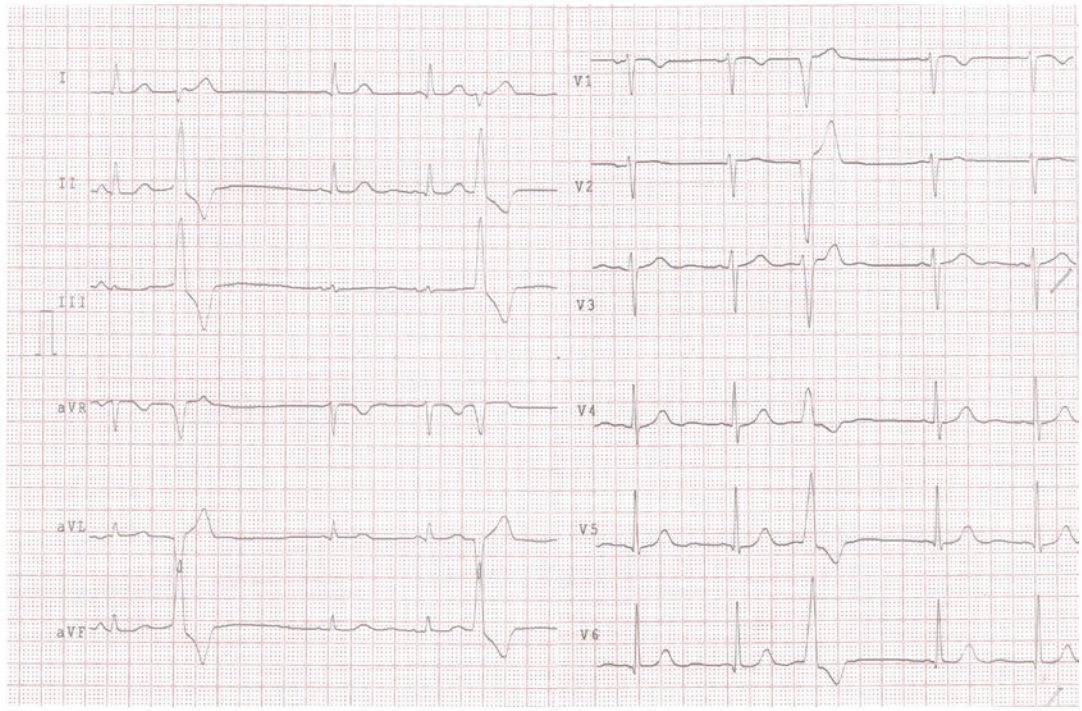

Fig. 4.1 Case 12-lead ECG

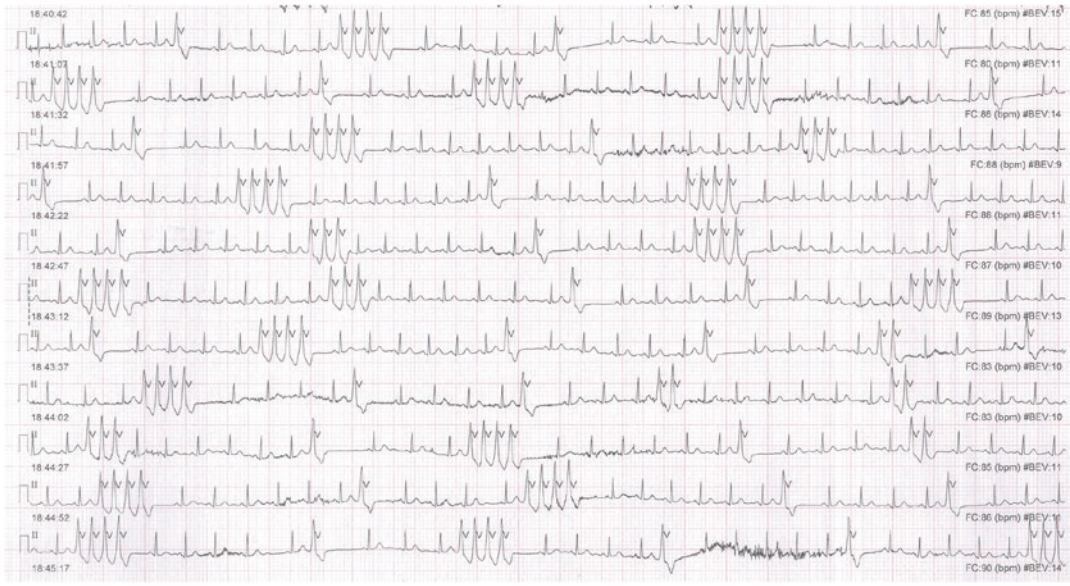

Fig. 4.2 Case ECG monitoring

ejection fraction (LVEF) of 42%. The left ventricle (LV) was mildly dilated. The walls' ventricular thickness was normal. A mild to moderate mitral regurgitation was present. Right ventricle sizes and function were also normal.

A coronary angiography and a cardiac magnetic resonance imaging with gadolinium were performed in order to exclude an ischemic or structural cardiomyopathy (i.e., arrhythmogenic right ventricular cardiomyopathy).

The *coronary angiography* did not reveal any appreciable coronary artery stenosis.

The *cardiac magnetic resonance* imaging confirmed the echocardiographic findings. Not any delayed myocardial enhancement was detected.

Furthermore, laboratory tests, comprehensive of catecholamine dosage and thyroid activity, resulted normal. It was then hypothesized that PVCs could have been the cause of the LV dysfunction instead of being the effect. We proposed to the patient a double option therapy: antiarrhythmic drugs or PVC focus ablation. The patient chose for ablation. The ablation of inferior right ventricle outflow tract focus was done and resulted effective. At follow-up, a 24-h Holter ECG and a TTE evaluated after 2 months from discharge showed absence of PVCs and a complete recovery of the LVEF to normal values.

4.1.2 Definition

Premature complexes may have a supraventricular origin (from the atria or from the atrioventricular junction) or may originate below the bifurcation of the His bundle (from the bundle branches or from the ventricular "common" myocardium).

PVCs may have an irregular or a regular distribution (a bigeminal rhythm could be present when PVC occurs every two sinus beats, trigeminal every three beats, and quadrigeminal every four beats). In the same patient, PVCs can have one morphology or more than one (monomorphic PVC or polymorphic PVC, respectively). Often the morphology of the QRS of PVC can be useful to define the site of origin, especially in patients without a structural heart disease. As a general rule, a left bundle branch block (LBBB) pattern-PVC takes its origin from the right ventricle and a right bundle branch block (RBBB) pattern-PVC from the left ventricle. QRS axis of the PVC allows to identify a more precise site of origin within ventricles [1, 2].

4.1.3 Epidemiology

PVCs are very common in the general population. In a study by Kennedy et al., 24-h Holter ECG monitoring of a healthy population showed a prevalence of PVCs of 40–75%; frequent PVCs (>60/h) were present in 1–4% [3]. The presence of PVCs increases with age: in a ECG ambulatory recording, it was less than 1% in a population younger than 11 years and 69% in individuals older than 75 years [4]. The prevalence of frequent PVCs increases in presence of a structural heart disease, particularly coronary artery disease. The Framingham Heart Study showed that frequent and complex PVCs (>30/h with multiple morphologies) in men with coronary heart disease increased the relative risk of all-cause mortality of 2.3 [5]. Finally special populations such as athletes have the same prevalence of PVBs as healthy individuals. However in some athlete study, a lightly higher prevalence was reported [6].

4.1.4 Mechanism

There are three main mechanism bases of PVCs:

1. Abnormal automaticity: the cells of the cardiac conduction system have a normal automatism, which is the capability to spontaneously depolarize when requested. Abnormal automaticity may derive from cells of "common" myocardium that have reduced diastolic membrane potentials (−50 mV) and consequently an "easier" but slower depolarization.
2. Reentry: to generate a reentry, it is mandatory an anatomical or functional circuit (where the impulse can "run"), with two or more pathways with different refractoriness and conductive velocity that generates an unidirectional block as basal reentry mechanism. In this condition, the impulse is blocked in one pathway and propagates slowly into the other with subsequent returning via opposite direction through the blocked pathway.
3. Triggered activity: it is caused by afterdepolarizations, which are oscillations in membrane potential that sometime can reach the threshold of activation. The afterdepolarizations can be divided into early afterdepolarizations (EADs) and delayed afterdepolarizations (DADs). EADs occur in the phases 2 and 3 of action potential, are

mainly pause dependent, and are involved in the genesis of ventricular arrhythmias in long QT syndrome. DADs occur in phase 4 of action potential, mainly tachycardia dependent, and involved in the genesis of ventricular arrhythmias during glycoside intoxications, electrolyte imbalances, and increased catecholamine conditions. They may have a role in adenosine-sensitive right ventricle outflow tract (RVOT) tachycardias [2, 7, 8].

4.1.5 PVCs and Cardiomyopathy: Chicken or Egg?

It is well known how cardiomyopathies may be associated with an increased number of PVCs. Ventricular arrhythmias, including PVCs, may be related also to the ischemic heart disease. The presence of ventricular arrhythmias in patients with left ventricular dysfunction and a previous myocardial infarction is accomplished with a 2-year mortality rate of 30% [9–14]. In addition, some studies showed that PVCs (>10/h) in patients with previous myocardial infarction have a poor prognosis and a worse mortality rate at 6 months follow-up [15–17]. Ventricular arrhythmias, including PVCs, are however also present in patients with nonischemic cardiomyopathy. Also in this population, a higher rate of mortality for sudden cardiac death (SCD) was demonstrated [18]. PVCs in structural heart disease are considered a marker of severity of the underlying cardiomyopathy [19].

In patients without significant structural heart disease, the presence of PVCs may also have some clinical impact. There are studies [3] and meta-analysis [20] that found a correlation between PVCs and a higher rate of SCD and all-cause mortality in this apparent "normal" population. In these patients, it is not clear whether PVCs are the first sign of a subclinical cardiomyopathy or whether PVCs are the cause of future development of heart disease. In the last years, the scientific interest is growing toward patients with frequent PVCs and a left ventricular dysfunction. A new concept was introduced: the PVC-induced cardiomyopathy (PVC-CMP).

This "disease" was defined: "presence of frequent PVCs and left ventricular dysfunction in absence of another possible etiology of cardiomyopathy."

The reversibility of dysfunction after PVC suppression (via ablation or pharmacological treatment) is mandatory for this final diagnosis [21]. In clinical practice not all patients with frequent PVCs develop a cardiomyopathy. Some predictors or risk factors of PVC-CMP have been proposed and are the following:

1. *Frequency and burden*: A frequency of 10,000 PVCs in 24 h or a PVC burden of 20% seems to be sufficient to develop the PVC-CMP [22], even if some authors demonstrated a PVC-CMP in population with less PVC number [23–25]. A precise threshold does not exist, probably because of interaction of other risk factors.
2. *Time duration*: the probability of development of PVC-CMP is directly correlated with the time onset. A patient with frequent PVC for a long time will generate more easily a left ventricular dysfunction. Several studies suggest a time-dependent mechanism [23, 24, 26, 27].
3. *PVC-QRS length*: a wide PVC-QRS could be associated with a cardiomyopathy development. A longer QRS prolongation, a higher likelihood of PVC-CMP. A 150 ms length seems to be an accurate cutoff (specificity 52%, sensitivity 80%, AUC 0.66) [23, 26, 27].
4. *Site of origin and morphology*: there are contrasting data about the different correlations between the LBBB and RBBB morphology of PVC-QRS and the cardiomyopathy [23].

- A higher risk of developing PVC-CMP was reported when the focus of origin of PVC is epicardial. The reason probably is the wider QRS of epicardial PVCs and the subsequent dyssynchronous contraction [24, 26, 27]. The standard 12-lead ECG can be useful to identify an epicardial origin of the PVC: long QRS duration, slurring, and notching of the initial part of QRS and a slow intrinsicoid deflection.

In the case of non-epicardial origin (in absence of structural cardiomyopathy), the PVC often starts from the sites of anatomic transition as the left and right outflow tract (usually near the aortic

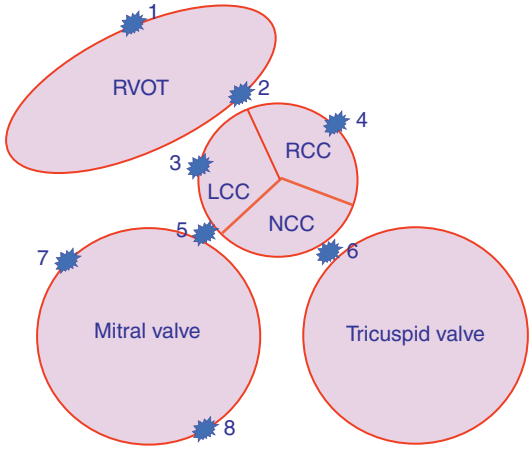

Fig. 4.3 Possible starting sites of non-epicardial PVC

and the pulmonary valve cusps, respectively), peri-atrioventricular valves zones, and papillary muscles and also from the conduction system (Fig. 4.3).

- A conduction system origin of the PVC is often caused by a reentry in one of the His bundles (anterior or posterior) and Purkinje's fibers. In this case the PVC can favor a fascicular ventricular tachycardia induction. In the 90–95% of cases, the left posterior fascicle is involved in the reentrant circuit. This specific origin of PVC can be suspected with a standard 12-lead ECG: the PVC-QRS has RBBB morphology and an axis high and leftward deviated (about −85°). Rarely the QRS might have a superior and right-deviated axis. In the remaining cases, the left anterior fascicle is part of the reentry. At a standard 12-lead ECG, this origin of PVC is characterized by RBBB morphology and inferior QRS axis (+90°, +100°).
- A narrow QRS is typical of the fascicular origin (usually <140 ms). This arrhythmia may appear in the young population (15–40 years); it has a good prognosis with a very low risk of SCD, and it is responsive to verapamil [28].

Other frequent anatomic origins of PVCs are the outflow ventricular tracts (VOTs, left (LVOT) and right (RVOT)). This last anatomic origin usually is not correlated with a structural cardiomyopathy, even if there are some rare exceptions as arrhythmogenic right ventricular cardiomyopathy, sarcoidosis, or regional myocarditis. Even if PVCs from VOTs usually have a benign prognosis, there are some described cases of PVC-induced left ventricular dysfunction [29]. Catheter ablation has been reported to be very effective to suppress PVCs from the VOTs. Some electrocardiographic clues might help to localize the arrhythmic focus in the ventricular outflow regions. In Fig. 4.3 the most frequent sites of PVCs origin from the VOTs are listed.

First of all it is fundamental to hypothesize when PVCs originate from LVOT or RVOT.

- PVC from LVOT has typically an inferior axis and a LBBB or RBBB morphology (Fig. 4.4).
- The RBBB morphology is very specific for LVOT origin.
- In case of LBBB morphology and LVOT origin, the precordial lead transition (first precordial leads with R/S waves ratio >1) occurs in earlier leads (V1, V2, or V3) (Fig. 4.5).
- When PVC originates from RVOT, the PVC-QRS has a LBBB morphology and inferior axis with a precordial lead transition at or after V3 [30, 31].
- In case of V3 transition, it is important to take into consideration all the small ECG variations caused by heart clockwise or counterclockwise rotation, respiratory acts, body size, thoracic conformation, and lead position. For this reason some authors proposed an ECG algorithm based on the PVC-QRS and the sinus rhythm (SR) QRS.
  When the precordial lead transition is V3, they suggest calculating the V2 transition ratio: R+R/S of PVC-QRS in V2 lead divided by the R+R/S of SR-QRS. A V2 transition ratio ≥0.6 is predictive of LVOT origin (sensitivity 95%, specificity 100%, AUC 0.992, positive predictive value 100%, negative predictive value 95%) [32]. An example of the application of V2 transition ratio is in Figs. 4.6 and 4.7.
- A qualitative observation of precordial lead transition of PVC-QRS compared to SR-QRS was also suggested. When PVC-QRS transition occurs at or before SR-QRS transition is likely LVOT origin (sensitivity 47%,

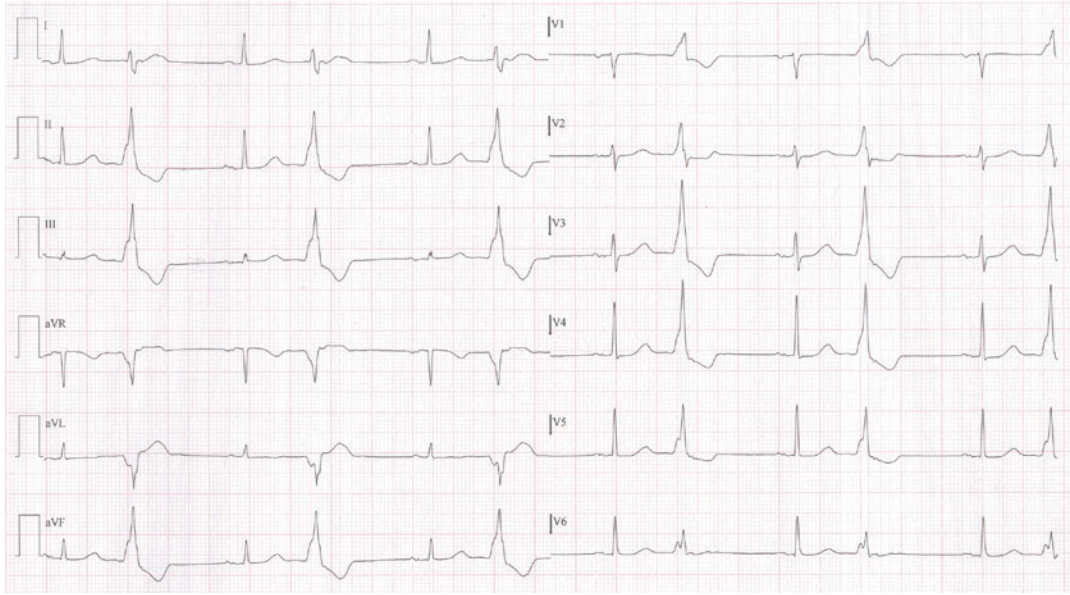

Fig. 4.4 PVC from LVOT: 12-lead ECG

specificity 64%). On the other hand, a PVC-QRS transition later than SR-QRS transition indicates a RVOT origin (sensitivity 19%, specificity 100%); this last case rules out a LVOT origin [32]. The knowledge of a "left or right heart origin" of PVC is primarily important in order to guide interventional procedures.

Furthermore there are other few ECG signs to hypothesize a more specific VOT-PVC origin.

- A wide QRS (>140 ms) with notching or RR' or Rr' morphology in inferior leads suggests an anterior free wall of RVOT origin (no. 1 in Fig. 4.3).
- A posterior RVOT wall (no. 2 in Fig. 4.3) origin is characterized by an earlier precordial lead transition and a less wide QRS than an anterior free wall one (Fig. 4.1).
- A narrow QRS (<140 ms) and the absence of notching in leads II and III are typical for anterior septal or para-Hisian origin; here the QRS is narrow for the conduction system proximity (no. 6 in Fig. 4.3).
- An origin from left or right coronary cusps (LCC or RCC) usually has precordial lead transition in V2–V3 (nos. 3 and 4 in Fig. 4.3) and never has R wave in a VL lead [33].
- A LCC origin is suggested by more prominent R or wave in V1 or V2, by a W- or M-shaped QRS in V1, and by a narrower QRS than a RCC origin.
- A R wave ratio in leads III and II (III/II) >0.9 predict a LCC origin (sensitivity 100%, specificity 64%, positive predictive value 80%, negative predictive value 100%) [33]. A non-coronary cusp (NCC) origin is very rare.

Other frequent PVC origins are from aorto-mitral continuity (no. 6 in Fig. 4.3) and peri-mitral valve region (nos. 7 and 8 in Fig. 4.3). PVCs with VOT-origin pattern cause less frequently PVC-CMP [26].

5. *Different morphologies*: polymorphic PVCs (two or more PVC-QRS morphologies in the same patient) are associated with a higher risk of developing a PVC-CMP.
6. *Interpolated PVCs*: this specific type of PVC is "sandwiched" between two consecutive sinus beats without altering the sinus rhythm. In some studies the presence of interpolated PVCs was a predictor of risk of PVC-CMP [34]. Its precise reason is not known. The authors hypothesized an uncorrected atrio-ventricular contraction synchronism. PR of

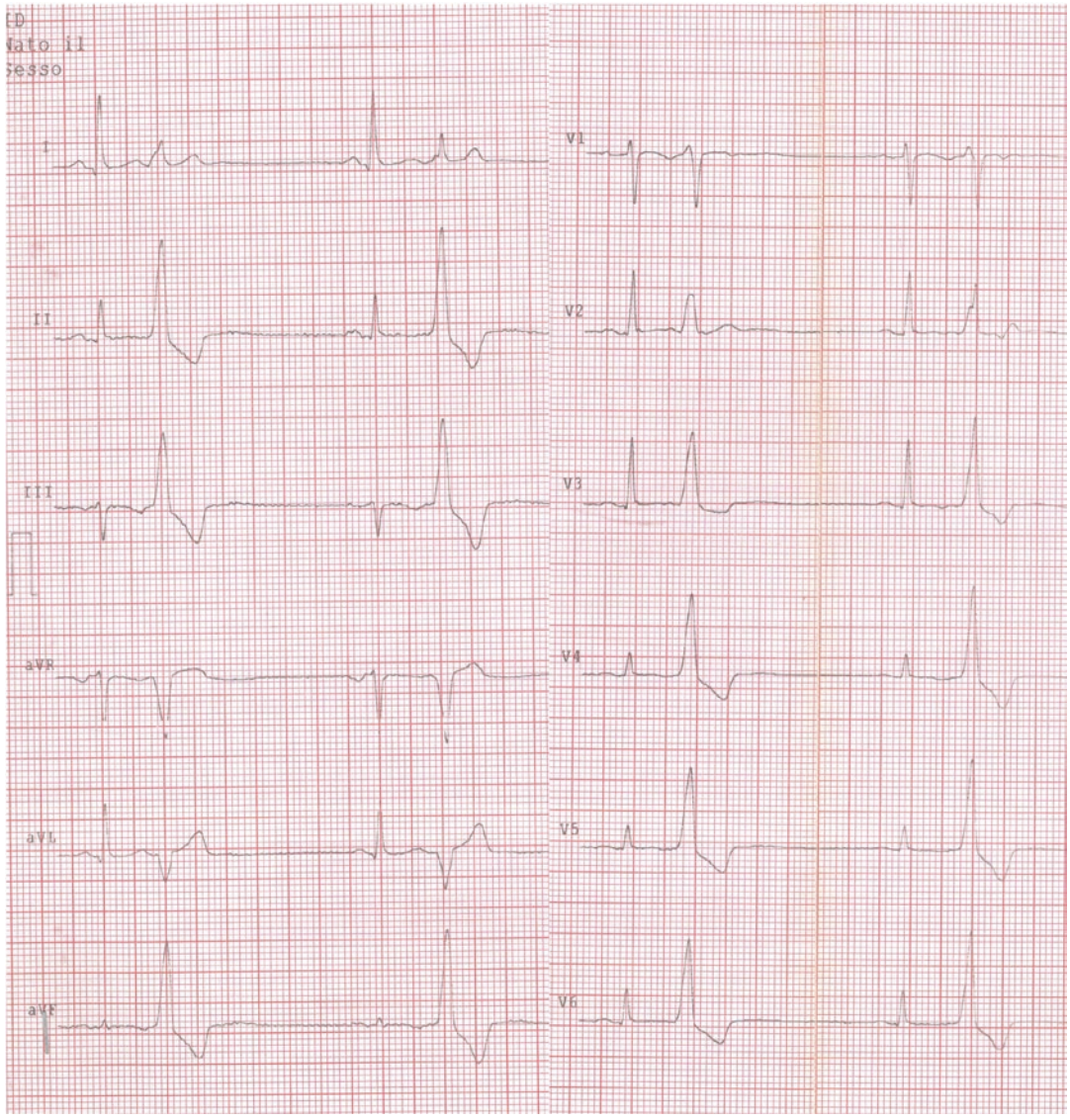

Fig. 4.5 PVC from with early precordial lead transition: 12-lead ECG

the sinus beat coming after the interpolated PVC is usually prolonged because of the concealed ventriculoatrial conduction. Furthermore the presence of interpolated PVCs is mainly directly associated with a higher PVC burden, that is, another independent risk factor of PVC-CMP.

7. *PVC coupling interval*: it is known that a short PVC coupling interval (the distance between the PVC and the previous sinus beat) can be associated to R-on-T phenomenon. This is a potential substrate of ventricular arrhythmias. In addition to the arrhythmic risk, short PVC coupling interval could be associated with PVC-CMP, even if not all authors are concordant [23, 24, 27]. An interesting study reported that in a population with PVC-CMP, a PVC coupling interval of less than 450 ms at baseline (before the LV dysfunction) was predictive of good LV function recovery [35].

Then after all how frequent PVCs can cause the PVC-CMP remains unclear. In literature there are different pathophysiologic hypotheses:

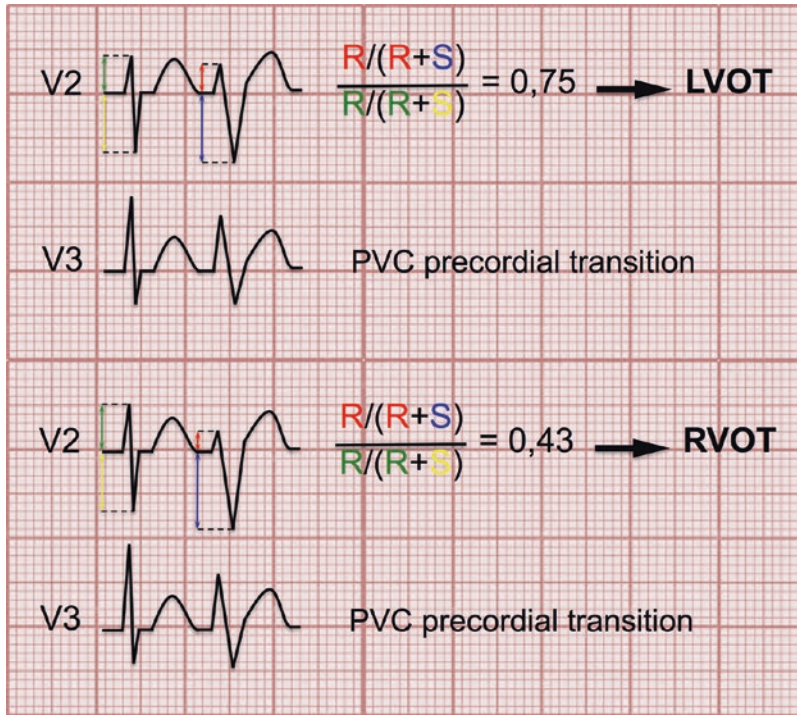

Fig. 4.6 Application of "V2 transition ratio" rule

1. *Tachycardia-induced cardiomyopathy*: it has been thought that frequent PVCs increase the average heart rate. This could be linked to the same mechanism responsible for LV dysfunction due to poor controlled ventricular response in atrial fibrillation. The time PVC duration related to CMP development could go to that direction. On the other hand, not all patients with PVC-CMP have a high average heart rate [35].
2. *Dyssynchronous ventricular activation*: the electrical impulse of PVCs comes from "common cells," and the depolarization wave propagates through "not-specialized conduction system cells." This may lead to a dyssynchronous electrical and then mechanical activation of the ventricular wall segments. It can be observed a parallelism with the LV dysfunction induced by ventricular pacing that is another condition where the electrical impulses do not rise from the conduction system [36].
3. *Impaired diastolic function*: in presence of PVCs, the abnormal interval coupling is often followed by the compensatory pause. This pause causes a prolongation of the diastolic period that might determinate an increase in the LV filling pressure. The association between PVC-CMP and short coupling interval, usually with a subsequent long compensatory pause, supports this theory [36].
4. *Ventricular volume overload*: the PVC is usually a not-perfusing beat. This PVC peculiarity may result in volume overload. In this case, the hypothesized PVC-CMP pathogenesis is similar to the chronic ventricular volume overload during valvular regurgitation [27].
5. *Channel dysfunction*: some authors in canine experiment documented modified calcium and potassium current and a decrease of calcium release from sarcoplasmic reticulum of cardiomyocytes (animals with PVC-CMP). Even if not yet clear, certainly there are alterations at cellular level that also contribute to PVC-CMP development [37].
6. *Genetic abnormalities*: finally the simple fact that not all patients with frequent PVCs develop PVC-CMP suggests that an individual predisposition must still be present.

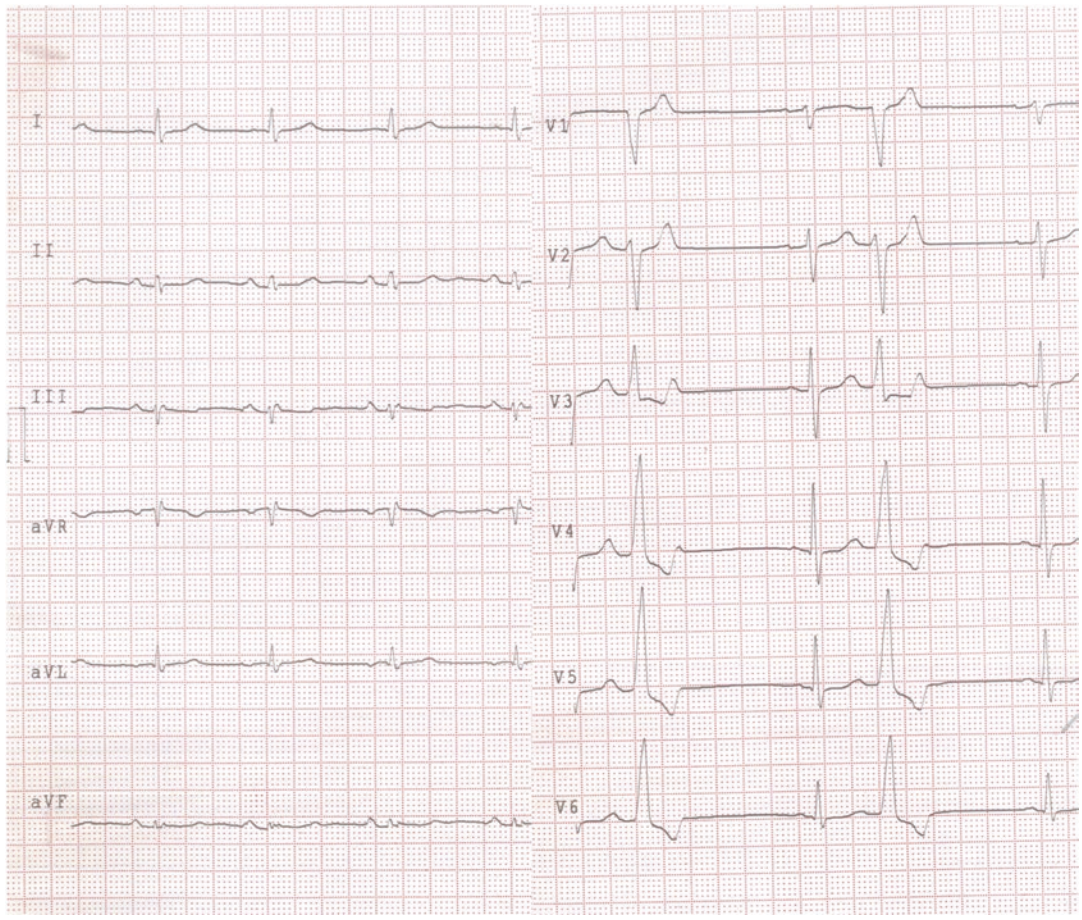

Fig. 4.7 Application of "V2 transition ratio" rule in a RVOT-PVC. PVC R wave = 2 mV, PVC S wave = 12.5 mV, SR R wave = 3 mV, SR S wave = 6.5 mV, V2 ratio = 0.44

Probably PVC-CMP is the result also of some genetic alterations.

All those reported mechanisms may trigger a negative left ventricular remodeling effect leading to dysfunction. None has been per se definitely proved, but few of them together may be basis of the PVC-CMP development.

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5 Supraventricular Tachycardias: How to Diagnose the Mechanism

Giulia Enea, Alessio Menditto, Francesca Patani, and Francesca Troiano

5.1 Case 1

F.R., a 62-year-old woman, went to the emergency department for tachycardia sudden onset. She was symptomatic for prolonged palpitations. Medical history and cardiovascular risk factors were negative, but she referred in the past years several episodes of palpitation without any recorded ECG. This time a 12-lead ECG was recorded (Fig. 5.1).

5.1.1 ECG Analysis

A narrow QRS tachycardia with regular R-R interval is present. R-R interval is 420 ms (heart rate 143 bpm). A P wave is visible and is flat in lead I, negative in inferior leads, and positive in leads aVR and aVL; P-wave axis is therefore −90°, and its duration is 40 ms. QRS complexes are 80 ms in length with a normally orientated axis in the frontal plane (+30°). PR interval is 80 ms. The P/QRS ratio is 1:1. ST segment is normal, and QTc is also normal (370 ms).

This is a clear case of supraventricular tachycardia. The differential diagnosis could be the following:

- *Sinus tachycardia*: this hypothesis can be immediately excluded because the P-wave axis (−90°) is different from that of a normal sinus P (range 0–75°).
- *Atrial tachycardia*: heart rate is compatible, but, if this hypothesis is correct, this atrial tachycardia should come from a lower part of the atrium near the interatrial septum; P waves have a concentric activation morphology (upper axis and short duration). The atrioventricular (AV) conduction is 1:1 with short PR duration (80 ms) that is not typical for this tachycardia type.
- *Atrioventricular node reentrant tachycardia (AVNRT)*: it could be an atypical AVNRT with anterograde conduction through the fast pathway and the retrograde conduction through the slow pathway (fast-slow type). This kind of circuit could well explain the RP duration longer than PR. Concentric atrial activation is also typical of AVNRT.
- *Permanent junctional reciprocating tachycardia (PJRT—Coumel tachycardia)*: this type of tachycardia is characterized by a macro-reentry circuit with anterograde conduction through the AV node and His-Purkinje system and a retrograde conduction through a slow-conductive (decremental conduction) concealed accessory pathway. Usually it has a posteroseptal localization. These ECG features (retrograde concentric P wave, P/QRS ratio 1:1, and RP greater than PR) are compatible with a PJRT.

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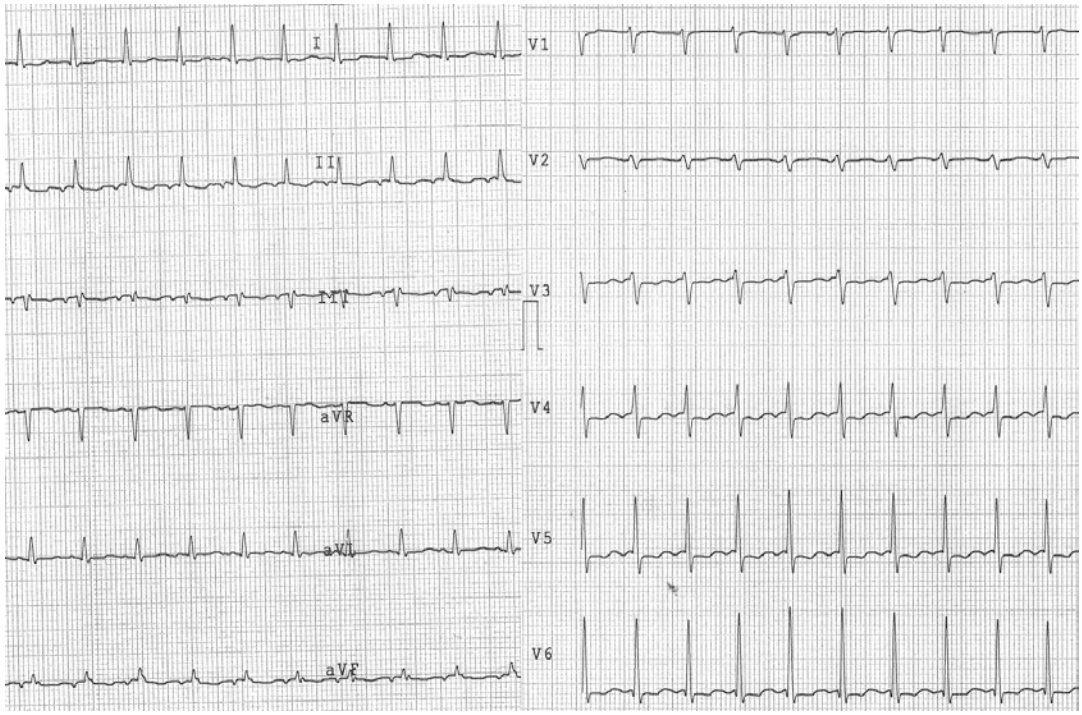

Fig. 5.1 Case 1: 12-lead ECG

Vagal maneuvers or adenosine administration may help to make a correct diagnosis during a SVT.

In this case, a carotid sinus massage was performed, and the tachycardia ended up abruptly with a QRS complex not followed by a P wave. At this point, the atrial tachycardia hypothesis could be excluded; in fact, typical response to vagal maneuvers is a transient high-grade AV block (P/QRS ratio from 1:1 to 2:1, 3:1, etc.) with contemporary persistence of the tachycardia. Only in rare cases atrial tachycardias end up with a vagal maneuver. Both atypical AVNRT and PJRT may stop during vagal maneuvers because of a block occurring within the slow pathway or in the decremental conduction accessory pathway. Therefore both of them may end with a QRS complex not followed by a P.

PJRT is a rare form of supraventricular tachycardia and is more common at a young age. Atypical AVNRT is the most valuable hypothesis in this case. However it is not possible to distinguish between these two forms only at this surface ECG. The right diagnosis was reached by an intracavitary electrophysiological study [1–3]. The atypical AVNRT (fast-slow pattern) was confirmed. The patient was treated by catheter ablation of the slow pathway.

5.2 Case 2

C. D. is a 50-year-old man with several cardiovascular risk factors (hypertension, hyperlipidemia, obesity, family history of cardiovascular disease) and was admitted to the emergency department for palpitations. A 12-lead ECG was recorded.

5.2.1 ECG Analysis

It is a narrow QRS tachycardia with regular R-R interval of 300 ms (heart rate is 200 bpm). It is possible to recognize a P wave that follows each QRS complex, more visible in leads II, III, and aVR. P wave is negative in lead I and aVL. Its length is 40 ms, and the RP interval is 100 ms (RP >70 ms). RP interval is shorter than PR interval. The P/QRS ratio is 1:1. QRS complex is narrow (80 ms) with a normally orientated axis in the frontal plane (+60°). QTc interval is 430 ms.

This is a case of supraventricular tachycardia with RP < PR. The differential diagnosis may include:

- *Sinus tachycardia*: unlikely because P-wave axis is not within 0° and 90°. Furthermore heart rate is not compatible with a simple sinus tachycardia at rest [6].
- *Atrial tachycardia*: if this hypothesis was correct, it should be possible to see more than three ectopic P waves, with regular PP intervals [7]. Any kind of P morphologies could identify an atrial tachycardia. The atrial activation is often eccentric (depending on the origin of the focus in the atria). In particular a P axis positive in the inferior leads is typical of an atrial origin of the tachycardia (with the exception of an AVRT with an anteroseptal accessory pathway). In case of appearance during the recording of a second-degree AV block, a diagnosis of atrial tachycardia (a reentrant tachycardia always conduct with a P/QRS ratio 1:1) could be more likely. In this ECG, a P wave negative in leads I and aVL makes this diagnosis unlikely.
- *Atrioventricular node reentrant tachycardia—typical (AVNRT)*: in the typical form (slow-fast), retrograde P waves are constantly related to the preceding QRS (RP<PR) and in the majority of cases are very close to the QRS complex (RP <70 ms). Indeed, P waves can be masked within the QRS or seen as a small terminal P wave that can simulate a right bundle branch block particularly in V1. In this ECG, P waves are well visible and distant from QRS; therefore the diagnosis of AVNRT is unlikely.
- *Atrioventricular reentrant tachycardia (AVRT)*: this kind of tachycardia is characterized by the presence of a P wave following a narrow QRS complex, with a RP interval longer than 70 ms. The atrial activation normally starts from the origin of the accessory pathway, which connects atria and ventricles, in a retrograde activation; P-wave morphology and axis during tachycardia depend on the circuit localization. In our ECG, it is possible to recognize all the features aforementioned. Moreover, the presence of QRS alternans (regular voltage variation >1 mm, at least 10 s after initiation of supraventricular tachycardia) is highly indicative of a retrograde accessory AV pathway included in the tachycardia circuit (Fig. 5.2) [8]. The arrhythmia was effectively interrupted by verapamil and adenosine.

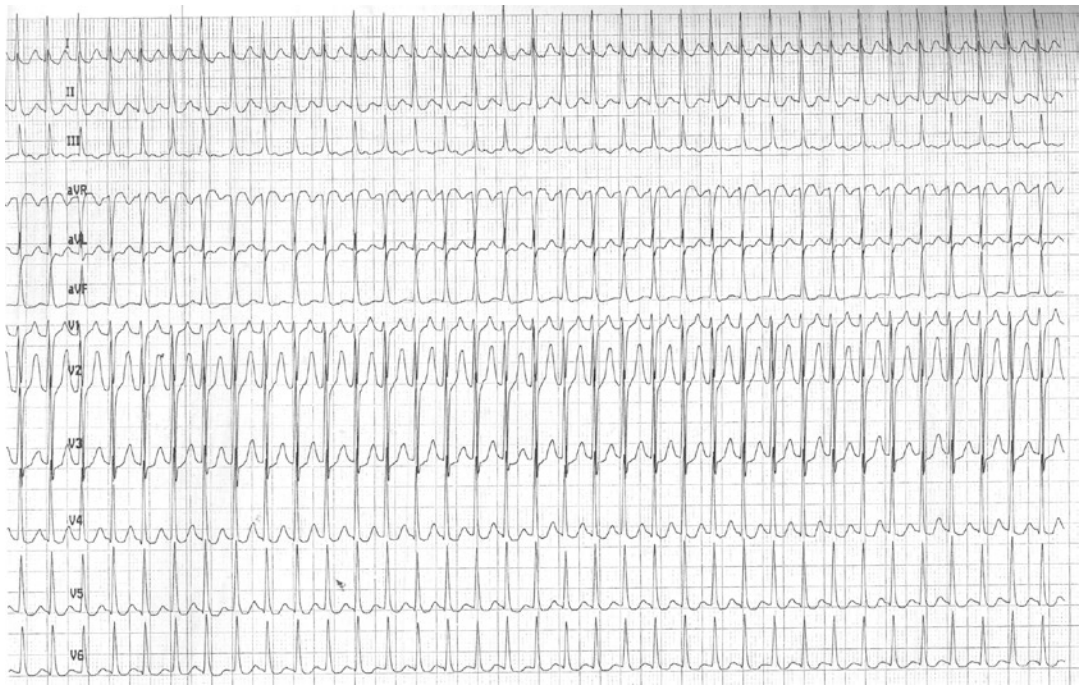

Fig. 5.2 Case 2: 12-lead ECG

An intracavitary electrophysiological study (EPS) was performed that confirmed inducibility of an orthodromic atrio-ventricular tachycardia. The localization of the accessory pathway was left lateral, as we could argue from the P-wave axis negative in lead I and aVL and positive in V1 [9].

The patient was successfully treated by radiofrequency catheter ablation of the accessory pathway.

5.3 Case 3

A 74-year-old female patient, with a history of palpitations, was admitted to ER for dyspnea at rest and palpitations. A 12-lead ECG was recorded (Fig. 5.3).

5.3.1 ECG Analysis

The ECG shows a narrow complex tachycardia with slight heart rate irregularity and a mean rate of 100 bpm. There is a regular-irregular rhythm. QRS axis is −30°. There are positive P waves in inferior leads (II, III, and aVF), in lead I, and from V3 to V6, while negative P are in aVR and V1. P-wave axis is therefore leftward and posteriorly directed. In some beats, P waves clearly precede the QRS complexes with a PR interval of 200 ms (1st, 4th, 8th, and 11th beats), while in other beats, they are inserted in the T wave of the previous ventricular complexes, either at the apex (as in the 2nd, 5th, 9th, 12th) or in the ascending part (3rd, 6th, 10th, 13th beats), with longer PR interval (of 300 and of 400 ms, respectively).

T waves of these beats have a different morphology, with sharp and nearly biphasic aspects. Looking carefully at the QRS complex of the 3rd, the 6th, the 10th, and the 13th beats, we observe a RSr' morphology that is different shape compared to the other QRS complexes. The r' is actually a deflection of QRS determined by the fusion of a P wave with the preceding QRS. Therefore PR and RP intervals are irregular, with some P waves clearly not conducted to ventricles.

PP intervals have an average duration of 460 ms with slight variations. P-wave length is 40 ms. Ventricular repolarization is normal, with a QTc of 410 ms.

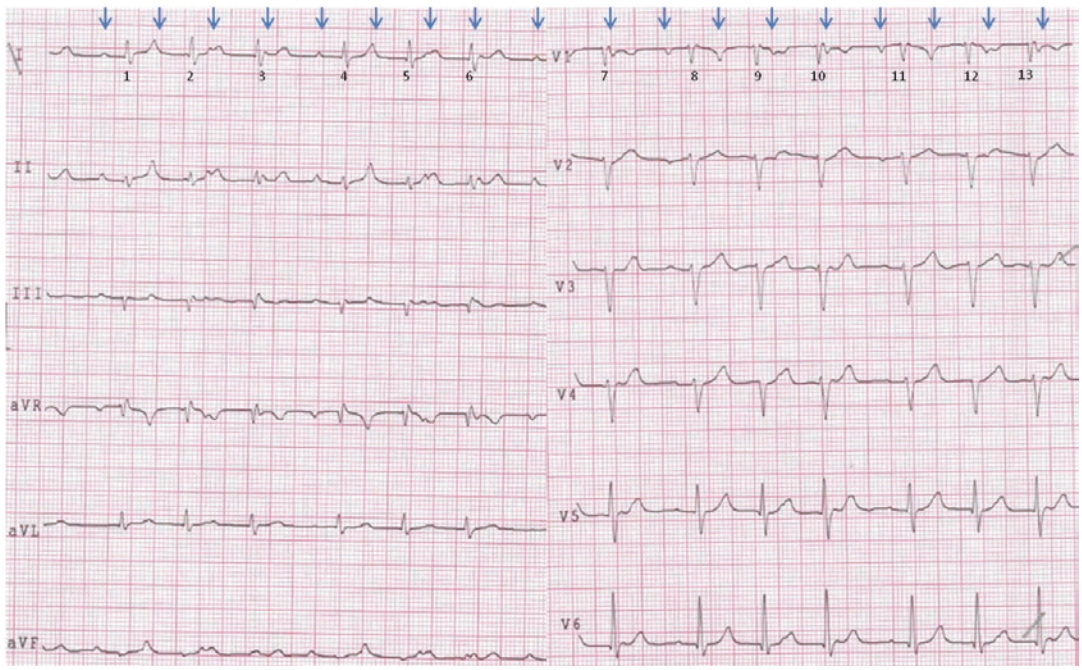

Fig. 5.3 Case 3: 12-lead ECG

This is a case of supraventricular arrhythmia, and the possible differential diagnoses are:

- *Sinus tachycardia with frequent PACs (premature atrial contractions) and PJCs (premature junctional contractions)*: this hypothesis was excluded because of the substantial regularity of PP intervals (there is only a slight variation of their length) and the absence of a real-anticipated QRS complex. R-R irregularity is due to a variable AV conduction rather than to premature beats.
- *Atrial tachycardia (AT)*: we have P waves at a rate of about 140 bpm, with a leftward and posteriorly directed axis. If this hypothesis is correct, this atrial tachycardia origins from the right atrium (negative P wave in V1) at the level of crista terminalis (negative P wave in aVR). There are irregular PR and RP intervals. By looking carefully at the PR intervals, there is a progressive prolongation until the atrioventricular (AV) conduction is blocked, and a P wave is not followed by a QRS complex (Wenckebach phenomenon). This AV relationship can be compatible with an AT.
- *Atrioventricular node reentrant tachycardia (AVNRT)*, *junctional tachycardia (JT)*, *and atrioventricular reciprocating tachycardia (AVRT)*: these hypotheses can be immediately excluded because of the irregularity of the tachycardia and the presence of a Wenckebach phenomenon. Diagnosis of reentrant or reciprocating tachycardia is unlikely.
- *Atrial fibrillation for the irregularity of the tachycardia*: it can be excluded because of presence of clear P waves in this case.

This supraventricular arrhythmia spontaneously terminated after a few minutes. The patients later underwent an electrophysiological study that showed an easy inducibility of a focal atrial tachycardia that showed an earliest depolarization point in left and right part of the interatrial septum and in the superolateral portion of the RA wall.

Focal atrial tachycardias (ATs) are characterized by atrial activations starting rhythmically within a small area (focus) outside the sinus node region, from which they spread out centrifugally. This focal activity can be caused by automaticity, triggered activity, or microreentry.

AT cycle length is usually ≥250 ms, but it can be as short as 200 ms and exhibit important variations over a certain period of observation (minutes to hours). AT ECG pattern shows typically discrete P waves at rates 130–240 bpm [10].

Focal ATs rise mainly from the right atrium (RA), and approximately two thirds of them are distributed along the long axis of the crista terminalis (from the sinus node to the coronary sinus) and the atrioventricular junction (tricuspid annulus). The pulmonary vein (PV) ostia are instead the most common sites of origin of left atrium focal tachycardias [11].

P wave morphologies can be used to localize approximately the site of the origin of the ATs. V1 and I leads are used for discriminating RA from LA origin. Leads II, III, and aVF may help to differentiate superior from inferior left atrial foci, while the P configuration in aVR can differentiate activation arising from crista terminalis from those originating from the tricuspid annulus or right atrium septum (Fig. 2.4) [6, 12, 13]. The final diagnosis is usually made through endocardial mappings.

P waves and QRS relationship depends not only from the tachycardia rate but also from the atrioventricular node conduction properties. If the rate of the tachycardia is faster than the AVN conductive capacity (e.g., in AVN disease or with a slowing conduction therapy), some of the P may be blocked, with a P/QRS ratio higher than 1 or sometimes a clear Wenckebach phenomenon [7]. This is the mechanism of Case 3.

5.4 Case 4

A 49-year-old male, with a history of recurrent paroxysmal supraventricular tachycardias (under Flecainide 100 mg/day), was admitted to our clinic with indication to perform an electrophysiology study. While in the hospital, he suddenly complained of palpitations, and a 12-lead ECG was recorded (Fig. 5.4).

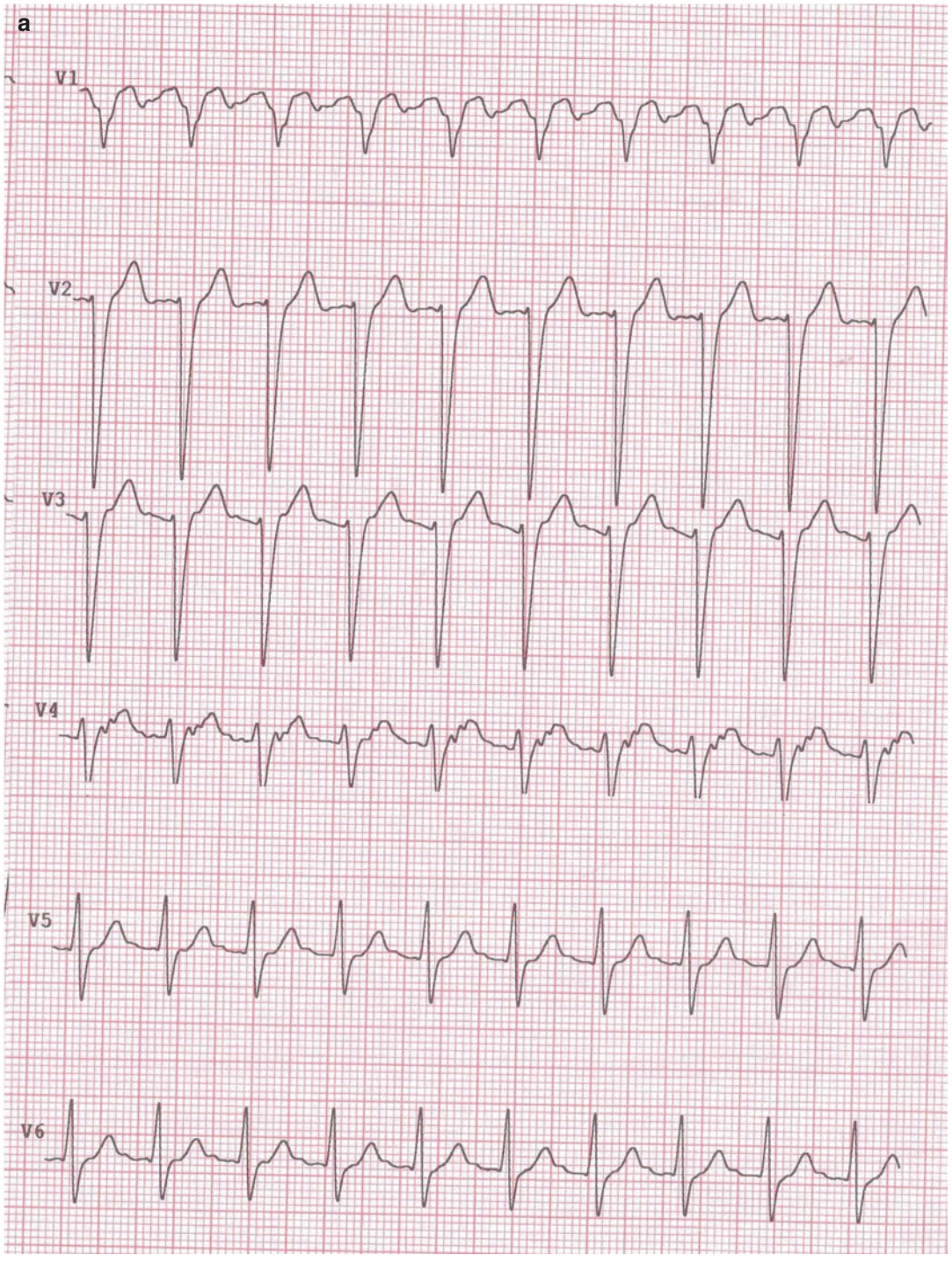

Fig. 5.4 (**a**, **b**) Case 4: 12-lead ECG

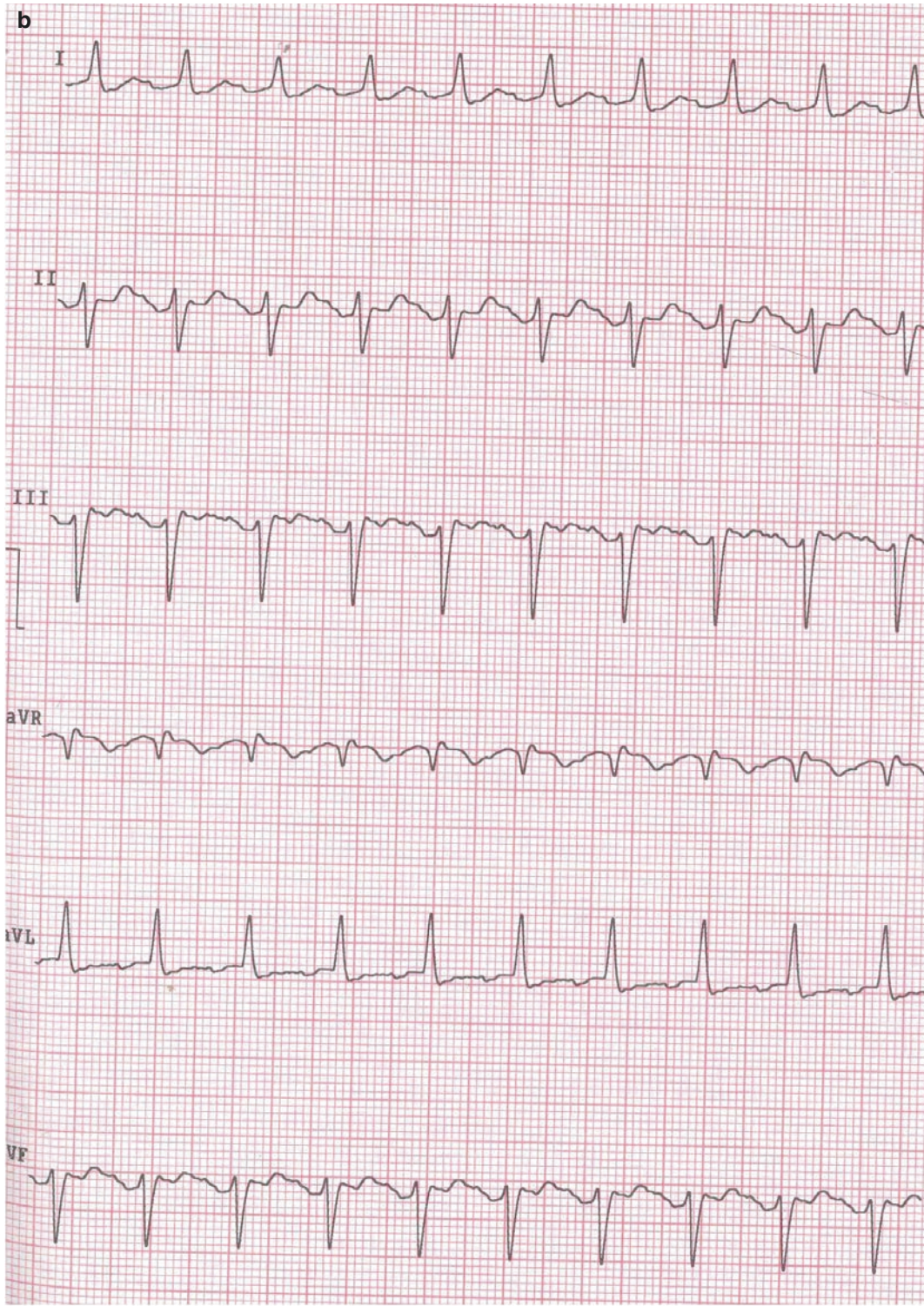

Fig. 5.4 (continued)

5.4.1 ECG Analysis

The ECG shows a narrow complex regular tachycardia with a mean heart rate of 130 bpm (R-R cycle length 450 ms). There are positive atrial waves before every QRS complex in inferior leads (II, III, aVF) and in V1, within the descending T-wave branches. We can also observe a notch within the T waves that can be interpreted as hidden atrial waves (i.e., V4 shows a notch in the ascending branch of T wave). P/QRS ratio is therefore 2:1. QRS length is slightly prolonged (110 ms); there is a left axis deviation (−45° on the frontal plane). The QRS has a qR pattern in aVR and rS in II, III, and aVF, probably secondary to the left anterior fascicular block. Ventricular repolarization is normal, and the QTc is 410 ms.

This is another narrow QRS tachycardia.

Differential diagnosis:

- *Atrial fibrillation (AF)*: it can be excluded because R-R are regular. Furthermore in this ECG, we can clearly identify the atrial activation waves, rarely present in case of AF (the atrial rate is so fast that the P waves are not identifiable, or only coarse fibrillatory waves are usually seen).
- *Sinus tachycardia*, *atrioventricular node reentrant tachycardia (AVNRT)*, *and atrioventricular reentrant tachycardia (AVRT)*: the P/QRS ratio is 2:1; therefore those hypotheses should be rejected.
- *Typical atrial flutter (AFL)*: counterclockwise AFL is characterized by pure negative deflections in the inferior leads. In clockwise (reverse typical) AFL, activation propagates in the opposite direction; therefore this time AFL generally has broad positive deflections in the inferior leads, with characteristic notching [11–15].
- *Atypical atrial flutter and atrial tachycardia*: because of the high-ventricular rate, these arrhythmias cannot be excluded.

In order to slow AV conduction and consequently better recognize the ongoing arrhythmia, adenosine 12 mg was administered. Figure 5.5 shows the ECG recorded during infusion.

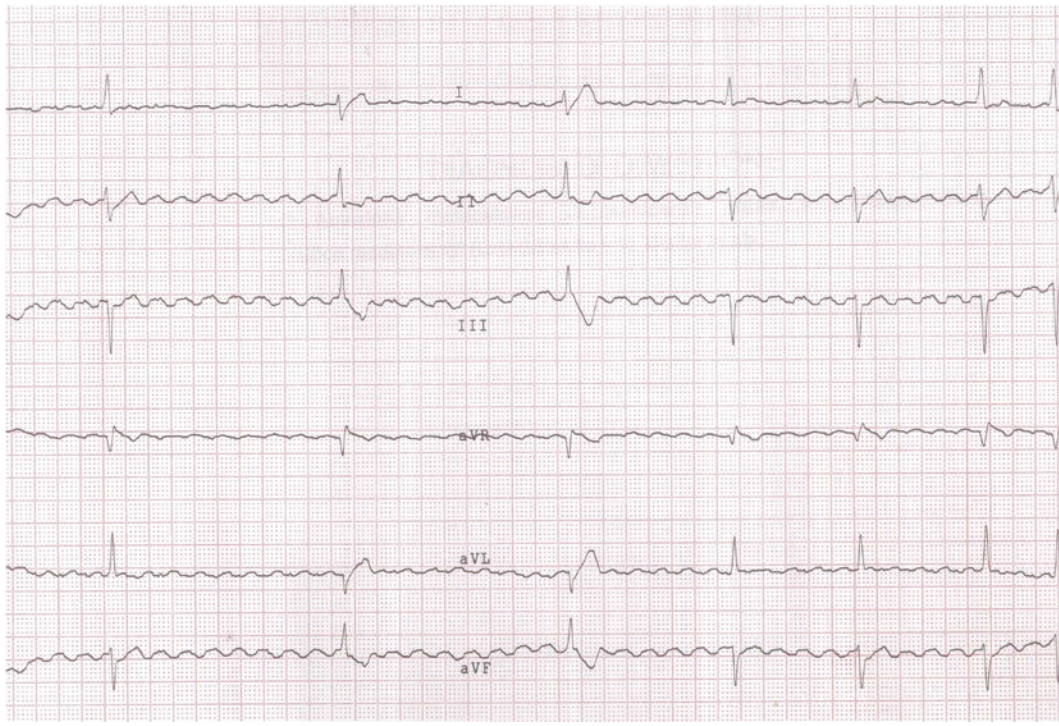

Fig. 5.5 Effect of adenosine on tachycardia

There are regular atrial activations, with a constant cycle length of almost 300 ms. The F-wave axis is positive in inferior leads. Furthermore, F waves show broad positive deflections, with notching in the ascending branch. With adenosine, AV conduction slowed abruptly down to 8:1, with wider QRS appearance and with different axis and morphology (such as ventricular escape beat). Then the arrhythmia speeded up again with a variable AV conduction (5:1, 3:1).

A diagnosis of clockwise typical atrial flutter with 2:1 AV conduction was therefore done. The QRS slight prolongation was considered to be secondary to chronic flecainide therapy.

The patient underwent successful isthmus catheter ablation and reverted to stable sinus rhythm.

5.5 Supraventricular Tachycardias: Systematically Approach to a Differential Diagnosis

In summary, a 12-lead ECG systematic approach could help us to understand the mechanisms and therefore make the correct differential diagnosis (Table 5.1).

The ECG correct analysis starts from R-R intervals, with a primary focus on the presence of regular or irregular R-R intervals. Then we should look for P waves and analyze the P/QRS ratio in order to understand a possible kind of relationship between atrial and ventricular activity. When the ratio is higher than 1:1, a primary atrial arrhythmic circuit is likely. If there is a 1:1 ratio, we can hypothesize a circuit that involves atria and ventricles. Assessing PR and RP intervals and P-wave morphology, it is possible to understand the kind of origin of atrial activation and the type of circuit. This approach is summarized in Table 5.2 [1, 4].

Other ECG features can be useful to understand the type of supraventricular tachycardia [3, 5]:

- *Effect of premature ventricular beat* (*PVB*): in PVB presence, it is important to evaluate its effect on the tachycardia cycle. If the PVB does not alter the tachycardia cycle and does not interrupt the tachycardia, an AVRT can be excluded. In this last case, the ventricle is part of the reentrant circuit, and therefore a PVB should influence at least the tachy-cycle.
- *Tachycardia onset and termination*: reentrant tachycardias have sudden onset and terminations. Instead focal tachycardias can be characterized by warm-up and cold-down phenomena with progressive heart rate increase when tachycardia starts and progressive heart rate decreases before stopping. It is of importance also the last tachycardia beat: if it is a P wave, atrial tachycardia, atrial flutter, atypical AVNRT, and, in the majority of case, PJRT could be excluded.
- *Electric alternans during tachycardia*: this is a rare phenomenon characterized by alternant QRS amplitude changes. It was initially described in orthodromic AVRT. Subsequent authors described it also in AVNRT and in rapid atrial pacing with an abrupt onset. Data suggest that electric alternans during tachycardia is a rate-dependent phenomenon due to sudden heart rate increase and does not have any precise correlation with the mechanism of a specific tachycardia. However reentrant tachycardia (AVRT and AVNRT) is characterized by a sudden onset and a heart rate higher than other supraventricular arrhythmias; that is the main reason why the electric alternans is more likely to appear in these last forms.

Table 5.1 Supraventricular tachycardia types and characteristics

Tachycardia	Mechanism	R-R interval	HR	P wave	P/QRS ratio	PR	QRS	Response to vagal maneuver
Sinus tachycardia	Increase activity of sinus node	Regular	100–180	Normal axis	Generally 1:1	Shorter than RP	Normal or conduction aberrant	Gradual slowing
Atrial tachycardia	Increase activity of ectopic focus (automaticity or microreentry)	Generally regular	75–200	Morphology related to origin	Often >1	Shorter than RP	Normal or conduction aberrant	High grade of AV block
MAT	Multiple atrial ectopic foci	Irregular	120–180	At least 3 types of P-wave morphology	Often >1	Variable	Normal or conduction aberrant	High grade of AV block
Atrial flutter	Macro-reentry in right atrium (typical flutter): counterclockwise or clockwise	Regular if P:QRS ratio is constant	75–175	Sawtooth F wave (typical flutter); no isoelectric line	>1	Generally constant	Normal or conduction aberrant	High grade of AV block
Atrial fibrillation	Chaotic atrial activation	Irregular	100–160	Absent; irregular atrial activation (F wave)	Not evaluable	Not evaluable	Normal or conduction aberrant	High grade of AV block
Typical AVNRT (slow-fast)	Dual AV nodal pathways. Macro-reentry with anterograde conduction by slow pathway and retrograde conduction by fast pathway	Regular	150–250	Hidden in QRS; pseudor' (V1); concentric atrial activation (narrow upper axis P wave)	Generally 1:1	Longer than RP	Normal or conduction aberrant	Terminate or anything
Atypical AVNRT (fast-slow)	Dual AV nodal pathways. Macro-reentry with anterograde conduction by fast pathway and retrograde conduction by slow pathway	Regular	150–250	Concentric atrial activation (narrow upper axis P wave)	Generally 1:1	Shorter than RP	Normal or conduction aberrant	Terminate or anything
Orthodromic AVRT	Macro-reentry with anterograde conduction by AV node-His-Purkinje system and retrograde conduction by AP	Regular	150–250	Eccentric atrial activation (morphology related to AP localization); concentric atrial activation in posterseptal AP	Mandatory 1:1	Longer than RP	Normal or conduction aberrant	Terminate or anything
PJRT	Macro-reentry with anterograde conduction by AV node-His-Purkinje system and retrograde conduction by decremental slow conduction AP	Regular	120–200	Concentric atrial activation (narrow upper axis P wave)	Mandatory 1:1	Shorter than RP	Normal or conduction aberrant	Terminate or anything

HR heart rate, *MAT* multifocal atrial tachycardia, *AVNRT* atrioventricular node reentrant tachycardia, *AVRT* atrioventricular reentrant tachycardia, *PJRT* permanent junctional reciprocating tachycardia (Coumel tachycardia)

Table 5.2 ECG features to assess

1st: assess RR	R-R regular					R-R irregular		
2nd: assess P wave and P/QRS ratio	P not visible	P:QRS = 1:1			P: QRS>1	No. of P waves	F waves	Different P waves
3rd: assess RP and PR	↓	RP<PR		RP>PR	↓	↓	↓	↓
		RP <70 ms	RP >70 ms					
4th: more probably diagnosis	Typical AVNRT		AVRT; AT	ST; AT; atypical AVNRT; PJRT	Aflu; AT	AF	Aflu with different AV conduction	MAT

AVNRT atrioventricular node reentrant tachycardia, *AVRT* atrioventricular reentrant tachycardia, *AT* atrial tachycardia, *ST* sinus tachycardia, *PJRT* permanent junctional reciprocating tachycardia, *Aflu* atrial flutter, *AF* atrial fibrillation, *MAT* multifocal atrial tachycardia (Table from Contadini D, Menditto A (2015) Supraventricular Reentrant Tachycardias. In: Capucci A. (eds) Clinical Cases in Cardiology. Springer, Cham)

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6 Wide QRS Tachycardias: Aberrant Conduction or Ventricular Origin?

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6.1 Case 1

6.1.1 Clinical Contest

A 76-year-old man was referred to the emergency room (ER) complaining of palpitation and fatigue. The patient reported a history of hypertension, dyslipidemia, type 2 diabetes mellitus, and chronic renal failure. The past history included also persistent atrial fibrillation episodes, a previous myocardial infarction 3 years earlier with severe left ventricular dysfunction. A biventricular ICD was implanted as primary indication because of 28% EF.

6.1.2 ECG Analysis

A 12-lead standard ECG was recorded at ER arrival.

There is a wide QRS tachycardia (Fig. 6.1).

Heart rate is 140 bpm. RR intervals are slightly irregular with RR intervals between 420 and 440 ms. Atrial fibrillation is therefore unlikely.

QRS is 160 ms length. To distinguish between supraventricular tachy with aberrant conduction and ventricular tachycardia, we have firstly to check for P waves and possible atrioventricular dissociation.

However P waves are not clearly evident in the trace, and therefore it is hard to recognize a possible atrioventricular dissociation. Fusion beats and capture beats would have been very useful when present in favor of a ventricular tachycardia, but they are not. In the precordial leads, there is no concordance among the QRS complexes that in case would have been a clue possibly suggestive of a ventricular origin of the arrhythmia. We may notice that the first part of the QRS measured from its beginning to the nadir of S wave is superior to 100 ms (VT criterion) in the precordial leads. Also the intrinsicoid deflection (Fig. 6.2), measured from the beginning of the QRS complex to the peak of the R wave, is slow being 60 ms length.

QRS axis is right deviated (+120°) and has a right bundle branch block morphology. In lead V1, a wide R wave pattern is present and in V6 an rS morphology with an R/S ratio inferior to 1. In VR, we can also notice an initial Q wave longer than 40 ms.

The ST segment is markedly downsloped.

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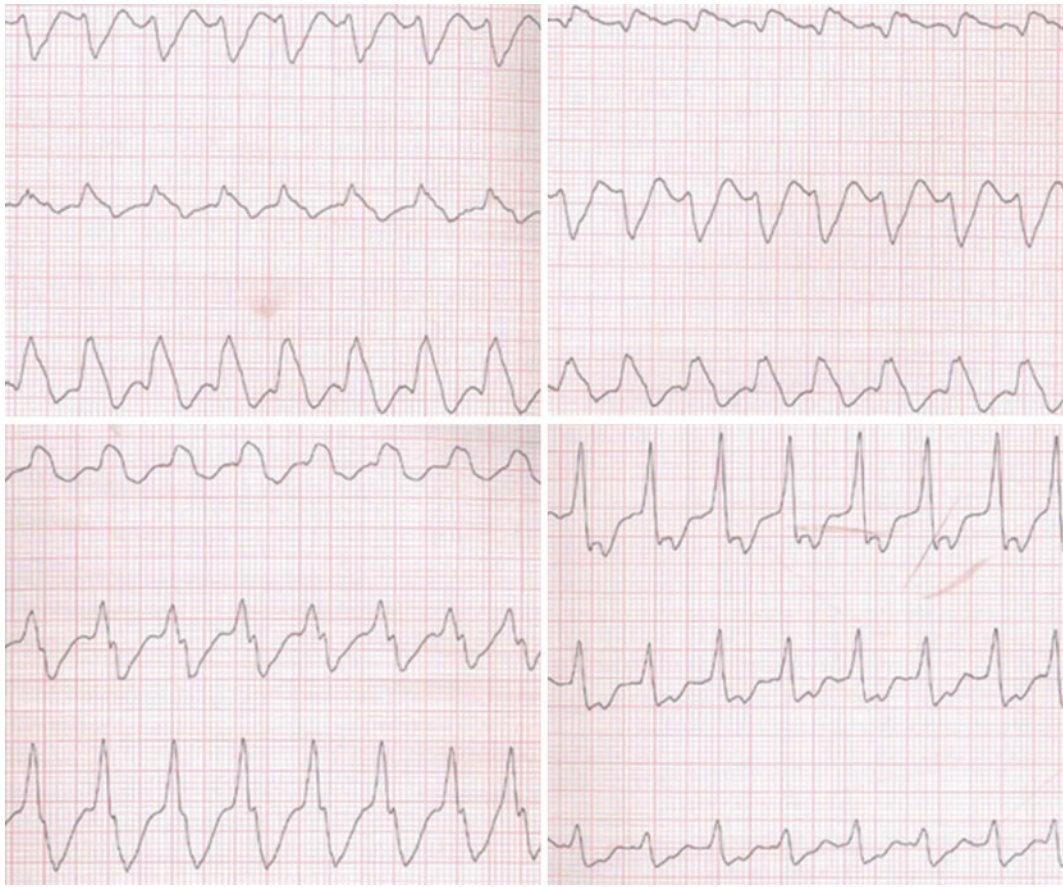

Fig. 6.1 Standard 12-lead electrocardiogram of case 1

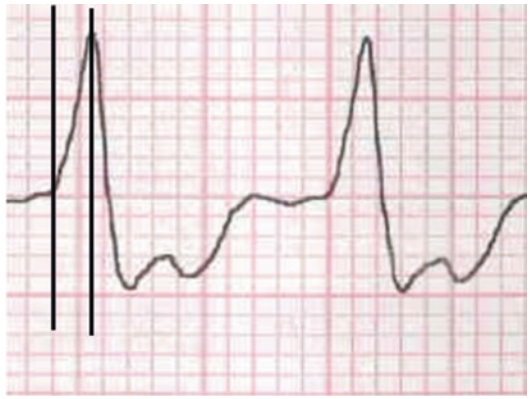

Fig. 6.2 Intrinsicoid deflection in lead V5 on standard 12-lead electrocardiogram of case 1

6.1.3 Diagnostic Summary

This ECG analysis only on the basis of morphologic-wide QRS complex criteria strongly suggests a ventricular tachycardia origin even in absence of a P/QRS clear dissociation.

The endocavitary-recorded ICD tracings (Fig. 6.3) did instead show a dissociation between atrial and ventricular activities. Atrial endocavitary signals are regular with an atrial rate of 115 bpm (RR 520 ms) that is lower than the ventricular rate. The endocavitary recording analysis therefore confirms the ventricular origin of the tachycardia.

This arrhythmia was interrupted by an ICD shock.

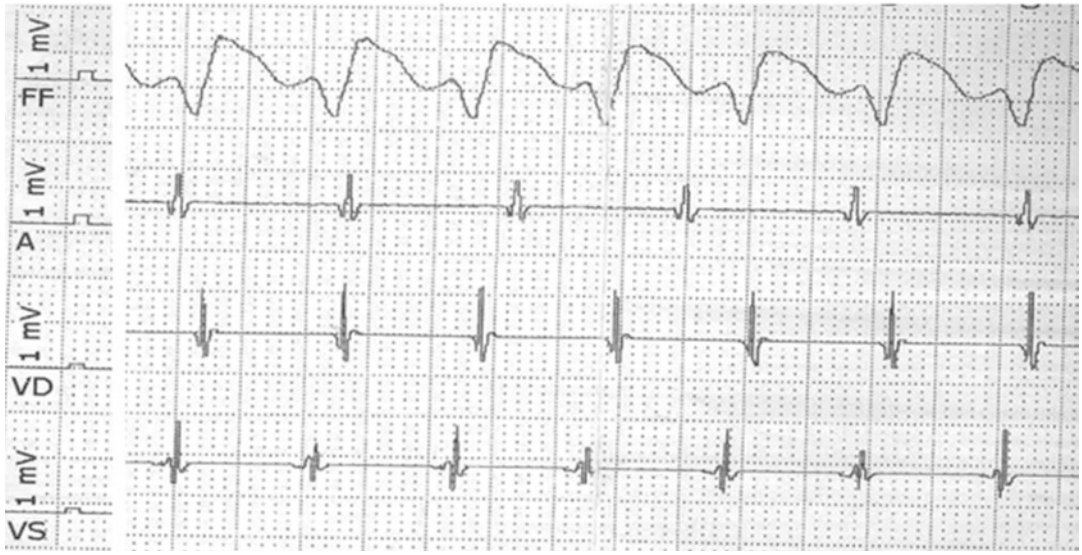

Fig. 6.3 Endocavitary tracing recorded by the ICD in case 1

6.2 Case 2

6.2.1 Clinical Contest

A 73-year-old male was admitted to ER complaining of palpitations and chest pain. The past medical history included arterial hypertension and dyslipidemia.

6.2.2 ECG Analysis

There is (Fig. 6.4) a wide QRS tachycardia.

Heart rate is 165 bpm. RR intervals look very regular (360 ms).

QRS complexes measure 140 ms. The presence of a regular rhythm certainly excludes an atrial fibrillation as a possible tachycardia mechanism.

Atrial activities (P or F waves) are not evident; thus a possible atrioventricular dissociation is not here a useful diagnostic criterion. Fusion beats and capture beats are not present either.

There is a positive concordance of the QRS complexes in the precordial leads, and the intrinsicoid deflection in V5 and V6 leads measures 60 ms. v_i/v_t is <1 (Vereckei criterion).

The QRS axis is right deviated (+110°). It has a right bundle branch block morphology with a wide R wave pattern in both V1 and V6 leads. There is an initial Q wave lasting 60 ms in VR

The ST segment is markedly downsloped.

6.2.3 Diagnosis

The morphologic criteria of QRS suggest therefore the diagnosis of ventricular tachycardia.

The patient was successfully treated with a DC shock of 200 J.

The following sinus rhythm ECG did show an ST segment elevation in the inferior leads.

A coronary arteriography was performed that showed a significant stenosis of the right coronary artery which was successfully treated with PCI and drug-eluting stent implantation.

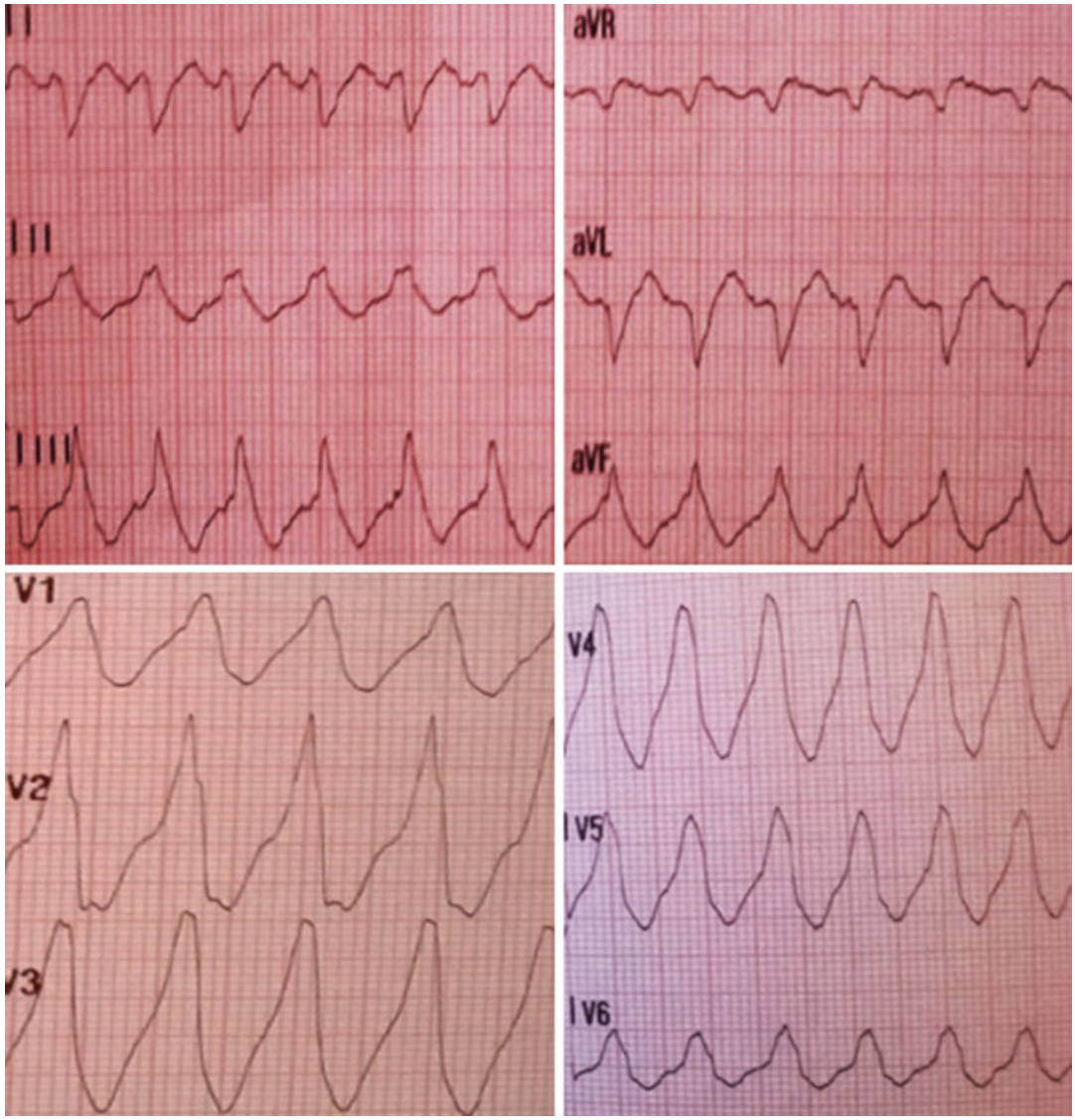

Fig. 6.4 Standard 12-lead electrocardiogram of case 2

6.3 Case 3

6.3.1 Clinical Contest

A 42-year-old male came to ER for persistent palpitations.

The past medical history included the presence of asymptomatic bicuspid aortic valve and ascending aortic dilatation for which a yearly follow-up was scheduled.

A 12-lead ECG was recorded.

6.3.2 ECG Analysis

There is (Fig. 6.5) a wide QRS tachycardia. Heart rate is 210 bpm, RR intervals are regular (280 ms), and QRS duration is 160 ms. The presence of a regular rhythm excludes the hypothesis of atrial fibrillation, and the heart rate is faster than in a classical 2:1 atrial flutter.

Not any atrial activity is evident, and we cannot ascertain any possible atrial ventricular strict relation. There are no fusion and capture beats.

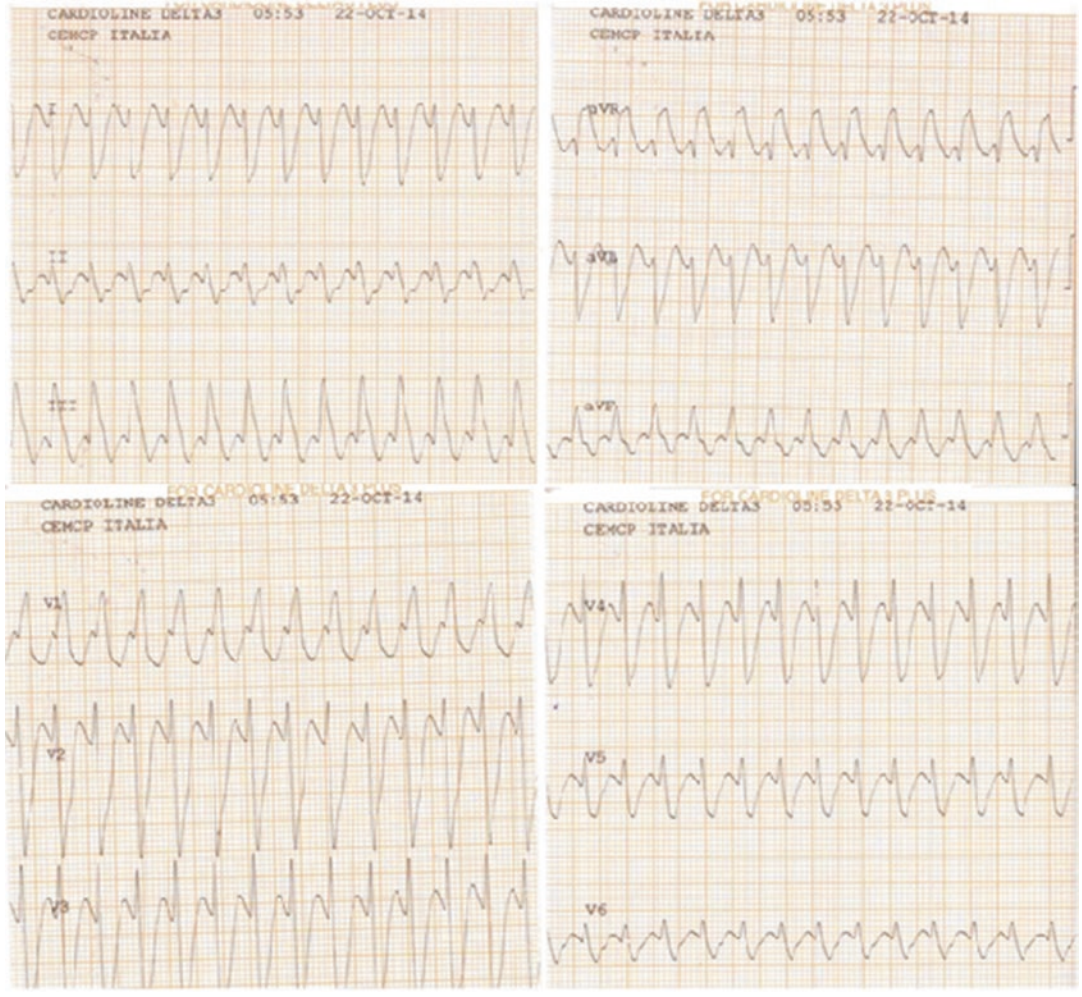

Fig. 6.5 Standard 12-lead electrocardiogram of case 3

Morphological criteria: no QRS concordance in the precordial leads. Time from QRS onset to S nadir in precordial leads is 80 ms. The intrinsicoid deflection in leads II, V4, V5, and V6 measures 35 ms. v_i/v_t is >1 (Vereckei criterion).

The QRS axis is right deviated (+160°). A right bundle branch block morphology is evident with an rR′ wave pattern in V1 and an rS morphology with an R/S ratio inferior to 1 in V6.

6.3.3 Diagnostic Conclusion

By considering the morphologic features, intrinsicoid deflection's characteristics, and Brugada and Vereckei algorithms, this is a supraventricular tachycardia with aberrant atrioventricular conduction.

The arrhythmia ended up spontaneously, and the sinus rhythm ECG did not show any conduction abnormality.

The patient underwent an electrophysiological study that wasn't able to induce any type of tachycardia, neither supraventricular nor ventricular. Nevertheless, during the incremental atrial stimulation up to 220/min, an aberrant conduction with right bundle brunch morphology and right axis deviation appeared with a QRS superimposable to the tachycardia's one.

Supraventricular tachycardia with aberrant atrioventricular conduction remains the most likely diagnosis.

6.4 Case 4

6.4.1 Clinical Context

A 68-year-old woman with past medical history of paroxysmal atrial fibrillation and arterial hypertension underwent cardiac surgery for ascending aorta replacement. At the 5th day after surgery, the patient complained of palpitations and dyspnea.

6.4.2 ECG Analysis

A 12-lead standard ECG was recorded.

There is (Fig. 6.6) a wide QRS tachycardia. Heart rate is 185 bpm, RR intervals are regular (320 ms), and QRS length is 120 ms. The rhythm is regular, so the hypothesis of atrial fibrillation is unlikely. Is a VT or a SVT with aberrant conduction?

There are visible notches inside the ascending branch of T waves in the inferior leads, possibly referable to P waves (or F wave). These P waves could be the result of a retrograde conduction or coming from atria (atrial tachycardia/flutter 1:1 or 2:1). P-wave axis is not clearly definable; however an atrioventricular dissociation can be excluded.

Fusion and capture beats are not present.

QRS complexes in the precordial leads are not concordant. Time from QRS onset to the nadir of S wave in V5–V6 is 80 ms. The R-peak time (intrinsicoid deflection) in leads II and V6 is 30 ms. In VR, there is an initial Q wave lasting about 40 ms. v_i/v_t is >1 (Vereckei criteria).

The QRS axis is extremely left deviated (−135°). A right bundle branch block morphology is evident with a wide R wave pattern in V1 and an rS morphology with an R/S ratio inferior to 1 in V6, both peculiar of ventricular tachycardia.

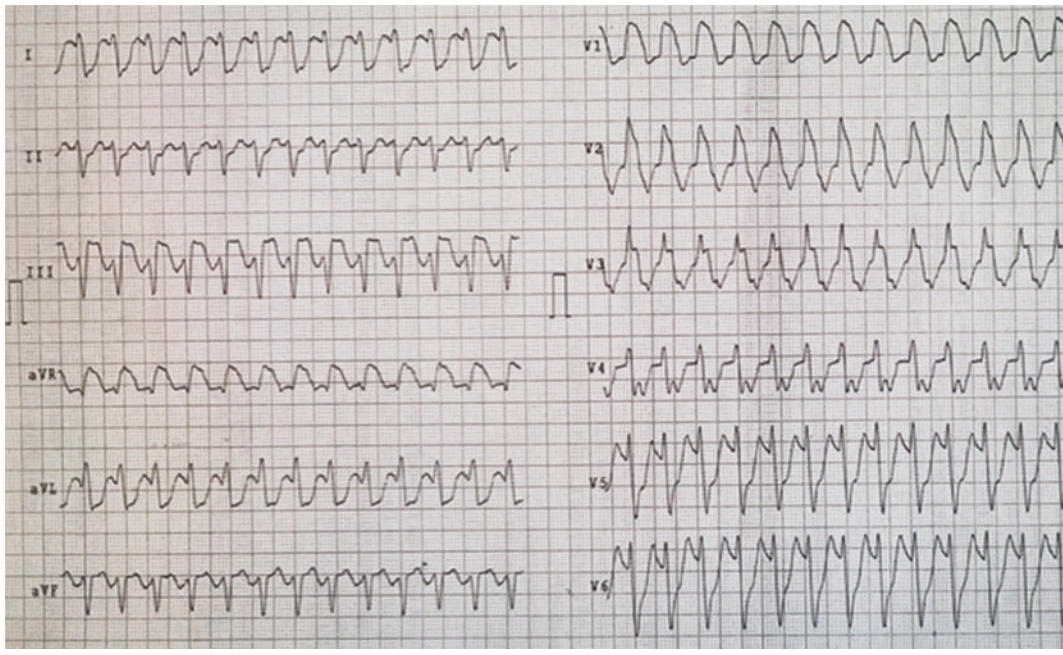

Fig. 6.6 First standard 12-lead electrocardiogram recorded for case 4

6.4.3 Diagnosis

The diagnosis is challenging because the classical criteria are discordant.

The tachycardia ended after a 5 mg metoprolol intravenous injection.

Some days later, the patients moved to our clinic where he had recurrence of the same symptoms. The following ECG was recorded (Fig. 6.7).

The ECG shows a narrow QRS complexes tachycardia. The heart rate is 150–130 beats/min. RR interval is not regular. F waves with an atrial rate of 280 bpm are visible. The F axis is oriented upward (−90°). QRS length is 80 ms, and no intraventricular conduction abnormality is present. T waves are negative in left precordial leads V4-V5-V6.

RR irregularities and F waves with a rate of 280/min suggest a common atrial flutter with a variable AV conduction (2:1; 3:1).

By going back to the previous medical records, it comes out that the patient was assuming flecainide 200 mg/day at the time of the initial tachycardia. The drug was then discontinued.

A posteriori, the first ECG was interpreted as atrial flutter with 1:1 AV conduction and aberrant QRS complexes. In the second ECG, there is a faster atrial rate because of lacking of the slowing atrial conduction influence of flecainide.

The patient underwent an electrophysiological study in which no ventricular arrhythmias were induced. However an atypical atrial flutter/atrial tachycardia with an atrial rate of 280/min was easily induced.

The class 1C drug flecainide is a sodium channel blocker which slows phase 0 of action potential, delaying conduction, with minimal effect on QT and with a mainly use-dependent effect.

Flecainide also prolongs the intra-atrial conduction and consequently reduce atrial rate. The decrease in atrial flutter rate to range of 180–200 beats/min can favor a 1:1 ventricular response.

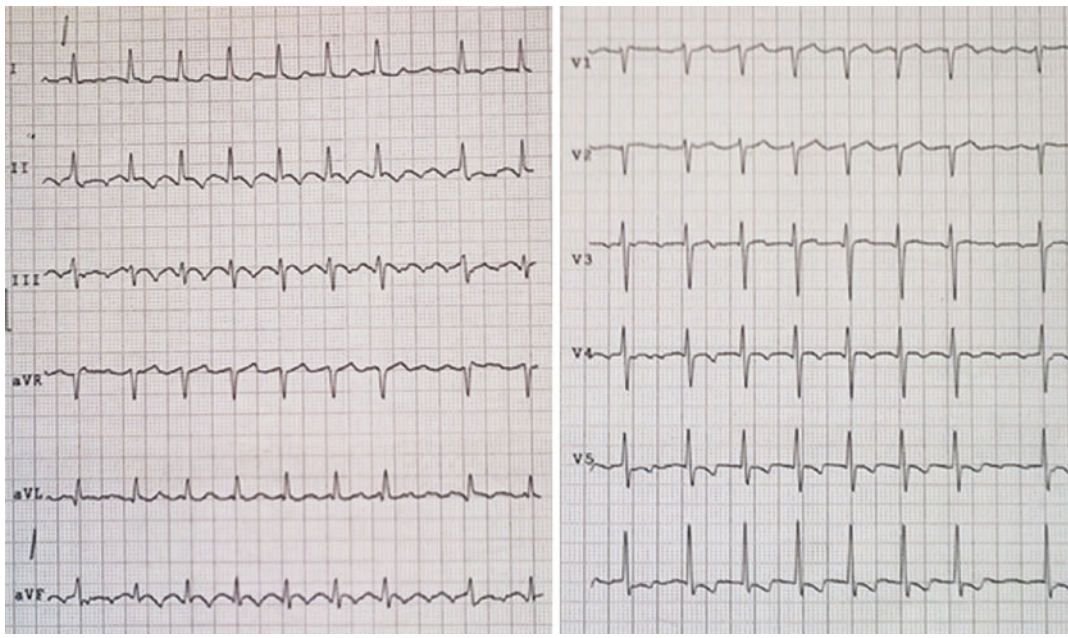

Fig. 6.7 Second standard 12-lead electrocardiogram recorded for case 4

This tachycardia effect happens in 0.5% of the treated patients during a chronic therapy.

6.4.4 From ECG to Pathology

Wide QRS complex tachycardias (WTC) are usually characterized by HR >100 bpm and QRS ≥120 ms duration.

Ventricular tachycardia (VT) is the most common cause (80% of cases); however a wide QRS could be supraventricular (SVT) and conducted with fixed or functional bundle branch block (BBB) (15–25% of WTC cases). The aberrancy may be favored by drug influences, electrolyte imbalances, or preexcitation (1–5%) [1].

A history of structural heart disease may be in favor of TV (>95% chances); however about 10% of patients with VT have no structural heart disease [1].

There are several electrocardiographic criteria for the differential diagnosis that are reported in Table 6.1 [6–10].

6.4.5 R Wave Peak Time (Intrinsicoid Deflection) Criterion

Intrinsicoid deflection, or R wave peak time, represents the early phase of ventricular depolarization and is defined as the time period from the onset of the QRS complex to the peak of the R wave (Figs. 6.8 and 6.9) [2–5].

The depolarization impulse travels through the normal His-Purkinje system faster than in the contractile myocardium and may be one reason why initiation of ventricular depolarization in VT

Table 6.1 Summary of the traditional criteria for the differential diagnosis of wide QRS tachycardias (WCT)

Atrioventricular dissociation	– No correlation between atrial and ventricular activity – It is diagnostic – 20–50% of VT	– P waves – Notches and irregularities repeated cyclically – 30% of VTs have 1:1 retrograde VA conduction
Capture beats	– Occur when a sinoatrial beat transiently captures the ventricles – It's an indirect sign of AV dissociation	– Narrow QRS complex usually close to normal duration
Fusion beats	– Occur when a sinoatrial beat and a ventricular beat coincide temporally in depolarizing the ventricles – It's an indirect sign of AV dissociation	– Hybrid QRS complex
Precordial concordance	– QRS complexes have the same orientation in all precordial leads	– Orientation of QRS complexes[a]
Morphology	– VT is suspected when QRS complexes do not resemble typical bundle branch block	RBBB morphology: – Wide R wave (V1) – qR or Rs (V1) – RSr′ (V1) – rS complex (V6) LBBB morphology: – Wide R wave (>30 ms) (V1 or V2) – A slurred or notched downstroke of the S wave (<60 ms) (V1 or V2) – Q wave, QS, or QR complexes (V6) [b] [c]

[a]QRS complexes have to be all positive or all negative from V1 to V6. A negative concordance has a higher specificity, while a positive concordance may also be caused by preexcited SVT through a left posterior accessory pathway

[b]In brackets is reported where to look for the morphologic features

[c]QR (but nor QS) complexes in any lead except aVR during WCT, especially when present in the same leads also in sinus rhythm; indicate a remote myocardial infarction and therefore are more suggestive for VT

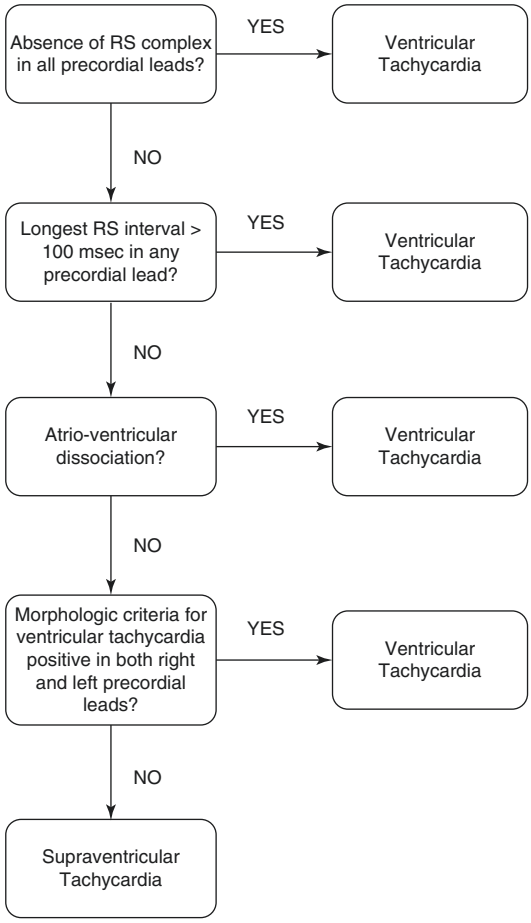

Fig. 6.8 Algorithm that summarizes Brugada's criteria for differential diagnosis of wide QRS tachycardias

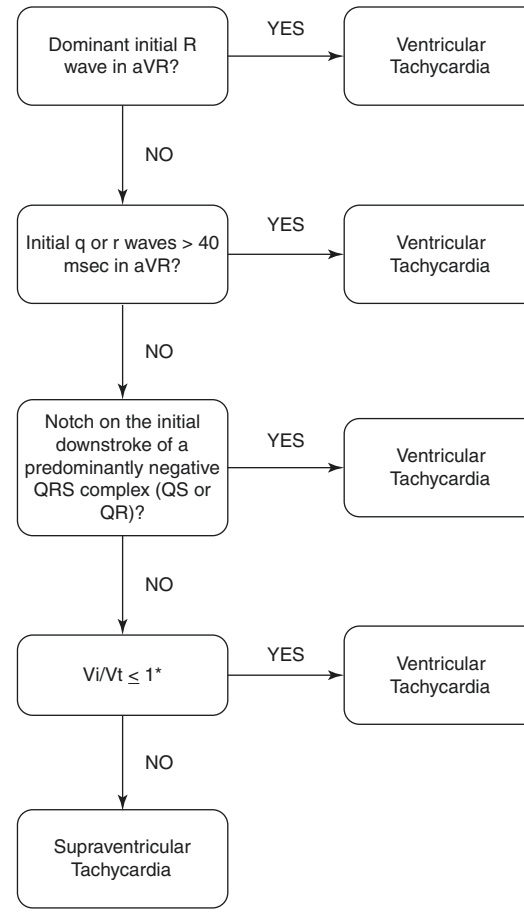

Fig. 6.9 Algorithm that summarizes Vereckei's criteria for differential diagnosis of wide QRS tachycardias. This algorithm adopts the conventional criteria of VA dissociation together with the morphologic analysis of the QRS complex in aVR. *v_i: total amplitude of the QRS in the first 40 ms; v_t, total amplitude of the QRS in the last 40 ms. During WCT due to VT, an initial slower muscle-to-muscle spread of activation occurs until the impulse reaches the His-Purkinje system, after which the rest of the ventricular muscle is more rapidly activated; thus, the $v_i/v_t \leq 1$ during VT

is longer than normal. The intrinsicoid deflection remains narrow or less wide during aberrance.

Pava et al. proposed that the deflection intrinsicoid in lead II (measuring the interval from the QRS onset to the peak of the first positive or negative wave) when ≥50 ms suggested VT and when <50 ms suggested aberrant conduction, with a high sensitivity (93.2%), specificity (99.3%), PPV (98.2%), and negative predictive values (NPV) (93.3%) for VT diagnosis [9].

Capucci et al. used a specific intracardiac ECG (iECG) to distinguish between an idioventricular activity (IVA) and an atrioventricular conduction (AVC) with wide QRS confirming that a prominent early iQRS velocity is generally observed with AVC and not with IVA [10].

Exception may occur depending on the underlying heart disease (MI scar, ventricular remodeling, or drug treatment) and a fascicular origin of the arrhythmia.

A precise evaluation of the initial ventricular activation represents therefore a strategic diagnostic criterion to differentiate any wide complex tachycardia. Indeed, the intrinsicoid deflection is an easy parameter to measure and therefore very much useful.

We believe that the integration of this parameter with the other reported ECG criteria (table) together with the patient history are of primary importance for a right etiologic definition of the tachycardia.

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7 QRS Morphologies of Difficult Interpretation

Agnese Fioranelli, Enrico Paolini, and Alessia Quaranta

7.1 Case 1: Hemiblocks

A preoperative ECG of a 48-year-old male affected by dyslipidemia, without any previous cardiological pathologies, was recorded. He complained of occasional palpitations (Fig. 7.1).

7.1.1 ECG Analysis

Regular rhythm at 67 bpm; every QRS is preceded by a P wave with normal axis, amplitude, and duration typical of a sinus rhythm; the atrioventricular conduction is at the upper limit (PR 200 ms); QRS duration is slightly prolonged (110 ms).

There is a left axis deviation −60° with poor R wave progression on the precordial leads and a delayed intrinsicoid deflection in aVL (60 ms), a terminal R wave in aVR, and a biphasic complex in V6. These findings suggest a left anterior fascicular block.

The QTc is slightly prolonged (Bazett = 465 ms).

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7.1.2 From ECG to Clinic

When a complete left axis deviation (≥ −30°) is recorded, there are usually two main causes:

(1) A simple left anterior fascicular block (or hemiblock, LAH) where the QRS complexes have an rS morphology
(2) Inferior or inferolateral myocardial infarction; with a possible Q wave in leads II, III, and aVF (5%)

Other possible clinical conditions coming together with a left axis deviation are:

(3) Left ventricular hypertrophy
(4) Ventricular preexcitation
(5) Pulmonary emphysema (COPD) (Table 7.1)

Some authors [1] further distinguished LAH in complete and incomplete; that may be apparent when premature beats are conducted with different degrees of LAH with a different QRS axis and S wave amplitude in II and III.

The electrocardiographic and vectorcardiographic expressions of LAH may have a high variability secondary to the fascicular speed and its anatomy (Fig. 7.2). It could be possibly more appropriate to substitute the term "block" with simply "delay" [2].

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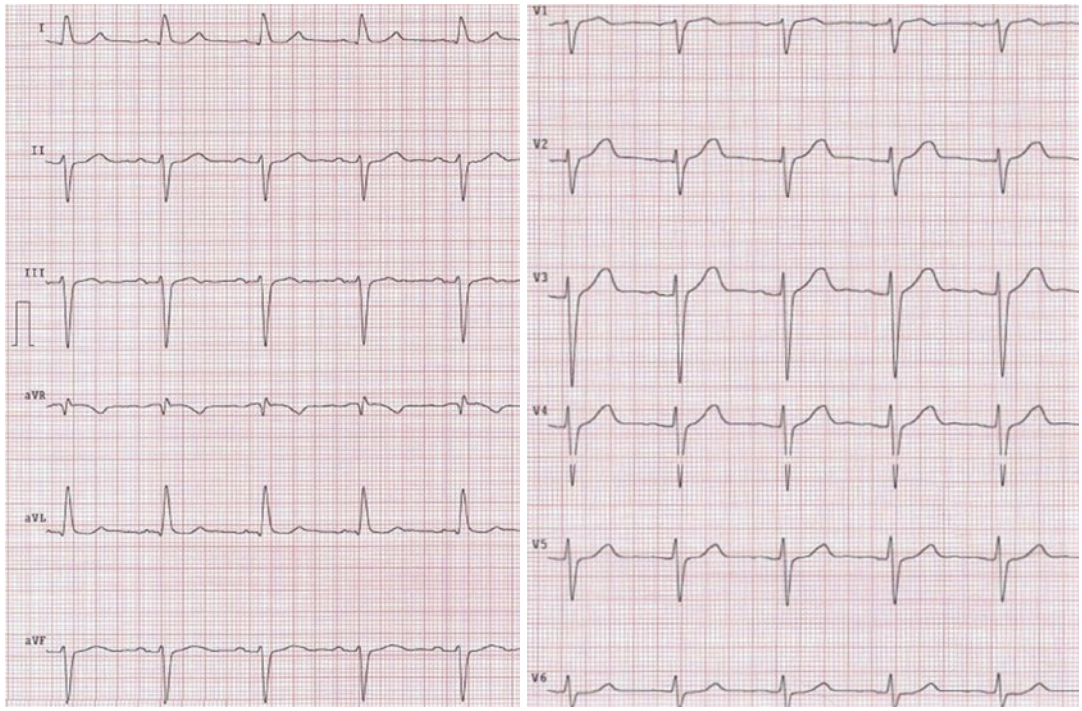

Fig. 7.1 Case 1 12-lead ECG

Table 7.1 Case 1 ECG features of LAH

ECG features of LAH	Additional findings
Left axis deviation of at least −30°[a]	Delayed intrinsicoid deflection (≥50 ms) in aVL
S wave II < III	Slurred R downstroke in I and/or aVL
qR complexes in aVL and I	Rs or rS without Q waves in V6[b]
rS complexes in III and aVF, and rS or RS in II	QRS duration ≤0.12 s
Secondary repolarization abnormalities of ST-T in I and aVL	r terminal wave in aVR

[a]In opinion of some authors, the lower limit should be set at -45° because of its specificity
[b]Or from V4–V6

Figure 7.3 reports a minor grade of left axis deviation (−30°) due to left anterior hemiblock. The AV conduction is at upper normal limit, and there is a slightly prolonged QTc. Are those figures clinically relevant features when compared to Fig. 7.1?

The prognostic value of a left anterior hemiblock depends on the clinical context. Previous studies [3, 4] that evaluated its prognostic significance in a general population with structurally normal hearts did not report any relationship with long-term mortality.

Biagini et al. [5] instead found that LAH is an independent predictor of total (1.5-fold) and cardiac (2.5-fold) mortality in a special patient population referred for a dobutamine stress test. Patients with LAH had a 10% higher incidence of ischemia at dobutamine stress echocardiography.

More recently, pre-existing isolated LAH was found to be associated with a higher incidence of permanent pacemaker implantation after a transaortic valve implantation (TAVI) [6].

However its natural history is benign since only 6% of LAH in people without apparent heart disease will evolve to complete left bundle branch block.

The latest European Guidelines [7] advise against preventive PMK implantation in asymptomatic patient with any bundle branch block (class 3, level of evidence B).

Fig. 7.2 Case 1 Diagrammatic sketches of the left-sided conduction system as observed in 20 normal hearts [taken from J.C.Demoulin and H.E. Kulbertus, 1972. Histopathological examination of concept of left hemiblock. Heart. 34(8) under concession of BMJ]

Possible misdiagnosis:

1. A right bundle branch block may mimic LAH; in that case, a possible wrong diagnosis of bifascicular block can be done.
2. A "standard lead" masquerading right bundle branch block coexisting with LAH.
3. A "precordial" masquerading right bundle branch block coexisting with LAH.

In the first case, the anterior direction of the terminal forces is missing, so an rSr' complex in precordial leads may be absent, and an rs or rS complex appears in II.

A close look at Fig. 7.4 reveals that S2 > S3 and there is a little s wave in aVL; those patterns are not typical of a simple LAH.

In the second and third cases, a right bundle branch block is masquerading by a left anterior hemiblock (respectively, Figs. 7.5 and 7.6):

- In the standard leads masquerading, there aren't S delayed waves in I and aVL.
- In the precordial masquerading, there are rSR' complexes in right precordial leads.

7.1.3 Left Posterior Hemiblock

Left posterior hemiblock is a rare finding.

Its electrocardiographic diagnosis is mainly made after a right ventricular pathology exclusion.

In a long-limbed patient, for instance, this diagnosis could be overdone since a right axis deviation could be due simply to the vertical heart position, in the absence of a true conduction delay.

In Fig. 7.7, there is an example of an ECG of a 31-year-old female: she was referred to the cardiologist for clinical evaluation before starting a physical training at the gym.

She was completely asymptomatic.

7.1.4 ECG Analysis

Narrow complex regular tachycardia; every QRS is preceded by a P wave with normal axis (+75°), high amplitude (0.25 mV in lead II), and normal duration typically of sinus origin. HR is 102 bpm; atrioventricular conduction is normal (PR = 180 ms); there is a small PR segment depression.

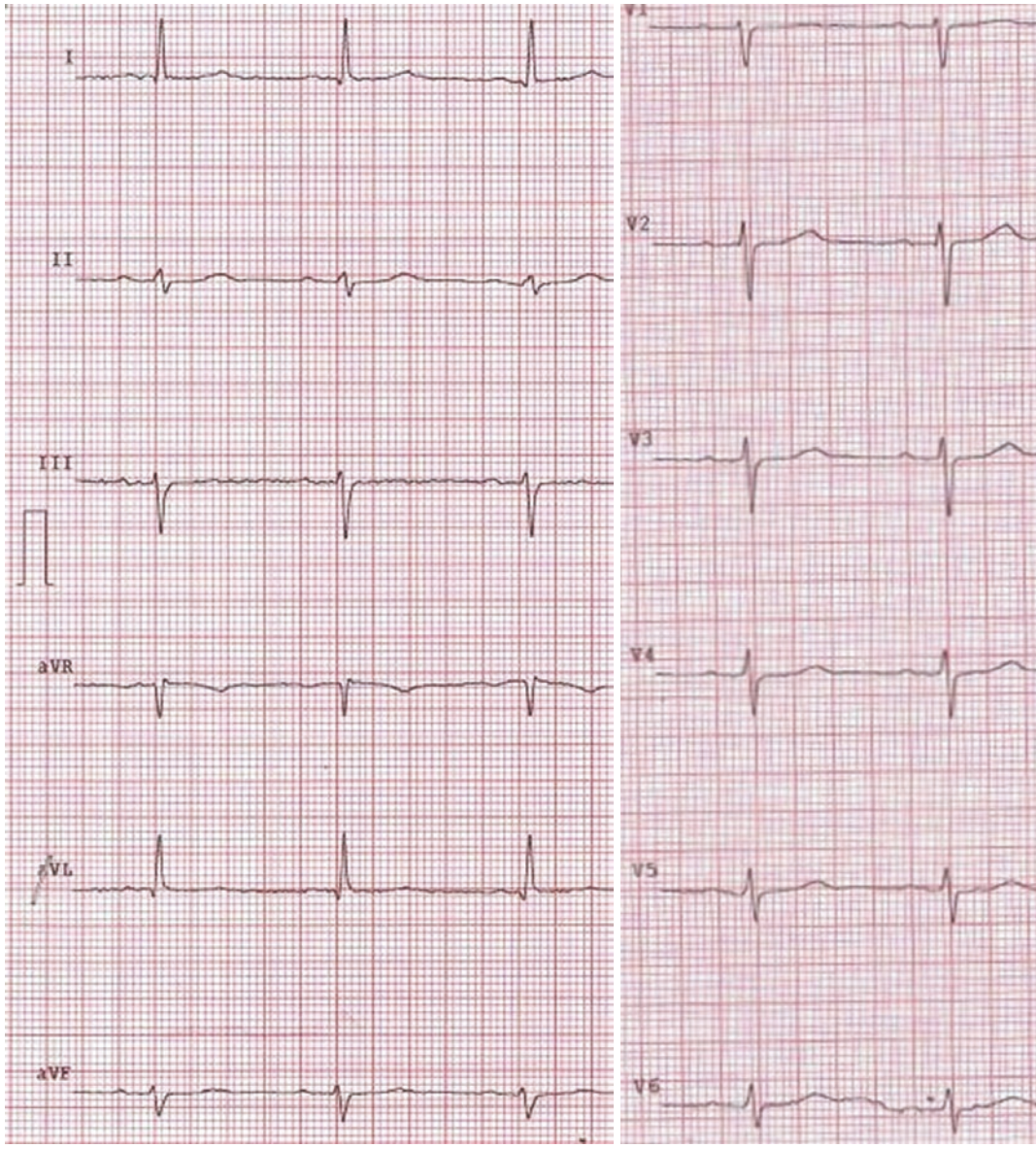

Fig. 7.3 Case 1 12-lead ECG

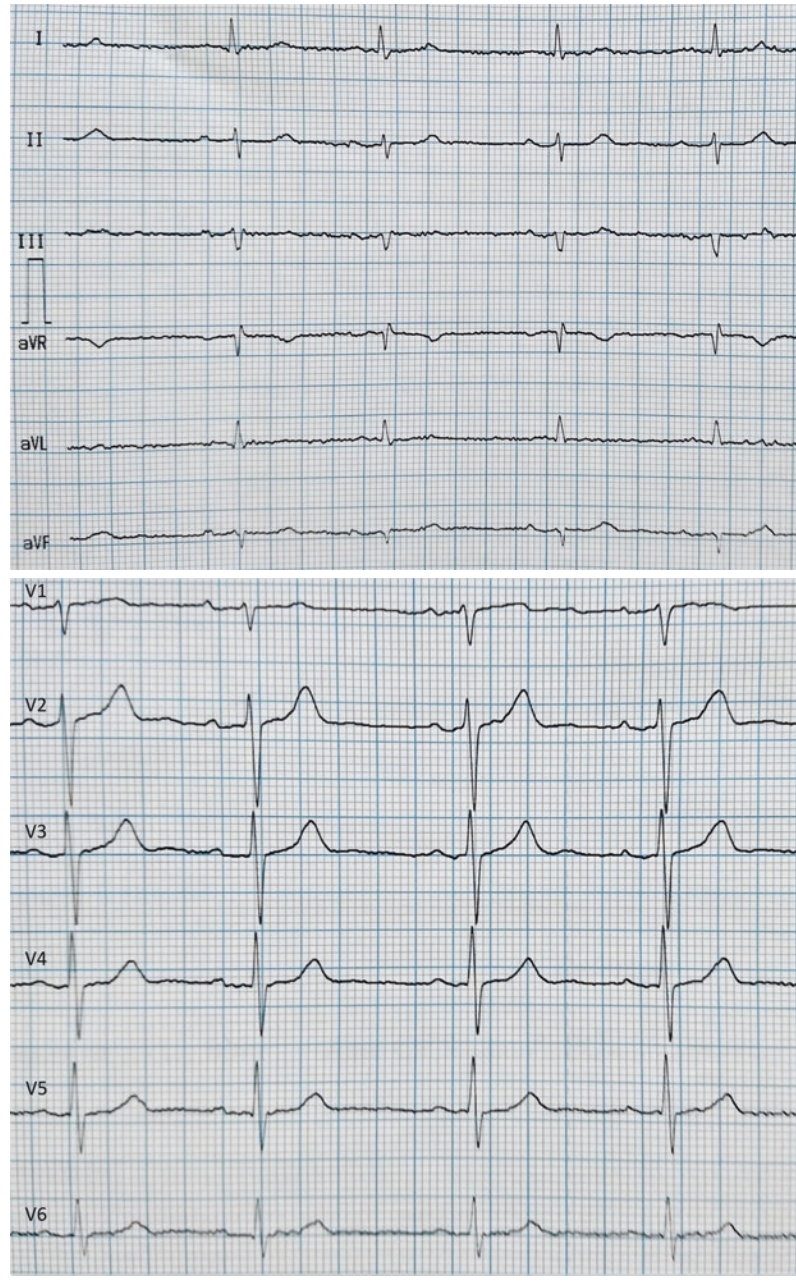

Fig. 7.4 Case 1 12-lead ECG

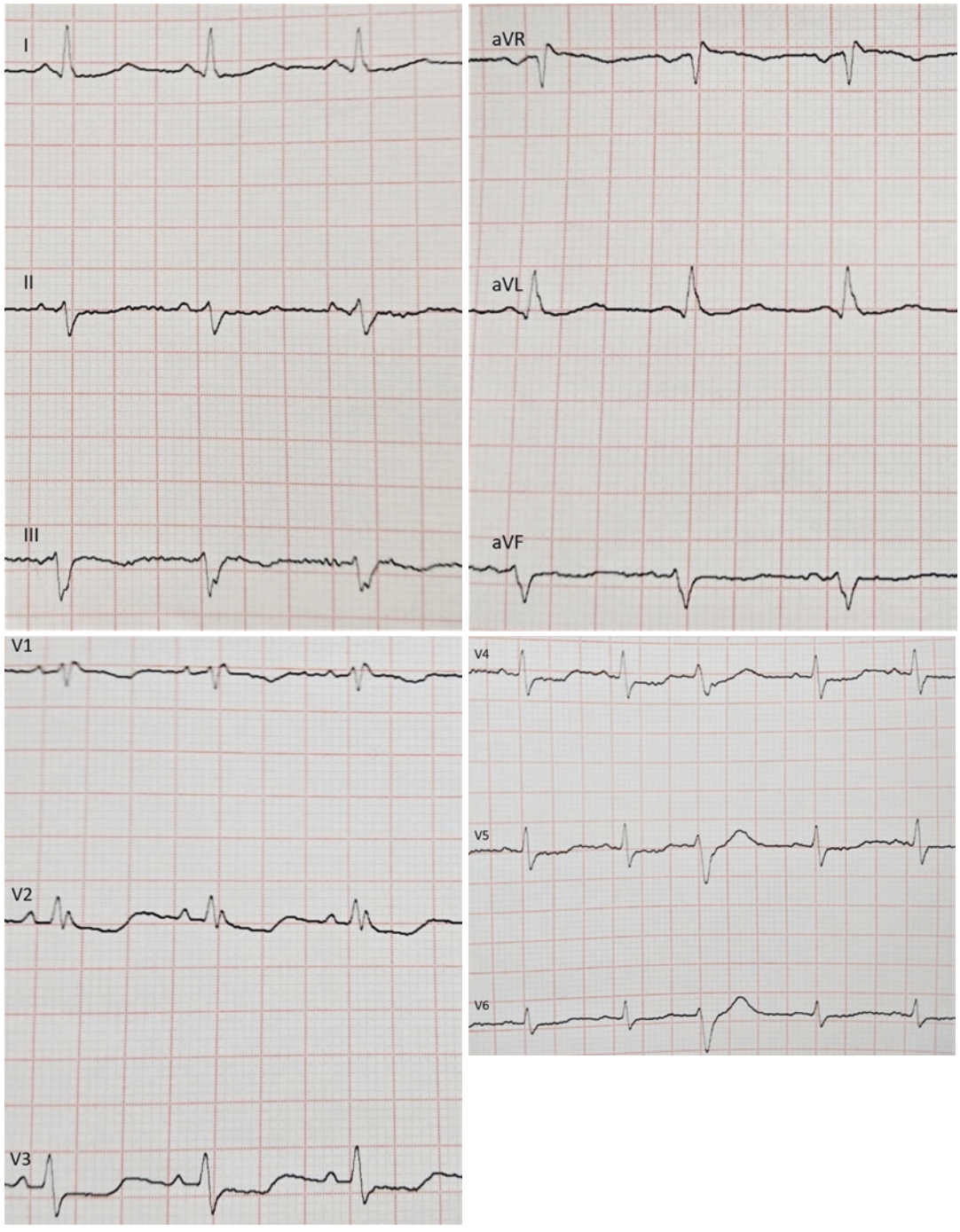

Fig. 7.5 Case 1 12-lead ECG

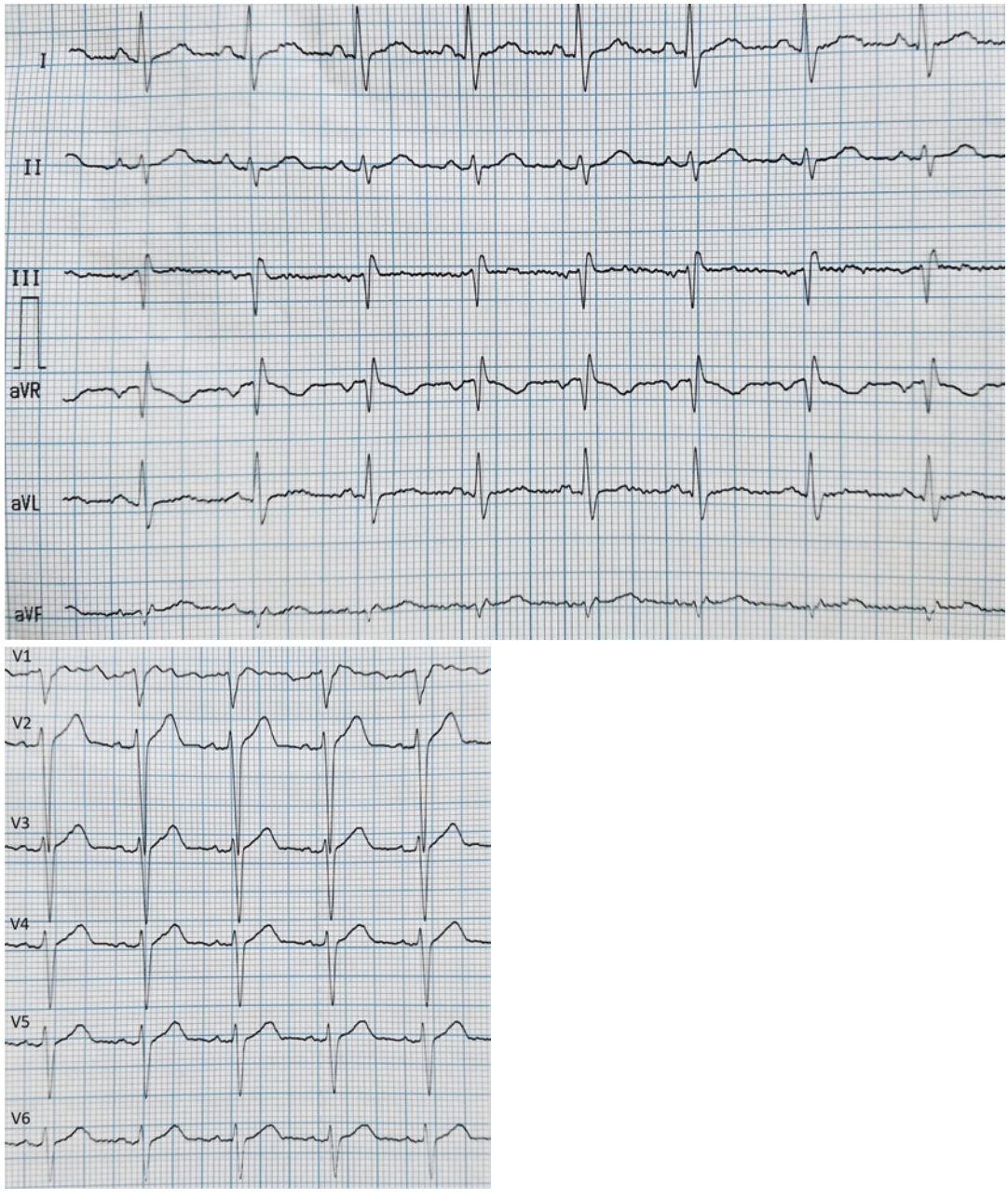

Fig. 7.6 Case 1 12-lead ECG

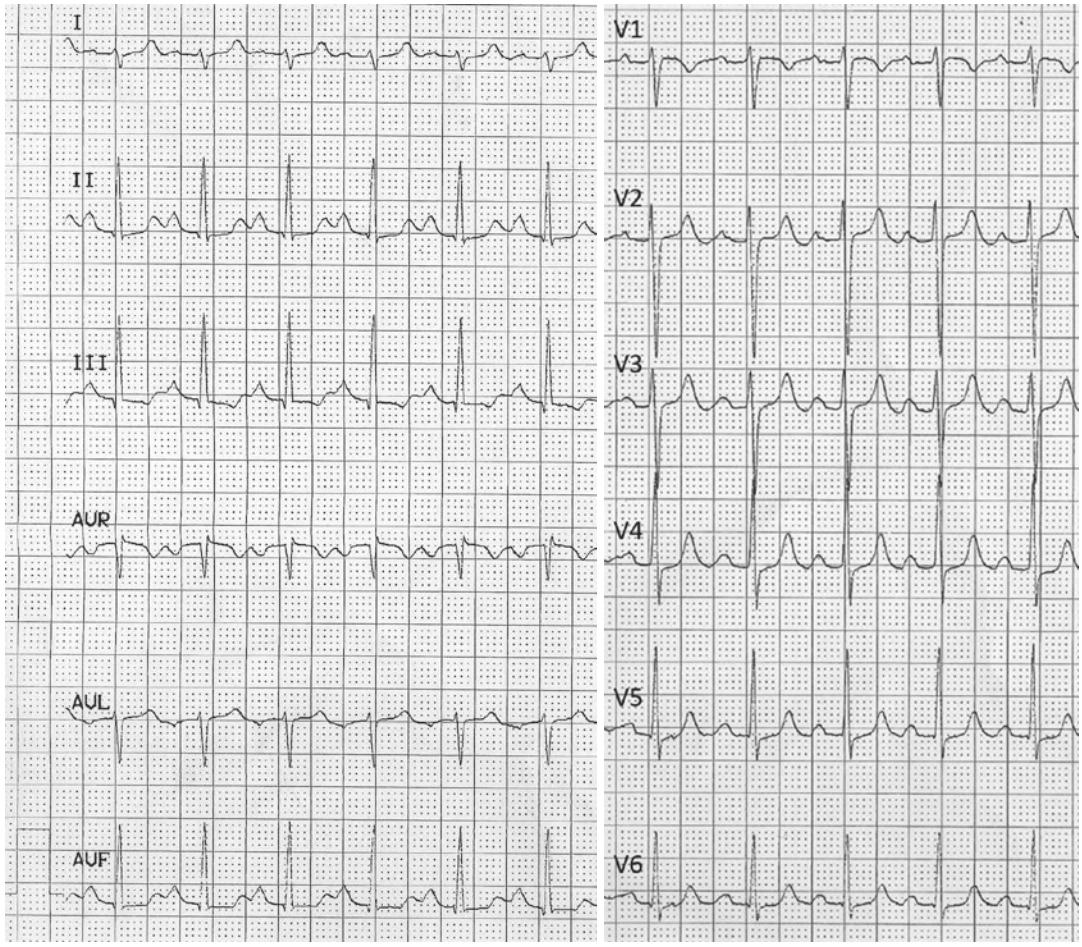

Fig. 7.7 Case 1 12-lead ECG

QRS duration is normal, with a right axis deviation (+115°).

There are diffuse ST-T alterations: flat ST segment with biphasic T waves in III and aVF, symmetrical in V2-V5.

QTc is normal (430 ms).

In summary, the ECG shows sinus tachycardia, normal AV conduction, right axis deviation secondary to left posterior fascicular hemiblock, nonspecific repolarization abnormalities, and normal QTc.

7.1.5 From ECG to Clinic

In the absence of any pathology, an echocardiogram was also recorded and confirmed a normal right ventricular morphology, dimensions, and function and normal pulmonary artery dimensions and gradients; there was only a mild mitral regurgitation due to anterior leaflet prolapse.

A pectus excavatum was present; that anatomical pattern by changing the normal topography of the chest/heart could influence on the axis deviation and thus question the diagnosis of left posterior hemiblock.

The diagnostic reported classical signs of this rare conduction disturbance are:

- Right axis deviation (>90°)
- qR complexes in II, III, and aVF
- ST-T inversion in the same leads
- Q wave absence in V6
- aVF intrinsicoid deflection delay slower than in V6
- QRS duration ≤120 ms

We believe that this reported ECG is a normal variant in a young woman with mild mitral valve prolapse and without other abnormal findings.

The diagnosis of left posterior hemiblock remains a conundrum, which is possible to solve only after an exclusion criteria work-up.

7.2 Case 2: Pathological and Physiological Q Waves

In Table 7.2, the common conditions that favor Q waves on the surface ECG are reported [8–10].

In Wolff-Parkinson-White (WPW) preexcitation a pseudo-infarction pattern may be a common finding in up to 70% of patients. That is due to negative delta waves in the inferior/anterior leads ("pseudo-Q waves") or to a prominent R wave in V1–3 (mimicking a posterior infarction).

Inferior lead pseudo-infarct Q waves are a common finding in the Wolff-Parkinson-White (WPW) syndrome.

In a retrospective study [11], pseudo-infarct Q waves in the inferior leads were associated with positive or isoelectric T waves in 47 of 50 examples (94%).

Table 7.2 Features of Case 2 pathological and physiological Q waves

Pathological Q waves
Physiologic and positional effects: *dextrocardia, rightward mediastinal shift in left pneumothorax, pectus excavatum, COPD, corrected transposition of the great vessels, congenital absence of the left pericardium*
Ventricular enlargement
Altered ventricular conduction: *left bundle branch block, WPW*
Misplacement of chest lead electrodes
Stress-induced (Tako-Tsubo) cardiomyopathy
Myocardial ischemia (without infarction)
Sign of previous myocardial infarction: *pathological Q waves are 25% or more of the height of the partner R wave, and they are greater than 40 msec in width and greater than 2 mm in depth*
Physiological Q waves
Physiologic activation of the ventricles begins at the left side of the interventricular septum: small "septal" Q waves occur in the lateral leads
QS complex can appear in aVL with a vertical axis and in leads III and aVF with a horizontal axis
Q wave in lead III may be positional and a normal finding

This characteristic Q wave-T wave vector discordance may be related to a nonhomogeneous ventricular activation.

A further cause of pseudo-infarct pattern could be left or right ventricular enlargement [12].

Q waves in these settings may reflect a variety of mechanisms, including a change in the balance of early ventricular depolarization forces and altered cardiac geometry and position; in fact, slow R wave progression in the precordial leads is commonly observed either in left ventricular hypertrophy or in right ventricular overload.

The acute pulmonary embolism develops the classic S1Q3T3 pattern of McGinn and White, but this sign is neither sensitive nor specific for pulmonary embolism (Fig. 7.8).

A prominent Q wave (usually as part of a QR complex) in lead aVF is also reported in this condition.

It was found that an acute right ventricular overload itself does not necessarily cause any pathologic Q wave in lead II [13].

7.2.1 ECG Analysis

Figure 7.9 shows a sinus tachycardia (HR 105 bpm) with PR interval of 160 ms, QRS axis of −15°, normal intraventricular conduction, 1 mm ST depression in lateral leads, biphasic T waves in leads I and II, and flattened T waves in precordial leads V3–V6. There is a classic pattern S1Q3T3.

The polarity of T waves may be useful in the differential diagnosis between hypertrophic cardiomyopathy and previous myocardial infarction.

T wave will be usually upright in an ECG of a patient with Q waves secondary to hypertrophy.

In case of myocardial infarction, prominent Q waves may be associated either with upright or also inverted T waves.

Figure 7.9 represents an equivocal ECG: there is a sinus rhythm at 55 HR, the QRS axis is −15°, and there is normal AV and IV conduction and nonspecific repolarization pattern.

There are clear Q waves in the inferior leads that could be related to previous infarction.

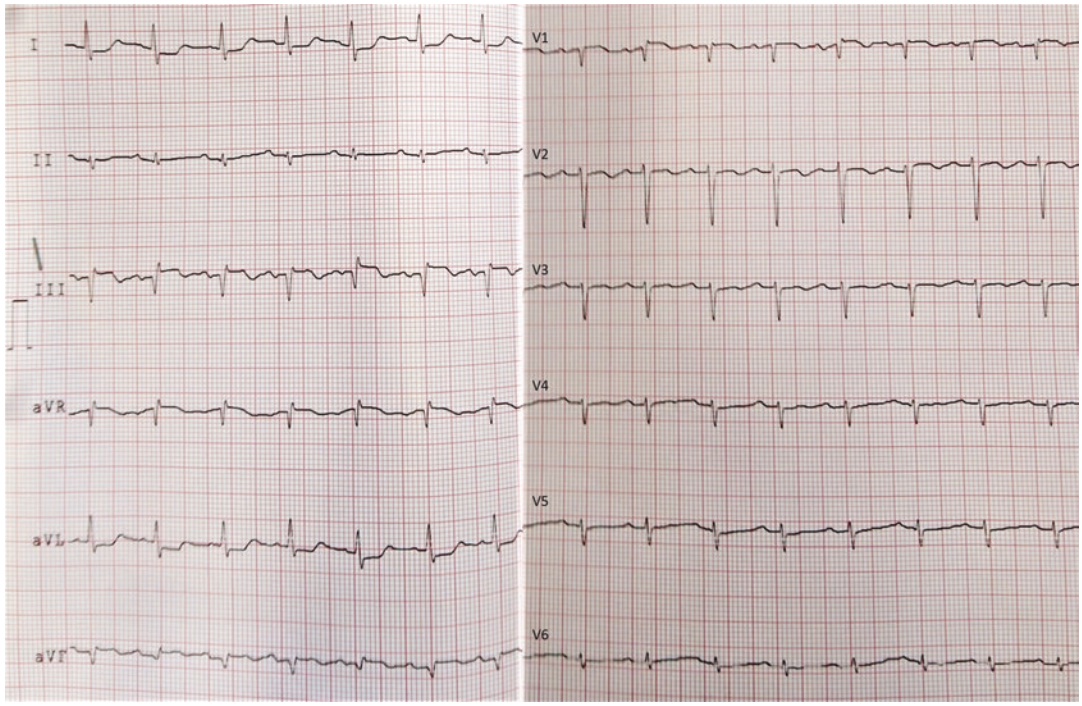

Fig. 7.8 Case 2 12-lead ECG

In Fig. 7.10 is shown the same ECG repeated during a deep inspiration.

7.2.2 ECG Analysis

Sinus rhythm at 60 bpm; QRS axis is −15°; normal atrioventricular and intraventricular conduction; Q wave in lead III with an r appearance in aVF (look at the arrow).

7.2.3 From ECG to Practice

Bodenheimer et al. [14] studied the effect of deep inspiration on Q waves in leads III and aVF in 31 patients by comparing with their cardiac catheterization results.

They found that the phasic inspiration can significantly influence Q wave duration in leads III and aVF, regardless of the presence or absence of significant associated coronary artery disease and asynergy. When that happens, those Q waves have no relevant values.

Nanni et al. [15] evaluated the diagnostic accuracy of electrocardiographic inferior Q wave persistence during inspiration by comparing with echocardiographic segmental wall motion abnormalities and using cardiac magnetic resonance as the gold standard.

They prospectively enrolled 50 apparently healthy subjects with inferior Q waves on routine electrocardiogram and high atherosclerotic risk profile.

From ten positive cardiac magnetic resonance subjects, eight showed persistence of inferior Q waves during inspiration, giving a sensitivity of 80% and a specificity of 95%.

The conclusion was that the inferior Q wave persistence during deep inspiration is a simple test with a high accuracy for the diagnosis of silent myocardial infarction, while the standard echocardiography result is less accurate.

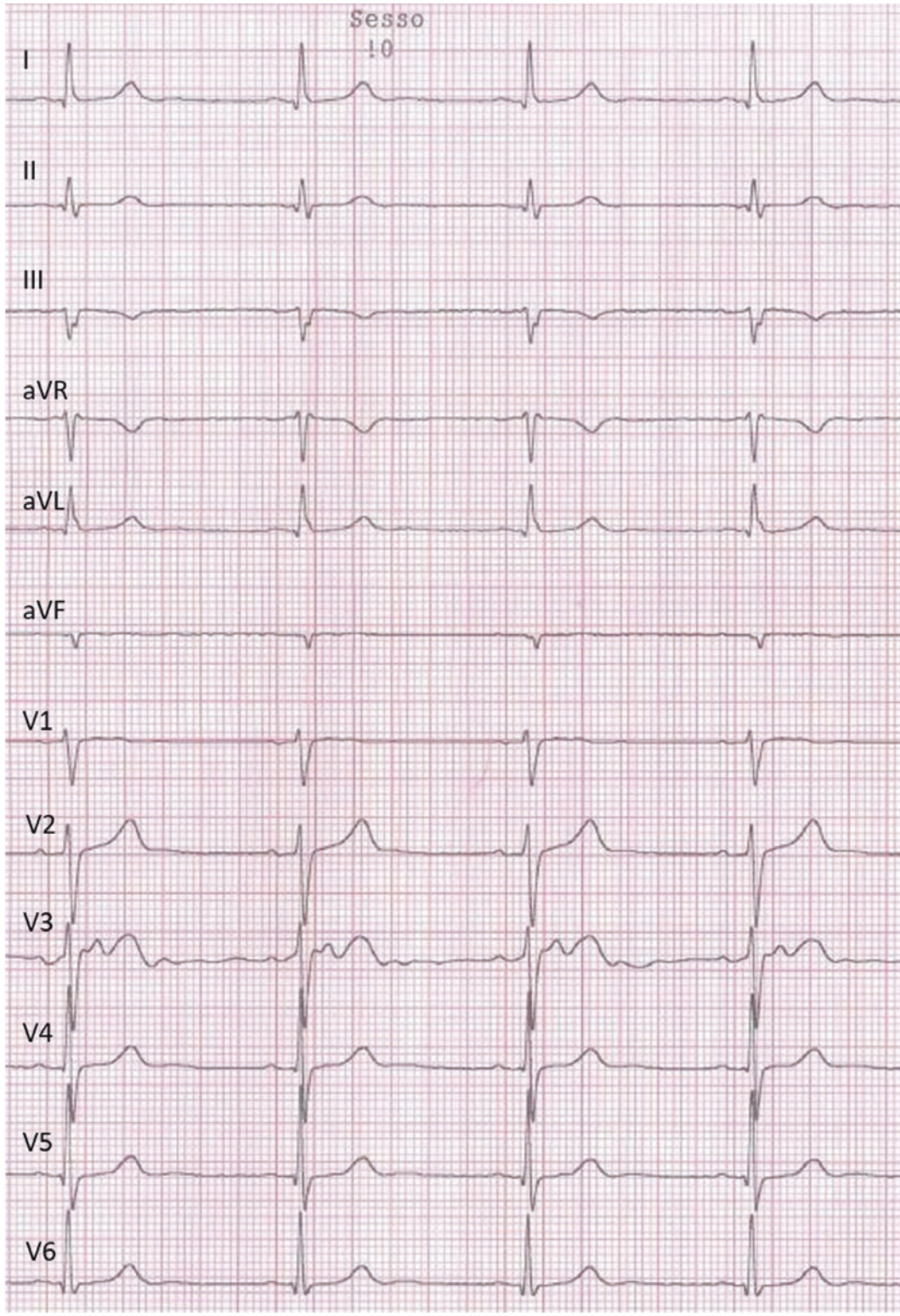

Fig. 7.9 Case 2 12-lead ECG

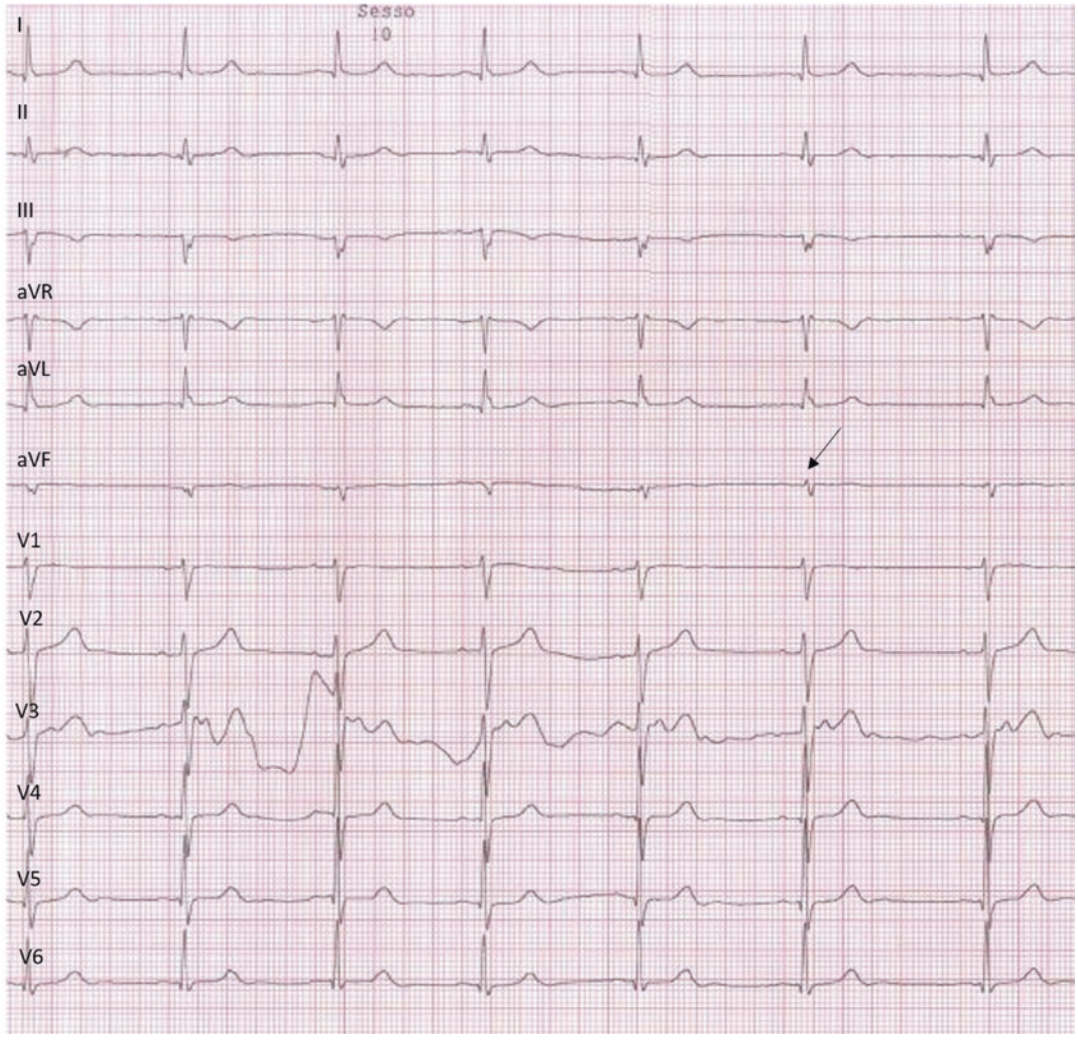

Fig. 7.10 Case 2 12-lead ECG

7.3 Case 3: rSr′ Complexes in the Precordial Leads

Male, 30 years old, without previous cardiovascular pathologies. Normal familiar medical history and physical examination; no echocardiographic signs of structural heart disease.

In Fig. 7.11 is shown his ECG:

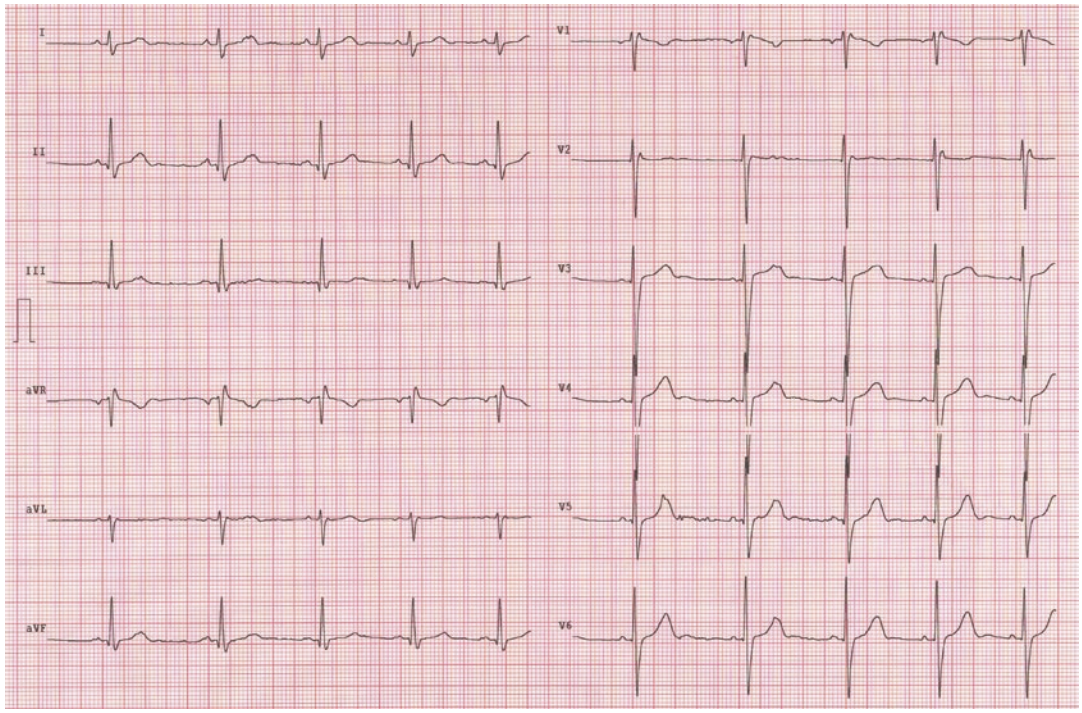

Fig. 7.11 Case 3 12-lead ECG

7.3.1 ECG Analysis

Regular rhythm is at 60 bpm; every QRS is preceded by a P wave with normal axis, amplitude, and duration, thus expression of sinus rhythm; the atrioventricular conduction is normal (PR 120 ms). QRS duration is normal (80 ms), showing rSR' morphology in the right precordial leads (V1-V2); QRS axis is vertical (+90°) with a clockwise QRS rotation on the longitudinal axis; there is an S wave in lead I and V6 and a wide terminal R wave in aVR.

QTc is normal (400 ms).

In summary, the ECG shows a sinus rhythm with normal atrioventricular conduction, incomplete right bundle branch block, and secondary repolarization abnormalities.

7.3.2 From ECG to Practice

Incomplete RBBB diagnosis is mainly QRS morphology related because the ventricular activation length could be in total poorly prolonged despite a significant delay already in the right ventricle [16, 18] (Table 7.3).

Table 7.3 Case 3 ECG features of RBBB

ECG diagnostic criteria [17]
• rSR' complex in the right precordial leads with R' wave usually higher than initial R wave in V1–V2
• Wide S waves in I, V5, and V6
• Wide terminal R wave in aVR
• QRS duration >120 ms and S waves duration >40 ms (complete RBBB)
• QRS duration <120 ms and S waves duration <40 ms (incomplete RBBB)

V1 QRS morphology depends on the amount of activation delay.

However, the increased conduction time can be related not only to a slower conduction velocity but also to an abnormal long right bundle branch or to a right ventricular outflow hypertrophy [19].

The QRS axis is usually normally oriented in RBBB, but there could be a mild right axis deviation or an undetermined axis.

A rSr' complex only in V1 (not extended to V2) could be often found in normal young people as a normal variant.

Some authors [20] identified the following features in the right precordial leads (V1, V2) that precede or accomplish the appearance of the rSr' as RBBB findings:

- Reduced S wave depth (100%)
- Inverted ratio of the S wave depth to SV1 > SV2 (93%)
- Slurred downstroke or upstroke of the S wave (27%)
- Prolonged QRS duration >0.10 s (73%)

The rSR' pattern is not associated with an increased risk of cardiovascular diseases and therefore may be considered as a benign finding [21].

The RBBB pattern could be confused so far with the "Brugada syndrome" since the last is characterized by a rSr' complex in lead V1 that resembles an incomplete RBBB.

Nevertheless, r' wave of the QRS complexes of Brugada pattern is not a sign of delayed activation of the right ventricle, but it is an expression of a repolarization abnormality with a consequent delayed initial repolarization, and it should be called more appropriately "J" wave [22].

Thus ST-segment elevation in Brugada and terminal r' wave are not synchronized with the extended S wave in leads I and V6.

Below (Fig. 7.12) there is an example of Brugada pattern.

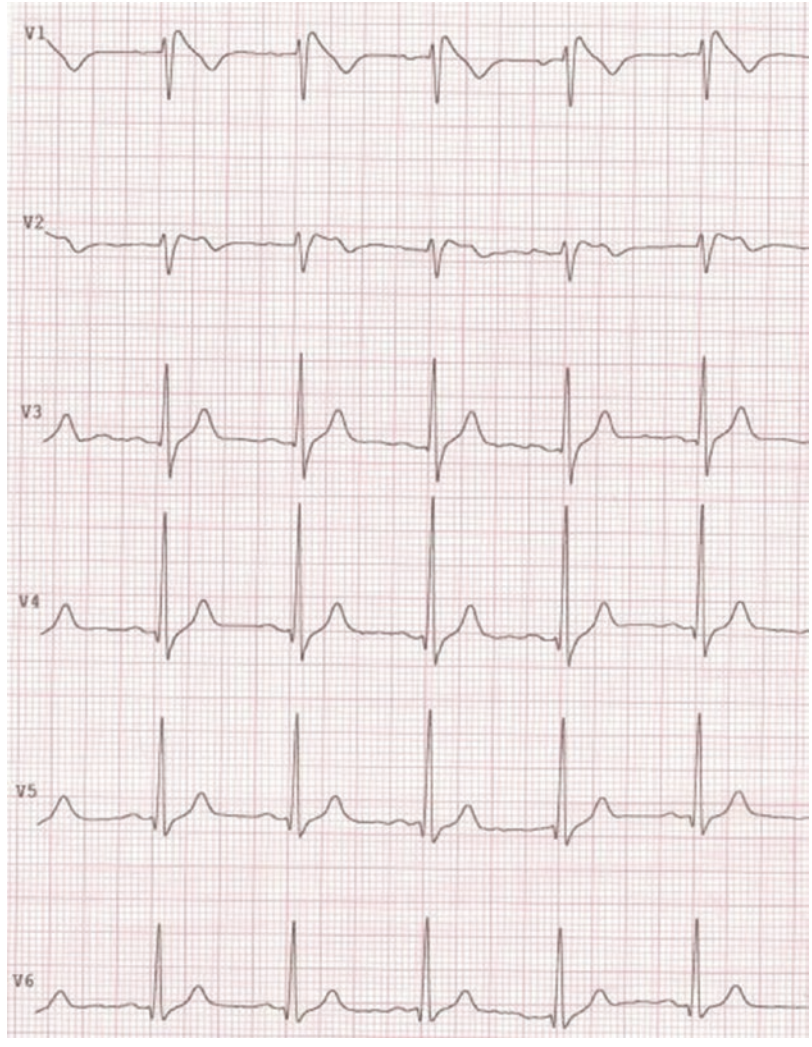

Fig. 7.12 Case 3 Chest lead ECG

7.3.3 ECG Analysis

Sinus rhythm with normal atrioventricular conduction; normal QRS duration of 120 ms with rSR' pattern in lead V1 and S wave in V6.

In V1 and V2, there are few features that can lead to the correct diagnosis:

- In lead V1, there is a J-point elevation of 3 mm and coved-type descending ST-segment elevation which merges into a negative T wave.
- In lead V2, there is J-point elevation (2 mm), a saddleback ST-segment elevation (1 mm in its terminal portion), and a biphasic T wave.

The V1 features are typically a Brugada type 1 pattern, whereas the V2 findings are typical of a Brugada type 2 pattern. The difference with an incomplete RBBB is striking.

This ECG belongs to a young man with a clear Brugada syndrome.

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8 Second-Degree Atrioventricular Blocks: Take It Easy

Francesca Patani, Francesca Troiano, and Jenny Ricciotti

8.1 Case 1

An 85-year-old man symptomatic only for dizziness wore a 1-day/three-channel Holter monitor ECG. He had a history of first-degree atrioventricular block (PR interval of 240 ms) and arterial hypertension.

8.1.1 ECG Analysis

The strip of Fig. 8.1 (recorded at 01.17 a.m.) shows a sinus rhythm with heart rate of 35 bpm. R-R intervals are slightly irregular, and the QRS complexes are 100 ms in width. P-P intervals are instead regular, and some P wave is not conducted to ventricles. The first three PR intervals have the same 210 ms duration, while the fourth shows a prolongation before the blocked P wave.

There is a 2:1 atrioventricular block in the first part of the strip and a type I second-degree atrioventricular block with a Wenckebach periodicity with an AV conduction ratio of 3:2 in the second part. After the blocked P, PR is shorter than the preceding and equal to the PR intervals of the 2:1 AV block.

In Fig. 8.2 another strip taken from Holter ECG of this patient shows two groups of narrow QRS complexes, with an average heart rate of 75–80 bpm, followed by pauses, respectively, of 1185 and 1200 ms. The two T waves within each of the pauses have a slightly different morphology from the others, because of the presence in their descendent branch of a blocked P.

We have to make a differential diagnosis between type I and type II second-degree AV block.

By considering the central beats of each group of QRS complexes, it could be a type II, being characterized by a substantial regular PR interval (280 ms) until a P wave is not conducted. By looking carefully, we observe a definite small incremental progressive conduction delay of PR before the non-conducted P; however, there is lack of RR shortening before the blocked P. PR interval after the block is shorter than PR just preceding the non-conducted P. This is therefore an atypical Wenckebach periodicity rather than a type II second-degree AV block (see after in Sect. 8.3.2). The right diagnosis in this case may have a prognostic implication, since the block localization is supra-hisian. The patient was totally asymptomatic during the all Holter recording and without any significant (≥3 s) pause.

Despite this analysis, the patient was sent from outside to our EP laboratory with an indication to implant a permanent pacemaker. We made an EP study that did confirm a supra-hisian con-

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A. Capucci (ed.), *New Concepts in ECG Interpretation*,
https://doi.org/10.1007/978-3-319-91677-4_8

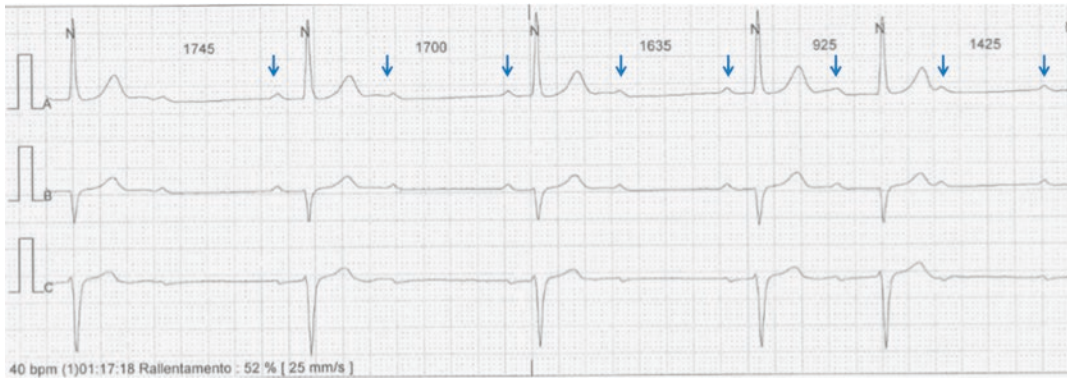

Fig. 8.1 Case 1; Holter ECG recorded at 01.17 am

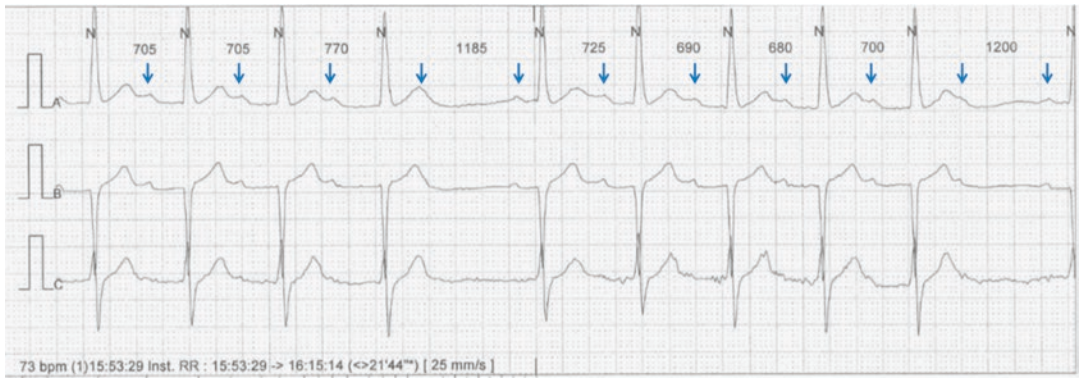

Fig. 8.2 Case 1; Holter ECG recorded at 03:53 pm

duction delay and a normal infra-hisian conduction (HV interval of 58 ms). The pacemaker was not implanted.

8.2 Case 2

An 86-year-old woman went to the emergency department for worsening dyspnea in the last 3 months (NYHA III); she also reported episodes of postural instability and dizziness. She had no history of cardiovascular disease but was affected by COPD.

8.2.1 ECG Analysis

Figure 8.3 shows the surface ECG recorded. There is a slightly irregular narrow QRS, with an average heart rate of 45–50 bpm. P waves are positive in inferior leads and negative in VR; therefore it is a sinus rhythm. QRS length is 120 ms with left axis deviation secondary to left anterior fascicular block. P-P intervals are regular (720 ms).

Differential diagnosis:

- *High-grade atrioventricular block with junctional escape complexes*. The P waves clearly visible in the precordial leads (especially from V1 to V3) are in a sort of repetitive sequence: they precede each QRS (with a constant PR interval of 240 ms) and can be found either at the end of each T wave or in its ascending part. P-P intervals are regular (720 ms). The slightly irregular R-R intervals and those P waves apparently conducted to ventricles make a third-degree AV block hypothesis unlikely.
- *Type II second-degree AV block*: If this hypothesis is correct, we have to believe that only the

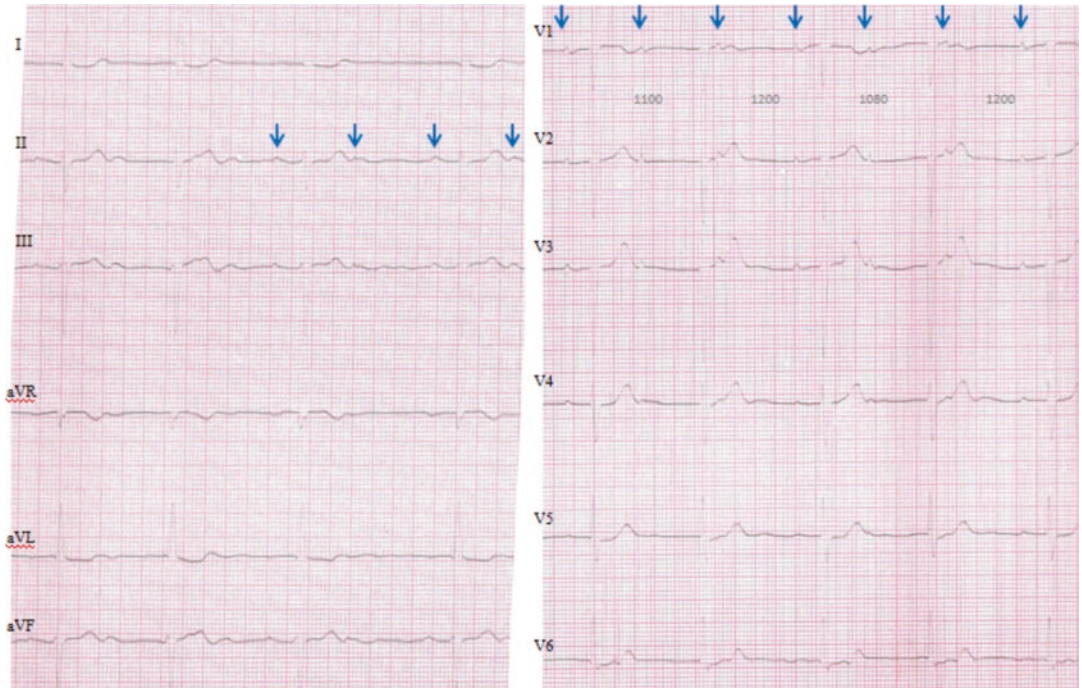

Fig. 8.3 Case 2; 12-lead ECG

first P wave in lead V1 (or V2) is actually conducted to ventricles; meanwhile the second one is blocked, and a junction escape beat ensues with a retro-conducted P. However also the second P could be regularly conducted with a very long AV delay (600 ms). The third P is not retro-conducted since it has identical morphology to the others. The pauses after each blocked P have the same duration. Therefore also the hypothesis of a type II atrioventricular second-degree block is unlikely.

- *2:1 atrioventricular block*. By looking carefully in the limb leads, especially the last two QRS complexes, we can see a very short phase of alternance of the conducted beats resulting in a 2:1 atrioventricular ratio. P waves conducted to ventricles have a PR interval of 260 ms, and blocked P waves are visible at the end of the T. Therefore the hypothesis of a 2:1 atrioventricular block could be possible.
- *Type I second-degree AV block.* By considering this hypothesis, we are in front of a Wenckebach block with an atrioventricular conduction ratio of 3:2. In lead V2, there is a progressive prolongation of PR of the two conducted P (240 and 600 ms) before the conduction failure of the third atrial impulse. Moreover, a shorter PR interval after the block is present, and each pause between QRS complexes containing a non-conducted P is less than the sum of R-R intervals. This is therefore the right hypothesis.

In this ECG, a type I atrioventricular second-degree block occurs with a 2:1 block and with a QRS width at the upper limit. This has a high chance to be a supra-hisian block.

The block disappeared during exercise and reappeared by the end (Fig. 8.4). The patient was asymptomatic during the all exercise. These further data strengthen the hypothesis of an atrioventricular nodal site of block that typically improves during exercise consequent of the higher sympathetic tone.

At the EP a type I second-degree atrioventricular block, with a supra-hisian delay and normal infra-hisian conduction, was found.

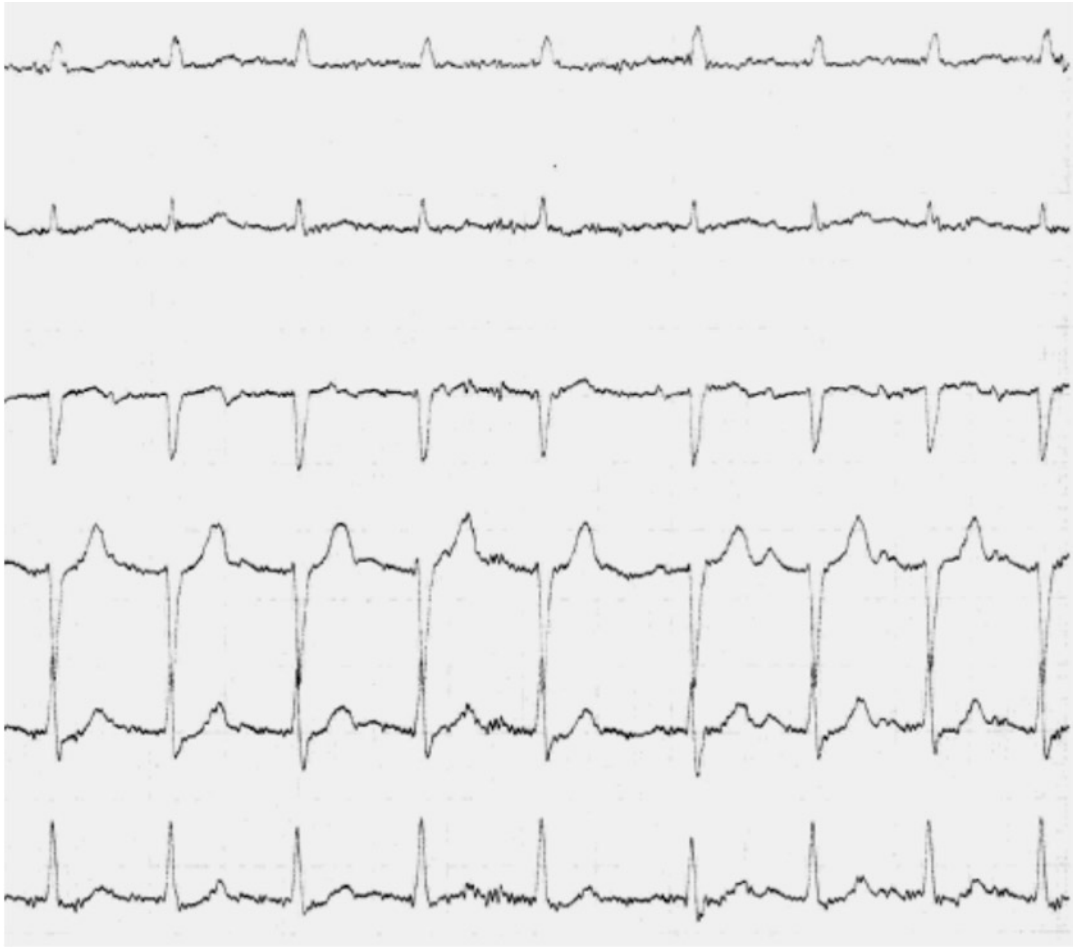

Fig. 8.4 Case 2; ECG during exercise stress rest

8.3 ECG Features of Atrioventricular Blocks

8.3.1 Types I and II Second-Degree Atrioventricular Blocks

Second-degree AV blocks can be classified in types I and II. The two reported cases are dealing with different ECG patterns that describe an intermittent failure of AV conduction [1]. The importance of a correct diagnosis in those cases is related obviously of the different prognostic implications. Type I is a benign condition, while type II usually requires a pacemaker implantation [2].

Table 8.1 illustrates the main diagnostic differences between the two types of block.

A second-degree AV block localized in the AV node can be reversed completely or partially to 1:1 conduction by altering the autonomic tone (e.g., during exercise or atropine infusion). Section 8.2 improved conduction during exercise when all P waves are conducted to ventricles with a first-degree AV block (Fig. 8.4).

Conversely, according to a higher vagal tone (as in carotid sinus massage), the AV conduction may delay, with a consequent shift to higher degree of block.

Those findings may help to evaluate the block localization.

Table 8.1 Second-degree atrioventricular blocks

Type of block	Site of block	Mechanism of block	Etiology	ECG features
Type I second degree AV block (Wenckebach or Mobitz type I)	AVN [3]	Prolongation of the *relative* refractory period	*Physiological* High level of resting vagal tone • Endurance athletes • Young *Pathological* Congenital • Maternal lupus • CHD Acquired • Drugs (digoxin, betablockers, calcium channel blockers, amiodarone) • Acute MI (*inferior* for AVN; *anterior* for infranodal blocks) • IHD • Degenerative disease • Rheumatic disease • Infiltrative processed • Neuromyopathies • Unfectious disease • Cardiac surgery	*Typical Wenckebach periodicity (20%):* • RP-PR reciprocity (progressive prolongation of the PR before not-conducted P; lengthening of the PR interval occurring at progressively decreasing increments; greatest increment of the second conducted PR after a blocked impulse) • Progressively shortening of R-R interval • Pause between QRS complexes containing the non-conducted P less than sum of R=R intervals of any two conducted beats *Atypical Wenckebach sequences (85%):* Not follow the traditional mathematical behaviour of PR intervals: • Second PR interval after the pause that fails to show the greatest increment • Shortening or lengthening of PR in the middle of a sequence • Very little incremental conduction delay with no discernible change in the duration of PR intervals (in long cycles and in case of increased vagal tone, accompanied by slow sinus rate [4]) • Sinus arrhythmia and sinus arrest instead of a dropped beat *Footprint to diagnose Wenckebach periodicity:* shortening of the PR interval after block comparing with the PR interval just preceding the blocked cycle or group beating
Type II second-degree AV block (Mobitz type II)	His bundle (30%) Bundle branches (70%) *Not yet been convincingly demonstrated in AVN* [5]	Prolongation of the *absolute* refractory period	*Pathological:* see above	Constant PR interval of all conducted P waves (at least two consecutive conducted P), followed by sudden failure of a P to be conducted to the ventricles Absence of RP-PR reciprocity Absence of slowing and stability of heart rate (substantial regularity of P-P intervals)

AVN atrioventricular node, *CHD* congenital heart disease, *MI* myocardial infarction, *IHD* chronic ischemic heart disease

8.3.2 *Pseudo-Mobitz II* or Atypical Wenckebach AV Block

Massie et al. reported that a vagal activity can cause simultaneous sinus slowing and AV block that could simulate a Mobitz II block. This phenomenon was called "apparent type II block" [6]. This pattern may be observed, for instance, secondary to a high vagal tone during sleep. In this case a Wenckebach block appears without any discernible or measurable increments in the PR intervals before the blocked P. Sinus slowing with AV block essentially excludes a Mobitz type II block. ECG features are summarized in Table 8.1.

The summary differential diagnosis between true or pseudo-Mobitz II AV block could be suggested by some clues [3, 7]:

- Mobitz type II AV block with a narrow QRS complex is relatively rare.
- Type I and type II second-degree AV blocks almost never coexist within the His bundle.
- Sustained advanced second-degree AV block is usually associated with true Mobitz type II block rather than with a Wenckebach block or its variant.

8.3.3 2:1 Atrioventricular Block

A 2:1 atrioventricular block is happening when only alternate beats are conducted to ventricles with a 2:1 ratio and a constant PR. A 2:1 atrioventricular block cannot be classified specifically as type I or type II AV block; it is a specific condition, not only because of the different ECG aspect but also for the possible different localization. Table 8.2 shows some features to differentiate the possible localizations of the conduction delay.

Both type I and type II blocks may progress to a 2:1 AV block, and a 2:1 AV block may also regress to a type I or type II block [1, 8].

Table 8.2 2:1 atrioventricular block

Type of block	Site of block	ECG features
2:1 atrioventricular block	AVN	• PR >300 ms
		• Narrow QRS
		• Presence of Wenckebach block
		• Improvement of the block with atropine or exercise
	His bundle/ bundle branches	• PR <160 ms
		• Wide QRS
		• Constant PR of all conducted complexes
		• Worsening of the block with atropine or exercise

AVN atrioventricular node

8.4 Case 3

A Holter ECG was recorded in a 29-year-old man who complained of palpitation occurring several times in the last 3 months. His personal and familial history was negative for cardiovascular diseases. He practiced everyday vigorous exercise (bodybuilding and jogging) in the last 10 years.

8.4.1 ECG Analysis

In Fig. 8.5 (recorded at 6:56 a.m. while the patient was asleep) we observe a bradycardia, with 40 bpm HR. Sinus P waves are followed by a narrow QRS complex (80 ms) in the first three beats and in the last one of the trace; the fourth P is not conducted.

There are two possible differential diagnoses: type II or type I second-degree AV block.

The first hypothesis is possible because the blocked P wave is suddenly not conducted, without any previous progressive PR prolongation. However, if carefully observed, there is indeed a minimal lengthening of AV conduction: The first PR interval is 200 ms and the latter before the pause is 220 ms. Moreover, the PR after the blocked P wave is shorter than the previous one.

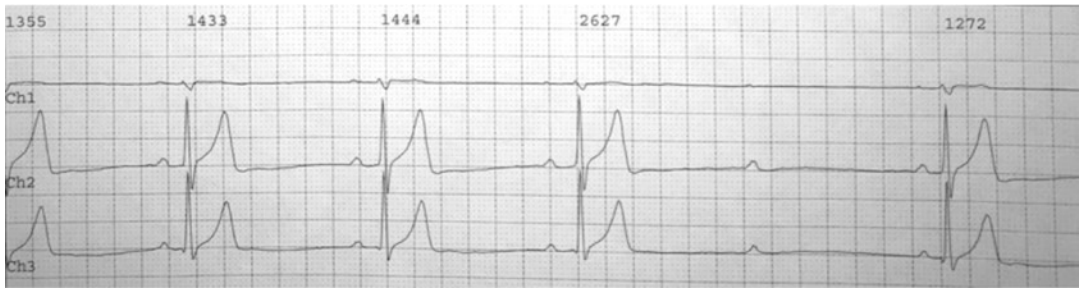

Fig. 8.5 Case 3; Holter ECG recorded at 06:56 am

Also in this case, we are facing a type I second-degree AV block, with an atypical Wenckebach periodism, associated with sinus bradycardia.

The patient was referred to our clinic and performed a maximal exercise stress test, during which there was a normal AV conduction and chronotropic competence. An echocardiogram was negative for structural abnormalities. Due to the high probability of a vagal-induced conduction delay, there were no indications to EP or to restrict the patient physical activity. The patient did well at follow-up.

8.5 Vagally Mediated Atrioventricular Blocks

The vagally mediated atrioventricular block is a paroxysmal block that may be of first, second, or third degree; it is often associated with sinus bradycardia.

Vagal influence is mainly acting on sinus and AV nodes and has a lower influence on the conduction velocity of the His-Purkinje system; the site of a vagally mediated atrioventricular block is likely to be within the AV node.

These types of block frequently occur during sleep and can be easily recorded during Holter monitoring. Most of the nocturnal AV blocks may be secondary to sleep disorders, such as obstructive or central sleep apnea (OSAS).

Other hypervagotonic conditions such as carotid sinus massage (CSM), tilt-induced syncope, or spontaneous neurally mediated syncope may also manifest a vagally mediated block. In patients with a normal AV conduction at baseline, CSM and tilt test may also favor a vagally mediated second- or third-degree AV block, although a sinus arrest is more common.

A vagal influence on sinus node could be prevalent, thus protecting the AV conduction.

In the ISSUE 2 study [9], when vagally mediated AV block and asystole were both present (8% of implantable loop-recorder patients), the isolated sinus node dysfunction was much more common than the AV blocks as a cause of syncope.

8.5.1 Vagally Mediated and Intrinsic Atrioventricular Blocks: How to Differentiate

Another differential diagnosis useful in clinical practice is between a vagally mediated AV block and an AV block secondary to anatomical involvement of the atrioventricular conduction (intrinsic AV block).

In these cases, the surface ECG can be similar. There are however some ECG features useful for the differential diagnosis that are listed in Table 8.3.

When a clear diagnosis is not possible, an electrophysiological study is indicated in order to evaluate the precise conduction times within the His-Purkinje system.

Table 8.3 Vagally mediated and intrinsic atrioventricular blocks: how to differentiate

	Vagally mediated	Intrinsic
QRS complexes	Narrow	Wide (bundle branch or bifascicular block)
PR interval	Prolongation	Generally normal
Association with sinus slowing	Yes	No

8.6 Atrioventricular Blocks in Athletes

A correct ECG interpretation in athletes can be sometimes challenging. Intensive sports participation can lead to electrical and structural modifications that can modify the surface ECG. Some of most common ECG findings in athletes, which are considered normal variants and therefore do not require further evaluations, especially in absence of symptoms are as follows:

- Sinus bradycardia, usually >30 bpm (only endurance athletes have extremely low heart rate, <30 bpm)
- Sinus arrhythmia
- Junctional escape and ectopic atrial rhythms
- Incomplete RBBB
- Isolated QRS voltage criteria for left ventricular hypertrophy
- Early repolarization
- Atrioventricular blocks

AV blocks may appear in 5–13% of athletes, mainly as first-degree AV block. Even if there is a PR prolongation up to 300 ms, this is usually asymptomatic and disappears during effort.

Mobitz type I second-degree AV block is also common (31%), and it's usually seen at night during Holter monitoring (as in the case 3). It's usually a functional block due to increased vagal tone related to physical training. Typically it reverts to normal during exercise or after physical deconditioning.

Mobitz type II second-degree and third-degree AV blocks are uncommon and eventually may be seen in endurance athletes (up to 0.5%). Only in case of symptoms we have to exclude an underlying cardiac disease.

A complete AV block particularly in these instances should be differentiated from AV dissociation; in the latter the junctional rhythm is faster than sinus node (also irregularity of R-R intervals—due to the intermittent ventricular capture—rules out a 3° AV block). AV dissociation without block is also an expression of autonomic different prevalence on AV and sinus nodal modulation and is not pathological. A complete and stable AV block needs anyway further evaluations to exclude a possible underlying disease.

8.7 Second-Degree AV Blocks: What Is the Appropriate Treatment?

Permanent pacing is the main treatment for symptomatic AV blocks. There is a strong consensus that permanent cardiac pacing is indicated in patients with type II second-degree AV block and with third-degree sub-hisian blocks irrespective of symptoms. In patient with type I second-degree AV block, the decision about pacing is instead controversial even taking into account the severity of symptoms and the risk of progression to complete AV block [2]. Supra-hisian blocks have a better prognosis than infranodal blocks, unless being symptomatic or when occurring in cases of pathological conditions and congenital heart diseases [8].

In this chapter we have reported two cases of patients with a supra-hisian block and few associated symptoms: the first patient was fully asymptomatic (case 1), while the second one (case 2) complained of dyspnea probably secondary to other causes. These patients did not receive any pacemaker implantation and were discharged from hospital with only a follow-up outpatient program.

First-degree and type I second-degree AV blocks are frequently recorded in athletes as we have reported in case 3. When asymptomatic, without any structural heart anomalies and narrow QRS, it is not necessary to perform any fur-

ther evaluation, and there's not any specific limitation to the physical activity [10, 11]. Hyperventilation or exercise AV normalization confirms its functional origin.

In case of a type II second-degree or a third-degree AV block, a careful diagnostic evaluation is mandatory and often a pacemaker is finally implanted [10].

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9 Does EKG Favor a Correct Localization of the Ischemic Areas?

Erika Baiocco, Paolo Compagnucci, and Daniele Contadini

9.1 Case 1

A 61-year-old man with a history of arterial hypertension, obesity (BMI = 42 kg/m^2), and tobacco smoking presented to ER complaining of severe oppressive chest pain for the past 2 h, radiated to the left upper arm and to the back side associated with profuse and cold sweating. The pain started at rest, worsened with minimal exertion and was unaffected by respirations.

An EKG was recorded (Fig. 9.1) and, given the persistence of symptoms, the patient was sent to cath lab for coronary angiography.

9.1.1 EKG Analysis

Sinus tachycardia, 105 bpm. P waves show a prominent negative terminal component in V1, which, together with a prolonged (110 ms) P wave duration in DII, is diagnostic for a left atrial strain. The PR segment is isoelectric and of normal duration (160 ms). QRS has a left anterior fascicular block morphology, with an axis of −45°; there is a slow progression of the R wave in the precordial leads and QS complexes in V1 and V2, possibly secondary to the left anterior fascicular block. ST segment is quite abnormal with an almost 1.5 mm ST-segment elevation (ST↑) in aVR and a 1 mm ST↑ in V1 together with reciprocal ST-segment depression (ST↓) in DII, aVF, DIII and from V3 to V6; negative T wave is recorded in DI and VL.

This EKG, coupled with the clinical presentation, is strongly suggestive for an acute coronary syndrome secondary to either acute *subocclusion* or even *occlusion with good collateral circulation* of the left main trunk or its equivalent (left anterior descending plus left circumflex coronary artery). The clues are the marked ST↑ in VR more than in V1, the reciprocal ST↓ in at least 7 other leads and the left anterior fascicular block.

A similar EKG may however be of difficult interpretation in all the patients with an acute coronary syndrome because of large interindividual variability of coronary anatomy, a possible presence of a well-developed collateral circulation, pre-existent myocardial infarction (MI), or a prior coronary artery bypass surgery [1].

The coronary angiogram showed as a culprit lesion an acute thrombotic occlusion of the proximal left anterior descending coronary artery distal to the origin of the first diagonal branch.

It was also evident a severe (70%) stenosis of the first diagonal branch, an 80% proximal stenosis of the left circumflex coronary artery, and a 50% stenosis of the right coronary artery. This was a left main trunk equivalent picture.

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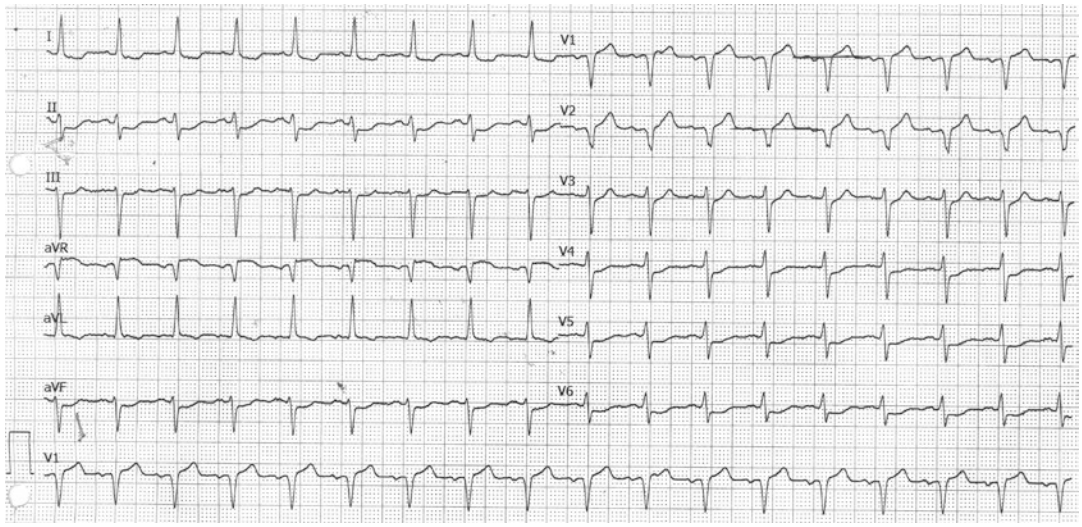

Fig. 9.1 Case 1, 12-lead EKG

The patient was treated with optimal medical therapy (aspirin, heparin, ticagrelor, atorvastatin) together with PCI on the proximal left anterior descending coronary artery; the pain solved. A week later a second PCI on the circumflex and on the first diagonal branch was performed. The echocardiogram upon presentation showed a dilated left ventricle with an ejection fraction (EF) = 35%, an akinesia of the inter-ventricular septum and of the anterolateral wall together with a moderate dilation of the left atrium.

During hospitalization, after PCI, the patient improved clinically and echocardiographically, with EF reaching 45% prior to dismission.

A left main trunk disease (or equivalent) may be somewhat nonspecific but an ST↑ in lead aVR > V1 should raise the suspicion for this severe condition, especially if accompanied by a diffuse ST↓ in at least 7 leads and presence of a conduction disturbance such as right bundle branch block or left anterior fascicular block.

9.1.2 Introduction and Definition

The term MI should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. The recently revised universal definition of MI [2] focuses on the rise and/or fall of cardiac troponins with at least one value above the 99th percentile upper reference limit (URL) as a mandatory sign together with at least another criterion among symptoms of myocardial ischemia, new or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB), development of pathological Q waves, evidence of new loss of viable myocardium or new regional wall motion abnormality, or identification of an intracoronary thrombus by angiography or autopsy.

9.1.3 Classification

The EKG allows clinicians to distinguish between ST segment elevation MI (STEMI) [3] and non-ST elevation acute coronary syndromes (NSTEMI, a broad term which encompasses non-ST elevation MI and unstable angina according to whether or not there's a rise and/or fall of cardiac troponins in the blood) [4]. This is a simple yet crucial distinction in that it influences the treatment, with the first group of patients going necessarily straight to the cath-lab.

The most widely accepted clinical/pathological classification distinguishes 5 types of MI:

- Type 1: MI is the spontaneous one, related to atherothrombosis;
- Type 2: MI is secondary to an imbalance between myocardial oxygen supply and/or demand;
- Type 3: MI is the one resulting in death when biomarker values are unavailable;
- Type 4a: MI is the one related to percutaneous coronary intervention (PCI);
- Type 4b: MI is the one related to stent thrombosis;
- Type 5: MI is related to coronary artery bypass grafting (CABG).

9.1.4 Epidemiology

Ischemic heart disease (IHD) is the most common cause of death worldwide. Its prevalence is increasing, even though IHD related mortality has been decreasing in Europe over the past three decades. IHD now accounts for 20% of all deaths in Europe. The relative incidences of STEMI and NSTEMI are decreasing and increasing, respectively, with NSTEMI presentation being more diffused nowadays.

9.1.5 Mechanisms of EKG Changes Under Ischemic Conditions

EKG is a fundamental diagnostic tool in the setting of suspected myocardial ischemia. Ischemia produces complex changes in the EKG, involving the QRS complex and, mostly, the repolarization phase (ST-segment).

It was since the 1960s [5] that the theories of diastolic and systolic currents were proposed to explain the ST-segment displacement, based on animal experiments. These theories rely on the observation that under ischemic conditions, the cardiac action potential is modified with shortening of the action potential duration, and a slowing of the rapid 0 phase of the action potential (upstroke); also an increase of the baseline potential (which becomes less negative) was demonstrated [6, 7]. This last is due to: (1) the depletion of ATP in the ischemic tissues, which determines an opening of ATP regulated K channels, thus increasing the extracellular K^+ content and (2) by the increased H^+ ions concentration in the cells due to the production of lactic acid (which is necessary to keep glycolysis active when the cell gets short of oxygen); the H^+ ions will then be exchanged for Na^+ ions, which in turn will be exchanged for Ca^{++} ions by the Na^+/Ca^{++} exchanger.

The increased intracellular Ca^{++} concentration will render the diastolic membrane potential less negative, thus provoking the inactivation of Na^+ channels; the result is a slowing of phase 0 (upstroke). This mechanism leads to the ischemic slowing of conduction, which may facilitate reentry circuits and thus ventricular arrhythmias.

Moreover, the repolarization phase will be accelerated, because of a reduction of Ca^{++} current flowing into the cell (due to a reduced outer to inner Ca^{++} gradient) and an increase in K^+ current flowing out of the cells, mainly because of the opening of the ATP regulated K^+ channel.

These changes inevitably produce an electric heterogeneity between the ischemic myocardium and the normally perfused myocardium, which provides the basis for both the electrocardiographic changes and the arrhythmic risk inherent to ischemia.

In particular, during diastole, there's a current flowing from the ischemic region (which is less negative) and the normally perfused myocardium; this is called the diastolic current of injury and is responsible for the TQ segment depression. In turn, this TQ segment depression will appear as an -ST↑ since EKG recorders used in clinical practice automatically compensate for any shift of the -TQ segment by placing it at the isoelectric line. In other words, according to the diastolic current of injury hypothesis, the ST↑ observed during transmural ischemia is an apparent phenomenon, reflecting the depression of the TQ segment.

However, there's also evidence for systolic currents of injury, because of the systolic voltage

gradient that determines a current flow from the normally perfused myocardium to the ischemic region. This happens mainly during phase 2 (plateau) of the action potential, since this phase is shorter and during this phase the myocardium is less positive in the ischemic region, but also during phase O (upstroke), which is slower in the ischemic myocardium as compared to the normally perfused one. This will be recorded as a positive displacement of the ST segment and as hyperacute giant T waves by an electrode exploring the ischemic region.

In addition to these diastolic and systolic currents, which flow parallel to the epicardial surface, there are several experiments that have suggested the presence of transmural currents, directed perpendicularly to the epicardial surface. This is due to the transmural differences in those cellular mechanisms that were explained previously; most notably, in particular, the Na^+ current mediating phase 0 shows different inactivation kinetics between the endocardium and the epicardium [8], inactivating earlier, at more negative membrane voltages in the latter as compared to the former. This produces a dramatic slowing of the conduction between the endocardium and epicardium and creates, once again, a voltage gradient, this time between the endocardium and the epicardium, which will contribute to the ST↑ as seen by electrodes over the transmurally ischemic area.

From these basic observations, we can understand how the correct EKG interpretation, focusing on repolarization alterations, may aid to identify the ischemic segment(s) in case of transmural ischemia and thus the vessel most likely involved.

9.1.6 Left Main Disease or Its Equivalents

There are two very different clinical and electrocardiographic presentations of patients with an acute coronary syndrome secondary to a left main trunk disease or its equivalents (proximal left anterior descending coronary artery plus left circumflex) (Fig. 9.2):

1. The occlusion of the left main trunk with a poorly developed collateral circulation;
2. The subocclusion with scarce collaterals or the occlusion with well-developed collaterals [9].

9.1.6.1 Occlusion of the Left Main Trunk with Poorly Developed Collaterals

In this case, patients usually show a significant hemodynamic compromise or even die before reaching the hospital because of cardiac arrest. When these patients survive, they usually show a cardiogenic shock and an EKG STEMI pattern with a significant ST↑ in multiple precordial leads starting from V2. This pattern differs from what is usually recorded in case of an acute occlusion of the left anterior descending artery proximal to the origin of the first septal and the first diagonal branches, in which there's a significant ST↑ even in V1 and VR. This difference is due to the concurrent involvement of left circumflex artery territory in case of a left main trunk occlusion with poorly developed collaterals [10].

Thus, an isoelectric ST segment in V1 (and usually aVR) in a patient with ST↑ in multiple precordial leads (V2 to V4–V6) and DI/VL and

Sub-occlusion of left main trunk or occlusion of left main trunk with well developed collateral circulation	Occlusion of left main trunk with a poorly developed collateral circulation
• aVR *ST*↑ ≥ 1 mm (aVR *ST*↑ > V1 *ST*↑) • *Reciprocal ST*↓ in at least 7 other leads	• *ST*↑ in V2-V6, I, aVL • *Reciprocal ST*↓ in aVF, II, III • Isoelectric ST in V1

Fig. 9.2 Different electrocardiographic presentation of acute coronary syndrome secondary to a left main trunk disease or its equivalents

ST↓ in the inferior leads [11] suggests an acute complete occlusion of the left main coronary artery with a poor collateral circulation, especially if accomplished with a newly developed right bundle branch block and/or left anterior fascicular block.

These conduction disturbances are due to the poor blood flow circulation to the right bundle and left anterior fascicle, which relies on the septal perforator branches (usually the first septal branch, S1) of the proximal left anterior descending artery. The development of a bifascicular block in patients with STEMI portends a poor prognosis, with a 30% risk of complete heart block [12, 13], that by itself carries an almost 80% risk of mortality in this setting [14].

9.1.6.2 Subocclusion of the Left Main Trunk or Occlusion of the Left Main Trunk with Developed Collaterals

The clinical and EKG picture of patients with an acute coronary syndrome secondary to a subocclusion of the left main trunk or to an occlusion of this artery with well-developed collaterals is that of an NSTEMI with an ST↓ in usually at least 7 leads and an ST↑ ≥1 mm in VR and often V1, with the ST↑ in VR > V1 (because the electrical forces due to posterior wall ischemia, secondary to left circumflex artery involvement, counterbalance the forces due to anterior wall ischemia secondary to left anterior descending artery involvement and thus bring the ST segment in lead V1 closer to the isoelectric) [15].

The lead VR is often ignored in EKG interpretation; it may be referred to as "the neglected lead" in past; however, in the ischemic condition may be of great diagnostic importance. Regarding the electrophysiological mechanisms underlying ST↑ in lead VR, there are two possibilities: the first is that a diffuse anterolateral sub-endocardial ischemia produces an ST↑ in VR as a reciprocal change; the other is that this may represent an acute transmural ischemic injury of the walls directly explored by lead VR, including the basal portion of the interventricular septum [16].

As for the prognostic significance of ST↑ in VR, there is discordance in the medical literature, with some but not all data suggesting a strong correlation to the 30-day mortality [17, 18]. Clinicians should be alert and aware of the clinical relevance of this EKG sign.

9.2 Case 2

A 57-year-old man, cigarette smoker, without any other risk factor, awakened early morning with a severe substernal chest pain, neck, shoulder and left arm radiated, associated with dyspnea. Because of pain persistence and its increasing intensity he called the emergency medical care.

9.2.1 EKG Analysis

The electrocardiogram was the following: irregular rhythm at 87 bpm. Absence of P waves and presence of small irregular oscillation in all leads, typical of atrial fibrillation. Narrow QRS complex. Evident ST segment elevation, of 6 mm, in lead V1–V3, I

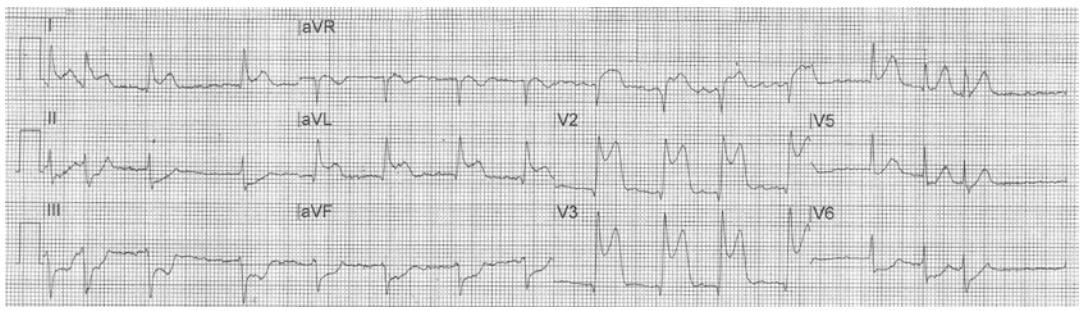

Fig. 9.3 Case 2, 12-lead EKG

and aVL associated with reciprocal ST-depression in inferior leads (II, III, aVF) and V6 (Fig. 9.3).

Clinical presentation and electrocardiogram both suggest an extensive acute anterior myocardial infarction.

A relevant ST elevation (>2.5 mm) in lead V1 and reciprocal changes in inferior leads with high ST deviation (>1 mm) suggest a proximal left anterior descending occlusion.

An echocardiography was performed and revealed hypokinesia of left ventricle anterior wall and apex. After 30 min the patient underwent coronary angiography which disclosed only a distal occlusion of the left anterior descending artery. Aspiration thrombectomy and angioplasty was performed with subsequent stent implant.

The discrepancy between the angiography result and the electrocardiographic pattern suggests that other mechanisms might be suspected such coronary vasospasm with possible occlusion, at the time of infarction, that lately may disappear due to recanalization or lysis of the thrombus. Moreover, atrial fibrillation is the most frequent cause of coronary artery embolism, a rare but important nonatherosclerotic cause of acute myocardial infarction.

9.2.2 Anterior Myocardial Infarction

Anterior myocardial infarction is the most relevant form of infarct because it is burdened by a high risk of short-term mortality and also of subsequent deterioration of left ventricular function. Prognosis following MI is mostly related to the infarct size rather than to infarct location and the more proximal the occlusion the less favorable is prognosis. Anterior MI is generally associated with the most extensive left ventricular damage [19].

Anterior wall infarct is due to occlusion of the left anterior descending artery (LAD), the most important of the three main coronary arteries that supplies over half of the heart muscle.

LAD gives rise to septal and diagonal branches and occasionally to intermediate branches. The septal branches supply the anterior two-thirds of the interventricular septum and the diagonal branches supply the anterolateral ventricular wall. Distal LAD supplies the inferoapical part and, when wrapped around the apex, supplies the area beyond that.

According to Engelen et al. [10], LAD occlusions at different sites led to electrocardiographically four different patterns (Fig. 9.4):

1. Proximal to the septal and diagonal branches;
2. Before the first diagonal but distal to the first septal branch;
3. Before the first septal but distal to the first diagonal branch;
4. Distal to the first septal and diagonal branches.

The ST↑ in leads V2 and V3 indicates occlusion of the LAD, especially when V3 ST↑ > V1 ST↑. These findings represent a specific marker of anterior MI and are common to all the above-mentioned cases.

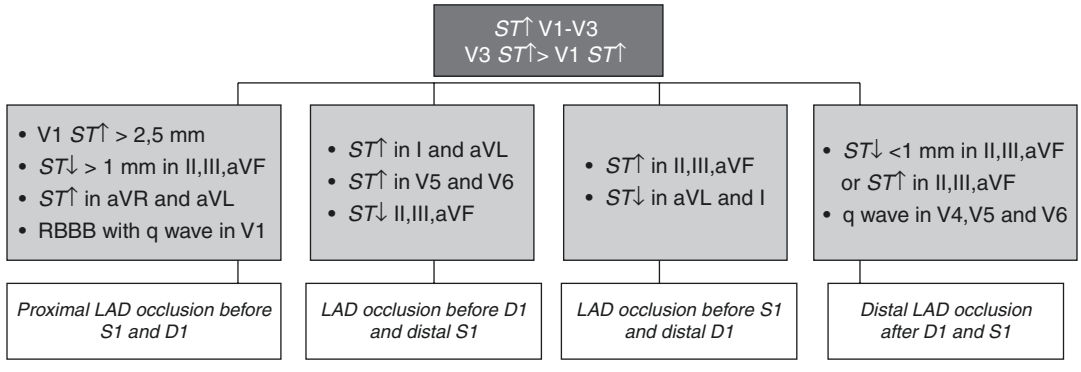

Fig. 9.4 Electrocardiographic patterns of left anterior descending artery (LAD) occlusion

1. The very *proximal LAD occlusion, before the septal and diagonal branches*, results in ischemia of all areas perfused by the left anterior descending coronary. Injury current vector is directed towards the damaged myocardium area, so it pointing superiorly (>−80 < −100°) and forward.

   EKG shows:

- ST↑ in leads V1-V3 (usually V1 ST↑ >2.5 mm);
- ST↑ in leads VR and VL;
- Reciprocal ST↓ II, III, VF (ST↓ >1.0 mm);
- Reciprocal ST↓ in leads V5-V6;
- Additionally, a new right bundle branch block (RBBB).

ST↑ in VR is specific for LAD occlusion proximal to S1 and it is consequent to transmural ischemia of the basal part of the septum. However, this finding could be absence due to the counterbalance of the septal ischemia by ischemia in other larger areas perfused by the LAD.

ST↓ in the inferior leads represents reciprocal changes associated with ischemia in the anterobasal region. It is the most important sign of a proximal occlusion of the left anterior descendant. The amount of deviation result is significantly higher in proximal LAD occlusion and ST↓ >1.0 mm is strongly predictive of a culprit lesion proximal to the origin of the first diagonal branch [20].

During an anterior MI, a new onset of right bundle branch block (RBBB) with a Q wave preceding the R wave in lead V1 is a specific marker of extensive myocardial damage and identify high risk patients. S1 supplies the distal part of the bundle of His and proximal bundle branches, thus RBBB may be a consequence of LAD occlusion proximally to S1. When RBBB occurs in association with a left anterior hemiblock, the risk of progression to a complete AV block is high [21].

2. *LAD occlusion of the first diagonal (distal to septal branches) or intermediate branches* results in ischemia of anterolateral wall. Therefore, ST segment vector is directed toward left leads. EKG pattern is characterized by:

- ST↑ in V2-V4 leads;
- *ST↑ mainly in I and aVL, fewer in V5 and V6 leads and possibly in II lead* (unlike the left circumflex artery (LCx) occlusion, when the anterior descending artery is involved, ST segment elevation is evident not only in the lateral leads, but also in anterior leads) [22].
- Mild reciprocal ST↓ in III and aVF

3. The o*cclusion of the LAD proximal to the main septal branch but distal to first diagonal branch* preserves the areas perfused by D1 and leads to the ischemia of the septum and inferoapical ventricular wall. This type of occlusion results in inferior and rightward direction of injury current vectors.

- ST↑ in V2–V4 leads;
- *ST↑ in inferior leads (II, III, aVF);*
- *Reciprocal ST↓ in I and VL leads* (unlike the inferior myocardial infarction supported by right coronary artery (RCA) occlusion, when the anterior descending artery is involved, ST segment elevation is evident not only in the inferior leads, but also in anterior) [10, 22].

4. *Occlusion of left anterior descending artery after the origin of the S1 and D1* produces ischemia of inferoapical ventricular area [8]. ST segment vector is directed inferiorly and leftward.

   EKG shows:

- ST↑ in V1-V3;
- Reciprocal ST↓ <1 mm in II, III, aVF, sometimes ST↑ in inferior leads
- *Pathological Q waves in V4-V5 and possibly in V6 leads* identify a preserved early septal activation with the vector directed away from the left leads. However, these waves have pathological characteristics consequent to

the slowed electrical activity in the ischemia areas [22].

9.3 Case 3

A 72-year-old man was referred to our hospital because of sudden onset of chest pain at rest irradiated to the neck and to the left arm lasting 30 min. The patient was also sweaty and dyspneic. He had a history of diabetes mellitus type II and was a tobacco smoker (20 cigarettes/day). A surface EKG was obtained (Fig. 9.5).

9.3.1 EKG Analysis

Sinus rhythm, heart rate 88 bpm, normal atrioventricular conduction (PQ 160 ms), electrical axis +75°, normal interventricular conduction (QRS width 90 ms), a high and unexpected high R wave in lead V3. There are significant ST-segment elevations in all inferior leads: 2 mm in lead III, 1 mm in lead aVF and 0.5 mm in lead II. In the peripheral lateral leads is visible an ST↓: 1.5 mm in lead VL and 1 mm in lead I. In VL the ST↓ is followed by a T wave inversion.

In lead I a biphasic (negative-positive) T wave is present. In the precordial leads V2, V3, and V4

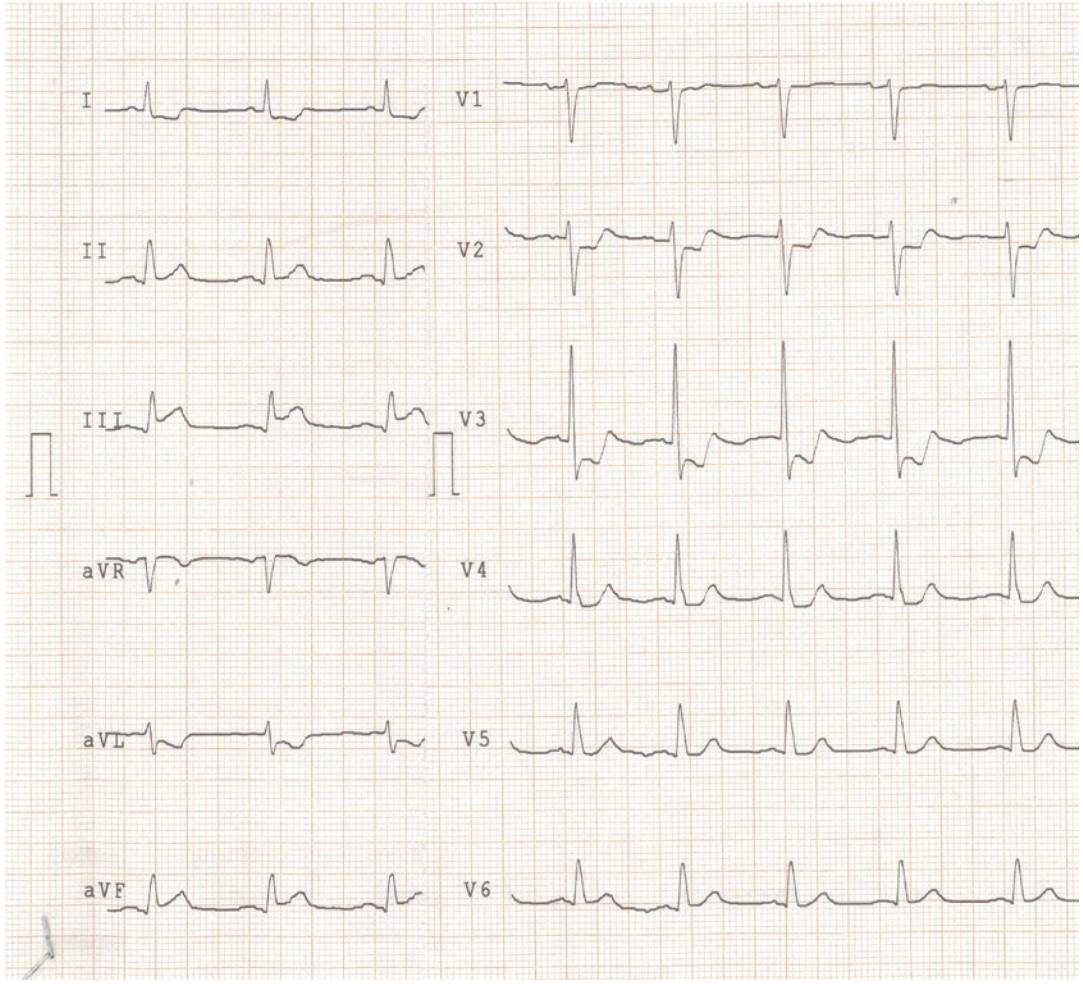

Fig. 9.5 Case 3, 12-lead EKG

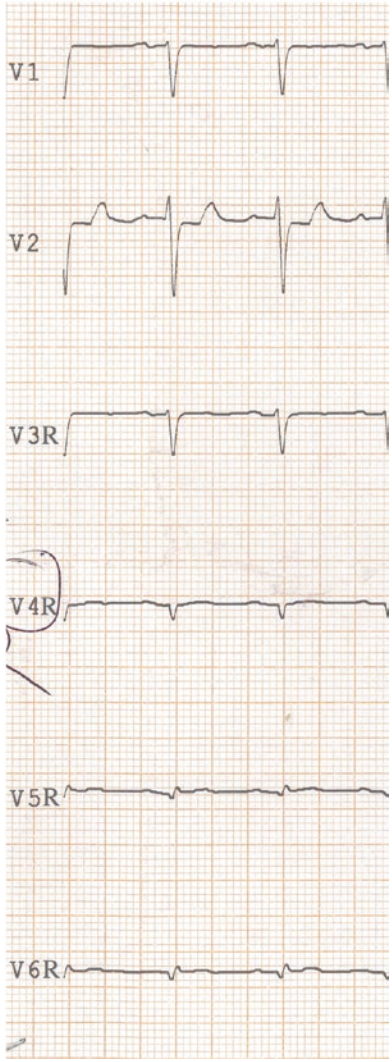

Fig. 9.6 Case 3 right precordial leads EKG

an ST↓ is visible: 1.2 mm in lead V2, 2.2 mm in lead V3, and 0.8 in lead V4. QTc 436 ms.

This EKG together with the patient's symptoms was strongly suggestive of inferior acute ST-elevation MI.

In order to find an ischemic involvement of the right ventricle, even if the ST-segment in lead V1 was not elevated, the right precordial leads (Fig. 9.6) were recorded. An EKG with posterior precordial leads (Fig. 9.7) was also recorded in order to exclude a posterior MI. This EKG showed an ST↑ of 0.5 mm in leads V8 and V9.

The patient was urgently brought to the cath lab for a coronarography and possibly PCI. We suggested the right coronary to be the culprit lesion.

1. ST↑ is higher in lead III than in lead II;
2. There is a reciprocal ST↓ in leads I and VL and the depression is deeper in lead aVL;
3. S/R-wave ratio in lead aVL is 1.4 (see below in the text);
4. The T-wave amplitude in lead III is greater than in lead II and there is a positive biphasic T wave in lead V5R (see below in the text).

All these signs are highly suggestive for a culprit lesion localized in RCA. Furthermore, we suspected the occlusion to be in the distal part of RCA (after the origin of acute marginal artery) since the right ventricle was not involved:

1. ST↑ in lead V1;
2. Not ST↑ in precordial right leads;
3. V3/III ratio 1.1 (see below in the text).

We also hypothesized that the RCA gave origin to the interventricular posterior artery (right dominancy). We thought of that because of the involvement of the posterior wall visible with a high R in V3 greater than in V4, ST-depression in leads V2 and V3 and a mild ST↑ in the posterior precordial leads V8 and V9. The coronary angiography revealed an acute thrombotic occlusion of a dominant RCA in the intermediate portion (after the origin of the marginal artery). The patient underwent a PCI with implant of two drug eluting stents (DES). The other major coronary arteries were free from severe stenosis. Transthoracic echocardiography (TTE) showed an akinesia of the inferior wall and of the basal segment of the posterior wall of the left ventricle and the LVEF was 41%. The right ventricle dimension and function was normal.

9.3.2 Acute Inferior Myocardial Infarction

The acute inferior MI is usually characterized by the clinical symptoms and signs together with

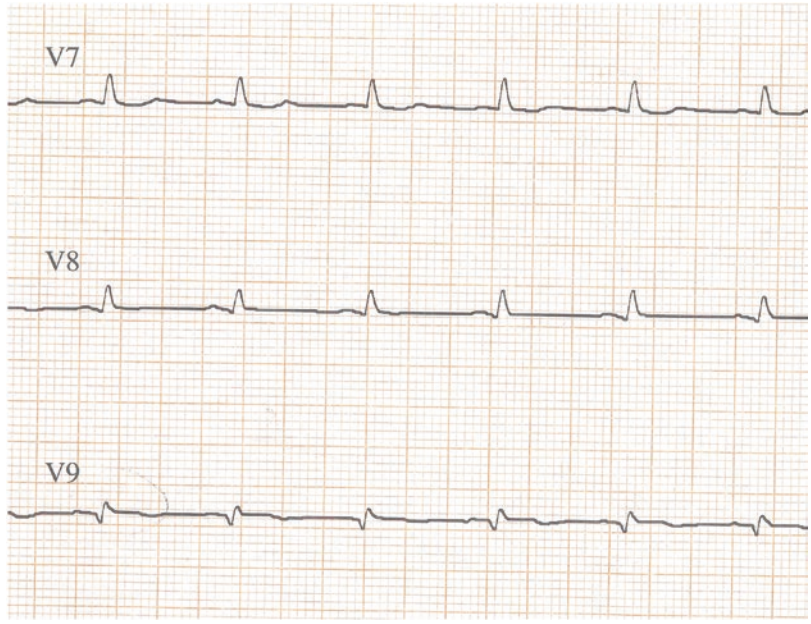

Fig. 9.7 Case 3 posterior precordial leads EKG

electrocardiographic modifications: ST↑ >1 mV in ≥2 inferior leads (II, III, VF). Sometimes other ST-segment modifications in I, aVL and precordial leads might be present. The vascularization of the inferior wall of the heart is often given by the right coronary artery (RCA) and in a less number of cases (10–18%) by the left circumflex artery (LCx). In 1% of cases the left anterior descending artery is responsible for this area [22, 23]. Prognosis is poorer in ACS due to RCA occlusion than when ACS is due to LCx. RCA is responsible for vascularization of sinus node in 60% of cases meanwhile LCx only in 40%; the atrioventricular node is vascularized by RCA in 90% of patients and by LCx in 10%; the RCA often supplies the bundle of His. An inferior infarction consequence of RCA occlusion can be more frequently complicated by conduction abnormalities such as sinus bradycardia, sinus-atrial blocks, and different degrees of atrioventricular block. Furthermore, an inferior ST-elevation ACS due to RCA occlusion may involve also the right ventricle especially when the occlusion is in the first part of RCA, before the origin of the marginal acute artery [8, 24].

When the RCA is involved the ST↑ vector is directed downwards and toward the right (Fig. 9.8). At the EKG this direction is visible as:

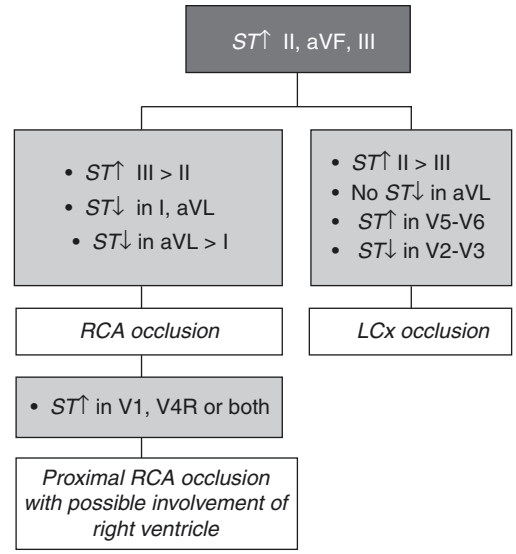

Fig. 9.8 Electrocardiographic patterns of inferior myocardial infarction due to right coronary artery (RCA) or left circumflex artery (LCx) occlusion

- ST↑ in lead III > lead II;
- ST↓ in leads I and VL;
- ST↓ in lead VL is greater than in lead I;
- Additional ST↑ in lead V1 can be a sign of a proximal occlusion of the RCA with involvement of the right ventricle.

On the other hand, when the inferior MI is due to an occlusion of LCx the ST↑ vector is directed downwards and towards left. This orientation means:

- ST↑ in lead II > lead III;
- Usually ST↑ in lead I;
- ST-segment isoelectric or ST↑ in lead VL;
- ST↑ in leads V5 and V6 can be present [8];
- ST↓ in leads V2 and V3, more frequently when the culprit artery is LCx or not-proximal RCA [24].

Not all these ST-segment variations are always present at the same time, but when more than one is visible the predictive power increases. There are some EKG-tricks that can help us to identify the culprit vessel more surely.

- ST↑ in lead III > II associated with ST↓ in lead VL > I is predictive of RCA occlusion. Conversely when the previous criteria are both absent the culprit lesion is LCx [25].
- The ratio between the magnitude of ST↓ in lead V3 and ST↑ in lead III (V3/III ratio) <0.5 is predictive for a proximal RCA occlusion (before the marginal artery), V3/III ratio ≥0.5 and ≤1.2 for distal RCA occlusion and V3/III ratio >1.2 for an LCx occlusion [24].
- The ratio between the S wave and the R wave in lead aVL (S/R-wave ratio) ≤0.33 associated to ST↓ in lead VL ≤1 mm is suggestive of LCx-related infarction. An S/R-wave ratio >0.33 and an ST↓ in lead VL >1 mm is a marker for RCA-related infarction [26].
- In the early phases of the infarction a T-wave amplitude in lead III ≥ lead II and an upright or positive biphasic T wave in leads V4R and/or V5R are predictive for RCA-related infarction [8, 27].

9.4 Acute Lateral Myocardial Infarction

The acute lateral MI usually is caused by the occlusion of the LCx or one of its principal branches as the first obtuse marginal artery. In a smaller number of cases the culprit lesion is in the first diagonal branch of the LAD. At the EKG it is characterized by:

- ST↑ >1 mV in leads aVL and I and/or in leads V5 and V6.

When all the lateral leads are not involved we can distinguish:

- High lateral infarction: ST↑only in leads VL and I;
- Low lateral infarction: ST↑only in leads V5 and V6.

Sometimes reciprocal ST↓ in inferior leads might be present. Usually ST in right precordial leads (V1-V3) is isoelectric or depressed [22, 23]. Sometimes an ST↑ can be visible in lead V3 when the first diagonal branch is involved [28]. The acute lateral infarction can often be a portion of larger infarctions such as the extended anterior infarctions or inferior-posterior-lateral.

9.5 Acute Right Ventricle Myocardial Infarction

The acute right ventricle MI is due to occlusion of the proximal RCA (before the acute marginal artery) or in case of isolated occlusion of the acute marginal artery. In the first option the EKG showed the already described modifications of the RCA-related inferior MI with the involvement of the right ventricle. The second and rarer option configures the "isolated" right ventricle MI.

This infarction can be recognized thorough EKG by some typical signs:

- ST↑ >1 mV in lead V4R;
- Upright T wave in lead V4R;
- ST↑ in leads V3R, V5R, and V6R (less enhanced ST↑ in case of concomitant inferior MI);
- Usually ST↑ in lead V1;
- ST↑ in leads V1, V2, and V3 (with ST↑ in V1 > V2 > V3) in case of right ventricle enlargement [8, 22, 23].

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Ischaemia or Pseudoischaemia? The Memory Hypothesis Revisited

10

Claudio Cupido, Giorgio Guidotti, Enrico Paolini, and Giulio Spinucci

10.1 Case 1

A 47-year-old man was admitted to ER because of recurrent mild to moderate chest pain (4/10).

The features were atypical for ischaemic origin (described as discontinuous, sometimes evoked by deep palpation of hypogastrium, sometimes precordial and associated with diaphoresis; it lasted 5–10 min and was recurrent and with spontaneous recovery).

In the past he complained also of headache and occasional palpitations.

A week before he had similar symptoms, but of less intensity, associated with two dizziness episodes.

ECG in Fig. 10.1 was recorded as the first.

10.1.1 ECG Analysis

Regular rhythm is at 71 bpm; P waves have normal duration, axis and morphology; PR interval is 140 ms; QRS has a +30° axis and 120 ms prolonged duration with RR' morphology in V1, a prominent R wave in aVR and an S wave in I and V6.

There is a widespread ST segment depression of ≤1 mm from V3 to V6, II, III and aVF.

T waves are also diffusely inverted in all the precordial and inferior leads with asymmetric morphology. There is a flat T wave in aVR.

QTc interval is normal (432 ms).

In summary, the ECG shows sinus rhythm at 71 bpm, normal AV conduction, incomplete right bundle branch block, widespread trivial ST segment depression from V2 to V5 and in inferior leads accomplished with T inversion.

Is that ischaemia or pseudoischaemia?

The widespread T and ST abnormalities that are therefore not confined to a specific "coronary area" are an important clue favouring pseudoischaemia or anyway are not towards a coronary classical origin.

The cardiac and inflammatory markers were also in the normal range.

Later an echocardiographic stress test was done and resulted to be normal.

Thus, a classical acute or subacute ischaemia is unlikely. Also a Takotsubo syndrome could not be supported because of good amplitude QRS, normal QTc and absence of the typical contractile pattern.

Once excluded an ischaemic origin, these clinical features of recurrent headache, palpitations and dizziness could suggest also possible brady or tachy paroxysmal episodes followed later by abnormal repolarization in accordance with the so-called "memory T wave inversion" hypothesis.

Later during the hospital stay, an electrophysiologic test was performed in order to exclude

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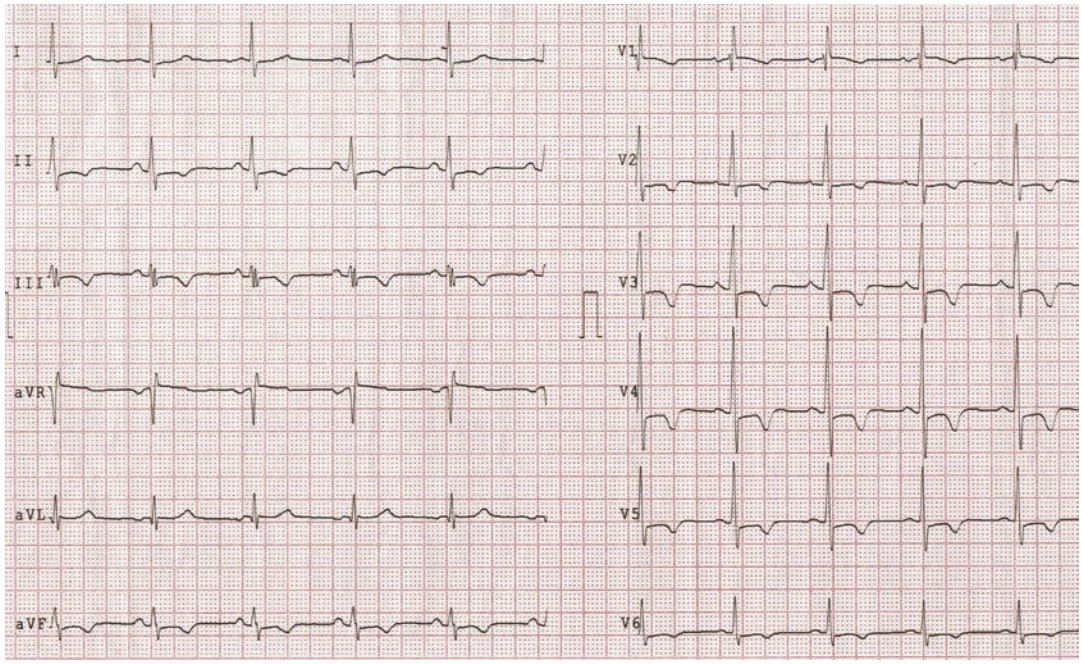

Fig. 10.1 Case 1: 12-lead ECG

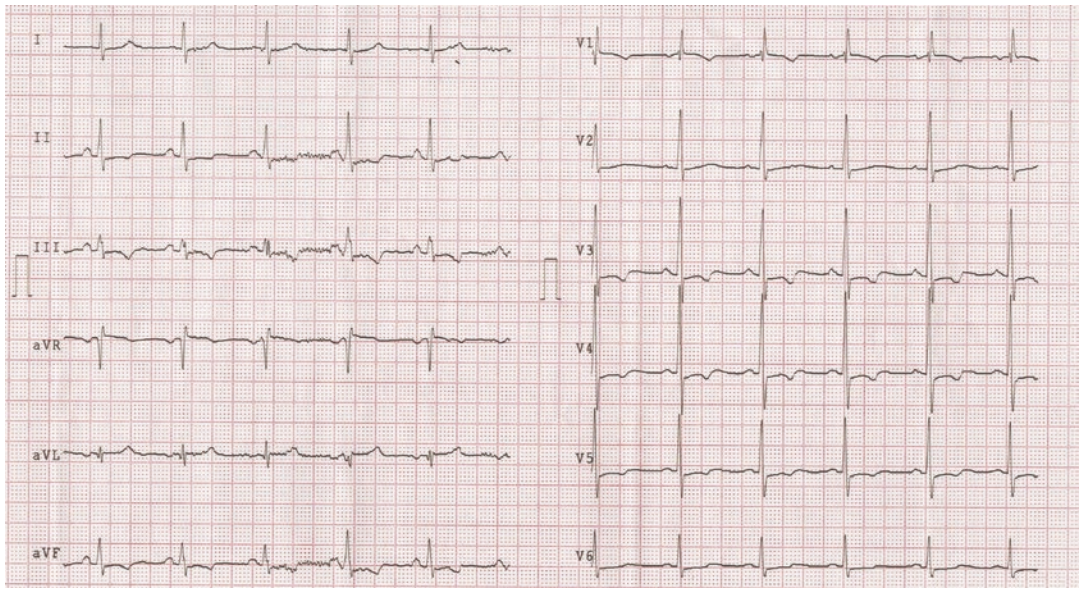

Fig. 10.2 Case 1: 12-lead ECG

possible paroxysmal tachycardia ensue: nothing was inducible; however a prolonged HV interval of 72 ms was recorded.

A hyperventilation test was done in order to evaluate the T wave modification in accordance with the rate abrupt change (Fig. 10.2; note the fluctuation of R wave amplitude due to chest movements). T changed from negative to biphasic in almost all the leads, except in V2 and V6 where they did normalize.

The T wave inversion in lead V1 secondary to the incomplete RBBB remained unchanged.

A brief hyperventilation may both increase HR and also speed up velocity on the conductive system. That can lead to shortening of the intrinsicoid deflection conduction time; if the repolarization abnormality is dependent on a conductive delay, the T tends to normalize with a simple hyperventilation [1].

This can be an easy method to disclose a harmless (functional) pattern of pseudoischaemic T wave inversion from a true ischaemia.

A further clarification of this repolarization/depolarization pattern is described in Sect. 10.4.

10.2 Case 2

A 73-year-old woman was admitted to the cardiology ward for ablation of a typical atrial flutter. The arrhythmia occurred while she was under a class IC antiarrhythmic drug for persistent atrial fibrillation rhythm control.

The drug was discontinued a month earlier. She denied any history of chest pain. An echocardiography showed mild left ventricular systolic dysfunction (EF 0.45 in Simpson's biplane) without any wall motion abnormalities.

ECG at admission (Fig. 10.3)

10.2.1 ECG Analysis

The rhythm is irregularly irregular with 104 bpm average rate; there are no visible P waves but irregular low-amplitude undulations of the baseline suggesting F waves of an atrial fibrillation.

QRS complexes are 80 ms in length with leftward shift in frontal plane axis at −45°; R wave transition occurs at V6 with a clockwise rotation; QRS morphology and duration are normal; the J point lies on the isoelectric line.

There is a beat-to-beat variable repolarization pattern.

The second of the beat series shows a less altered repolarization than the other two.

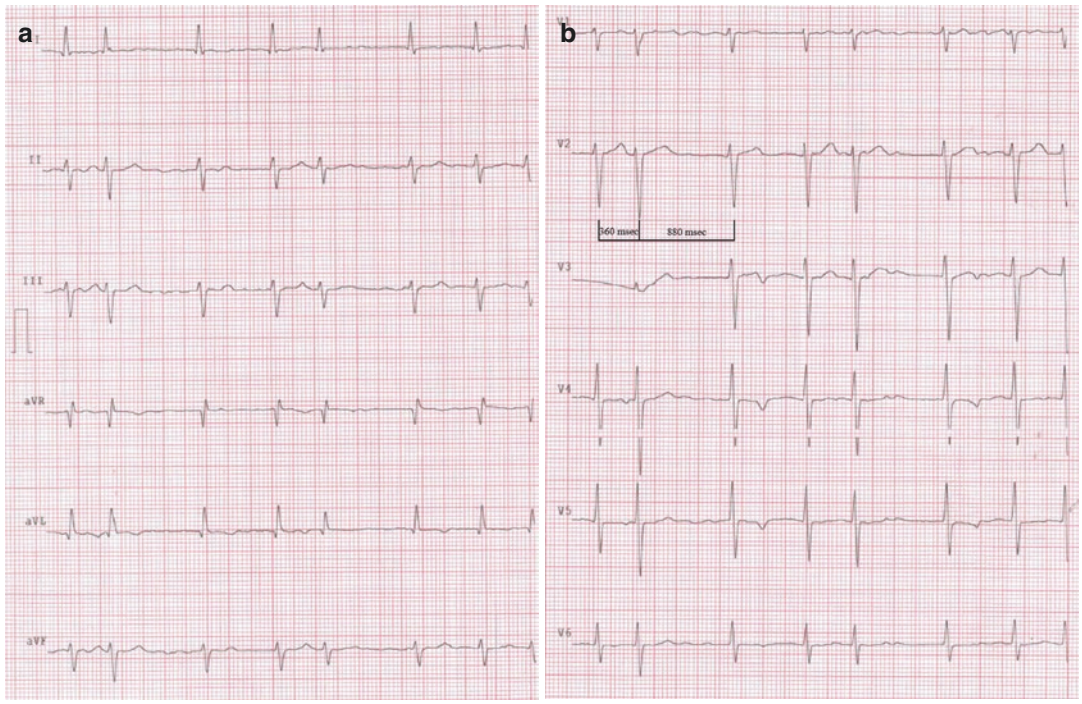

Fig. 10.3 (**a**) Case 2: limb lead ECG. (**b**) Case 2: chest lead ECG

In addition (Fig. 10.4), the R wave peak time (intrinsicoid deflection) of the second beat is slightly shorter than the other two, although the exact difference cannot be easily calculated at this electrocardiogram paper speed (25 mm/s).

The T wave polarity of the first beat is in a middle range between the T of the second (positive deflection) and of the third one (completely negative T wave).

Finally, the QRS amplitude of the second complex is slightly longer than the one of the other two beats.

This ECG shows a supraventricular arrhythmia that is atrial fibrillation.

It is possible that the previous AAD discontinuation contributed to disorganize the atrial flutter to atrial fibrillation.

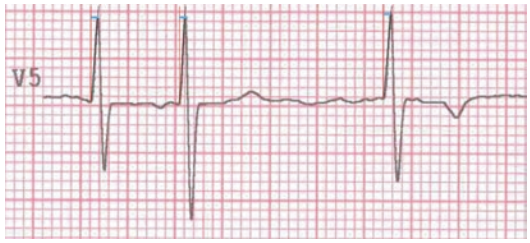

Fig. 10.4 Case 2: detail of the Fig. 10.3b, intrinsicoid deflection speed related to T wave polarity

In this ECG there are clues that make the possible diagnosis of ischaemia related to the inverted T waves unlikely:

- T wave polarity changes dynamically according to cycle length; in fact the recurrent negative T after the longer RR suggests that morphology is closely related to the cycle change.
- An ischaemic pattern may also have minor beat-to-beat changes but does never show a complete T normalization strictly related to the cycle length.
- Indeed, it is not unusual to observe T wave abnormalities mimicking ischaemic heart disease during atrial fibrillation in non-ischaemic patients (more details in Sect. 10.4).

10.3 Case 3

An 86-year-old woman, with a medical history of first-grade essential hypertension and a mild chronic renal disease, was admitted to the emergency department because of syncope. The ECG recorded soon after the episode is shown in Fig. 10.5.

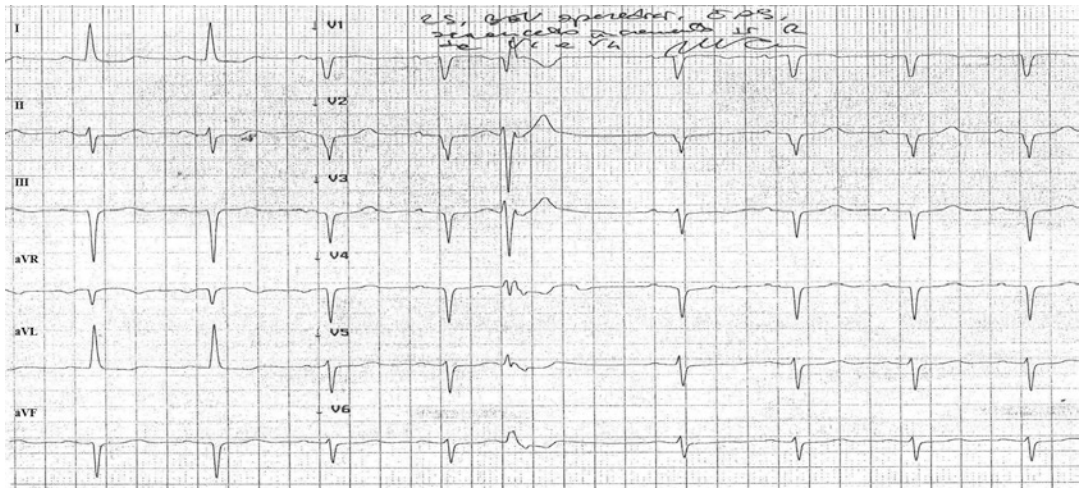

Fig. 10.5 Case 3: 12-lead ECG

10.3.1 ECG Analysis

The rhythm is regular at 84 bpm; P waves have normal axis and duration; the PR interval is normal (160 ms).

QRS is of normal duration (80 ms): left axis deviation (QRS axis −50°) with poor R wave progression and clockwise rotation on the precordial leads.

There are non-specific repolarization abnormalities.

The QTc interval is normal (403 ms).

There is an isolated ventricular ectopic beat with RBBB morphology.

In summary, the ECG shows sinus rhythm, normal AV conduction, left anterior hemiblock, non-specific repolarization pattern and a ventricular premature beat.

The patient was by that time completely recovered and subsequently was discharged without any clear diagnosis. She was referred as outpatient to our cardiology department to investigate later the cause of syncope.

One month later being in good condition and asymptomatic, she was admitted to our clinic, and a new ECG was recorded (Fig. 10.6).

10.3.2 ECG Analysis

There are striking differences comparing with the previous ECG:

- Giant negative T waves (negative T waves with an amplitude ≥1 mm in at least two consecutive electrocardiographic leads) in all the precordial leads, I, II, aVL, biphasic in aVF and positive in III and aVR
- ST segment depression in V2–V5
- Slightly prolonged QTc (474 ms)

She complained only of an isolated syncopal episode 2 months earlier; at this time the physical examination was normal together with the laboratory tests and the standard transthoracic echocardiography. It was suggested a pseudoischaemic pattern of T wave inversion.

To definitely rule out an ischaemic origin, a stress echocardiography with dobutamine was done that had a normal response.

During that test the negative T waves became positive at the peak stress time and later negative again during the recovery time (Fig. 10.7). That is usually called "pseudonormalization".

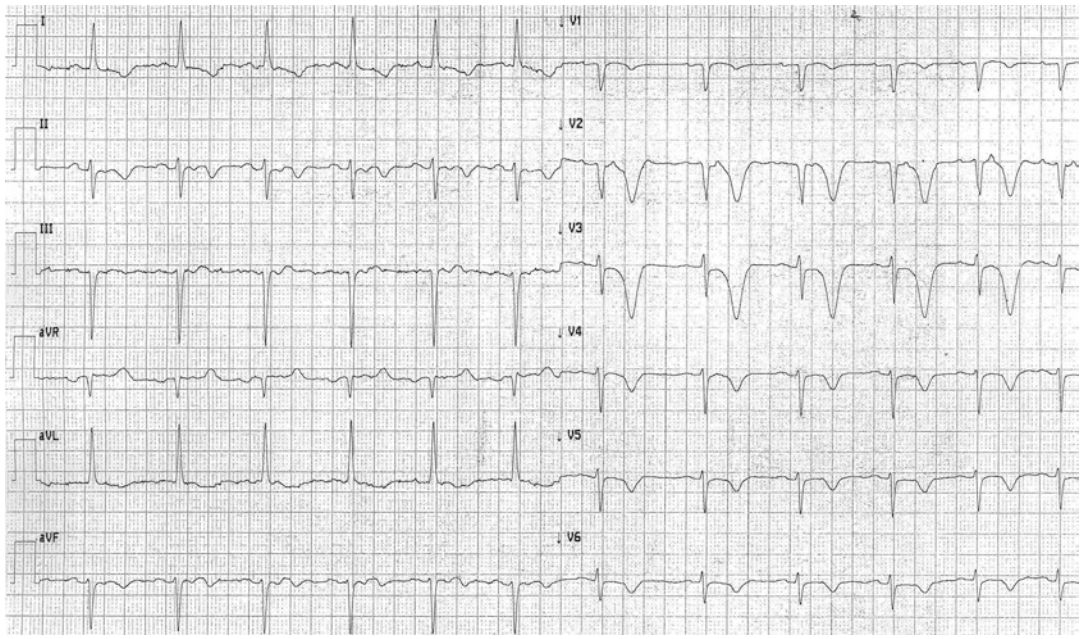

Fig. 10.6 Case 3: 12-lead ECG

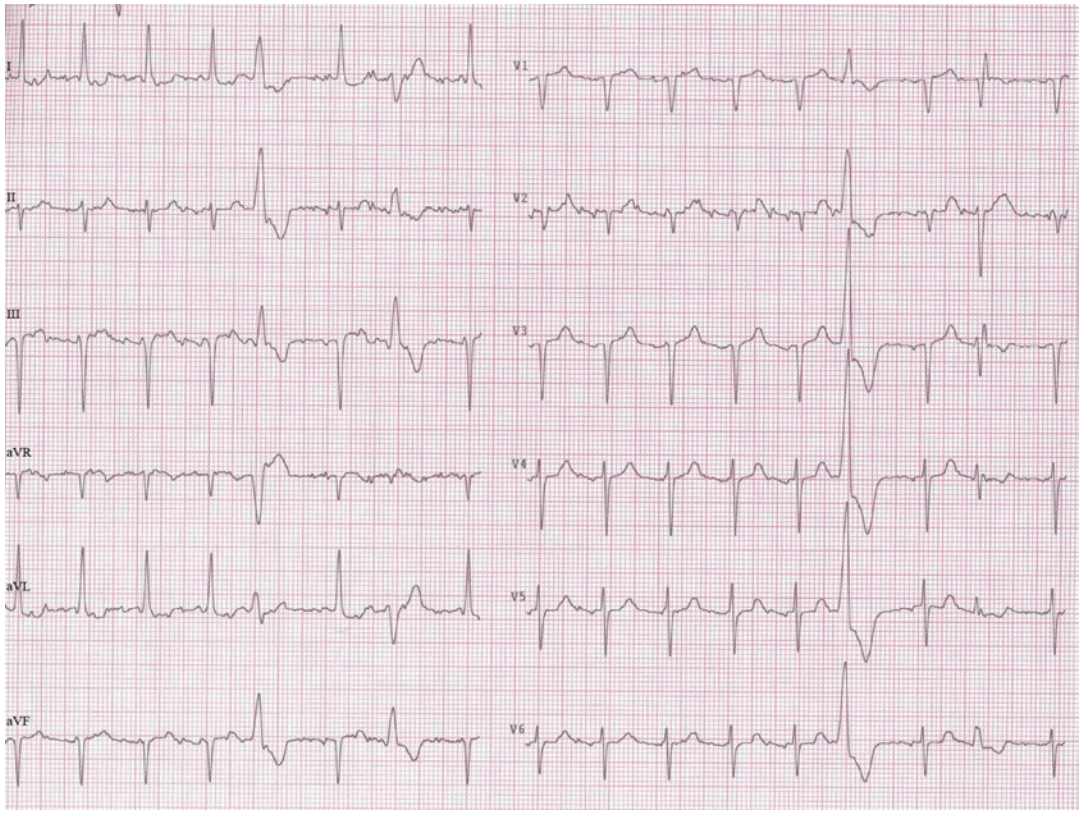

Fig. 10.7 Case 3: 12-lead ECG

10.3.3 ECG Analysis

The dobutamine, a catecholamine analogue, speeds up the normal node function and also atrioventricular and intraventricular conduction.

The ECG shows therefore a sinus tachycardia (114 bpm) with isolated ventricular ectopic premature beats, normal P wave axis and duration, PR 120 ms, QRS 60 ms and persisting left anterior hemiblock.

The negative T waves normalize in all the leads. QTc shortens to 372 ms.

Considering the history of syncope and the possible deep influence of intraventricular conduction on repolarization, an electrophysiological study (EPS) was performed, which showed a delayed infra-Hisian conduction time with a prolonged HV interval (70 ms) (Fig. 10.8), increasing to 92 ms after intravenous flecainide 2 mg/kg (Fig. 10.9).

A dual-chamber pacemaker was implanted, and no other syncopal episodes occurred in the following year.

A posteriori by comparing the intrinsicoid deflection of basal- and stress-recorded ECGs, it is visible the initial part QRS narrowing only of the beats that precede the T normalization (Fig. 10.10), thus confirming a strict relationship between conduction time and repolarization behaviour.

This finding will be discussed in Sect. 10.4.

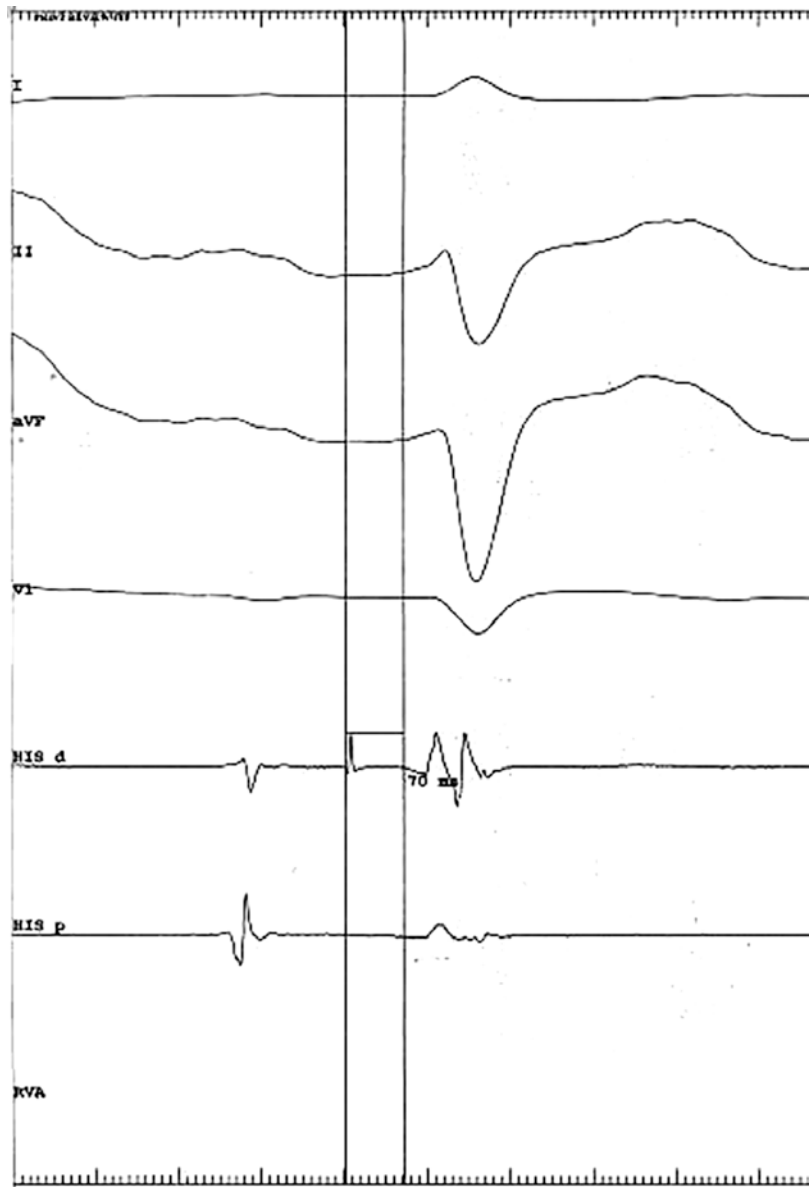

Fig. 10.8 Case 3: EPS showing HV interval of 70 ms

10.4 From ECG to Theory

Action potentials and functional refractory periods of the subendocardial cells last normally longer than the subepicardial ones; for this reason repolarization begins in the subepicardium and moves to subendocardium that is the opposite direction of the depolarization wave-front.

Thus, because of the inverted electron movements, the exploring electrode of the surface

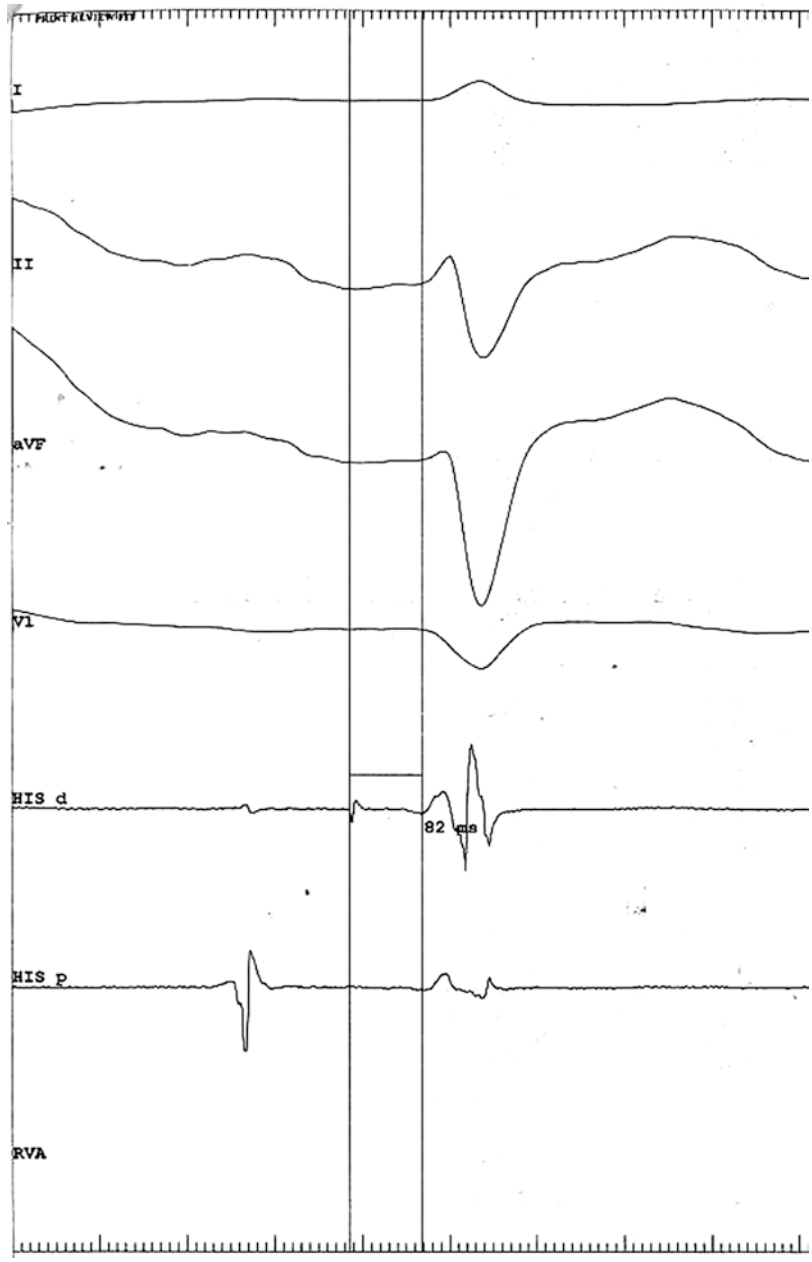

Fig. 10.9 Case 3: EPS showing HV interval of 82 ms

ECG records a vector consistent to the depolarization phase.

This is the classical hypothesis made by Wilson et al. [2] to explain why the QRS (summation of its deflections) and the T wave have the same direction.

The two phases of depolarization and repolarization are closely linked together: the first one moves like a wave-front of about 1 mm in a mosaic pattern that starts from few Purkinje-myocell junction in three different areas of the left ventricular endocardium and myocardium and then proceeds from cell to cell through conduction (gap junctions).

That is not a true wave-front since every myocardial cell repolarizes independently, and the T

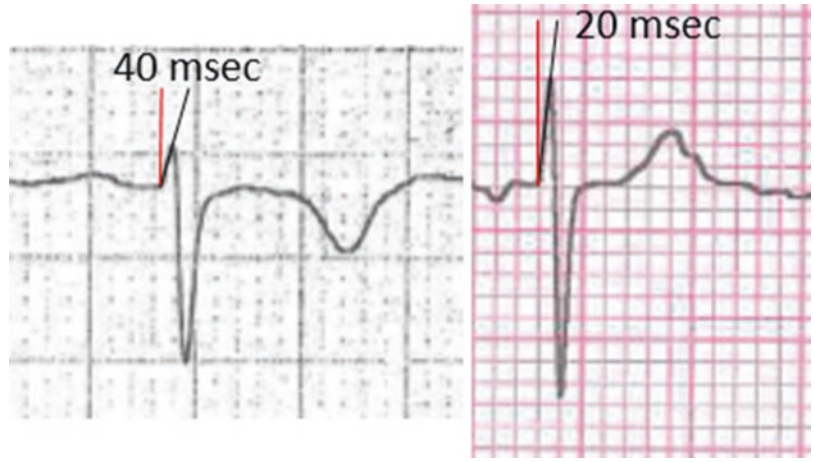

Fig. 10.10 Case 3: detail of Figs. 10.6 and 10.7, intrinsicoid deflection speed related to T wave polarity

wave resultant vector represents the surface measure of this inhomogeneity [3]:

- Different zero time of depolarization
- Different action potential duration
- Different action potential configuration (amplitude and slope of phases 2 and 3, the last one is also frequency dependent)
- Different spatial distribution of the same fibres during diastole and systole
- Effect of blood flow direction during diastole
- Filter effect made by the distance from myocardial wall and skin for a low-amplitude phenomenon like repolarization

Antzelevitch et al. [4] in the early 1990s discovered M cells that have a tendency to have their action potential prolonged disproportionately compared with epicardial or endocardial cells.

That is related with ionic features of M cells including the presence of a smaller slowly activating delayed rectifier potassium current I_{Ks} but a larger late sodium current I_{NaL}.

Therefore the difference between the I_{Ks}:I_{Kr} density ratio among the three transmural cell types (endocardium, M cells, epicardium) contributes importantly to a heterogeneous repolarization.

If it is true that T wave inversion means that the repolarization starts from subendocardium and moves to subepicardium, every phenomenon that could slow down depolarization (i.e. ischaemia, left ventricular hypertrophy, drugs, bundle branch blocks, etc.) by increasing the transmural and/or trans-ventricular gradient (the last one is zero in normal conditions) may favour the subendocardium to repolarize first; consequently the T waves reverse.

T waves have normally asymmetrical branches, being the proximal less steep than the distal one.

T wave abnormalities have to be classified into three groups: primary (due to ischaemia), secondary (or pseudoischaemic) and diffuse/non-specific.

Typically, ischaemic T waves are due to alterations in myocardial cellular electrophysiology and do not appear in the hyperacute phase, when conversely it is often possible to find the elevation of the J point with an increase in the T wave amplitude [5].

The ischaemic vector, depicted by T wave inversions, looks like a subacute phenomenon that appears after hours or days and sometimes may persist several months after the ischaemic event; the T waves are narrow, symmetrical or biphasic, with a sharp final component.

Figure 10.11a–c shows the normal evolution of ST-T segments on the first and second day after presentation, respectively.

Pseudoischaemic inverted T waves are associated with several conditions (Table 10.1).

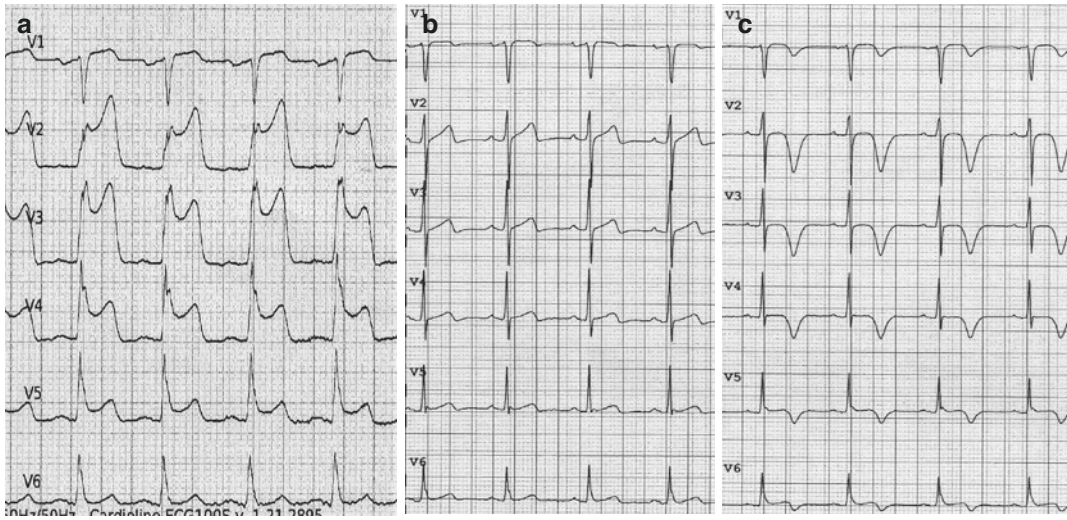

Fig. 10.11 (**a**) Chest lead ECG at presentation. (**b**) Chest lead ECG at first day after index event. (**c**) Chest lead ECG at second day after index event

Table 10.1 Conditions associated with pseudoischaemic inverted T waves

Organic cardiac disease
• Hypertrophic cardiomyopathy
• Left ventricular hypertrophy
• Cardiomyopathy in Friedreich's ataxia
• Arrhythmogenic right ventricular dysplasia (ARVD)
• Mitral valve prolapse
Conduction disturbances
• Electric memory after ventricular pacing (electrotonic modulation)
• Intermittent left bundle branch block
• Post-ventricular tachycardia
• Supraventricular tachycardia conducted with aberrancy
• Ventricular preexcitation (WPW)
Drugs
• Drugs acting in action potential duration (e.g. amiodarone)
Neurological conditions
• Cerebrovascular accidents in particular subarachnoid haemorrhage
Trauma
• Neoplasia
Cardiac tissue inflammation
• Recent pericarditis
• Post-pericardial surgery
Other causes
• Pulmonary embolism
• Takotsubo syndrome
• Idiopathic T wave inversion in athletes or in middle-aged females

10.4.1 The Memory Hypothesis Revisited

This phenomenon was described in the early 1980s by Rosembaum et al., the so-called cardiac memory [6].

The authors demonstrated that changes in the activation sequence persistently modify the order of ventricular repolarization (electrotonic modulation); such modulations accumulate and represent the basis of the "memory" occurrence. It takes time to become apparent, reach its maximal effect and then revert.

This theory came by observing patients with intermittent left bundle branch block (LBBB), referring to inverted T waves that appear after a period of abnormal ventricular activation once the conditioning stimulum ceases and normal ventricular depolarization resumes.

Furthermore, because of the effects of T wave modulation on the surface electrocardiogram are mainly determined by the order and duration of the depolarization process, and by accumulation and memory effects, the post-tachycardia T waves show the same direction as that of the QRS forces during the tachycardia.

Later, Costard-Jackle et al. [7] found that during baseline atrial pacing, ventricular action potential duration was inversely related to the

activation time (sites with earlier activation repolarized later), but after 2 h of ventricular pacing, there was a loss of the inverse relationship (sites with earlier activation repolarized earlier).

Recently, Chiale et al. [8] described that pacing "ad hoc" alters the direction of ventricular depolarization, causing not only the classical abnormal pattern of cardiac memory (inverted and symmetrical T waves) but also leading to peaked positive T waves or even partial or total normalization of abnormal T waves.

Moreover, pseudonormalization or pseudoworsening of repolarization can occur following transient events that alter the depolarization sequence, raising the concepts of "short- and long-term T wave memory".

Short-term T wave memory develops after minutes to hours of continuous abnormal ventricular activation and disappears rather rapidly; meanwhile long-term T wave memory is fully expressed after days or weeks and vanishes in a slow and gradual fashion.

Short-term T wave changes sometimes overcome the changes underlying long-term memory: LBBB repolarization abnormalities occur instantaneously, and their magnitude is proportional to the area of the conditioning QRS complex but of opposite direction.

After a variable period, the increase of opposite forces which generates in the same direction of the conditioning QRS forces is responsible of the long-term memory T wave inversion.

Our three clinical cases offer another possible electrophysiological explanation of the origin of the pseudoischaemia and could help the clinicians to better interpret the ECG in some specific clinical setting.

When spontaneous or provoked by atrial pacing (not ventricular), the so-called short-term memory could be due to a small conduction delay inside the His bundle (see patients of Sects. 10.1 and 10.3) that could lead to a proximal depolarization delay within closest areas (inhomogeneous conduction).

The depolarization delay within the His bundle causes delays of conduction in nearly zones that is followed by inhomogeneous and delayed repolarization [8].

The consequence is a T inversion.

The speed of the intrinsicoid deflection, that is, the first depolarization site of the QRS that has to depend on the hisian conductivity, may reflect therefore an intrinsic conduction delay (phases 0 and 1 of the action potential) and thus be related to normal or instead to inverted T waves.

A close look at the intrinsicoid deflection thus may give useful information especially when (see Sects. 10.2 and 10.3) there is T wave alternans like in Sect. 10.2.

The electrophysiologic study (Fig. 10.12) performed on the patient presented in Sect. 10.1 shows how repetitive atrial extra stimuli may influence the infra-Hisian conduction and at the same time the repolarization pattern.

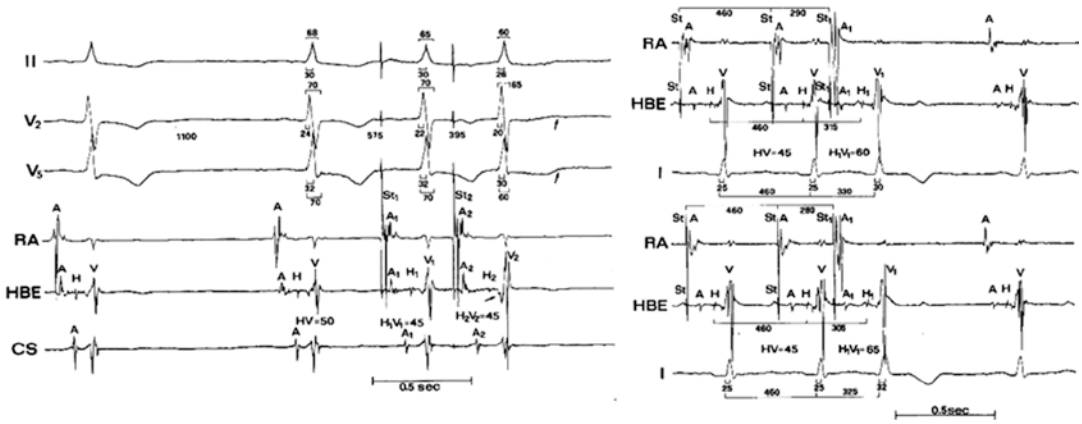

Fig. 10.12 EPS referred to case 1

When the conduction speeds up, it follows a corresponding shortening of the intrinsicoid deflection, and the T wave normalizes.

On the contrary, when the intra- or infra-Hisian conduction prolongs, the negative T wave worsens or appears.

It is conceivable that the cardiac memory is only an expression of the delay of the first QRS activation vectors sited within the His bundle.

It is therefore fairly possible that patients affected by a proximal left bundle block will show a T inversion although their conduction does not yet show a classical LBBB pattern because an infra-Hisian conduction delay is not visible at the surface ECG.

Accordingly, a strict relationship between intrinsicoid deflection time and T could help in suggesting the proper diagnosis.

In the reported case when HV is 65 ms, a deep T inversion ensues that was not visible at HV of 45 ms.

The molecular mechanisms underneath these phenomena aren't understood at all: in canine model cardiac memory induced by ventricular pacing was attenuated by I_{CaL} blockers, suggesting that increased intracellular calcium concentration, as it is a secondary messenger, may change nuclear transcription factors that express membrane channels like I_{Kto}, I_{Kr} and I_{CaL} that determine long-term T wave memory.

As for long-term, also short-term memory is generated by molecular changing, started by local synthesis and liberation of angiotensin II: there is an increase of internalization of macromolecular complex ATII/KV3,4/KCH_{ip2c} that modulates the transmural gradient of this current [9].

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Early Repolarization: When Is It a Normal Pattern?

11

Erika Baiocco, Daniele Contadini, Alessandro Maolo, and Maria Vittoria Matassini

11.1 Case 1

A 38-year-old man was referred to an emergency room for a chest pain that started 2 days before and worsened with a deep breath. He also complained of dizziness. He was recently discharged from the neurology clinic where a diagnosis of migraine, nystagmus and ataxia was made. In the past he was admitted once to an emergency room for agitation and alcohol abuse. The cardiologic past medical history was unremarkable.

The initial 12-lead ECG revealed:

Sinus rhythm, heart rate of 60 bpm, normal atrioventricular conduction (PQ 160 ms), electrical axis 0° and normal interventricular conduction (QRS width 80 ms).

An end-QRS notch in inferior (II, III and aVF) and anterolateral (I and V2–V6) leads is present, with an elevation of J point ≥0.1 mV in lateral and anterior precordial leads (I, aVL and V2–V4) and a rapidly upsloping ST segment and tall T waves. QTc 400 ms (Fig. 11.1).

At hospital admission baseline parameters were normal and stable: blood pressure 125/75 mmHg, arterial blood saturation of 98% without oxygen supplementation and body temperature 36.4 °C.

The preliminary diagnosis was ST-elevation myocardial infarction. Therefore, the patient went to coronary angiography, which revealed normal coronary arteries.

At echocardiography only a mild concentric hypertrophy of the left ventricle with normal wall motion was recorded, without any pericardial effusion or valve abnormalities. The patient was transferred to our clinic for further evaluation.

The laboratory tests showed normal values of blood count, haemoglobin, troponin, creatinine, electrolytes and negative C-reactive protein.

Hyperkalaemia and hypothermia as possible causes of the ECG abnormalities were excluded. Subacute pericarditis was also an unlikely hypothesis because of the absence of pericardial effusion and of the normal inflammatory markers. Moreover, the ST elevation was not associated to a PR depression that is usually present during the acute phase of a pericarditis. We could reasonably exclude also a myocarditis, considering the normal troponin in three consecutive blood samples, the normal left ventricle ejection fraction and the absence of history of recent fever, flu or gastroenteritis.

A treadmill stress test was performed in order to investigate possible repolarization changes during physical activity. During the exercise ST segments normalized and returned to baseline during recovery. Any arrhythmias or symptoms

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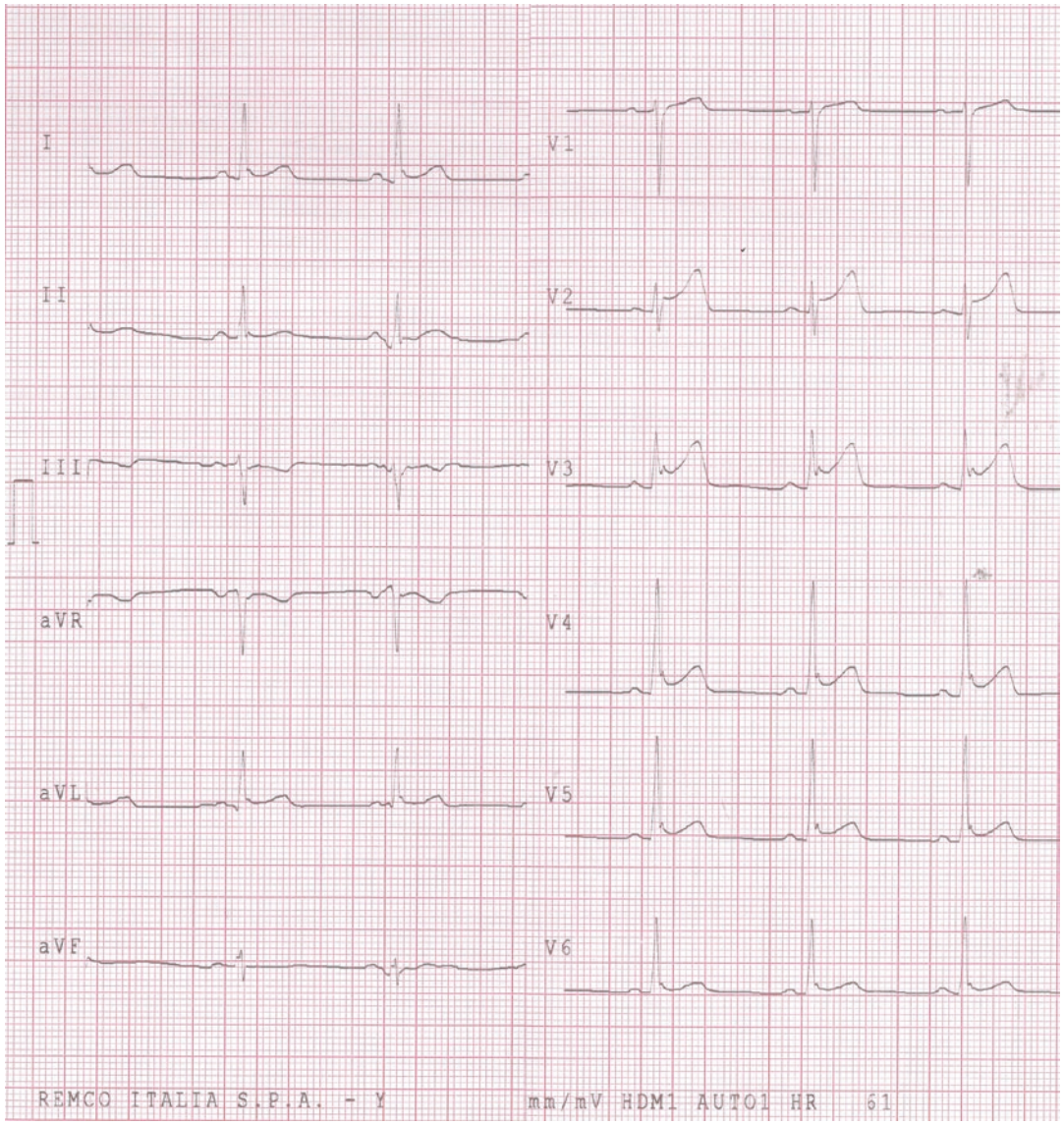

Fig. 11.1 12-lead ECG

occurred. Thus, we were left with an early repolarization likely diagnosis (Fig. 11.2).

The patient was then dismissed with the diagnosis of nonspecific chest pain and early repolarization ECG pattern.

11.1.1 Definition

Early repolarization is usually defined by the presence of three electrocardiographic features: J wave, concave ST-segment elevation and tall symmetrical T wave in two contiguous leads.

More recently, a consensus paper focused on the terminology of early repolarization proposed a new definition including some new measurements and parameters.

Early repolarization is identified by presence of an end-QRS notch or slur with an elevation of the QRS-ST-segment junction (J point) ≥0.1 mV above the isoelectric baseline, in at least two contiguous leads (e.g., inferior or lateral leads;

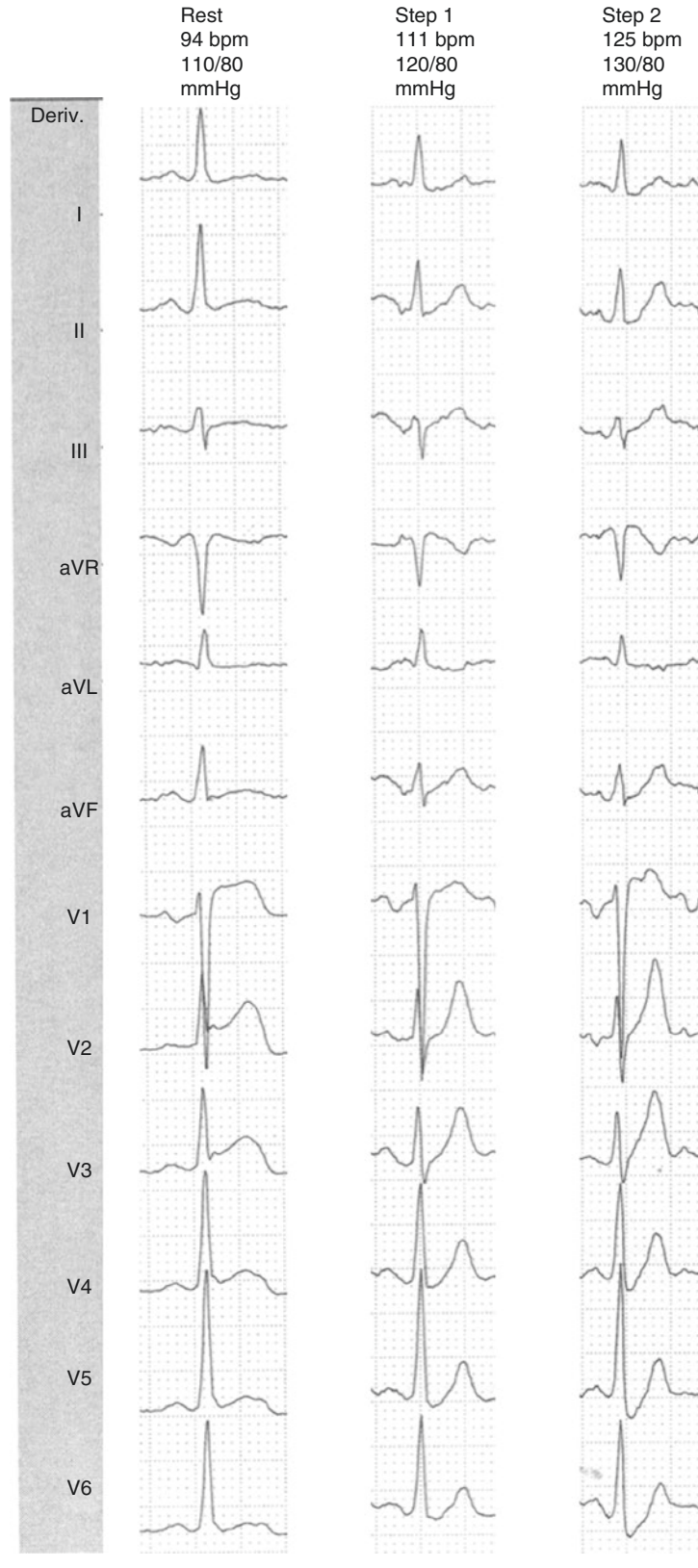

Fig. 11.2 ECG treadmill stress test

excluding leads V1–V3), accompanied by a narrow QRS (duration <120 ms).

End-QRS notch is a positive deflection with a dome morphology occurring on the final 50% of the downslope of R wave, whereas the end-QRS slur is an abrupt slowing of the end of QRS complex.

The J point is the site where the QRS ends and the ST segment begins. The correct way to define J-point elevation is to measure the amplitude of the peak of the notch or the onset of a slur, named J peak (Jp) (Fig. 11.3).

ST-segment slope should be distinguished in three different morphologies: ascending/upsloping, horizontal or descending/downsloping. The amplitude of the ST segment should be measured 100 ms (interval M) after the J termination (Jt), defined as the end of slur or notch (Fig. 11.4).

If the amplitude of the ST segment is inferior to the amplitude of Jt, the ST segment is defined as descending, if it is equal as horizontal and if it is superior as ascending.

QRS duration should be measured on leads where slur or notch is not present [1].

When an early repolarization pattern is associated with aborted cardiac arrest, documented ventricular fibrillation (VF) or polymorphic VT, in absence of any structural heart disease, we can diagnose an early repolarization syndrome (ERS) [2].

11.1.2 Epidemiology

Prevalence of early repolarization pattern in normal population ranges from 2 to 31% [1].

This wide variability could reflect differences in the criteria used for its definition, the demographic features of the population and dynamicity of this pattern with the time along.

Early repolarization pattern is more frequent in young men, African ethnicity people and athletes [3].

The higher prevalence in males could be due to testosterone, which physiologically increases

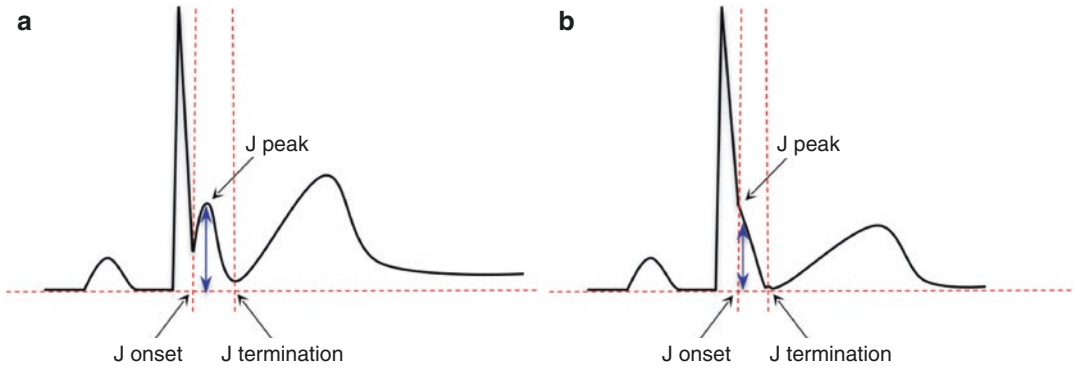

Fig. 11.3 End-QRS notch and slur terminology: end-QRS notch (**a**); end-QRS slur (**b**)

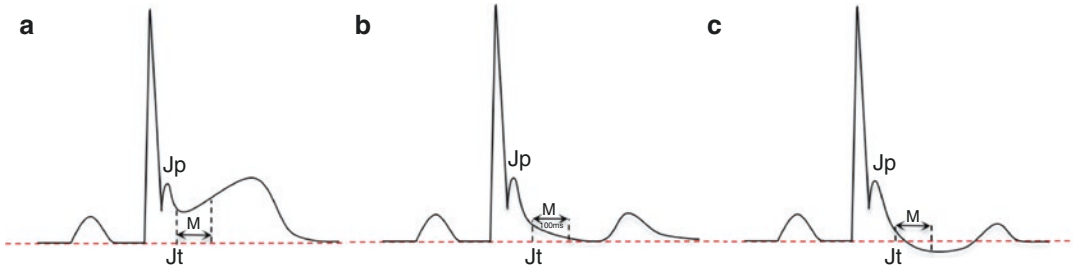

Fig. 11.4 ST-segment slope: ascending/upsloping (**a**); horizontal (**b**); descending/downsloping (**c**)

the outward repolarizing currents of cardiac action potential (AP). Moreover, in males the prevalence of this pattern decreases with age [4].

Also the association between ER and physical activities is largely mentioned. This correlation may be explained by high prevalence of males and black individuals among athletes and by the lower heart rate and pronounced vagal tone typical of sportsmen [3].

This electrocardiographic finding is located preferentially in the inferior and lateral leads, ranging from 0.6 to 7.6% and from 0.4% to 9%, respectively [3].

Early repolarization features in inferior and/or lateral leads together with a rapidly ascending/upsloping ST segment are the most common pattern in healthy and young people practicing physical activity, leading to the conviction that this aspect might be related to athlete-type ECG changes such as a physiological left ventricular hypertrophy. On the other hand, horizontal/descending ST-segment morphology is usually seen in middle-aged population [5].

ER has a heritable basis and it is more prevalent in siblings and offspring of ERP-positive individuals [3].

11.1.3 Pathophysiology

The electrophysiological basis of early repolarization pattern is not completely clear, and it is still a matter of debate.

Experimental evidence indicates that the J wave ECG inscription is a manifestation of a transmural voltage gradient from the epicardium to endocardium, occurring in the early phases of action potential (AP).

During AP phase 1 (early repolarization), the membrane repolarizes rapidly through a progressive attenuation of sodium inward current (I*Na-late*) and simultaneous activation of outward currents (current I*to and* I*Cl*).

In the human heart, both density and properties of recovery of transient outward K+ current (I*to*) vary between epicardium and endocardium. These differences create a physiologic transmural voltage gradient.

However, an imbalance between outward and inward repolarizing currents may result in a prominent I*to* current capable of developing a further faster repolarization in the epicardial cells. As opposed, the action potential is maintained normal in endocardial cells, with a consequent increase of transmural repolarization heterogeneity [6].

These regional differences might increase dispersion of repolarization, thereby facilitating a local re-excitation (phase 2 re-entry). This, in turn, may develop closely coupled premature beats, sometimes degenerating in ventricular arrhythmias.

The ERP response to pharmacologic therapy could confirm the central role of I*to* current. In this regard, studies have reported that quinidine, the only agent with significant I*to*-blocking properties available around the world, is useful to suppress both the J wave and arrhythmic manifestations of ERS. Similarly, beta-adrenergic agonist (isoproterenol) and some phosphodiesterase III inhibitors (milrinone, cilostazol) have been shown to act in reversing the repolarization abnormalities by suppressing the I*to*, augmenting the I*ca* or both [7].

However, discrepant response to I*Na* blockade, in particular ajmaline, pointed out that the mechanism underlying early repolarization still remains to be completely clarified [6].

The response to an increase in heart rate can differentiate a repolarization defect from a conduction defect. At faster rates, as during premature beats, J waves usually are reduced whereas are accentuated by bradycardia or long pauses.

11.1.4 A New Marker of Arrhythmic Risk

Sudden cardiac death prevention has always been one of the main goals of the cardiologists.

For decades the early repolarization was considered a normal variant with a benign outcome.

However, recently case-control and large population studies revealed an association between early repolarization and an increased risk of arrhythmic death, mostly due to idiopathic ventricular fibrillation (IVF) [8, 9].

Some clinical and electrocardiographic characteristics have been evaluated with the aim to improve our ability to distinguish "benign" from "malignant early repolarization".

In multiple studies, the J wave amplitude, distribution and dynamicity as well as the ST-segment morphology have been reported to reflect a different arrhythmic risk.

The observation that a J-point elevation >0.1 mV is increasingly associated with idiopathic ventricular fibrillation (IVF) in patients without structural heart disease has focused on the height of J-point elevation, rather than on its mere presence, as increased arrhythmic risk. In these subjects, early repolarization pattern occurred mainly in the inferior leads and less commonly in lateral leads [10]. It is noteworthy though that a lateral J wave position heralds the lowest risk; the risk progressively increases when early repolarization manifests itself in inferior or even widespread in all the leads [8, 11].

While early repolarization pattern with horizontal or descending ST segment has been linked to an increased risk of arrhythmic death, a rapidly ascending ST-segment morphology has not yet been associated with adverse outcomes, and it is considered generally benign, with few exception [5, 12].

Several studies showed that the presence of high J wave amplitude (>0.2 mV) in the inferior leads together with a horizontal or descending ST segment is a strong predictor of death for arrhythmic causes that is the same percent of other well-known electrocardiographic risk markers, such as long QTc interval and left ventricular hypertrophy [11].

In consideration of ER pathophysiological background, the J wave accentuation during bradycardia or after long pauses could be explained by the pause-dependent augmentation in transient outward current I*to*. Since this behaviour has been noticed only in patients with idiopathic ventricular fibrillation, J wave dynamicity is considered an important predictor of arrhythmic risk in the setting of ER [13–15].

It is also easily understandable how patients with frequent and short-coupled ventricular premature beats (VPBs) have a significant increased risk of arrhythmic deaths [8, 14].

Syncope is also common in early repolarization population. It may occur at rest or during sleep, and it may suggest an early repolarization-related arrhythmic event.

However, syncope has a low specificity in predicting future events in these early repolarization patients, where sudden death is rare compared to a high syncope frequency [14].

A positive family history of sudden cardiac death may be a good sign of a higher arrhythmic risk.

Finally, it is important to point out that in patients with other arrhythmic syndromes, such as short QT and Brugada syndromes, the simultaneous presence of early repolarization pattern does correlate with a worse outcome [16, 17].

None of these clinical or electrocardiographic findings per se has a valid stratification risk tool [18].

Currently, in early repolarization setting, provocative pharmacological and functional tests do not improve accuracy in arrhythmic risk stratification [14]. However, persistence of ERP during exercise and/or ajmaline testing seems to identify patients at higher risk of arrhythmic events, but further prospective evaluation is required to confirm their positive predictive value [19].

Also, ventricular fibrillation inducibility during electrophysiology study (EPS) does not predict risk for future arrhythmias. Moreover, a positive EPS doesn't correlate with the presence of more "malignant" ECG variant of the early repolarization pattern [20].

In conclusion, to date we have difficulties to distinguish the very common "benign early repolarization" from the truly rare malignant form. That is anyway a rare complication.

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Channellopathies: New ECG Criteria for Risk Stratification

12

Paolo Compagnucci, Simone D'Agostino, Alessia Quaranta, and Giulio Spinucci

12.1 Brugada Syndrome

A 39-year-old man was sent to our outpatient clinic before ENT surgery for cardiological evaluation. He reported some episodes of sudden nocturnal awakening associated with palpitations. He did not complain any previous syncope or presyncope, and the family history of sudden cardiac death (SCD) was negative (Fig. 12.1).

12.1.1 ECG Analysis

Sinus rhythm: 72 beats/min; normal PR interval (180 ms); QRS with a right bundle branch block (RBBB) morphology (QRS length 120 ms, S wave in leads I and V6, rSR′ pattern in lead V1). However a closer look at V1 and V2 reveals some features that are not just consistent with RBBB:

- In V1 there is a J point elevation of 3 mm and coved type descending ST-segment elevation which merges into a negative T wave. These features are diagnostic of Brugada type 1 pattern and of Brugada syndrome (BrS).
- In V2 moreover there is J point elevation (2 mm), a saddleback ST-segment elevation (1 mm in its terminal portion), and a biphasic T wave. Those findings identify a Brugada non-type 1 pattern.

12.1.2 Diagnosis and Management

The ECG is therefore diagnostic of a spontaneous type 1 Brugada pattern in the right precordial lead V1. The patient was admitted to our department for further examination. He was asymptomatic and had normal body temperature. A transthoracic echocardiography showed normal cardiac anatomy and function. Laboratory tests were normal.

In the reported ECG, there is therefore an S wave in lead I. As some studies have shown, this electrocardiographic sign (S wave ≥0.1 mV and/or ≥40 ms) could be a strong predictor of life-threatening ventricular arrhythmias that ensue during follow-up of patients with diagnosis of type 1 Brugada even in the absence of a history of cardiac arrest [1].

For a better risk stratification, the patient underwent an electrophysiological study with programmed ventricular stimulation; a single extrastimulus delivered in the right ventricular apex induced a "torsades de pointes" VT type which soon after degenerated into ventricular fibrillation (VF) that was reverted with prompt DC shock. The patient was then implanted with a cardioverter-defibrillator (ICD) (Fig. 12.2).

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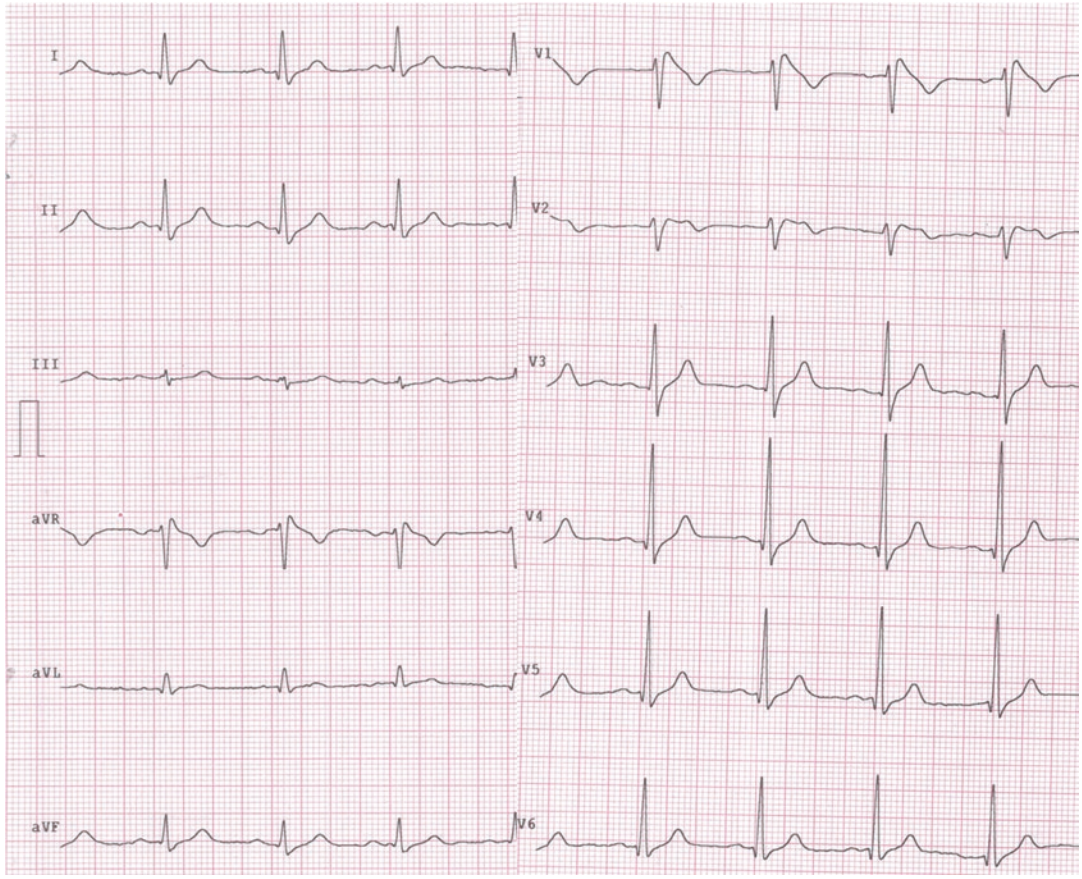

Fig. 12.1 ECG case 1

12.1.3 From ECG to Pathology

Brugada syndrome (BS) is an inherited disease described for the first time in 1992. It is inherited as an autosomal dominant trait with variable expression and is associated with an increased risk of sudden cardiac death (SCD), syncope, and ventricular tachyarrhythmia in young people with no structural heart disease [2].

12.1.3.1 Epidemiology

Prevalence of Brugada syndrome ranges from 1 in 1000 to 1 in 10,000, and it is higher in Southeast Asia (Thailand, Japan, the Philippines) than in Western countries. Brugada syndrome is the leading cause of death in men younger than 40 years in Southeast Asia [3].

12.1.3.2 Pathophysiology

The syndrome is a channellopathy caused by an alteration in the transmembrane ion currents that constitute the cardiac action potential. Particularly, it is associated with mutations of the sodium channel genes. The most frequent gene involved is SCN5A of which almost 300 mutations have been described [4].

12.1.3.3 Clinical Features

A large number of patients with a Brugada pattern may be asymptomatic or instead might have palpitations, syncope, nocturnal agonal respiration, and sudden death. Sudden cardiac death is due to polymorphic ventricular tachycardia (VT) or VF. Fever, use of some specific drugs, dehydration states, alcohol abuse, and large meals may increase the

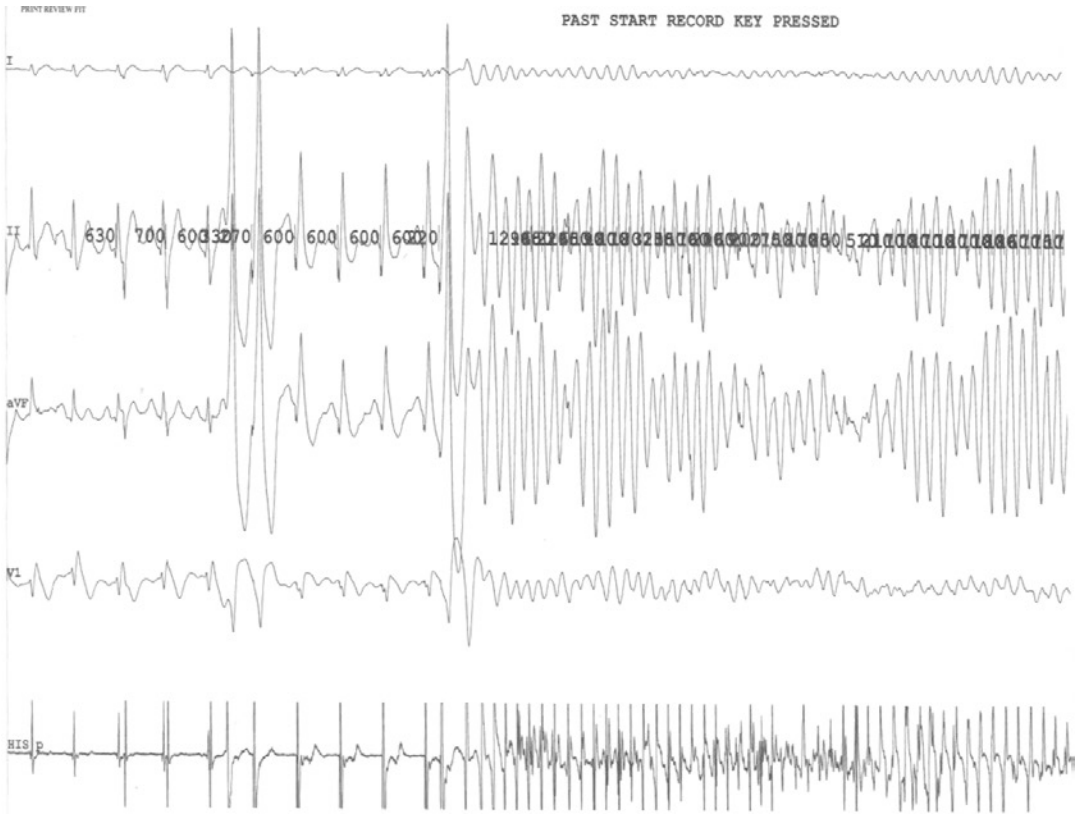

Fig. 12.2 Electrophysiological study with programmed ventricular stimulation

risk of arrhythmic death. Moreover patient with Brugada syndrome is more prone than the general population to develop supraventricular arrhythmias, including atrial flutter, fibrillation, and atrioventricular (AV) nodal reentry tachycardias [5].

12.1.3.4 Electrocardiogram Findings

Brugada Pattern

In the latest consensus document, BrS is classified in type 1 and type 2 (the latter unifying previous types 2 and 3 into a unique pattern [6]):

- Type 1 Brugada pattern (coved pattern): "coved" ST-segment elevation on the J point (≥2 mm), descending with an upward convexity to an inverted T wave in at least one right precordial chest lead (V1–V2). Additional criteria are listed in Table 12.1.

Table 12.1 Typical coved pattern: additional criteria

• The high takeoff (J point) is higher than ST segment after 40 ms, that is, higher than ST after 80 ms
• At 40 ms from the J point, the decrease in amplitude is less than 0.4 mV
• QRS duration is longer in V1–V2 than in mid-left precordial leads due to right ventricular conduction delay

Adapted from "Current electrocardiographic criteria for diagnosis of Brugada pattern: a consensus report."; A. Bayés de Luna et al. (2012) Journal of Electrocardiology, with permission

- Type 2 Brugada pattern (saddleback pattern): "saddleback" pattern with J point (≥2 mm) followed by ST-segment elevation (≥0.05 mV) that descends toward the baseline and then rises again to an upright or biphasic T wave. Some additional criteria are useful for differential diagnosis (Table 12.2) (Figs. 12.3 and 12.4).

Table 12.2 Differential diagnosis between type 2 Brugada and incomplete RBBB

• The high takeoff of r' is not peaked and the descending arm has a gradual slope (Fig. 12.1)
• The angles between both arms of r' are wider (α and β angle). The sensitivity (SE) and specificity (SP) are higher in β angle (79% and 84%, respectively) with a threshold of 58° (Fig. 12.2)
• The measurement of the duration of the base of triangle of r' at 5 mm from the high takeoff is more than 3.5 mm in BrP type 2, with an SE of 81% and an SP of 82%. This criterion is easier to measure than the α and β angles
• The duration of QRS is longer in Brugada pattern type 2

Adapted from "Current electrocardiographic criteria for diagnosis of Brugada pattern: a consensus report."; A. Bayés de Luna et al. (2012) Journal of Electrocardiology, with permission

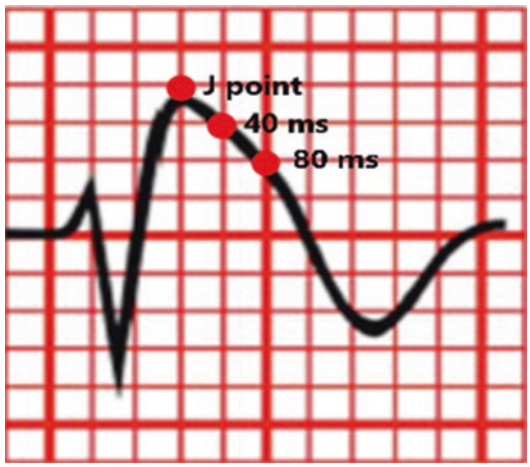

Fig. 12.3 Typical characteristics of coved and saddleback pattern and additional criteria useful for differential diagnosis

In case of a suspected Brugada, it is recommended to record ECG also in 2nd and/or 3rd intercostal space. By moving up the right precordial chest leads (V1–V2) to the 2nd or 3rd intercostal space, we may increase the sensitivity to detect the clues of Brugada type 1. In case of inconclusive findings but still highly suspicious, it is advisable to provide a pharmacologic challenge with intravenous administration of sodium channel blocker agents like flecainide or ajmaline that can unmask the typical pattern [6].

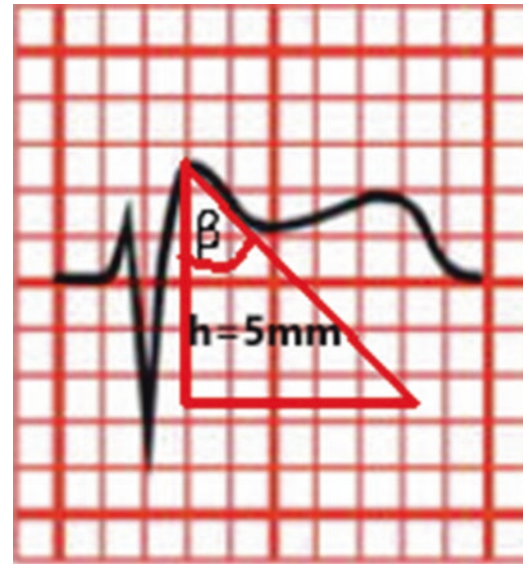

Fig. 12.4 Typical characteristics of coved and saddleback pattern and additional criteria useful for differential diagnosis

According to 2013 HRS/EHRA/APHRS Expert Consensus Statement on the Diagnosis and Management of Patients with Inherited Primary Arrhythmia Syndromes [7]:

- BrS is diagnosed in patients with ST-segment elevation with type 1 morphology ≥2 mm in ≥1 lead among the right precordial leads V1 and V2, positioned in the 2nd, 3rd, or 4th intercostal space occurring either spontaneously or after provocative drug test with intravenous administration of Class I anti-arrhythmic drugs.
- BrS is diagnosed in patients with type 2 or type 3 ST-segment elevation in ≥1 lead among the right precordial leads V1 and V2 positioned in the 2nd, 3rd, or 4th intercostal space when a provocative drug test with intravenous administration of Class I anti-arrhythmic drugs induces a type 1 ECG morphology.

Several conditions which may mimic BrS have been reported.

They are classified into Brugada phenocopies, which are transient, and Brugada-like patterns which are generally permanent.

Brugada phenocopies represent cases of ECG Brugada pattern (mainly type 1) induced by transient events. These electrocardiographic patterns disappear as soon as the injury is resolved, so it is not correct to make a Brugada syndrome diagnosis. They include *acute myocardial ischemia or infarction, dissecting aortic aneurysm, acute pericarditis, myocarditis, pulmonary embolism, metabolic disorders (metabolic acidosis), ionic disorders (hyperkalemia, hyponatremia, hypercalcemia), abuse of some drugs (e.g., tricyclic and tetracyclic antidepressants), cocaine overdose, thiamine deficiency, electrocution, hypothermia, and mechanical compression.*

Brugada-like patterns are generally permanent conditions that may resemble the Brugada type 1 or type 2 patterns: *incomplete RBBB, early ventricular repolarization, ventricular septal hypertrophy, arrhythmogenic right ventricular cardiomyopathy, athlete's heart, pectus excavatum* [8, 9].

12.1.4 ECG Risk Stratification

The main risk factors of the Brugada patients are ventricular tachyarrhythmias (typically polymorphic VT, TdP and VF) leading to syncope or cardiac arrest; in these patients an ICD implant is recommended. Current practical guidelines and consensus recommend implant of an ICD in patients surviving a SCD with class of recommendation I (level of evidence C) and in patients with unexplained syncope and spontaneous type 1 ECG (class IIa, level of evidence C) [10].

In addition to clinical features, a series of findings can help to evaluate the arrhythmic risk, especially in medium- to low-risk patients, in the presence of inconclusive diagnostic assessment, and in asymptomatic patients.

In the population of asymptomatic individuals, the event rate of SCD is around 0.5% per year; but the cumulative risk is not negligible because individuals diagnosed with BrS are often young and have a long life expectancy. EPS with evidence of inducible ventricular arrhythmias may help stratifying their risk, even if there are controversies on this test because different studies showed discordant results [11].

Some noninvasive information could be taken even from the 12-lead ECG.

Patients displaying the spontaneous type 1 pattern have a worse prognosis, with a hazard ratio (HR) of 4.0 for events.

Patients with fever inducing a type 1 ECG pattern have an arrhythmic incidence of 0.9% per year, that is, an intermediate risk between patients with a drug-induced type 1 ECG pattern and those with a spontaneous diagnostic pattern.

The coexistence with sinus node dysfunction or with atrial fibrillation is associated with a worse prognosis. Atrial fibrillation (AF) is more common in patients with BrS than in the general population and can be a marker of a more severe disease with a consequent worse long-term prognosis [12–14].

Similarly, concomitant sinus node dysfunction can be related with a more evident clinical presentation of BrS [15].

Some novel risk factors, such as QRS fragmentation, T-peak to T-end interval, T wave alternans, the VR sign, and S wave in lead I, might help in the management of BrS and also for taking clinical decisions.

QRS fragmentation (defined as the presence of two or more in V1–V3) has been found to predict worse prognosis. It is an independent risk marker and can be useful in asymptomatic patients [16].

Among the other ECG markers of risk, a recent study described that S wave in lead I, a deep and/or large S wave (>4 ms, >1 mV), strongly correlates with malignant ventricular arrhythmias during follow-up. The presence of a significant S wave could be related to a delayed activation in the right ventricular outflow tract (RVOT). This substrate could favor reentrant ventricular tachyarrhythmias and can be used as a potential novel marker of SCD risk stratification [1].

12.2 Short QT Syndrome

A 33-year-old male presented to our clinic after a syncope. He reported on an abrupt and transient loss of consciousness associated with sudden loss of postural tone that lasted for few seconds and

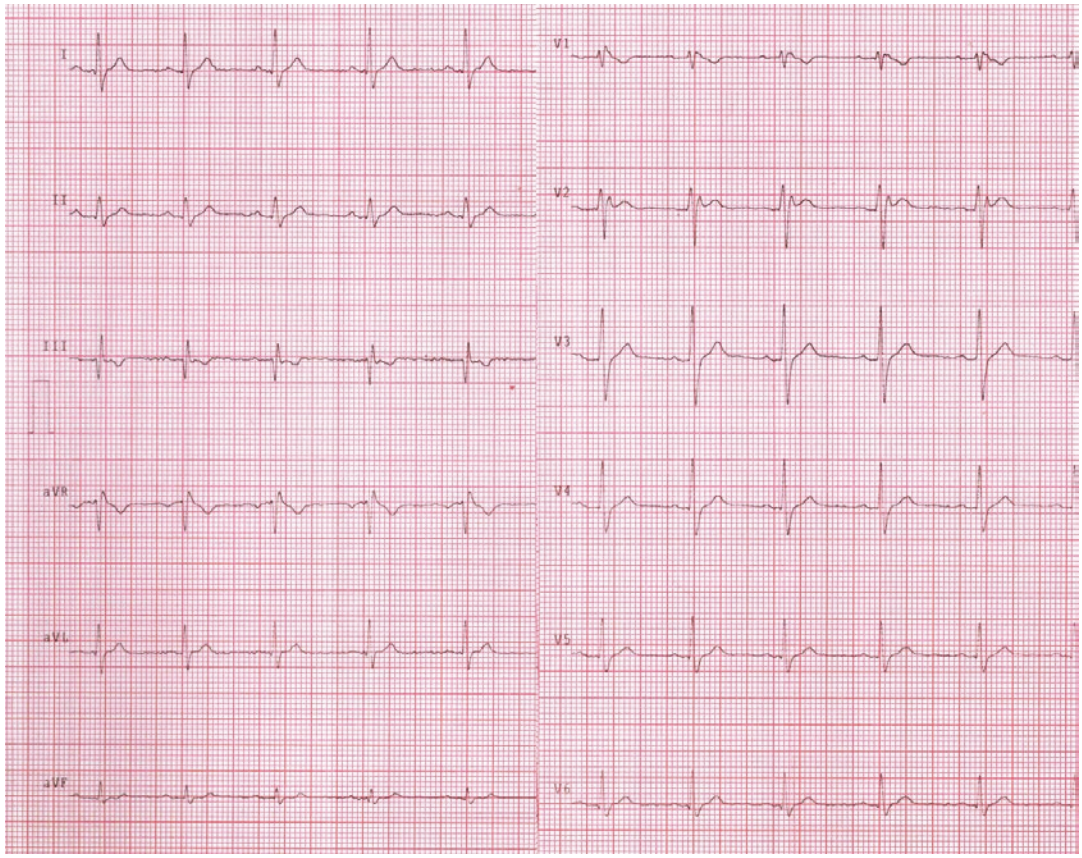

Fig. 12.5 ECG case 2

had a spontaneous recovery. He reported also a warmth sensation, diaphoresis, and nausea preceding the syncope, which occurred after he was standing for 30 min in a warm room. His family history was positive for sudden death of his father at the age of 36. His past medical history was positive for two previous episodes of syncope with similar features (Fig. 12.5).

12.2.1 ECG Analysis

Sinus rhythm, heart rate: 85 beats/min. P wave morphology is normal as well as the PR interval which lasts 160 ms. QRS has a Brugada type 2 pattern in lead V2 (a nondiagnostic pattern). There is a short QT interval: in lead II, it is 280 ms, with a corrected QT interval (using Bazett's formula) of 330 ms.

12.2.2 Diagnosis and Management

This electrocardiogram is diagnostic of a short QT syndrome (SQTS) that can be diagnosed in case of a corrected QT interval (QTc) ≤340 ms or a QTc ≤360 ms in the presence of a family history of short QT syndrome, a confirmed pathogenic mutation, together with a family history of sudden cardiac death prior to the age of 40 or a previous documented ventricular tachycardia/ventricular fibrillation episode in the absence of any significant structural heart disease. Our patient's father died suddenly at the age of 36. The patient was not taking any drugs or medications, and serum calcium levels were normal.

He underwent a genetic testing which confirmed the diagnosis by showing a loss-of-function mutation in the alpha subunit of cardiac

L-type calcium channel (CACNA1C), a mutation which has been associated with a short QT interval, a Brugada pattern, and a familial sudden cardiac death syndrome [17]. The patient received a diagnosis of STQS type 4.

Since the syncopal episodes could be reasonably attributed to a neuro-mediated mechanism, after a discussion of the possible therapeutic options, we decided with the patient assent not to implant an ICD but to prescribe hydroquinidine, a drug which has been shown to prolong QT interval and to reduce the arrhythmic risk in patients with short QT syndrome [18, 19]. Furthermore, the patient received an implantable loop recorder, which has not revealed any sustained ventricular arrhythmias so far (2-year follow-up).

12.2.3 From ECG to Pathology

12.2.3.1 Historical Background

Short QT syndrome (SQTS) is one of the rarest cardiac channellopathies.

Until the 1990s, the main interest was focused on the association between QT prolongation and risk of sudden death; a study conducted in 1986 on kangaroos [20] showed that those animals, which are known to have a very short QT and also a high risk of sudden death, are extremely prone to induction of ventricular fibrillation upon contact of a catheter tip with the endocardial surface. The authors postulated that the short QT interval could portend an arrhythmic risk. A subsequent human study in 1993 [21] reported a high sudden death risk in subjects with a corrected QT (QTc) interval shorter than 400 ms and similar to those people with a QTc longer than 440 ms. The association of a short QT interval with both atrial and ventricular fibrillations was first recognized by Gussak et al. [22] in 2000 and was later confirmed by other authors. The short QT syndrome was then described after further observations made on two families with a strong history of sudden death and short QTc intervals by Gaita et al. in 2003 [23].

12.2.3.2 Epidemiology

Until recently, fewer than 200 confirmed cases have been reported in medical literature worldwide. Studies on healthy populations estimate the prevalence of QTc intervals under 360 ms and under 340 ms to be far less than 2% and 0.5%, respectively [24]. Even though SQTS may be fatal as early as in the first months of life or as late as in the 80s, some data suggest that risk of sudden death by the age of 40 is higher than 40% [25]. This may at least in part explain why the prevalence of subjects with QTc <300 ms is negligible in studies conducted on adult populations.

12.2.3.3 Definition and Diagnostic Process

SQTS definition has been a matter of debate with regard to the optimal cutoff value for QTc interval. Current guidelines [26] suggest that SQTS can be diagnosed in subjects with a QTc interval (calculated using Bazett's formula thus avoiding both bradycardia and tachycardia in order to prevent an overestimation and an underestimation of the QTc interval) ≤340 ms or a QTc ≤360 ms and *one or more* of the following: (a) a confirmed pathogenic mutation, (b) a family history of SQTS, (c) a family history of sudden death at age <40 years, and (d) survival from a ventricular tachycardia/ventricular fibrillation episode in the absence of heart disease (see Table 12.3).

Secondary causes of a short QTc have to be excluded before making a diagnosis such as bradycardia, hypercalcemia, digitalis, Class IB antiarrhythmic drugs, or antiepileptic drugs acting on voltage-gated sodium channels.

Table 12.3 Short QT syndrome diagnosis

Short QT syndrome in diagnosed in the presence of a QTc ≤340 ms
Short QT syndrome should be considered in the presence of a QTc ≤360 ms and one or more of the following (a) A confirmed *pathogenic mutation* (b) A *family history* of SQTS (c) A *family history* of sudden death at age <40 years (d) Survival from a *VT/VF episode* in the absence of heart disease

It is also wise to record several ECGs to observe QT intervals and T wave morphologies at different heart rates, because of possible underestimation of the QTc by Bazett's formula at heart rates under 60 and an overestimation at rates over 100/min.

Patients with the SQTS typically show a reduced adaptation of the QT interval to changes in heart rate; therefore, these subjects may have QTc intervals in the low to normal range at heart rates around 60, with the interval failing to shorten at higher heart rates. Also an exercise test ECG may be of help by showing a flat QTc/R-R relationship [27].

12.2.3.4 How Should the QT Interval Be Measured?

The QT interval should be measured from the beginning of the QRS complex to the end of the U wave. Even though this might seem a straightforward task, it is a little complicated matter [28].

Lead Selection

QT interval may be different in various leads. It is the electrical axis that determines which lead has the longest or shortest QT. QT interval is usually best measured in lead II, as proposed by Bazett in 1920. The best reason for this is that the QRS and the TU axes are usually directed infero-laterally (in the direction of II) and this makes II the preferred lead for QT measurement. The reference values are measured in lead II [29].

U wave

The QT interval, by definition, does not include U wave, even though cardiac repolarization is not finished until the end of the U wave. What complicates the routine QU interval measurement is the suppression of the U wave by standard ECG filtering and also by the P wave at high heart rates; thus, the QT interval is preferred as the standard measurement of the cardiac repolarization duration.

T wave End

Defining where the T wave ends may be a complex task both in normal ECGs and in ECGs with abnormal T-U wave morphologies. The classic method for the definition of the end of the T wave is the tangent method (Fig. 12.6), initially proposed in 1952 [30]. A tangent is drawn to the steepest portion of the descending limb of the T wave, and the point at which this tangent intersects the baseline (i.e., the U-P segment) is the end of the T wave and thus of the QT interval. Other authors, however, have proposed the use of the T wave nadir (Fig. 12.7), that is, the point between the T wave and the U wave that is closest to the baseline, to define the end of the T wave [31]. This produces slightly longer QT intervals.

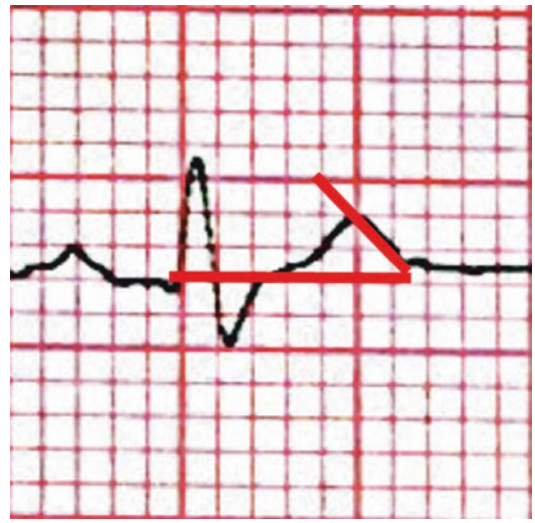

Fig. 12.6 The tangent method

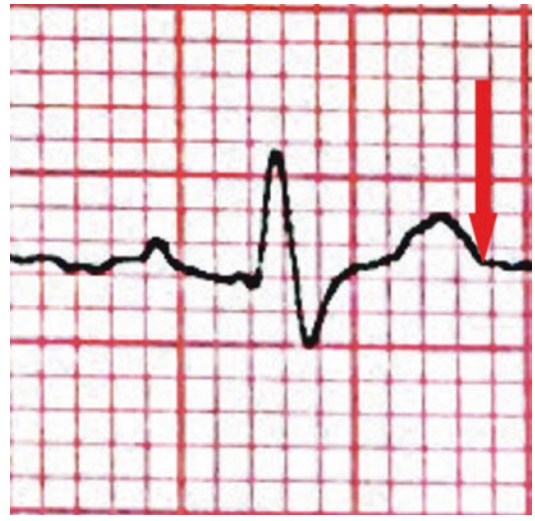

Fig. 12.7 T wave nadir

Heart Rate

The duration of the cardiac repolarization process and thus the duration of the QT interval adapt to changes of the heart rate. The standard method to account for this adaptation process is the use of the formula initially proposed by Bazett in 1920 [32]. The QTc is calculated as $QT/\sqrt{RR}$ (where the RR interval is determined as the RR preceding the measured QT interval). This enables the comparison among QT intervals at different heart rates. Nonetheless, this method works best at normal heart rates (between 60 and 100) and produces an underestimation of the QTc interval at slow heart rates and an overestimation at fast heart rates. A different measurement used in clinical practice is the linear Framingham formula: $QTc = QT + 0.154 * (1 - RR)$. This method produces a more uniform correction over a wide range of heart rates. Even though many other correction methods have been proposed, Bazett's formula remains the standard one.

Arrhythmias

QT interval measurement is a complicated issue in cases of irregular rhythms (sinus arrhythmia, premature complexes, and atrial fibrillation) where there is a risk of overestimation. It should be measured in stable sinus rhythm and calculated as the average value of three measurements.

12.2.3.5 SQTS Pathophysiology

SQTS is a disease in which there is an acceleration of the repolarization process which is responsible for both the short QT interval on the electrocardiogram and the predisposition to develop atrial and ventricular fibrillation. This is due to an excessive and inhomogeneous shortening of myocardial action potential duration and thus of refractoriness, which promotes arrhythmogenesis mainly by functional reentrant circuits [33].

SQTS is a genetic disease with an autosomal dominant mode of transmission. Until recently, mutations in five genes have been recognized as causative: three of these genes encode voltage-gated potassium channels (KCNH2, KCNQ1, KCNJ2), and two encode the subunits of voltage-gated L-type calcium channel (CACNA1C and CACNB2). Mutations in genes encoding potassium channels produce a gain of function of these channels, thus accelerating the repolarization process by shortening the plateau phase of the action potential; on the contrary, mutations in genes encoding L-type calcium channel subunits produce a loss of function of the channel, which portends similar electrophysiological consequences.

Given the rarity of this disease, few studies evaluated the relationship between genotype and phenotype; from the data available, SQTS produced by mutation in the KCNH2 gene is characterized by the shortest QT intervals, a late age of manifestation, and an optimal response to the drug hydroquinidine, which is able to restore a normal QTc duration. This is called SQTS type 1.

Mutations in KCNH2 (SQTS type 1) and KCNQ1 (SQTS type 2) are associated with the highest risk of atrial fibrillation and flutter, usually occurring at a young age in the absence of structural heart disease. Furthermore, mutations in L-type calcium channel subunits (SQTS type 4 and SQTS type 5) often produce an overlap of STQS and Brugada syndrome, as in the case described above.

Unfortunately, the diagnostic yield of genetic testing is very low, with only 15% of patients with SQTS having a positive result [25]. Each of the causative mutation affects no more than 5% of the SQTS population. Thus, much work still has to be done to reveal other causative mutations.

12.2.3.6 Clinical Features

As already pointed out, SQTS may present as early as in the neonatal period or as late as in the eight decade. Cardiac arrest is the initial presenting symptom in about 30% of patients in the largest case series; the prevalence of cardiac arrest by the age of 40 is >40%. Both male and female subjects are at risk of malignant arrhythmias, but the risk is homogeneous during the entire life span for female subjects, whereas it is highest between adolescence and 40 years of age in male, suggesting a role for androgens in the modulation of genotype-phenotype correlations. The arrhythmic risk, as is true for Brugada syndrome, is maximal at rest, and cardiac arrests usually recur in the same circumstances. Patients

with SQTS, mainly SQTS type 1 and type 2, are also at high risk of atrial arrhythmias, usually occurring in the absence of structural heart disease.

12.2.3.7 Therapeutic Approach

Unfortunately, we do not have yet enough information to determine which asymptomatic patient will have a malignant arrhythmia. Both genetic classification and QT interval duration have proven unsatisfactory risk stratification tools (as opposed to long QT syndrome, where a QTc >500 ms predicts a higher arrhythmic risk).

Thus, guidelines recommend implantation of an ICD for secondary prevention in patients who survived a cardiac arrest or experienced a sustained ventricular tachycardia, given that the risk of recurrence is very high (10% per year).

Syncope of undetermined origin is not a strong predictor of cardiac arrest; thus an implantable loop recorder might be useful to assess the correlation of symptoms with arrhythmias and to detect asymptomatic arrhythmias in that setting.

No data support the use of the electrophysiological study with premature ventricular stimulation as a tool for risk stratification so far.

Hydroquinidine, by blocking potassium channels and thus restoring a normal action potential duration, is an effective therapeutic option that might be considered in patients who qualify for the implantation of an ICD for secondary prevention but refuse it or have a contraindication for it (e.g., the pediatric population) or in subjects with a strong family history of sudden death. Also, hydroquinidine can be very useful in patients experiencing multiple ventricular fibrillations and appropriate ICD shocks.

12.3 Long QT Syndrome

A 34-year-old patient was admitted to ER for syncope occurring while he was walking, not preceded by prodromes. The syncope was complicated by facial and thoracic trauma with rib fractures at the left hemithorax. Recovery of consciousness was spontaneous and complete.

Our patient had been diagnosed with long QT syndrome type 3 (LQT3) while he was a child. Indeed he had always been asymptomatic in the past, and LQT3 diagnosis had been done during a family screening. He inherited a pathogenetic mutation from his mother who had already undergone ICD implant in secondary prevention (Fig. 12.8).

12.3.1 ECG Analysis

Sinus rhythm, 58/min, normal atrioventricular and intraventricular conduction (PR 160 ms), normal QRS axis (+45°) and isoelectric ST segment. The distinctive traits of this ECG are the prolonged QT interval (QT = 520 ms measured in lead V4–V5, while QTc is 510 ms with Bazett's formula) and the typical T wave morphology of LQT3 (late-onset and narrow T wave).

12.3.2 Diagnosis and Management

During hospitalization the patient underwent further investigations for the study of syncope, in order to exclude alternative causes of syncope. At 2D echo there were normal dimensions and function of the cardiac chambers. Laboratory findings did not show electrolyte abnormalities, and not any reversible cause of QT interval prolongation was found. An exercise stress test was negative for inducible ischemia and also arrhythmias; a tilt-up test resulted negative; and a coronary angiogram excluded any hemodynamically significant stenosis.

On the ground of family history, characteristics of the syncope, and genetic mutation, the patient received an implantable cardioverter-defibrillator (ICD).

12.3.3 From ECG to Pathology

12.3.3.1 Epidemiology

Long QT syndrome (LQTS) is a congenital disorder with variable penetrance characterized by a prolongation of the QT interval and an increased

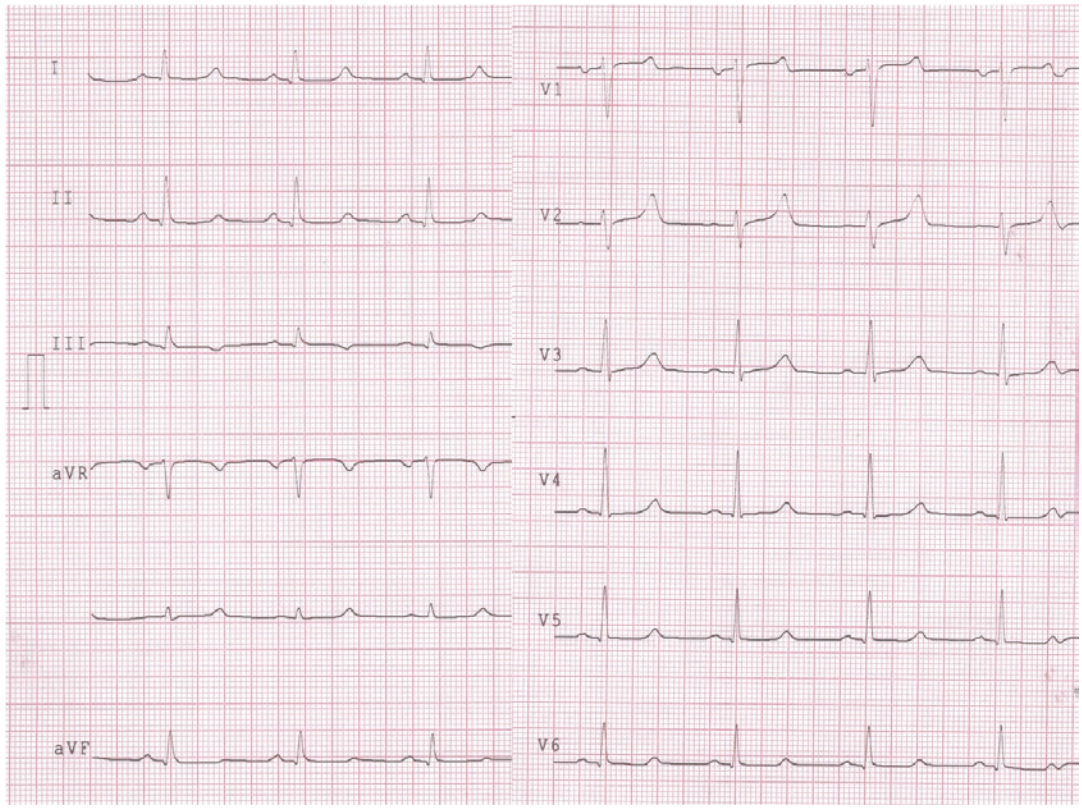

Fig. 12.8 ECG case 3

propensity to life-threatening ventricular arrhythmias. The prevalence in general population is estimated to be between 1:5000 and 1:2000 subjects, but the real prevalence may be higher since many patients with LQTS are asymptomatic [34–37].

12.3.3.2 Pathophysiology

In the majority of cases, LQTS is inherited as an autosomal dominant trait with incomplete penetrance. Sporadic (de novo) alterations occur in 5–10% of cases. Like all electrical heart activities, QT interval depends on specific ion current (Fig. 12.9).

Molecular studies show that all genes linked to the LQTS phenotype encode for various subunits of cardiac ion channels or channel-associated structural proteins. More than 500 mutations have been described so far [35, 39].

The most frequent clinical types of LQTS are LQT1, LQT2, and LQT3. The remaining ten types (LQT4 to LQT13) make up less than 5% of the genotype-identified LQTS. Genetic mutations involved are the following:

- KCNQ1-encoded Kv7.1 channel subunit (IKs potassium channel alpha subunit; LQT1)
- KCNH2-encoded Kv11.1 subunit or hERG (IKr potassium channel alpha subunit; LQT2)
- SCN5A-encoded Nav1.5 (INa sodium channel alpha subunit, LQT3)

Genetic mutations in other types of LQTS may involve auxiliary subunits to KCNQ1 or KCNH2, other potassium channel subunits (Kir2.1 current involved in Andersen-Tawil syndrome, characterized by skeletal abnormalities), L-type calcium channel subunit associated with LQT8-Timothy syndrome (characterized by syndactyly in both hands and feet and autism), or cytoskeletal proteins (ankyrin-B).

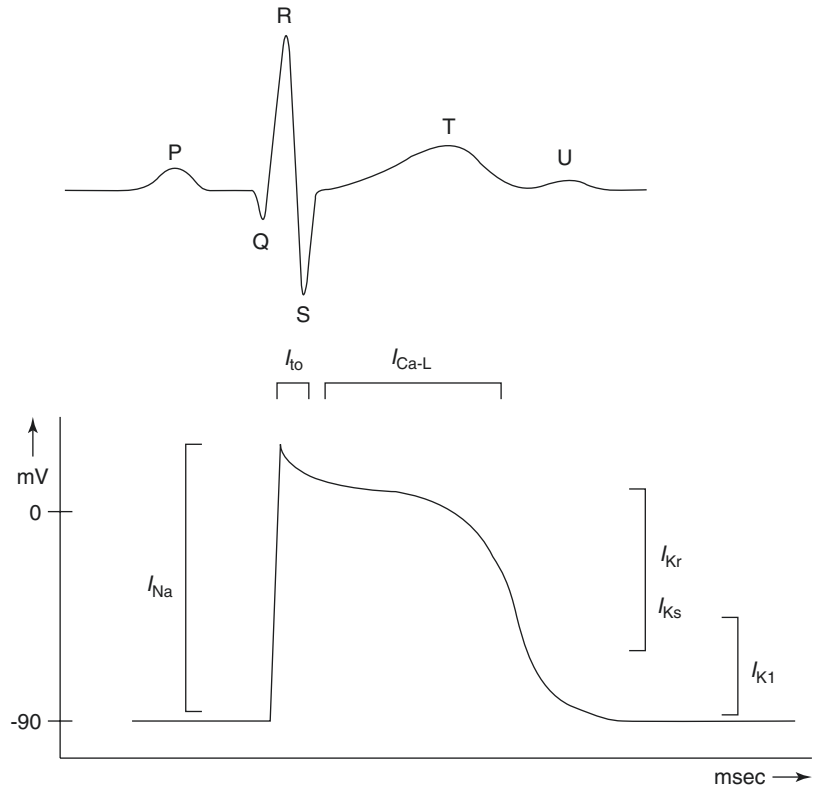

Fig. 12.9 Ionic currents contributing to the action potential and its phases. On courtesy of P.G. Postema, "The measurement of QT interval" [38]

12.3.3.3 Clinical Features

The clinical course of patients with LQTS is variable, owing to incomplete penetrance; prognosis is influenced by age, genotype, gender, environmental factors, therapy, and possibly other modifier genes. LQTS patients have an increased propensity to life-threatening ventricular arrhythmias, in particular torsade de pointes (TdP). This arrhythmia can be self-limiting and asymptomatic or manifest with palpitations, presyncope, syncope, or sudden cardiac death (SCD). Death is usually due to degeneration of TdP in VF. Nonfatal events (syncope and aborted cardiac arrest) in LQTS patients remain the strongest predictors of subsequent LQTS-related fatal events [37].

LQTS often manifests before puberty in males and after puberty in females. Among untreated symptomatic patients, mortality is high, with 20 % of deaths in the first year after the first cardiac event and approximately 50% within 10 years [34]. Unfortunately SCD is the first sign in up to 15% of patients.

The three main genotypes (LQT1, LQT2, and LQT3) are associated with distinctive clinical phenotypes with important implications in diagnosis, treatment, and long-term clinical course. Each one of these genotypes is more frequently associated with specific triggers. In patients with LQT1 and LQT2, cardiac events are typically associated with adrenergic stimulation. Diving and swimming are common triggers in LQT1 patients, while acoustic stimuli (such as alarm clock ringing) and sudden awakening are common triggers for LQT2 patients [37, 40–42]. On the contrary LQT3 is often associated with arrhythmic events at rest or during sleep.

The frequency of cardiac events is significantly higher among LQT1 (63%) and LQT2 (46%) patients than among patients with the LQT3 genotype (18%). However, the likelihood of dying during a cardiac event is significantly higher among LQT3 patients (20%) than among those with the LQT1 (4%) or the LQT2 (4%) genotype [40–42].

Each genotype has a different response to exercise. LQT1 patients fail to appropriately shorten their QT interval during exercise, and QTc may further lengthen. On the contrary, patients with LQT3 show shortening of QT interval during exercise. In LQT2, QTc behavior is variable [43]. Finally, LQT1 patients have a peculiar response to epinephrine. Epinephrine infusion has an excellent performance in the detection of LQTS1 because it provokes a significant and stable QTc prolongation in these patients [31, 44, 45].

12.3.3.4 Electrocardiogram Findings

The ECG abnormalities are very different and they depend in part on QT syndrome type. Abnormal QT interval prolongation on the surface ECG, reflecting delayed ventricular repolarization, is the hallmark of LQTS. T wave abnormalities are also encountered in the majority of patients.

Normal values have been extensively discussed, and usually QTc prolongation is considered in the presence of QTc >440 ms in men and >460 ms in women.

QT prolongation is not always present at rest. In some patients the QT interval can be normal (up to 10% in LQT3 and 37% in LQT1) at rest, while a diagnostic prolongation can be evident only during exercise or epinephrine test [31].

The QT interval is measured as the interval from the onset of the QRS complex (i.e., from the onset of ventricular depolarization) to the end of T wave, at the point where T wave intersects the isoelectric line. It is recommended that the QT be measured in the leads not showing U waves (Fig. 12.10).

The QT interval is measured in all ECG leads where the end of the T wave can be clearly defined (preferably leads II and V5 or V6), with the longest value being used.

In 40% of patients with LQTS diagnosis, QTc intervals fall in the normal range; hence LQTS

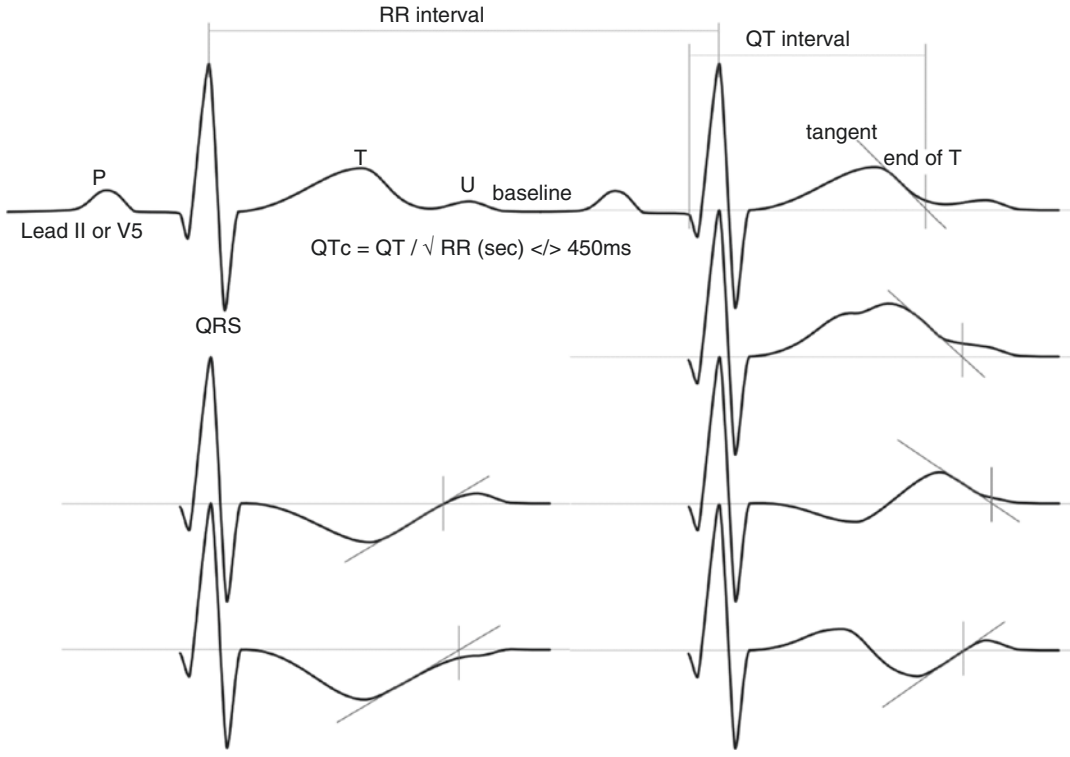

Fig. 12.10 Schematic illustration of the use of the tangent method to define the end of the T wave in normal and abnormal TU morphologies. On courtesy of P. G. Postema, "The measurement of QT interval"

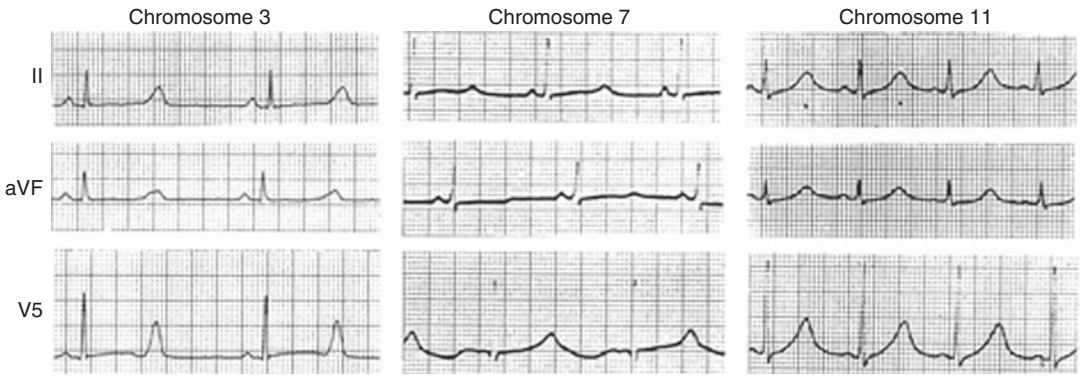

Fig. 12.11 Distinctive ECG patterns of the three main LQTS genotypes (With permission from Prof. Arthur Moss with the consent of the original publisher (Circulation)) [49]

cannot be excluded merely by the presence of a normal QTc interval, since QTc variability is common. In the case of borderline QT prolongation, serial ECG is recommended [46, 47].

Table 12.4 Rate-adjusted QT interval formula

Bazett	$QT_c = \frac{QT}{\sqrt{RR}}$
Fridericia	$QT_c = \frac{QT}{\sqrt[3]{RR}}$
Framingham	$QT_c = QT + 0.154 * (1 - RR)$
Hodges	$QT_c = QT + 1.75 * (HR - 60)$

The diagnosis of QT interval prolongation can be challenging because of the difficulty in defining the "end" of the T wave and the need for correction for heart rate, age, and gender.

Since QT changes with heart rate, QT interval must be corrected for the RR interval. The most used formula for QTc calculation is the Bazett's one (which is less reliable for high and low rates). Other correction formulas, such as the Fridericia, Framingham, and Hodges formula, have been proposed [48] (Table 12.4).

In typical cases of LQT, differential diagnosis is not even considered. When dealing with borderline cases, several conditions should be considered including *vasovagal syncope, orthostatic hypotension, arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVD), CPVT, and hypertrophic cardiomyopathy. Causes of abnormal prolongation of the QT interval include myocardial ischemia, cardiomyopathies, hypokalemia, hypocalcemia, hypomagnesemia, autonomic influences, drugs, and hypothermia* [37].

LQTS ECG Patterns

Each one of the three major genotypes (LQT1 to LQT3) seems to have a distinctive T wave repolarization pattern on the standard 12-lead ECG.

LQT1 commonly presents a smooth, broad-based T wave that is present in most leads, particularly in the precordial. LQT2 generally has low-amplitude T waves, which are notched or bifid in approximately 60% of cases. LQT3 often show late-onset, narrow, peaked, and/or biphasic T waves with a prolonged isoelectric ST segment [34, 37, 43] (Fig. 12.11).

12.3.4 ECG Risk Markers

Arrhythmic risk in LQTS patients is elevated in symptomatic patients, and nonfatal events (syncope and aborted cardiac arrest) remain the strongest predictor of subsequent SCD.

Moreover arrhythmic risk is influenced by genotype and possibly by other modifier genes, age, gender, environmental factors, and therapy. Sex influence shows an interaction with age: young male patients have a higher risk, but after the second decade, girls exhibit and maintain higher risk than male patients throughout adulthood.

ECG findings may help either diagnosis or risk stratification.

The frequency of cardiac events is higher among LQT1 (63%) and LQT2 (46%) patients than patients with LQT3 genotype (18%). However, the likelihood of dying during a cardiac event is significantly higher among LQT3 patients (20%) than among those with the LQT1 (4%) or the LQT2 (4%) genotype [40–42].

12.3.4.1 QT Interval Prolongation

The QTc is the best prognostic ECG parameter in LQTS families. A QTc interval ≥0.470 is a predictor for increased risk for symptoms, whereas ≥0.500 predicts an increased risk of life-threatening cardiac events. The maximal QTc duration measured at any time before age 10 was shown to be the most powerful predictor of cardiac events during adolescence, regardless of baseline, mean, or most recent QTc values [50–52].

12.3.4.2 Dispersion of Repolarization

Besides QT interval prolongation, several studies suggest that heterogeneity of myocardial repolarization can be involved in the genesis of torsades de pointes. Some ECG indices have been proposed for estimating transmural dispersion of repolarization. Several studies have demonstrated tha endo-, mid- and epicardial cells have different electrical properties. In particular, the end of repolarization in subepicardium, which exhibits shorter action potentials, might coincide with the peak of the T wave, whereas the end of repolarization of the midmiocardium, with longer action potentials, coincides with the end of the T wave [38, 53].

The interval from the peak of the T wave to the end of the T wave ($T_{peak} - T_{end}$) in each surface ECG lead has been proposed as an index of transmural repolarization, and it can potentially be a more sensitive predictor of arrhythmogenic risk than the QT interval, which represents the total duration of electrical ventricular activation and not necessarily the dispersion of transmural repolarization [52]. However the role of T-peak to T-end interval is not clearly defined, and no study has established a reference normal value.

A second index proposed to estimate repolarization heterogeneity is the *QT interval dispersion*. The QT dispersion index measures interlead variability of QT and is obtained measuring the difference between the maximal and minimal QT intervals ($QT_{max} - QT_{min}$) in the 12 ECG leads. It is a marker of cardiac electrical instability and reflects the spatial heterogeneity of repolarization more accurately than single QT values. Accurate measurement on the ECG at a paper speed of 25 mm/s is difficult, and a 50 mm/s might be useful [54].

Nevertheless further studies and adequately validated data are needed to establish the value of these QT dispersion indices in practice.

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Drug Effects on ECGs

13

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Maria Vittoria Matassini, and Alessio Menditto

13.1 Case 1

A 54-year-old female without any previous cardiovascular medical history but with many cardiovascular risk factors (diabetes mellitus (DM) type 2, dyslipidaemias, smoking habit) was hospitalized for psychiatric disorders. She was affected by schizoaffective disorders since the age of 30 with frequent hospital readmissions. During a new hospitalization, her ECG was referred to our cardiology consulting service for evaluation. She has been treated with zuclopenthixol 10 drops per os b.i.d. and intramuscular haloperidol 75 mg/die (Fig. 13.1).

13.1.1 ECG Analysis and Diagnosis

The ECG shows a regular rhythm, 99 beats/min. Each QRS complex is preceded by a P wave with a normal axis (P wave axis =45°). The P morphology could hint slight left atrium enlargement (P duration 50 ms, with a small notch in II and negative in V1). Atrioventricular conduction is normal (PR segment 100 ms); QRS is 90 ms with normal axis (+75°) and normal R wave progression throughout the precordial leads. QT segment duration is 380 ms with a QTc of 488 ms.

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We concluded for normal sinus rhythm with slightly prolonged QTc interval.

QT prolongation may be related to congenital or acquired causes [1] (see previous chapter). Congenital causes of prolonged QT are long QT syndromes (LQT1, LQT2 and LQT3) and other genetic variants associated with QT interval duration [2, 3].

Considering the acquired long QT, many variables should be taken into account: age, female gender, left ventricular hypertrophy, heart failure, myocardial ischemia, hypertension, diabetes mellitus, increased thyroid hormone concentrations, elevated serum cholesterol, high body mass index, slow heart rate and electrolyte abnormalities (including hypokalaemia and hypomagnesaemia) [1, 2, 4].

Our patient's familiar story was negative for sudden cardiac death and QT prolongation; therefore a congenital long QT syndrome was unlikely. Blood sample did not show any electrolyte and thyroid disorders.

Given her pharmacological therapy, the most likely cause of QT prolongation is *psychotropic drugs.* The therapy was temporarily discontinued with full QT interval recovery.

13.1.2 From ECG to Clinical Contest

QT interval represents the entire ventricular electrical activity duration (both depolarization,

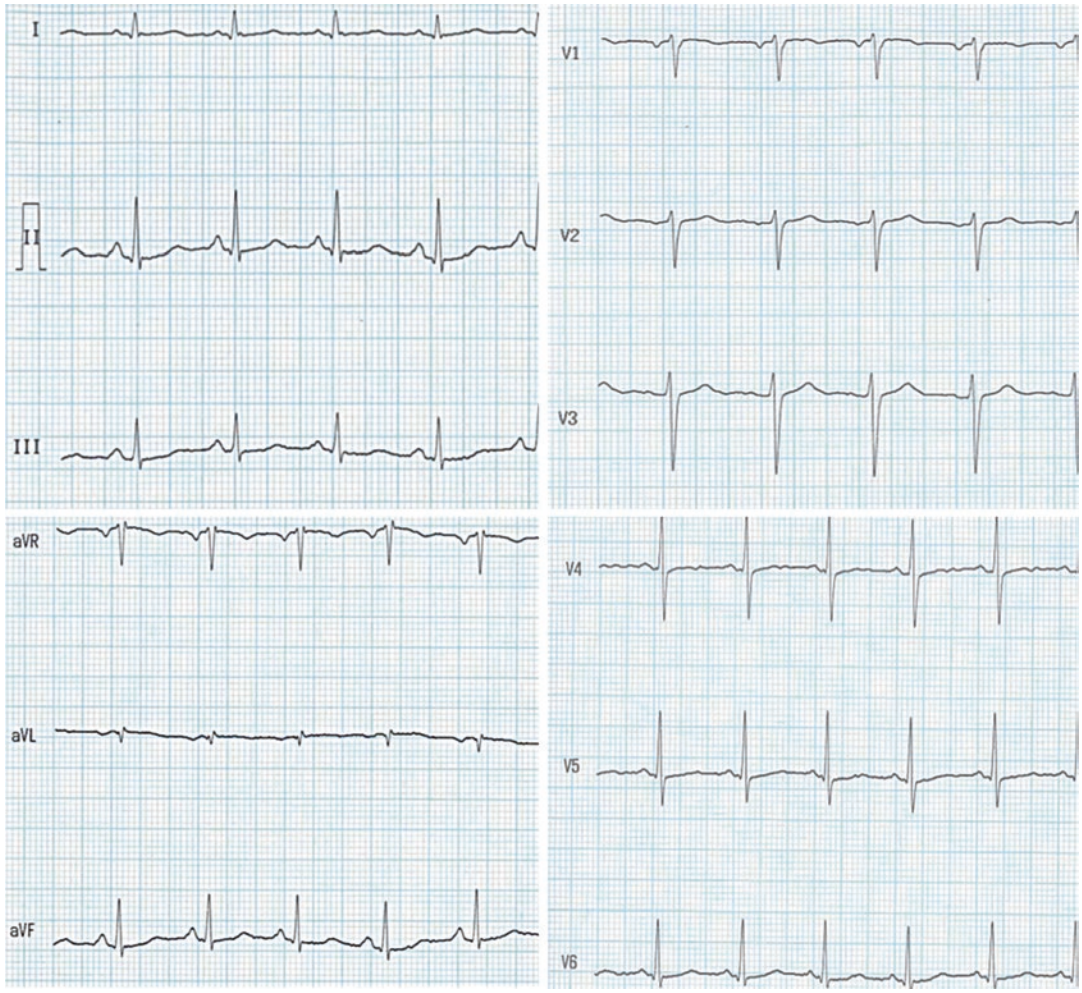

Fig. 13.1 Case 1, 12-lead ECG

represented by QRS interval, and repolarization, represented by JT interval and T wave), but it is used only to evaluate ventricular repolarization due to the difficulties to recognize precisely the beginning of repolarization on surface ECG ("ventricular electrical systole") [4]. It has to be measured from the beginning of the Q wave until the end of the T wave [5] and correct QT based on heart rate. For this reason, many methods have been studied to measure QT interval in relation with the associated heart rate. Although many formula are reported in literature (see previous chapter), none is totally perfect (e.g. they usually may overcorrect for heart frequency <60 beats/min and undercorrect for frequency >100 beats/min [6]), Bazett's type of correction is the most common actually used.

QT interval depends mainly on phase 3 of the action potential. In this phase the action potential moves from the plateau to the resting potential membrane. The balance between inactivating calcium current and rising potassium current I_{Ks}, I_{Kr} and I_{K1} (so-called I_{Kr} "inward rectifier") is the main responsible for that modification [7]. Phase 3 potassium conductance (direct mainly from

inside to outside cell membrane) influences total duration of the action potential.

Haloperidol is a typical butyrophenone antipsychotic drug; zuclopenthixol belongs to thioxanthene antipsychotic class. Both are widely used in many psychiatric conditions. Their mechanism of action involves many different receptors, and the effect on cardiac cells is only partially known. Haloperidol, available from 1958 [8], in particular, has been associated with QT prolongation, torsade des pointes (TdP) and sudden cardiac death [9]. Molecular basis studies of these effects have pointed out that haloperidol blocks I_{Kr} current (concentration dependent effect), prolonging phase 3 and total duration of action potential (even at standard dose and with every somministration modality). The same mechanism has been proposed for other antipsychotic drugs such as zuclopenthixol and pimozide [10]. In general drugs may be divided into four groups based on the association with QT prolongation and TdP [11]:

1. Drugs at known risk of TdP
2. Drugs at possible risk of TdP
3. Drugs at conditional risk of TdP
4. Drug to avoid in congenital long QT

Haloperidol is a drug considered at known risk of TdP. Zuclopenthixol is not classified in any of those risk categories. Antipsychotic drug association is discouraged in clinical practice; if done in that case, the QTc interval must be monitored because of well-known risk of TdP. When the QTc arrives to >500 ms, it is mandatory to stop the antipsychotic therapy. Lead II is the most suggested for QT interval measurement, and we must pay attention to exclude a U wave in the QT measurement.

13.2 Case 2

A 60-year-old male with a history of hypertension and previous episodes of paroxysmal atrial fibrillation was admitted to ER because of palpitations and dizziness, with a suspicion of an atrial fibrillation recurrence. He was in chronic therapy with propafenone 425 mg bid and valsartan/hydrochlorothiazide 160/25 mg (Fig. 13.2).

13.2.1 ECG Analysis and Diagnosis

The ECG shows broad complex tachycardia (180/min) with QRS duration of 180 ms with a left bundle branch morphology. Ventricular axis is +10° with extreme clockwise rotation on the horizontal plane and there is absence of concordance in the precordial leads. In peripheral leads especially in inferior leads (II, III and VF), it is noticeable how the main QRS width is related to its second part; the first part (intrinsicoid deflection) has a short duration (less 40 ms). This pattern of conduction delay is generally a typical aberrancy. Atrial activations were not evident.

To facilitate a correct diagnosis, a carotid sinus stimulation was performed (Fig. 13.3).

By carotid massage an AV block came out with clear appearance of atrial flutter F waves that enlightened the correct diagnosis.

This is therefore an atrial flutter with 1:1 atrioventricular conduction in a patient on propafenone therapy.

13.2.2 From ECG to Clinical Contest

Propafenone is an orally active sodium channel blocking agent, β-adrenoceptor antagonist with a weak calcium antagonist activity. Like other IC antiarrhythmic drugs, it prolongs depolarization by reducing sodium influx and, hence, delays the conduction velocity. At high heart rates, class IC drugs cannot dissociate completely from the sodium channel resulting in progressive conduction delay, with the so-called "frequency or use-depend" effect. This may result in a very broad QRS complex, mimicking a ventricular tachycardia [12].

The extreme aberrant conduction reverts by slowing ventricular rate with carotid sinus

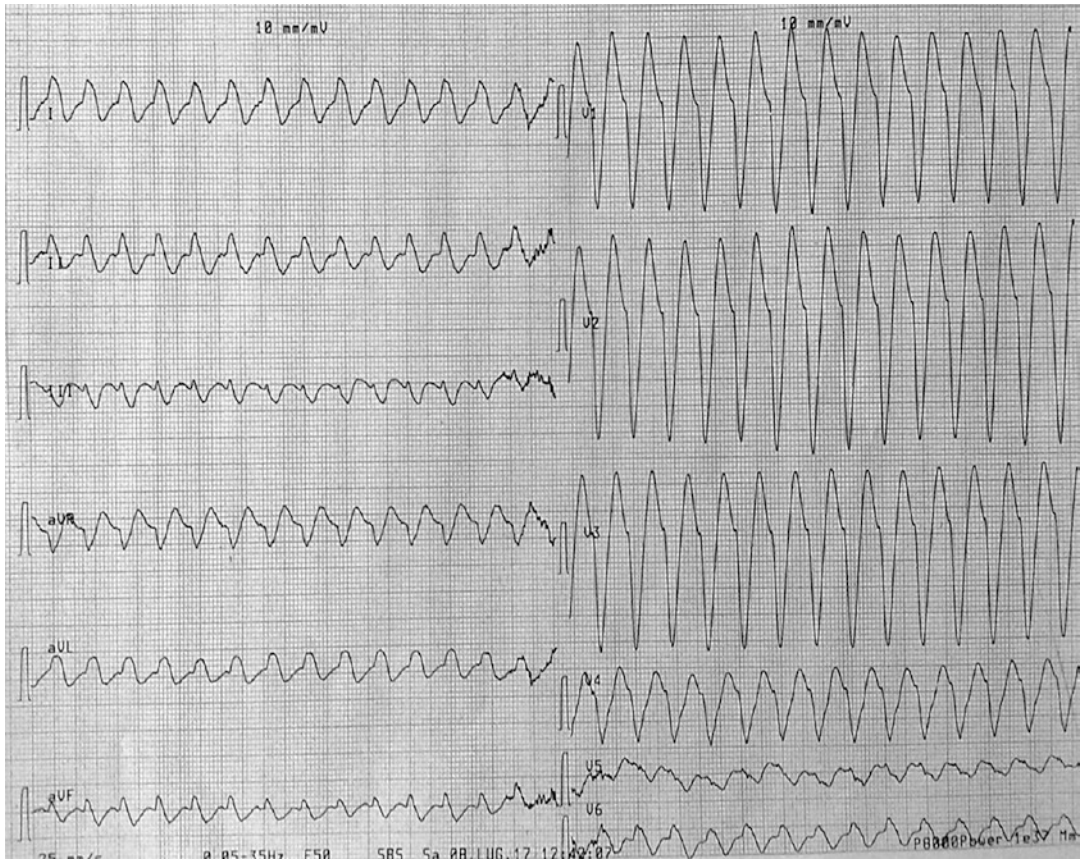

Fig. 13.2 Case 2, 12-lead ECG

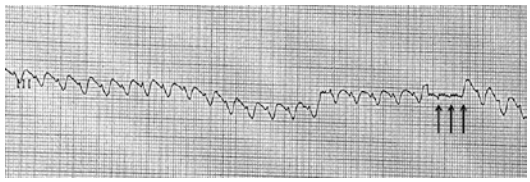

Fig. 13.3 Sinus carotid massage effect: flutter waves (arrows)

pressure or using a negative chronotropic drug. Antiarrhythmic drugs belonging to class IC have therefore a possible proarrhythmic potential, causing either ventricular tachycardia or atrial flutter with 1:1 atrioventricular conduction [13].

The proarrhythmic effect is present in 0.5–3% of cases and is related to a concomitant high adrenergic tone (exercise) or high catecholamine level [14]; therefore the concomitant use of β-blocker agents or Ca^{2+}-antagonists may probably reduce this negative drug effect.

IC drugs affect atrial velocity of conduction and refractory period duration and cause rate-dependent prolongation of the atrial refractory period balancing the drug-induced conduction slowing. The explanation regarding the transformation of atrial fibrillation into atrial flutter resides into the electrophysiologic effects of these drugs: class IC antiarrhythmics prevent the formation of smaller secondary circuits, decrease the number of existing circuits and increase the size of the existing circuits leading to a macro-reentrant loop [15, 16].

Atrioventricular node may allow a 1:1 conduction because of concomitant lower atrial rate together with a slow atrial conduction velocity caused by cycle length prolongation.

The ventricular response during atrial flutter is determined by the refractory period of the AV node, and a pre-existing rapid AV nodal conduction can also be a predisposing factor. The acceleration of the ventricular rate leads to widening QRS complex during tachycardia, representing a diagnostic challenge in differentiating from ventricular tachycardia [17, 18].

It is not possible to predict who will develop class IC atrial flutter; therefore, to avoid atrioventricular 1:1 conduction, the development of high ventricular rate and the secondary negative hemodynamic impact, it may be useful at least in chronic therapy to associate drugs that slow nodal conduction such as beta-blockers and calcium antagonist. Only a possible summing of the negative inotropic effects has to be considered.

A coronary angiography did not show any stenotic lesion. That exam was done because at echocardiogram there was a moderate reduction of cardiac systolic function (EF 40%) with segmental medioseptal and apical akinesia.

The observed segmental kinetic disorder and even the low ejection fraction value could be a posteriori consistent with the negative inotropic IC drug effect.

These antiarrhythmic agents are contraindicated in patients with congestive heart failure, coronary artery disease and reduced ejection fraction as they reduce stroke volume index and left ventricle function [19, 20].

The IC negative hemodynamic effect is exerted by Na^+ and subsequently Ca^{2+} entry reduction into the myocardial cells [21]. There are also blocks of the intracellular interaction between Ca^{2+} and the ryanodine receptor preventing diastolic Ca^{2+} waves [22].

It has also been demonstrated a slight reduction of cardiac output and stroke volume during the first 90 min after propafenone infusion given to restore sinus rhythm, even in healthy subjects.

Final reported diagnosis is:

Atrial flutter with 1:1 conduction and aberrant QRS secondary to propafenone effect in a patient with paroxysmal high ventricular rate AF episodes.

13.3 Case 3

A 63-year-old man was admitted to ER for acute dyspnoea. His history was characterized by ischemic heart disease with previous heart failure episodes, systemic arterial hypertension, paroxysmal atrial fibrillation and peripheral artery disease. Home medications were aspirin 100 mg, digoxin 0.125 mg, furosemide 25 mg, ramipril 5 mg bid, and bisoprolol 2.5 mg.

An ECG was recorded (Fig. 13.4).

13.3.1 ECG Analysis and Diagnosis

The ECG shows a narrow QRS tachycardia. R-R intervals are irregular, and heart rate is 135 bpm on average. There are no P waves; it is therefore an atrial fibrillation. QRS complexes have normal duration (80 ms) and frontal plane axis (+45°). There are no pathological Q waves. ST-segment depression is visible in lateral leads (V4–V6) and flat T waves in peripheral leads. QT interval is normal (QTc 420 ms).

We conclude for a diagnosis of high ventricular rate atrial fibrillation. Valuable hypotheses for these repolarization pattern abnormalities are:

- Hypertrophy with strain
- Acute pericarditis
- Ischemia
- Drug-related changes of repolarization

The first hypothesis can be excluded because in this ECG, there are no signs of left ventricular hypertrophy (we are however at the upper normal range, near the Sokolow cut-off). Modified Sokolow-Lyon criteria and other hypertrophy ECG signs like RaVL >1.1 mV and left axis deviation of QRS are not satisfied.

Also acute pericarditis could be excluded. Typical acute pericarditis ECG modifications include diffuse coved ST-segment elevation. Sometimes ST-segment depression and T wave inversion are present in acute pericarditis, but these patterns are diffuse (not limited to lateral leads), and also they are not coved ST-segment depressions.

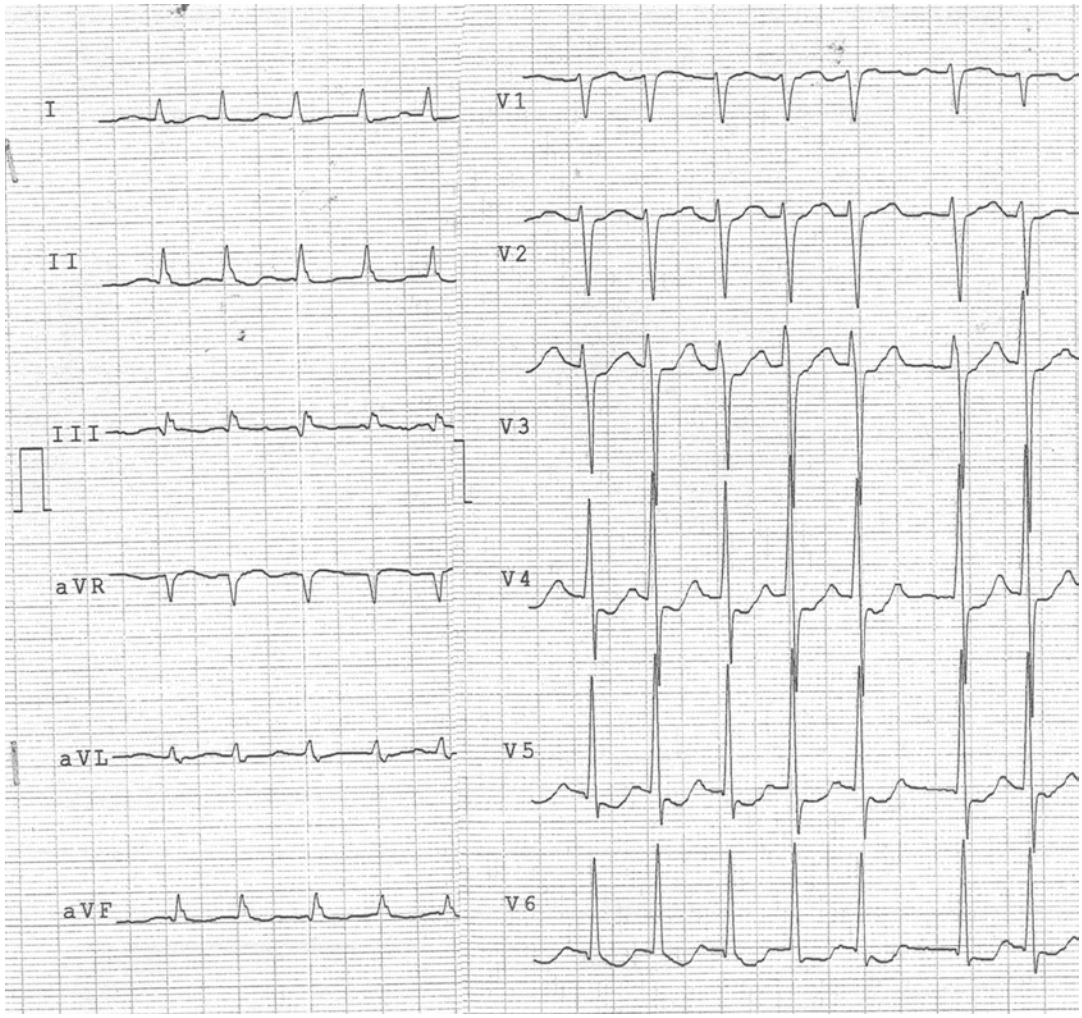

Fig. 13.4 Case 3, 12-lead ECG

Ischemic alteration of repolarization, in particular acute coronary syndrome without ST elevation (NSTE-ACS), is a valuable hypothesis. However in ischemia, the ST-segment depression pattern is generally different: the most typical morphology is a descendent ST-segment depression with a negative T wave associated or a rigid descending ST.

In this ECG, ST-segment depression in lateral leads has a coved shape, and this aspect associated with flat T waves in other leads is a typical ECG sign in patients treated with digoxin (also known as "digitalis effect"). These features are visible even at therapeutic dose. Digoxin may be followed by QT shortening that in this case is not evident.

A blood sample showed digoxin of 1.2 ng/ml (normal therapeutic range 0.5–2.0 ng/ml) and negative troponin I in several blood samples. This confirmed digoxin as the main cause of ST-segment depression and therefore of the repolarization abnormalities.

13.3.2 From ECG to Clinical Contest

Digoxin and other cardiac glycosides are sodium-potassium ATPase pump inhibitor in outer cell membrane that result in intracellular sodium increase and activation of Na^{+}/Ca^{++} exchanger. This increase of intracellular Ca^{++} causes a higher

contractility. Electrophysiological actions are mediated by the increase in vagal tone that slows sinus rate, shortens atrial refractoriness and slows also AV conduction. At therapeutic dose the effect of the digitalis on the His-Purkinje system and on ventricles is minimal. Typical ECG features with digoxin at therapeutic range are prolonged PR interval due to AH interval prolongation, ST-segment depression with typical coved morphology, flat or diphasic (negative/positive) T waves (*spoon like*), shortening of QT interval and increasing U wave amplitude [4, 23].

In case of digitalis toxicity, the manifestations are premature unifocal or multifocal ventricular beats, with bigeminal or trigeminal rhythms. Other arrhythmias during digitalis toxicity are atrial tachycardia with AV block, accelerated junctional rhythm, low heart rate atrial fibrillation and bidirectional tachycardia (junctional or ventricular) [23].

Digitalis interaction with AAD such as amiodarone and dronedarone may favour torsade des pointes and sudden cardiac death [24].

13.4 Drug Effect on ECG: An Overview

Many drugs and toxins may affect electrophysiology and therefore influence electrocardiographic changes. The main mechanisms are related to drug action on membrane channels (sodium channel, slow calcium channel, outward potassium channel and sodium-potassium adenosine triphosphatase pump) or on autonomic nervous system. Moreover, factors such as hypoxia, hypotension, acid-base and electrolyte imbalance may favour or contribute to drug effects on ECG [4, 5, 23, 24].

In the following paragraphs and in Table 13.1, we classify drugs acting on ECG according to the main mechanism involved, and we resume the main alterations induced.

1. *Fast sodium channel blockers:* they act mainly on phase 0 of the action potential through the inhibition of fast sodium channels and, therefore, slowing the upslope of depolarization. Sodium channel blockers could cause QRS widening until the extreme grade; they can favour an unidirectional block with consequent reentrant circuits (especially during acute ischemia) that may lead to final VT or VF. In poisoning conditions a bradycardia with very wide QRS complex may develop.
2. *Slow calcium channel blockers:* they play their effect on voltage-sensitive L-type calcium channels that are involved in phase 2 of the action potential through the influx of positive ions and in maintenance of membrane potential. These channels are primarily responsible of depolarization of sinoatrial node and atrioventricular node cells, and their block causes a slowing or inhibition of impulse conduction, exiting in sinus bradycardia, various degrees of AV blocks, sinus arrest, junctional bradycardia and asystole. Ischemic ECG alterations may also appear because of hypotension.
3. *Outward potassium channel blockers:* they act on phase 3 where the potassium efflux from cells lets the action potential to return to the resting potential. The outward potassium flow is responsible of QT interval; therefore the main effect of these channel blockers is QT prolongation. The repolarization is slowed, and early after-depolarizations are favoured, promoting triggered activity that may lead to torsades de pointes (TDP) or other polymorphic VT.
4. *Sodium-potassium ATPase blockers*: cardiac glycosides belong to this category, acting on the sodium/potassium ATPase pump. Pump inhibition implies intracellular calcium concentration increase with positive inotropic effect and increased automaticity. These drugs also increase vagal tone with secondary AV nodal conduction inhibition, a therapeutic effect mainly pursued in clinical practice. We already reported digitalis effect on ECG (case 3, from EG to pathology) and related arrhythmias.
5. *Drugs acting on autonomic nervous system*: they include a broad spectrum of drugs that may be resumed in sympathetic inhibitors and sympathomimetic drugs and anticholinergic and cholinomimetic drugs.

Table 13.1 Drug effecting on ECG: a schematic classification

Mechanism	Drugs		ECG changes
Inhibitors of fast Na^+ channels	Type IA antiarrhythmics	Disopyramide, quinidine, procainamide	QRS widening, right bundle branch pattern, R wave elevation in aVR lead, rightward deviation of QRS axis Ventricular tachycardia (VT) and ventricular fibrillation (VF) Bradycardia with wide QRS complex Asystole
	Type IC antiarrhythmics	Flecainide, propafenone	
	Psychiatric drugs	Cyclic antidepressants (amitriptyline, imipramine, nortriptyline, maprotiline) neuroleptics (thioridazine, mesoridazine), other antidepressants like carbamazepine	
Inhibitors of slow Ca^{2+} channels	Dihydropyridine Ca-channel blockers	Nifedipine, amlodipine, lercanidipine	Sinus bradycardia Reflex tachycardia (e.g., nifedipine) Varying degrees of AV block Sinus arrest with AV junctional rhythm Asystole Wide QRS complex ST/T changes
	Non-dihydropyridine Ca-channel blockers	Verapamil, diltiazem	
Inhibitors of outward K^+ channel	Type IA antiarrhythmics	Disopyramide, quinidine, procainamide	QT interval prolongation T or U wave abnormalities, premature ventricular beats (PVB) followed by TdP sinus tachycardia
	Type IC antiarrhythmics	Flecainide, propafenone	
	Type III antiarrhythmics	Amiodarone, dronedarone, sotalol	
	Psychiatric drugs	Antipsychotics (chlorpromazine, haloperidol, quetiapine, risperidone, ziprasidone), cyclic antidepressants (amitriptyline, imipramine, nortriptyline, maprotiline), other antidepressants (citalopram, venlafaxine), phenothiazines	
	Antimicrobials and antimalarics	Ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin, sparfloxacin, clarithromycin, erythromycin, pentamidine, chloroquine	
Inhibitors of Na^+/K^+ ATPase	Digoxin, digitoxin		Excitant activity: premature beats, atrial tachyarrhythmia suppressant activity: sinus bradycardia, sinoatrial block, AV block Combination of these: atrial tachycardia with AV block
Sympathetic-inhibiting agents	Beta-blockers	Propranolol, atenolol, metoprolol, nebivolol, bisoprolol, esmolol, carvedilol	Sinus or nodal bradycardia, AV blocks (first-degree AV block is common). Prolonged PR and QTc intervals, asystole (rare)
	Other than beta-blockers	Methyldopa, prazosin, clonidine	
Sympathomimetic agents	Drugs	Amines and inotropic agents, theophylline, beta-agonist bronchodilator (albuterol)	Sinus tachycardia atrial tachycardia, AF ventricular premature beats VT, VF myocardial ischaemia or infarction
	Illicit drugs	Cocaine, amphetamine, LSD	
	Toxins	Ethanol, hydrocarbon solvents	

Table 13.1 (continued)

Mechanism	Drugs		ECG changes
Anticholinergic agents	Drugs	Antihistamines, atropine, scopolamine, tricyclic antidepressants, antipsychotics (clozapine, olanzapine, phenothiazines)	Sinus and atrial tachycardia premature ventricular beats
	Toxins	*Atropa belladonna*, *Amanita muscaria*	
Cholinomimetic agents	Drugs	Direct muscarinic agonists (methacholine), succinylcholine indirect neuronal nicotinic agonists (chlorpromazine, local and volatile anaesthetics, ketamine), anticholinesterases (physostigmine, pyridostigmine, neostigmine), central cholinesterase inhibitors (rivastigmine)	Sinus bradycardia, AV block, sinus tachycardia (seen in early stages of cholinesterase inhibition and nicotine poisoning due to ganglionic stimulation), VT associated with QT interval prolongation asystole
	Toxins	Nicotine, muscarine, organophosphate and carbamate pesticides	

The most known sympathetic inhibitors are beta-blockers, acting on beta-adrenergic receptors and commonly leading to sinus bradycardia. In case of toxicity, various forms of bradycardia with increasing severity may develop (AV blocks, junctional rhythms, asystole). Some beta-blockers as sotalol also prolong QT interval through action on potassium flow and may predispose to bradycardia-dependent TDP.

Sympathomimetic agents embrace drugs, often illicit, and cause sinus tachycardia, atrial tachycardia and less frequently ventricular arrhythmias with malignant rhythms, triggered also by other mechanisms as the ischemia in the case of cocaine abuse.

Anticholinergic drugs usually cause sinus and atrial tachycardia; in case of toxicity ventricular premature beats may develop. Cholinomimetic agents, instead, induce ECG effects that change over time: the first sign may be sinus tachycardia because of the nicotinic receptor stimulation. Then, sinus bradycardia could follow for the action on muscarinic receptor. In advanced phase AV blocks, atrial and ventricular bradyarrhythmias and asystole may develop. Also QT prolongation and secondary TDP are described (Table 13.1).

To conclude, cardiologists and generally physicians could run into many alterations of ECG due either to cardiovascular or non-cardiovascular drugs and toxins, both at therapeutic range and in case of poisoning. These ECG changes are related to two main mechanisms, membrane channels and autonomic nervous system interactions, on whom temporary factors (hypoxia, hypotension, ischemia, electrolytes or acid-base imbalance) or a pre-existing cardiac disease or comorbidities could negatively overlap.

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14 Electrolytic Influences on the Depolarization/ Repolarization Patterns

Claudio Cupido, Giulia Enea, Agnese Fioranelli, and Jenny Ricciotti

14.1 Case 1

A 72-year-old woman was admitted to ER for loss of consciousness.

She had a history of ischemic heart disease (ACS-NSTEMI) in the previous 5 years treated with PTCA and stent on the right coronary artery. Risk factors are hypertension, dyslipidemia, and type 2 diabetes mellitus.

Blood pressure was 75/45 mmHg.

Laboratory tests showed leukocytosis with neutrophilia (WBC 10.760/mmc), creatinine of 1.44 mg/dL, and potassium of 6.9 mEq/L.

There was oligo-anuria with signs of acute renal failure; creatinine was 1.9 mg/dL.

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14.1.1 ECG Analysis

The ECG showed a junctional rhythm with a heart rate of 36 b/min, left axis deviation, symmetrically high *peaked T waves*, and *QTc 411* ms. It was a typical ECG of hyperkalemia (Fig. 14.1).

The patient had an *intravenous calcium gluconate*, *insulin*, *glucose*, *normal saline*, *and oral kayexalate therapy*, with a progressive potassium blood concentration reduction and consequent ECG normalization (normal sinus rhythm, heart rate of 55 b/min, normal repolarization) (Fig. 14.2).

A urinary tract infection was treated with antibiotic therapy, with progressive improvement of the renal failure framework as well. Blood pressure was 105/60 mmHg.

The final diagnosis was junctional rhythm secondary to hyperkalemia, during acute renal failure secondary to urinary tract infection.

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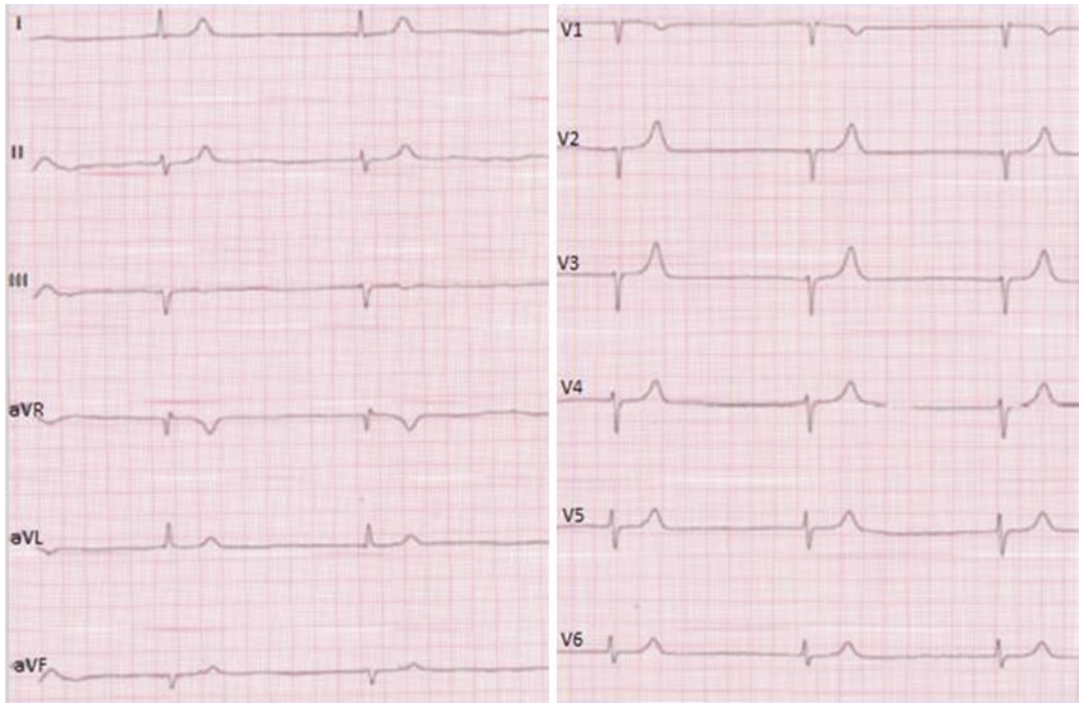

Fig. 14.1

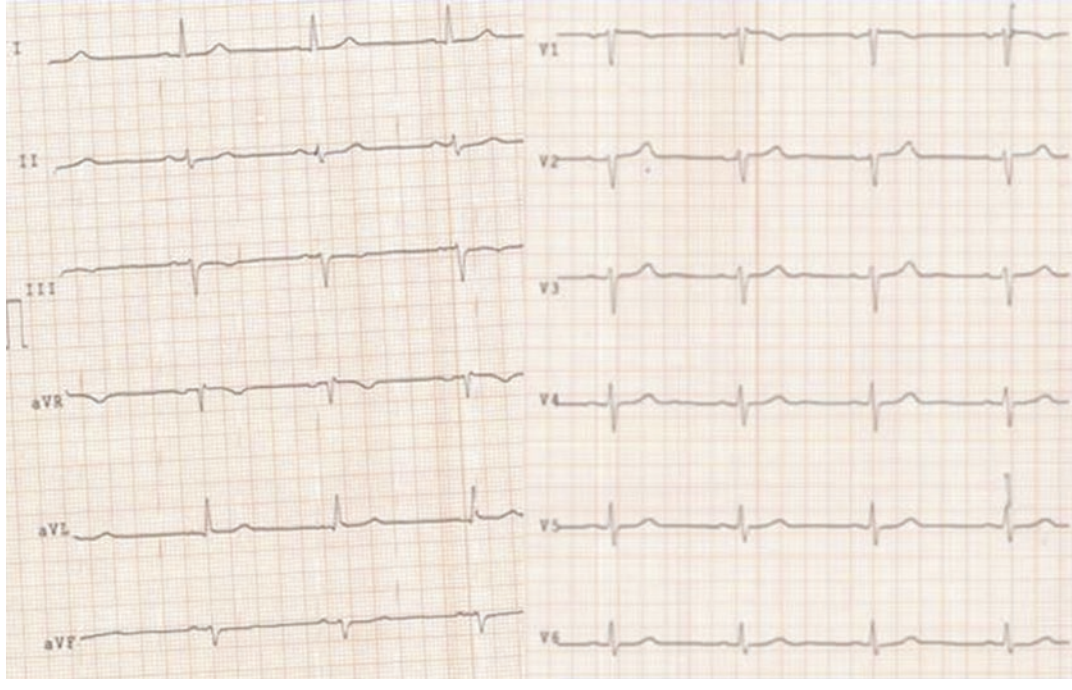

Fig. 14.2

14.2 Case 2

An 89-year-old woman, with previous episodes of heart failure, had diabetes mellitus, dyslipidemia, chronic renal failure, and COPD. The daughter called the 118 ambulance because of mother's syncope; ECG was recorded by nurses at their arrival.

14.2.1 ECG Analysis

Wide QRS complex tachycardia, HR 150 bpm, AV dissociation, QRS axis shift, and left bundle branch block morphology. ECG diagnosis of polymorphic ventricular tachycardia (torsades de pointes) (Figs. 14.3 and 14.4).

Lidocaine (70 mg) IV was injected and the tachycardia became monomorphic before ending up (Fig. 14.5).

IV therapy was effective in terminating VT; but an atrial fibrillation ensued (HR 85) with numerous polymorphic PVCs. The QRS axis is now −30°, left anterior fascicular hemiblock, QRS length 100 ms, and secondary repolarization abnormalities with QTc 476 ms (Figs. 14.6 and 14.7).

Main blood samples: Hb 11.2, creatinine 6 mL/dL (GFV 6 mL/min), INR 9, blood glucose 282, Na^+ 128 mEq/L, K^+ 3 mEq/L, P 6.9 mEq/L, Cl^- 84 mEq/L, and Ca^{++} 7.7 mEq/L.

The patient was hospitalized for intensive treatment, with a diagnosis of COPD with respiratory/metabolic acidosis, acute renal failure, and ventricular tachycardia secondary to electrolyte imbalance.

A few days later (Fig. 14.8), there were sinus rhythm, HR 60 bpm, PR 200 ms, and QRS axis −30°, with left anterior fascicular hemiblock morphology, QRS length 100 ms, and QTc 380 ms.

There are important interactions between K+ and acid-base balance. In metabolic acidosis, more than one-half of the excess hydrogen ions are buffered in the cells. Electroneutrality is maintained in part by the movement of intracellular potassium into the extracellular fluid. The net effect in some cases is overt hyperkalemia; in other patients who are potassium depleted, the plasma potassium concentration is normal or even reduced. The ECG changes are influenced by the K^+ level.

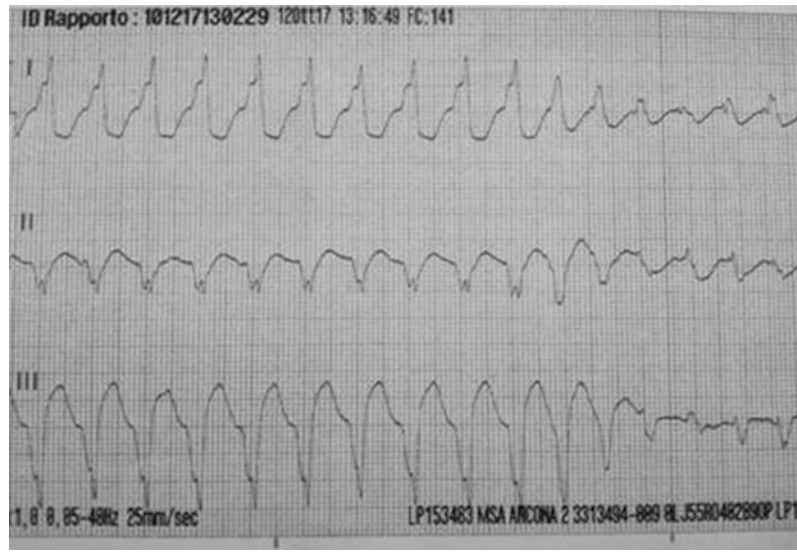

Fig. 14.3

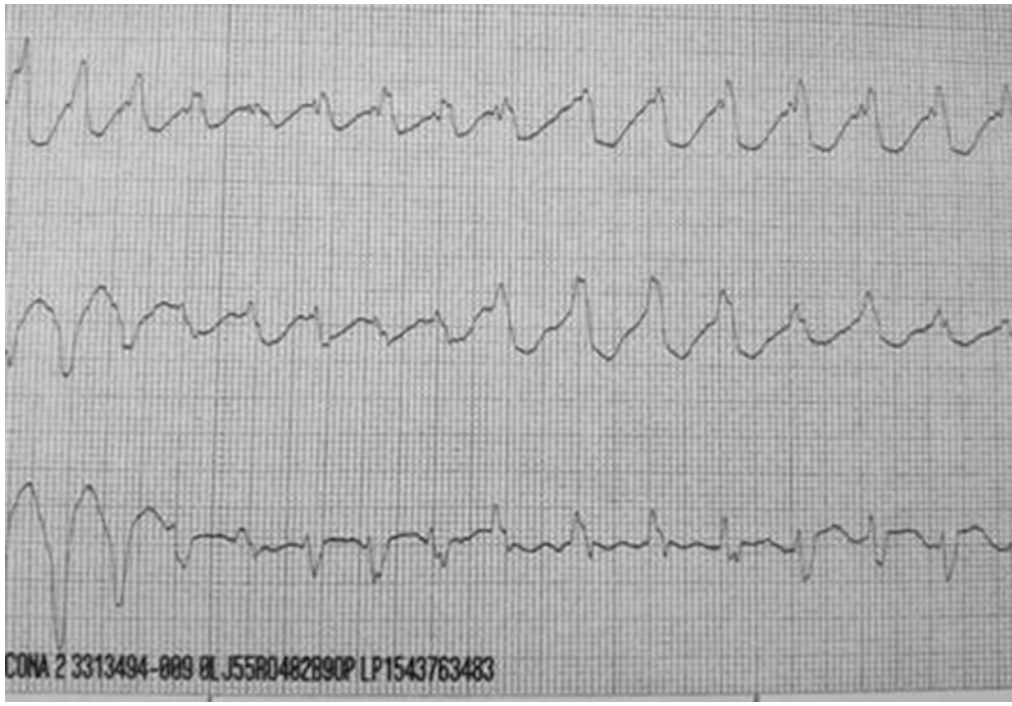

Fig. 14.4

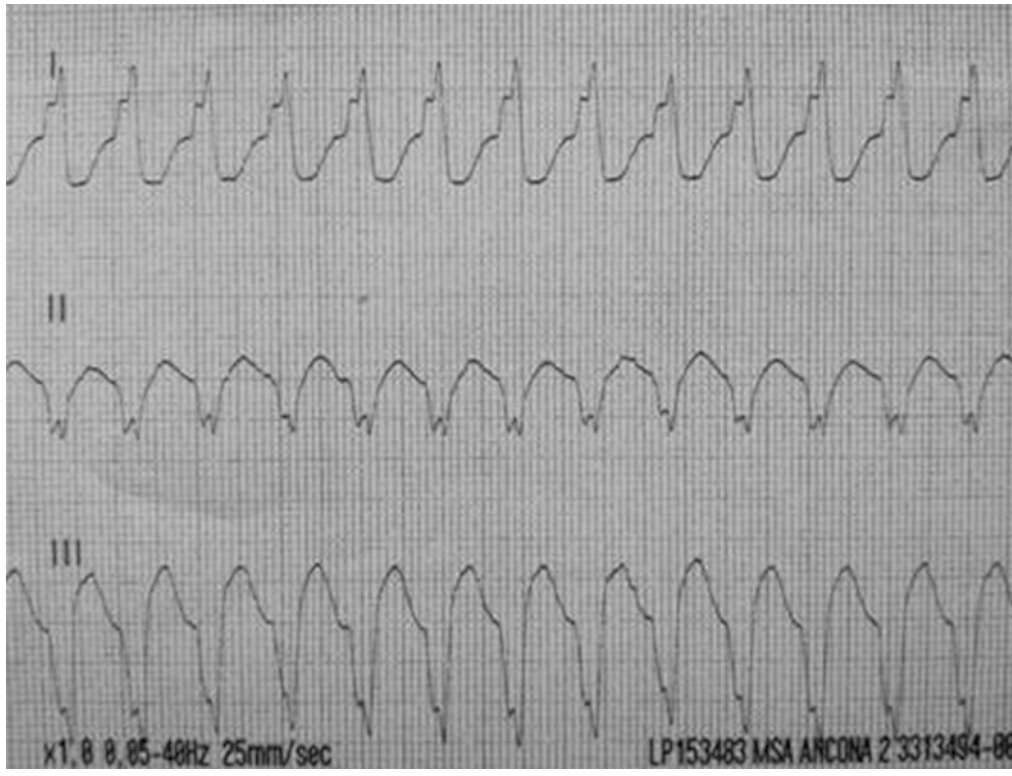

Fig. 14.5

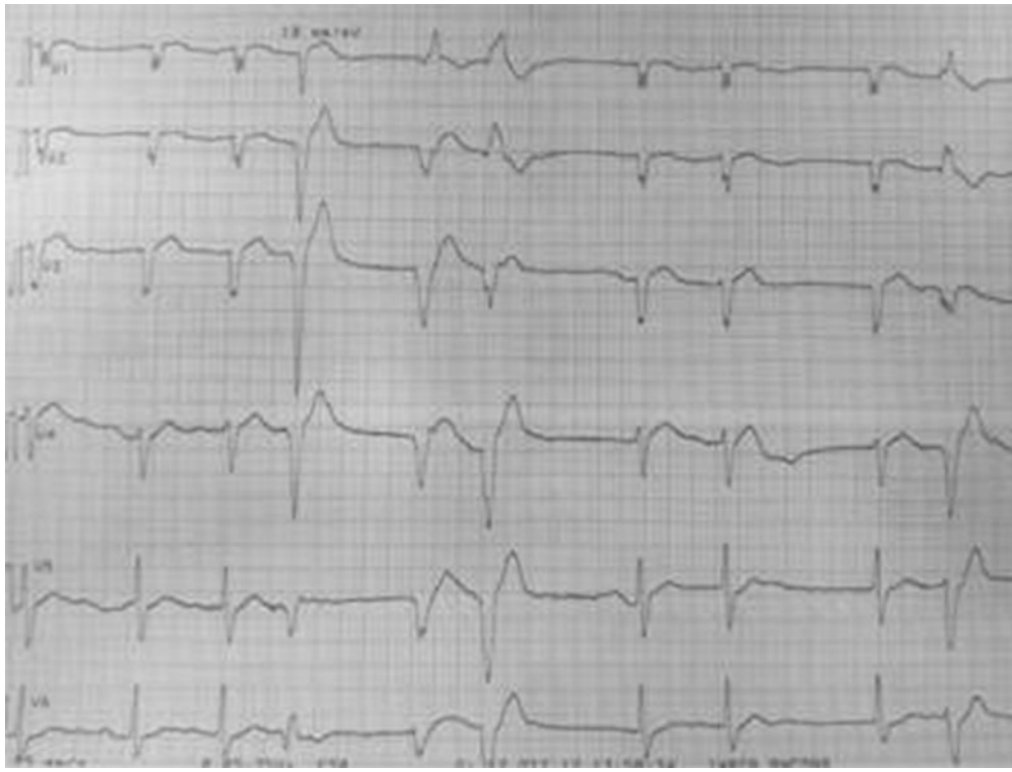

Fig. 14.6

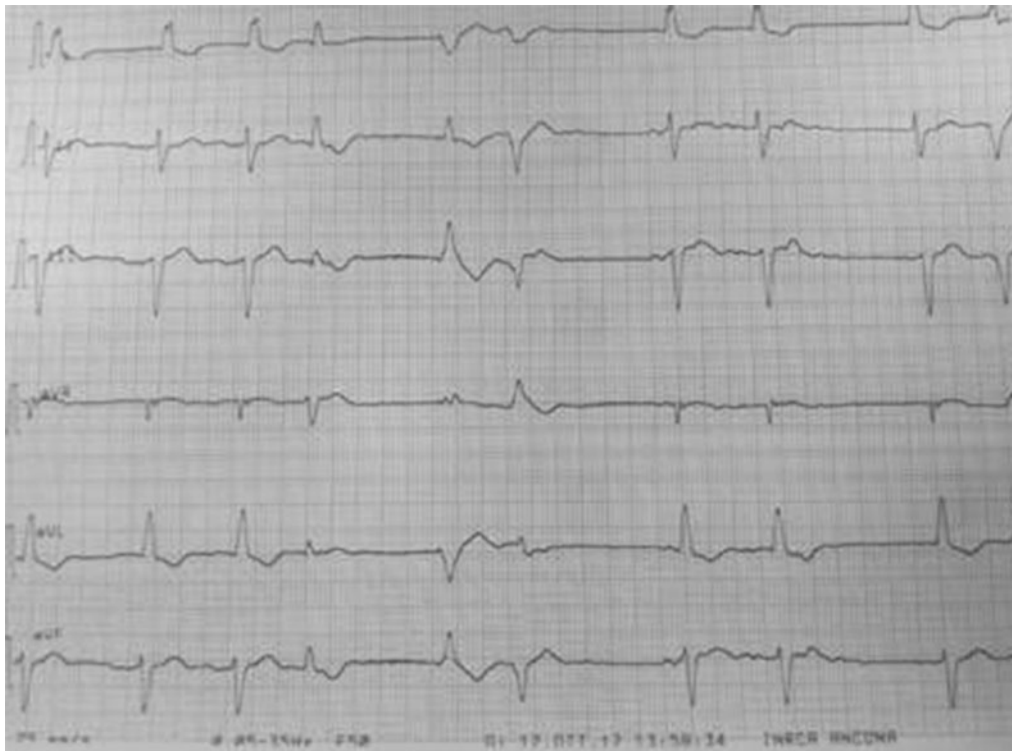

Fig. 14.7

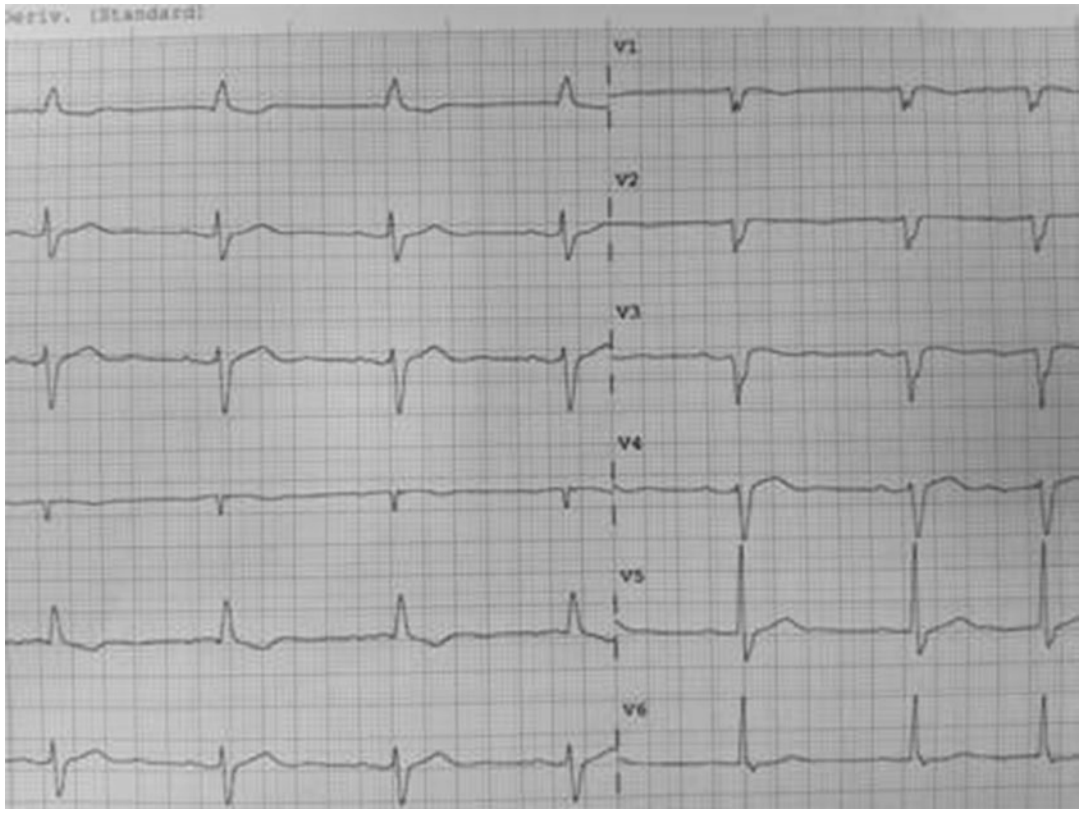

Fig. 14.8 ECG

14.3 Case 3

A 75-year-old woman, with a systemic arterial hypertension, had a previous colon cancer operation and lately worsening of renal function with creatinine values of 1.6 mg/dL.

Home therapy: ASA, candesartan, doxazosin, trazodone, and potassium canrenoate.

In the previous 2 weeks, the patient was admitted to a hospital four times (the first time for an accidental fall, the other three times because she was sleepy and felt tired).

A palpable nodular mass was found on the right flank.

14.3.1 ECG Analysis

Sinus tachycardia; HR 110 bpm; normal AV conduction (PR 160 ms); normal IV conduction; QRS axis +30°; QRS length 80 ms; ST depression of 1 mm in the leads II and III, AVF, V4, V5, and V6 of a horizontal-ascending type; and QTc 378 ms (Fig. 14.9).

Main blood exams:

- Hemoglobin values decreased from 14 g/dL to 8.1 g/dL in the last 4 months
- Hypercalcemia up to 15.4 mg/dL
- Hypokalemia down to 2.4 mEq/L

The patient had a rapid cognitive deterioration associated with hypercalcemia. Because of the presence of an abdominal mass, she needed a short-term diagnostic investigation.

At protein electrophoresis there was a monoclonal peak in gamma area.

A multiple myeloma was diagnosed.

Multiple myeloma is a malignant proliferation of plasma cells resulting in a monoclonal immunoglobulin production. The plasma cells proliferate in the bone marrow, resulting in skeletal

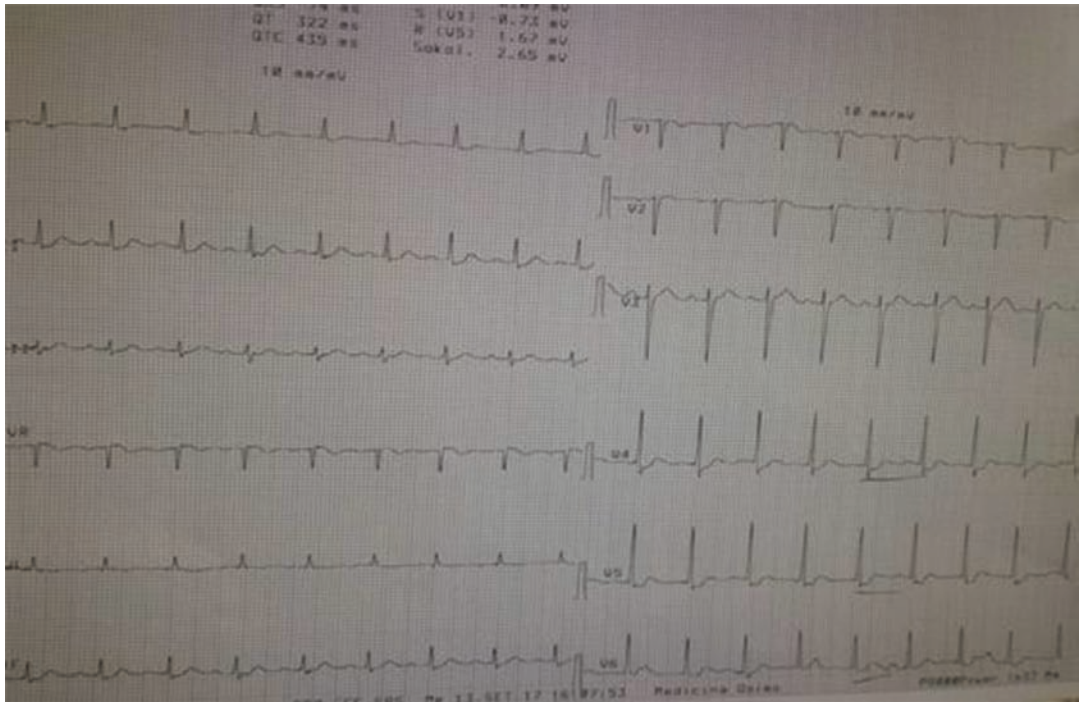

Fig. 14.9

destruction. Anemia is the most common finding in these patients; and then there are reversible ECG ST-segment depression and tachycardia because of an imbalance between oxygen myocardial supply and demand.

The pathophysiology of renal failure in multiple myeloma is often multifactorial but is mostly due to the high excretion of immunoglobulin-free light chains. Hypercalcemia is due to numerous destructive bone lesions; in this case reported hypercalcemia was associated with hypokalemia, and then the ECG shows low-voltage T waves followed by apparent U waves. The QTc in these cases may be short or normal.

14.4 Case 4

An 83-year-old man presented with systemic arterial hypertension and chronic renal failure and in dialysis three times/week.

Soon after arriving at the nephrology department, he experienced a syncopal episode with subsequent consciousness restoration. An ECG was recorded.

14.4.1 ECG Analysis

Sinus rhythm, HR 75 bpm, advanced second-degree AV block (most P are not conducted to the ventricle), QRS of 160 msec with a complete right bundle branch block morphology, QRS axis +75°, tall and peaked T waves in V2-V3-V4, and QTc 537 ms (Figs. 14.10, 14.11, 14.12, and 14.13).

This ECG pattern is compatible with hyperkalemia.

14.5 Case 5

An 86-year-old woman was suffering from systemic arterial hypertension, diabetes mellitus, and chronic renal failure in dialysis. She went to a hospital for an abnormal and persistent asthenia.

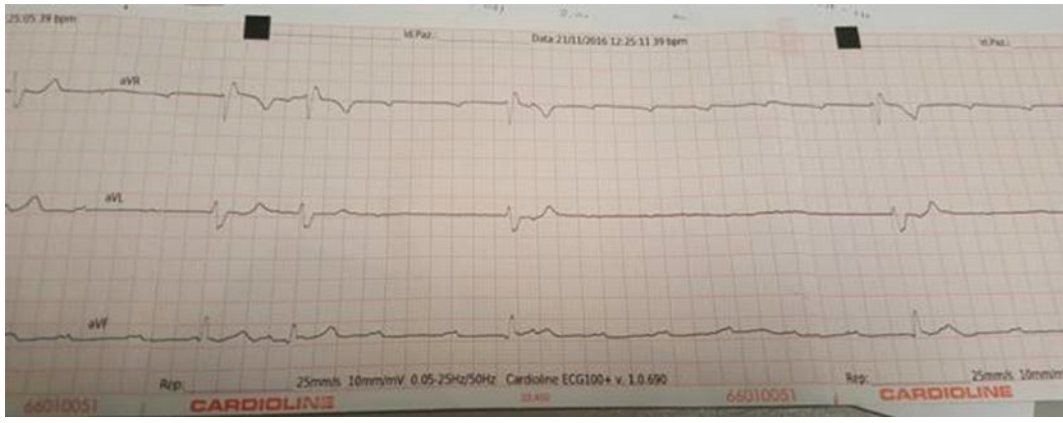

Fig. 14.10

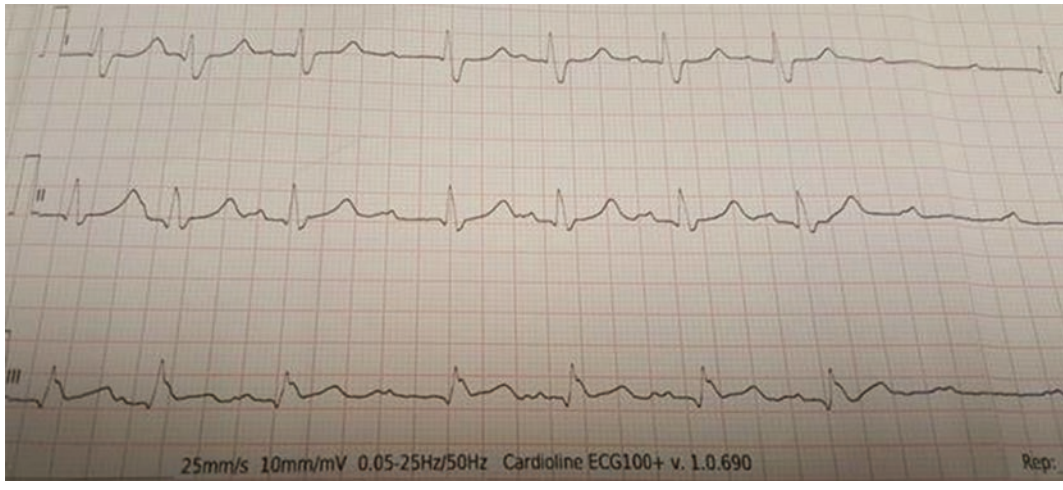

Fig. 14.11

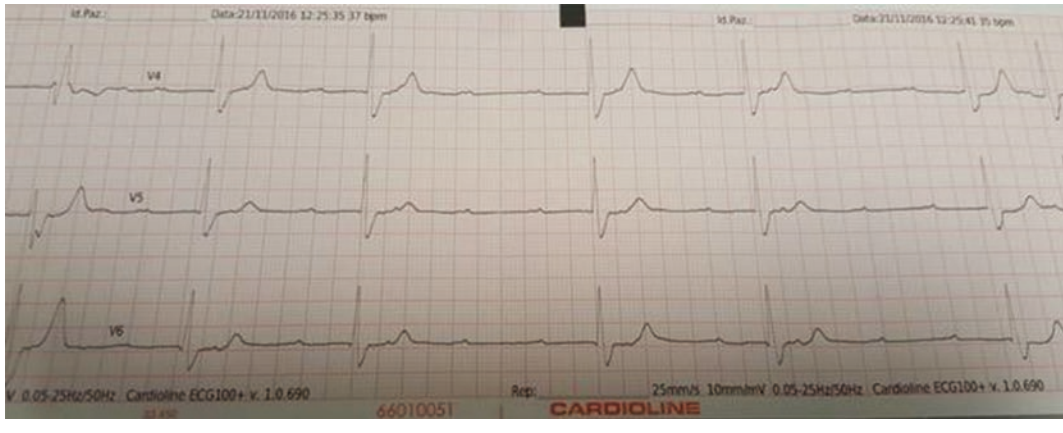

Fig. 14.12

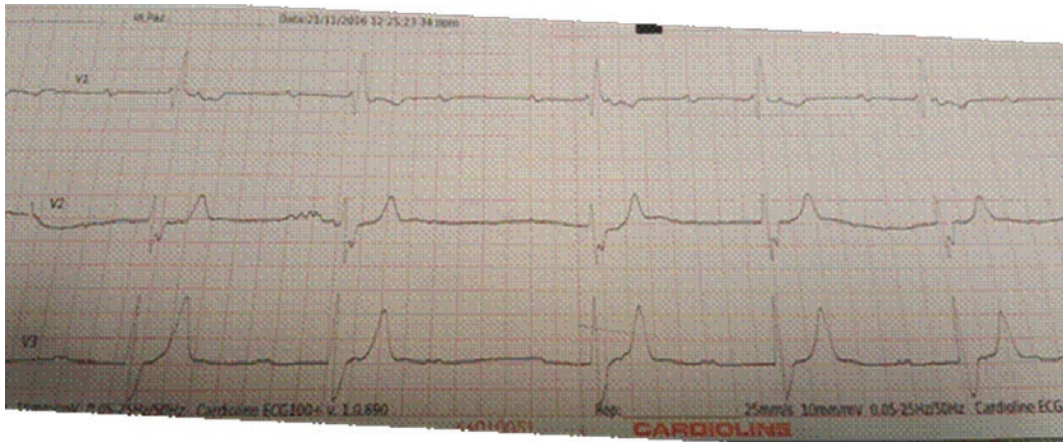

Fig. 14.13

14.5.1 ECG Analysis

The following is the ECG result:

Sinus bradycardia (P axis +60°), HR 50 bpm, normal AV conduction (180 ms), QRS right axial deviation (+135°), QRS 180 ms, right bundle branch block morphology, tall and peaked T waves with voltage increase (hyperkalemia), and QTc 447 ms (Fig. 14.14).

After dialysis, the ECG modified (Fig. 14.15):

Sinus bradycardia, HR 50 bpm, normal AV conduction, QRS 120 ms, right bundle branch block, QRS +15° axis, T wave voltage reduction, and QTc 402 ms.

14.6 Case 6

An 82-year-old woman went to the hospital for dyspnea at rest. She got therapy at home for systemic arterial hypertension and osteoporosis.

Ca^{++} 7 mEq/L, K^{+} 3.3 mEq/L, and Na^{+} 143 mEq/L.

14.6.1 ECG Analysis

Sinus rhythm, HR 87 bpm, normal AV conduction (180 ms), QRS 120 ms, QRS axis −30°, right bundle branch block and left anterior fascicular hemiblock, and QTc 494 ms (Figs. 14.16 and 14.17)

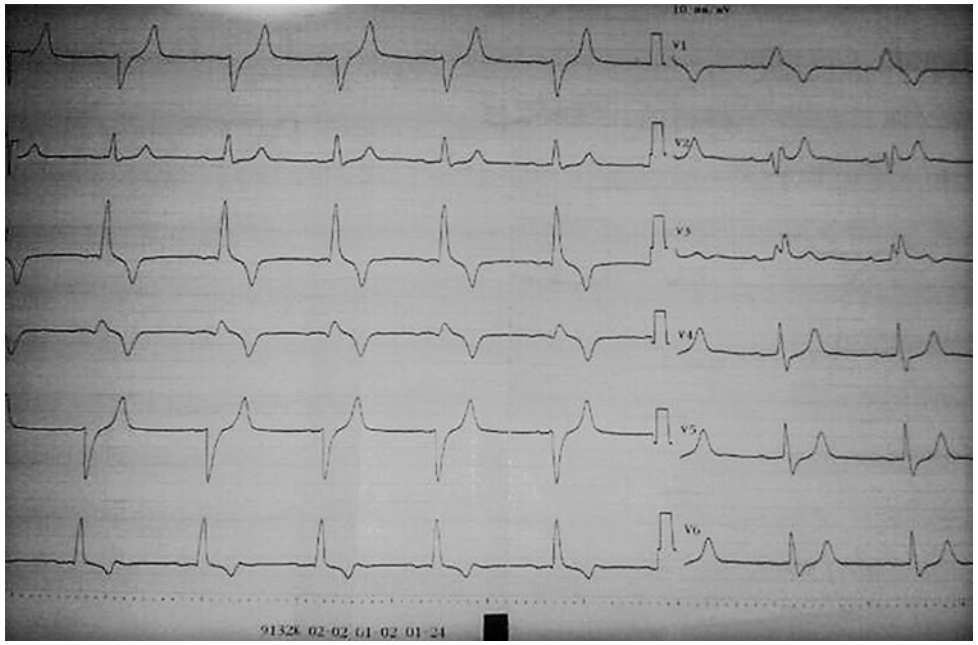

Fig. 14.14

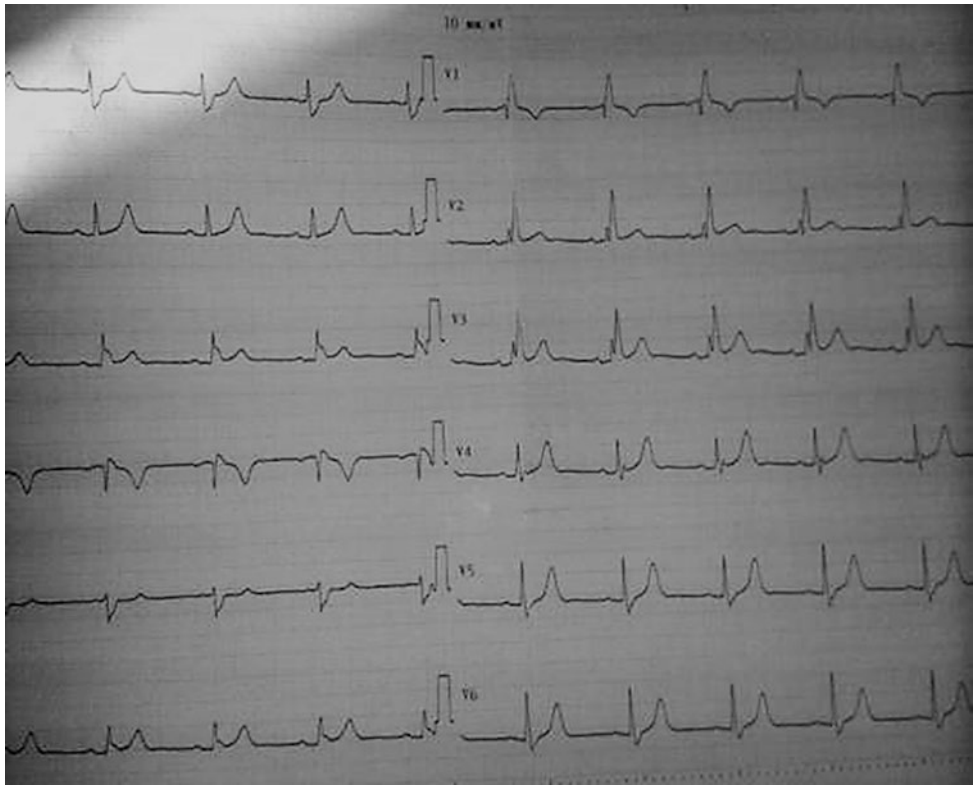

Fig. 14.15

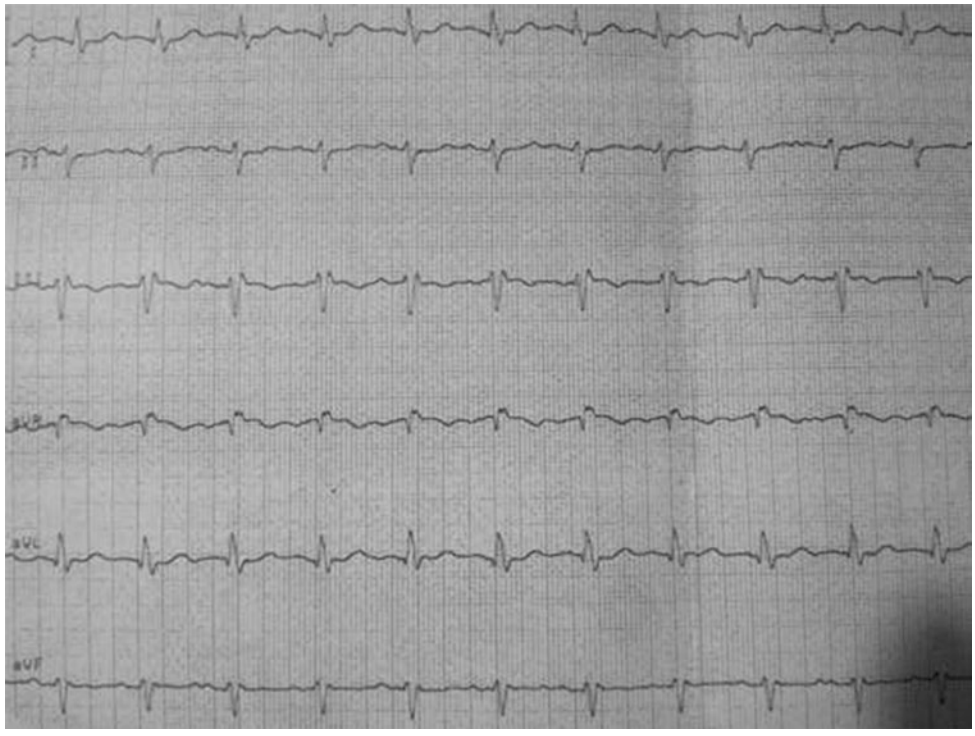

Fig. 14.16

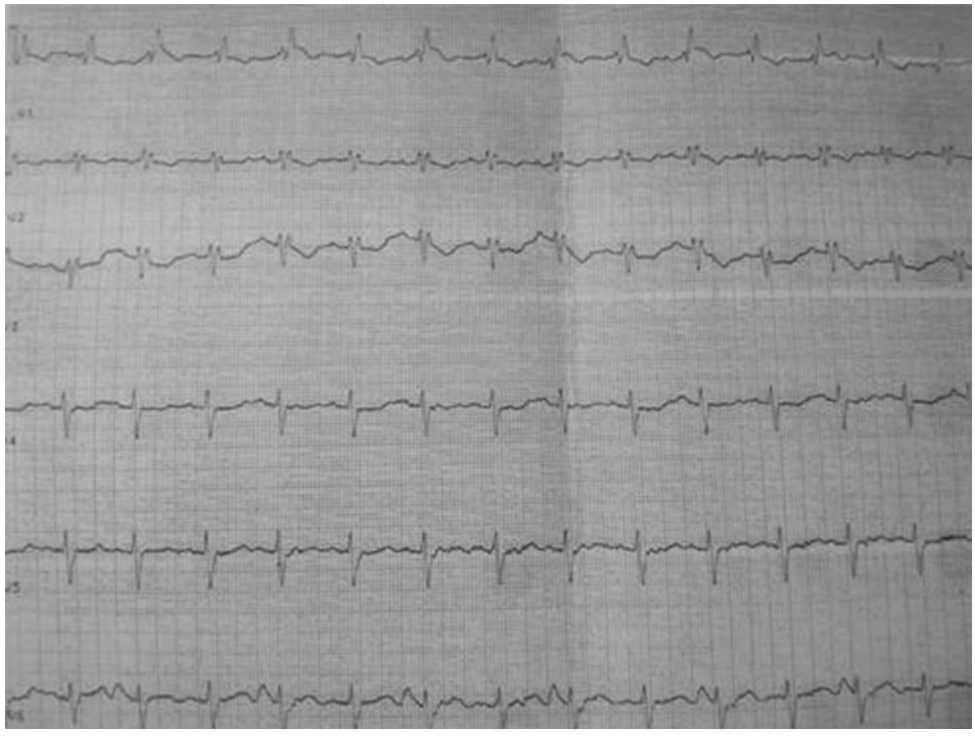

Fig. 14.17

14.7 Electrolytic Imbalances and ECG

Normal cardiac action potentials may be influenced by electrolyte imbalance, owing to changes in intra- and extracellular electrolyte concentrations. The ECG may be a way to estimate the severity of electrolyte imbalances and to judge whether there are risks for life-threatening arrhythmias [1–3].

14.7.1 Hyperkalemia

Hyperkalemia is defined as a serum potassium concentration higher than 5.0–5.5 mEq/L in adults.

Hyperkalemia is often the result of multiple conditions, in particular the most common contributors are impaired renal function, medication use, and hyperglycemia.

In general, the causes of hyperkalemia are:

- Impaired potassium excretion: acute kidney injury/chronic kidney disease, medications, decreased distal renal flow, hypoaldosteronism, and primary renal tubular defects
- Transcellular shifts: insulin deficiency/resistance, acidosis, hypertonicity, medications, cell breakdown/leakage, and hyperkalemic periodic paralysis
- Increased intake: potassium supplementation, red blood cell transfusion, foods high in potassium, potassium-containing salt substitutes, protein calories supplements, penicillin G potassium, and pica (certain forms)
- Pseudohyperkalemia: hemolysis, blood sample cooling, intravenous fluids with potassium, cell hyperplasia, and familial pseudohyperkalemia

Hyperkalemia is often an asymptomatic condition. In the case of severe hyperkalemia, the symptoms are nonspecific, as weakness, fatigue, palpitations, paresthesias, nausea or vomiting, and ascending paralysis.

Laboratory analysis is mandatory to make the correct diagnosis. It may be useful to repeat serum potassium measurements and also to exclude pseudohyperkalemia (common condition that results from potassium moving out of cells during or after potassium sample collection).

When hyperkalemia occurs, the action potential duration is reduced; phase 3 myocardial action potential verticalizes its slope, thus shortening its duration. The hypopolarization of the myocardial cell membrane causes partial inactivation of the Na channels, resulting in a decrease in Vmax and amplitude of phase 0. When kalemia exceeds 6 mEq/L, it is possible to identify the typical electrocardiographic modifications.

At a serum potassium level of 6.0–7.0 mEq/L, it is possible to identify the following findings:

- *Tall, peaked T waves with a narrow base*, with a prominent or sharp apex, best seen in precordial leads. The ECG differential diagnosis of hyperacute T wave includes transmural acute myocardial infarction, but the T wave of STEMI is typically wide (in contrast with the narrow based T wave of hyperkalemia) [4].
- *Normal or little shortened QT interval*

At a serum potassium level of 7.0–8.0 mEq/L, the ECG frequently shows the following:

- *Peaked T waves*.
- *Decreased amplitude of P waves*.
- *Prolonged PR interval* (first-degree AV block).
- *Sinoatrial*, *atrioventricular*, *and intraventricular conduction depression*, causing escape rhythms.
- *Widening of the QRS* (because the phase 0 of the action potential slows down, a nonspecific intraventricular conduction occurs): wide QRS often mimics a RBBB with left axis deviation, or rarely a LBBB; actually in hyperkalemia the conduction delay persists throughout the QRS complex and not just in the initial or terminal portions.
- *Apparently normal or prolonged QT interval* (due to QRS widening).
- *ST-segment elevation* (less common): it can be more evident in leads V1–V3 and mimic myocardial infarction (described as “pseudoinfarction”

pattern) or Brugada syndrome. Recently, the terminology "Brugada phenocopy" was proposed, including those clinical entities that present with identical ECG patterns to those of Brugada syndrome but are elicited by various other clinical circumstances. Metabolic conditions, particularly hyperkalemia, represent one of the etiological categories [5–8].

At a serum potassium level higher than 8.0 mEq/L [9], the ECG shows the following:

- *Absence of P wave*. This finding depends on the sinoventricular conduction, represented by sinus impulse conduction to ventricles without atria activation. Sinus impulse reaches atrioventricular node going through internodal pathways, while atria are inexcitable.
- *Progressive QRS widening* (>200 ms). The progressively widened QRS can fuse with the T wave, forming a typical *sine wave pattern*. Ventricular fibrillation or asystole can follow.

14.7.2 Hypokalemia

Hypokalemia, defined as a serum potassium level <3.5 mEq/L, is a common finding in clinical practice. The most frequent causes are:

– Gastrointestinal loss (diarrhea, laxatives, gastroileal anastomosis)
– Renal loss (potassium-depleting diuretics, hyperaldosteronism, severe hyperglycemia, carbenicillin, sodium penicillin, amphotericin B)
– Intracellular shift (alkalosis, insulin overdose)
– Inadequate intake (malnutrition, anorexia, total parenteral nutrition)

Symptoms of mild hypokalemia are weakness, fatigue, paralysis, dyspnea, constipation, paralytic ileus, and leg cramps; more severe hypokalemia can alter cardiac tissue excitability and conduction and represent a life-threatening condition. Indeed the myocardium is extremely sensitive to the effects of low serum potassium since hypokalemia disrupts the fine balance of ion currents across the cell membrane, causing a prolongation of action potential (loss of repolarization reserve) [1]. The result is an increased risk for ventricular arrhythmias, especially in the setting of preexisting conditions such as cardiac ischemia, bundle branch block, ventricular pacing, digoxin treatment, or heart failure. Nevertheless, the inhomogeneous distribution of action potential duration changes and conduction slowing represent an arrhythmogenic substrate for reentrant circuits even in structurally normal hearts [10]. Pulseless electrical activity or asystole may also develop with severe potassium depletion.

A definite correlation can be established between hypokalemia and ECG pattern, with magnitude of development of the electrocardiographic changes paralleling the decrease in serum potassium. We can observe a progressive depression of the ST segment, a flattening and inversion of the T wave, and an increase in amplitude of the U wave lowering the serum potassium levels. The typical ECG pattern of hypokalemia, which appears most frequently in precordial leads V3, V4, and V5, has been described as an ST segment and a T wave of opposite polarity to a U wave of increased voltage, thus resembling a letter "S" lying on its side [12] (Figs. 14.18 and 14.19).

ECG shows sinus bradycardia at 58 bpm, PR 200 ms, QRS duration 80 ms, and QRS axis −30°. Note the slightly depressed ST segment, flattened T wave, and prominent U wave best seen in leads V4-V5-V6. QTc is 492 ms (Bazett). Serum K^+ was 3.2 mEq/L.

In particular, the hallmarks of hypokalemia-induced ECG changes are the following [11–13]:

ECG changes due to hypokalemia	
P wave	Increased in height and width
PR interval	Prolonged (first-grade atrioventricular block)
ST segment	Depressed
T wave	Flattened/inverted, low amplitude
U wave	Prominent (deepened and broadened) with T/U <1; polarity is not affected
QT interval	Apparently prolonged (long QU interval with fusion of T and U waves)

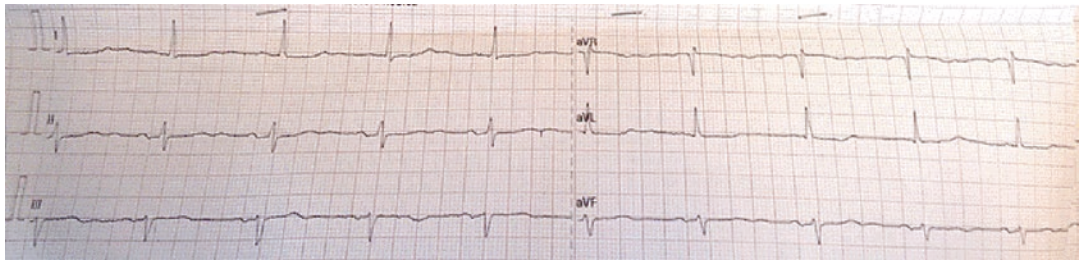

Fig. 14.18

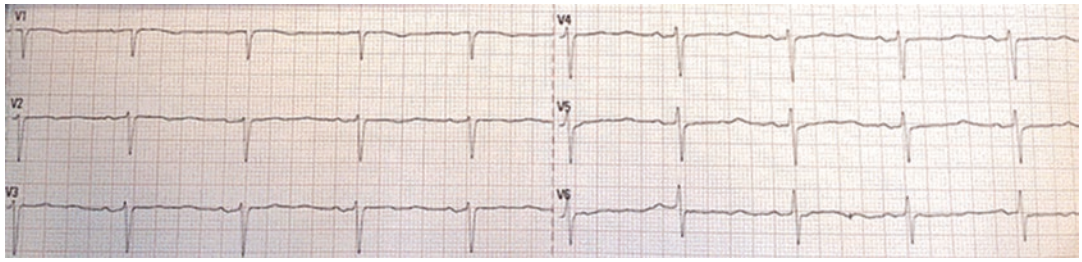

Fig. 14.19

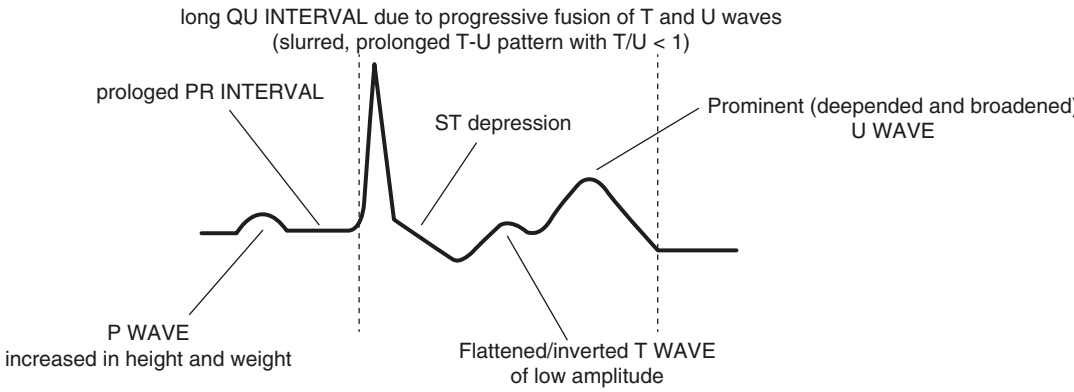

Fig. 14.20

The recognition of hypokalemia can be difficult if there are marked ST and T alterations due to the currents of injury of a myocardial infarction or concomitant administration of antiarrhythmic drugs or digoxin or in the presence of tachycardia or a prolonged PR interval causing the merging of the P wave with the U wave [12] (Fig. 14.20).

14.7.3 Calcium Disorders

Hypercalcemia and *hypocalcemia* influence predominantly the duration of the action potential: an increase in extracellular calcium concentration reduces the duration of the ventricular action potential by shortening phase 2; instead, hypocalcemia extends this phase and the actual refractory period. Phase 3 is not significantly altered by calcium disorders.

14.7.4 Hypercalcemia

Hypercalcemia is defined as a total serum calcium concentration >10.5 mg/dL (or ionized calcium >4.8 mg/dL).

The most common causes of hypercalcemia are primary hyperparathyroidism and malignancy

with metastatic bone disease (accounting for more than 90% of reported cases). Vitamin D intoxication may represent another cause of hypercalcemia.

Patients with hypercalcemia can show the following symptoms:

- Neurologic: depression, weakness, fatigue, confusion (lower levels), hallucinations, disorientation, hypotonicity, seizures, and coma (higher levels)
- Gastrointestinal: dysphagia, constipation, peptic ulcers, and pancreatitis
- Renal: diminished ability to concentrate urine with abundant dieresis leading to loss of sodium, potassium, magnesium, and phosphate

Hypercalcemia can determine different effects on cardiovascular system depending on its severity.

At a calcium level <15 mg/dL, myocardial contractility may be increased, while above this level myocardial depression occurs. Hyperkalemia represents a proarrhythmic condition since it shortens the refractory period; concomitant hypokalemia may increase the risk of life-threatening arrhythmias.

Typical ECG features are QT interval shortening with ST segment almost disappearing. The latter phenomenon is due to T wave beginning directly on QRS complex, thus mimicking a RSr' in right precordial leads. Furthermore ST segment can present a mild elevation. Both these conditions can simulate a Brugada phenomenon if present in leads V1 and V3. During hypercalcemia T wave often presents low voltage, though at high levels (>16 mg/dL) it can be prolonged and become inverted; QRS complex can increase its amplitude [14].

ECG changes due to hypercalcemia:

– Shortened QT interval
– Lengthened QRS duration
– Bradycardia
– All degrees of AV block
– Sinus node dysfunction and tachy-brady syndrome
– Ventricular tachycardia, ventricular fibrillation, and torsades de pointes

14.7.5 Hypocalcemia

Hypocalcemia is defined as a total serum calcium concentration <8.5 mg/dL (or ionized calcium <4.2 mg/dL).

The most common causes of hypocalcemia are thyroid surgery, abnormalities in serum magnesium, and tumor lysis syndrome (rapid cell turnover with resultant hyperkalemia, hyperphosphatemia, and hypocalcemia). Symptoms of hypocalcemia, which usually occur when ionized levels decrease below 2.5 mg/dL, are paresthesias, muscle cramps, carpopedal spasm, tetany, stridor, and seizures. On clinical examination, typical features are Chvostek and Trousseau signs and hyperreflexia. ECG can be a valid help in the diagnosis of severe hypocalcemia. Indeed hypocalcemia deeply affects both atrial and ventricular repolarizations by prolonging phase 2 of action potential, although on a surface ECG, only the ventricular one can be recognized. The hallmark of hypocalcemia is QT interval lengthening or, more properly, of Q-0T interval: the prolongation involves the ST segment, while T wave duration is not significantly affected. QT prolongation usually does not exceed the 140% of the upper limit of normal values.

ECG changes due to hypocalcemia [15]:

– Lengthened QT interval
– Shortened QRS duration
– AV block
– Sinus bradycardia
– Sinoatrial block
– Torsades de pointes and ventricular fibrillation are uncommon

ECG is recorded from a patient with severe hypoparathyroidism. It shows sinus bradycardia at 52 bpm, PR 160 ms, QRS duration 100 ms, and nonspecific repolarization pattern. QTc is 465 ms (Bazett), and its prolongation is due to a lengthened Q-0T interval (ST segment is prolonged, while T wave duration is not altered). Serum Ca^{++} was 4.4 mg/dL (Figs. 14.21 and 14.22).

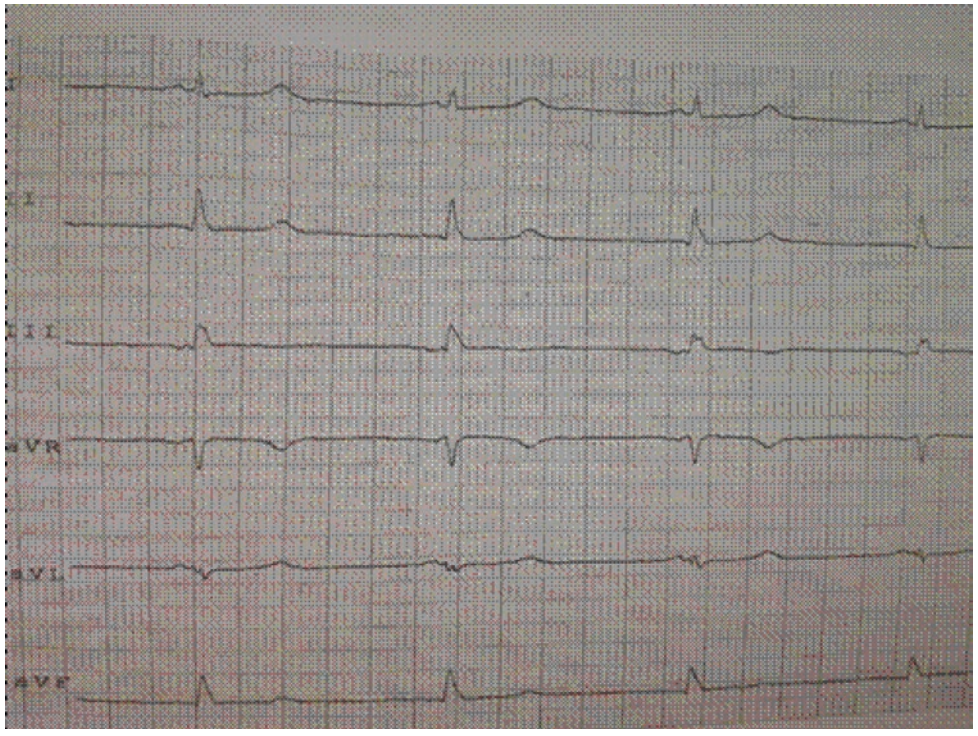

Fig. 14.21

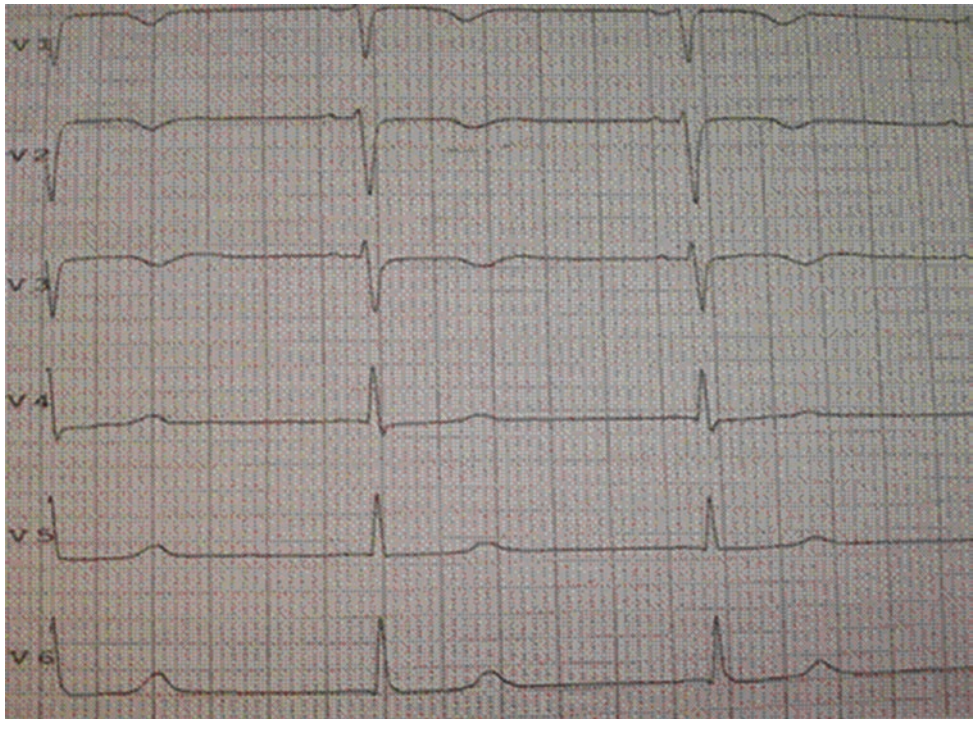

Fig. 14.22

14.7.6 Magnesium Disorders

If the values of calcium and potassium are normal, magnesium alone does not cause significant effects on the ECG.

Hypomagnesemia is usually associated with hypocalcemia or hypokalemia and can potentiate some digital toxicity arrhythmias. Torsades de pointes cases have been observed in patients with QT prolongation due to hypomagnesemia. These sporadic cases, however, do not allow to establish a reliable correlation between hypomagnesemia, QT prolongation, and rhythm turbulence. A magnesium reduction of magnitude such as to enhance the electrophysiological effects of hypocalcemia can only occur if not at a concentration of the two electrolytes so low as to be incompatible with life.

Severe *hypermagnesemia* can cause AV and IV conduction disorders that can culminate in complete AV block and asystole (Mg >15 mEq/L) by inducing an increase in sinus node recovery time and a slowing of AV and IV conduction.

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Critical ECGs from Non-cardiologic Patients

15

Irene Giannini, Cristina Pierandrei, and Alessia Quaranta

15.1 Case No. 1

F. A. B. is a pregnant young female (30 years old) that came to our attention because her gynaecologist requested an ECG together with other antenatal tests before the nearing delivery.

Childbearing course was characterized by gestational diabetes, but foetal development was regular at the 33rd week.

She complained only of rare mild palpitations.

She had no personal and familiar history of cardiovascular diseases (Fig. 15.1).

15.1.1 ECG Analysis

Narrow QRS tachycardia (110 bpm) with a constant and regular cycle length; AQRS is +70°; R-wave progression is normal in precordial leads. In limb leads, there is a clear P wave preceding every single ventricular complex, but its morphology changes during the first three beats. The atrial depolarization axis is positive in inferior leads and in I, negative in VR and negative/isodiphasic in VL that is consistent with an atrial activation coming from the sinus or perisinusal area.

The following atrial deflections are melted with the early ventricular signal. In the last beat, there is a completely different feature of P with its axis upward directed, negative in inferior leads, positive in VR and VL and isodiphasic in I.

A minor ST elevation in the lateral precordial leads is noticeable.

15.1.1.1 Diagnosis

Automatic junctional tachycardia with AV dissociation.

15.1.2 From ECG to Clinic

Supraventricular tachyarrhythmias could occur during pregnancy. It is largely a third-trimester phenomenon (20–44%) [1]. The underlying mechanisms are volume overload, increased levels of circulating catecholamines and greater sensitivity of adrenergic receptors [2].

The heart remodelling during pregnancy may cause enlargement of all the four cardiac chambers, with particular involvement of the left atrium which usually returns to normal only 2 weeks after delivery [3].

In this case, an atrial enlargement could be expressed by the tall P wave of the first three beats.

Heart rate physiologically increases during pregnancy, and an enhanced automatic activity has been described being not unusual for a pregnant woman complaining of palpitations [4].

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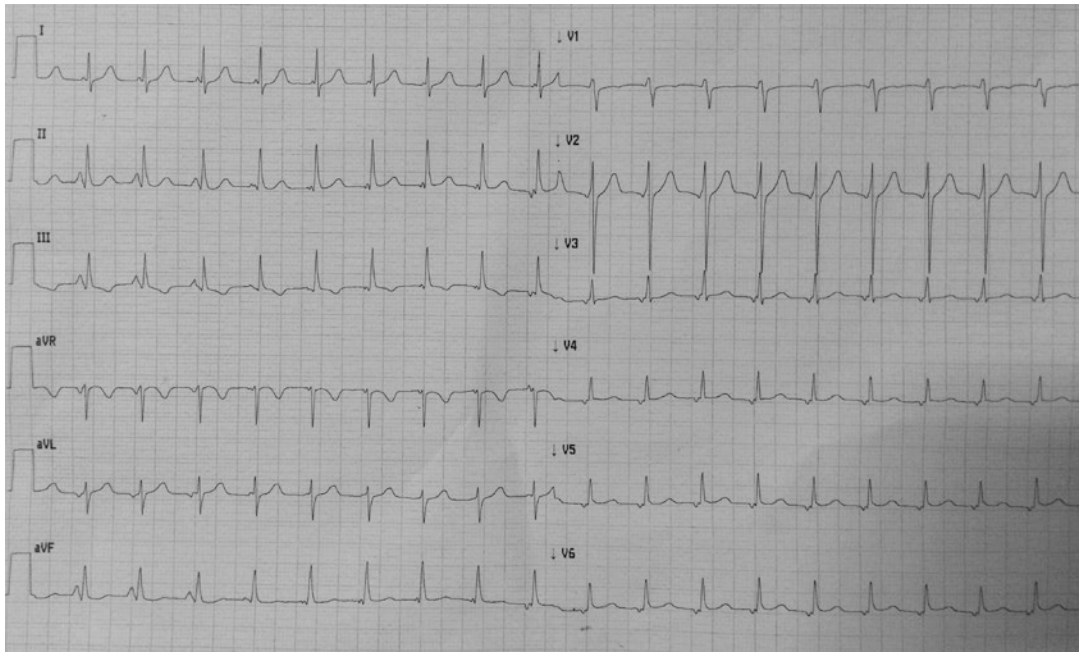

Fig. 15.1 12-lead ECG: automatic junctional tachycardia in pregnant

Automatic junctional tachycardia begins when automatism rate of the junction overcomes the sinoatrial rate or the main pacemaker and ends when sinus node fires at a higher frequency.

That is the reason why, in this case, the sinus P progressively disappears inside the QRS and a junctional P subsequently appears.

The automatic junctional tachycardia could be secondary also to digoxin toxicity, but many cases have been reported in the literature in pregnant women without any cardiac structural heart disease and with quite a good outcome.

This kind of SVT tends to be persistent and drug resistant.

Our patient tolerated the arrhythmia quite well.

She was treated with metoprolol 5 mg IV that was ineffective. A similar injection was repeated 1 h later (5 mg IV) with successful arrhythmia termination.

It is known how during pregnancy a higher dosage of drugs is required to achieve an effective therapeutic plasma concentration because of an increased volume of distribution and a higher renal and hepatic clearance.

Adenosine is an exception; it works at standard dosages (6–12 mg IV) because of levels thus allowing a successful conversion of specific supraventricular arrhythmias without any risk for foetus [5].

Metoprolol and propranolol are also safe and effective in pregnancy [6]; guidelines suggest to employ these drugs in case of failure of adenosine and of vagal manoeuvres.

Verapamil and diltiazem are recommended when beta-blockers are ineffective with a preference towards verapamil because it is less hypotensive [7].

The decision to interrupt the arrhythmia must be taken not only because of possible haemodynamic consequences on the mother and foetus but also considering the possible intrauterine growth impairment, the risk of preterm delivery and the possible heart failure induction.

15.2 Case No. 2

C. M., male, 44 years old, smoker, is admitted to the ER because of sudden chest pain onset that slightly reduced while sitting. He had no history of fever nor upper airway inflammation in the previous days (Fig. 15.2).

15.2.1 ECG Analysis

Sinus rhythm is at 62 bpm. QRS axis is normodirected (+60°).

Atrioventricular and intraventricular conductions are normal, with 140 ms PR interval and 80 ms QRS.

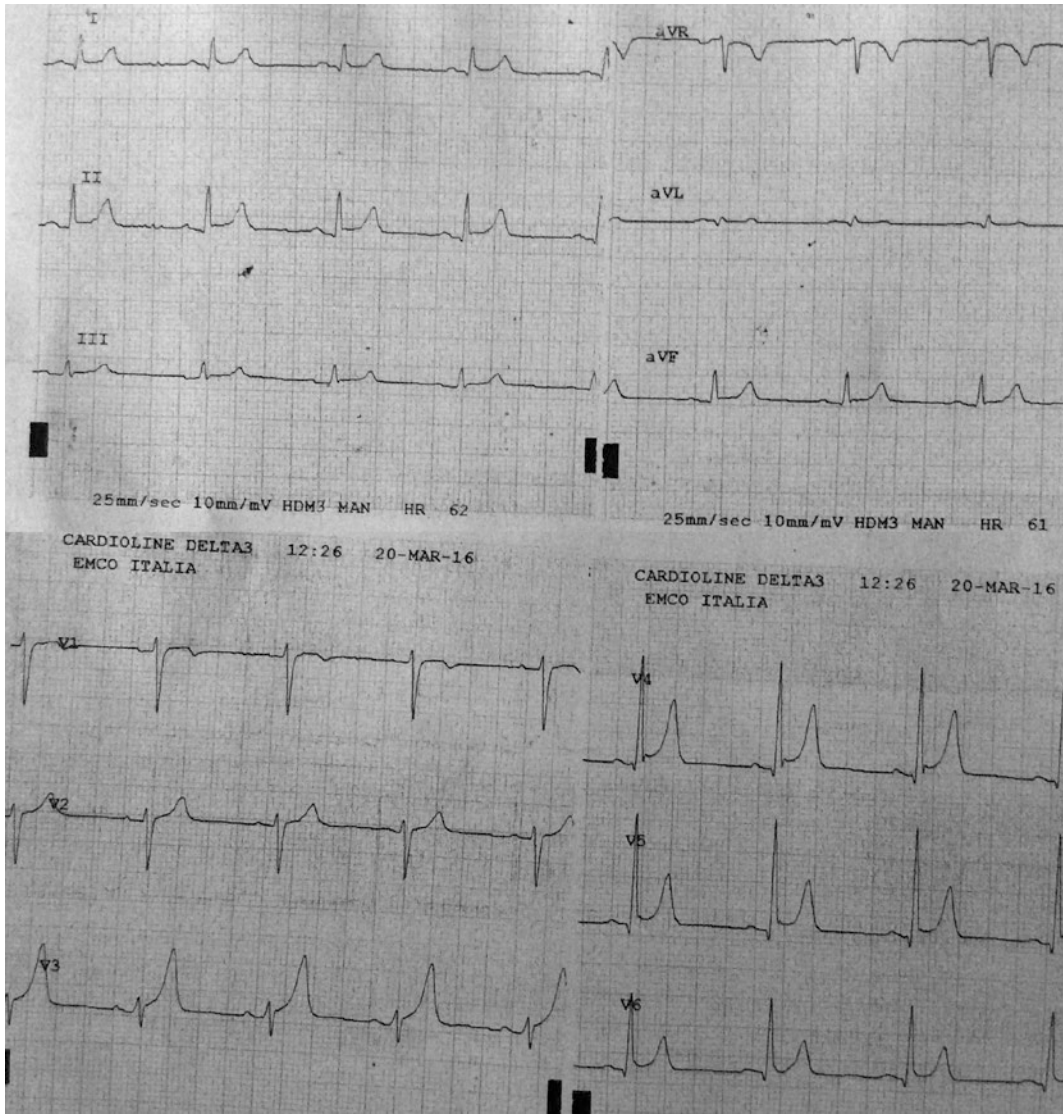

Fig. 15.2 12-lead ECG: acute cholecystitis

A downslope PR interval is noticeable in inferior leads.

Repolarization is characterized by diffuse concave ST elevation (+1.5 mm max) in I, II, VL, VF and V3–V6 with also a pointed T wave (tent type).

This ECG is highly suggestive of acute pericarditis.

The widespread diffusion of ST abnormalities in the absence of any electrolyte imbalance and the extension beyond a single coronary territory exclude other diagnosis.

15.2.1.1 Diagnosis

Young age, few cardiovascular risk factors and PR interval depression are in favour of a diagnosis of acute pericarditis. In the case of ST elevation, an acute myocardial infarction should be ruled out. In this case, also cardiac markers were not elevated even after several hours thus excluding both an acute ischemic episode and also acute myocarditis. Few hours after admission, chest pain migrated to the abdomen (right upper quadrant), and an echography showed signs of acute gallbladder inflammation, despite the absence of lithiasis.

Those last findings led us to hypothesize the inflammatory origin of the ECG changes secondary to an acute cholecystitis episode.

15.2.2 From ECG to Clinic

ST elevation could be encountered in several clinical conditions out of cardiac ischemia: cholecystitis, gastric distension, pancreatitis, acute stroke, subarachnoid haemorrhage, neoplastic invasion of the myocardium and hypothermia are just some examples [8].

Its mechanism remains still unclear and interestingly these changes often disappear after surgery [9].

Other studies demonstrated that during acute cholecystitis, negative T waves and ST-segment depression may appear at ECG; meanwhile, ST elevation is quite a rare event [10].

Previous studies on animal models have demonstrated that gallbladder distension may cause an increase of heart rate, blood pressure and circulating levels of renin thus affecting coronary circulation and predisposing to ECG acute modifications [11].

More recent observations hypothesize that dehydration and electrolyte imbalance, as a consequence of the abdominal disorder, could also play a role in ECG changes in the acute setting [12].

The overt abnormal repolarization shown in this ECG, not accomplished by troponin elevation, without echocardiographic signs of cardiac involvement, does not fit with any ischemic mechanisms and is per se not a contraindication to cholecystectomy [13].

The most likely hypothesis in this case is for an inflammatory reaction with a pericardial inflammation whose etiologic agents were coming from the gallbladder.

The patient was referred to surgeon who, even in presence of a ‘not reassuring ECG’, did not hesitate to operate him in order to prevent abdominal complications. It did quite well with subsequent symptoms disappearance and ECG normalization.

15.3 Case No. 3

A 78-year-old man, who has a clinical history of hypertension, impaired glucose tolerance, prostatectomy and duodenal ulcer, went to the ER because of poor appetite, sleepiness and dysuria; those symptoms did follow a flu of 2 weeks before. The relatives reported that these symptoms followed a laparotomy done 1 month before. He was conscious and apyretic. His blood pressure is 130/70 mmHg and heart rate 105 bpm. EGA: pH 7.49 SpO2 93% pCO_2 28 mmHg (respiratory alkalosis) (Fig. 15.3).

15.3.1 ECG Analysis

Sinus tachycardia is at a heart rate of 105 bpm. There are ‘pulmonary P waves’ with high voltage in II and in III leads; atrioventricular conduction is within the upper limits; there is clockwise QRS rotation on the longitudinal axis with an incomplete

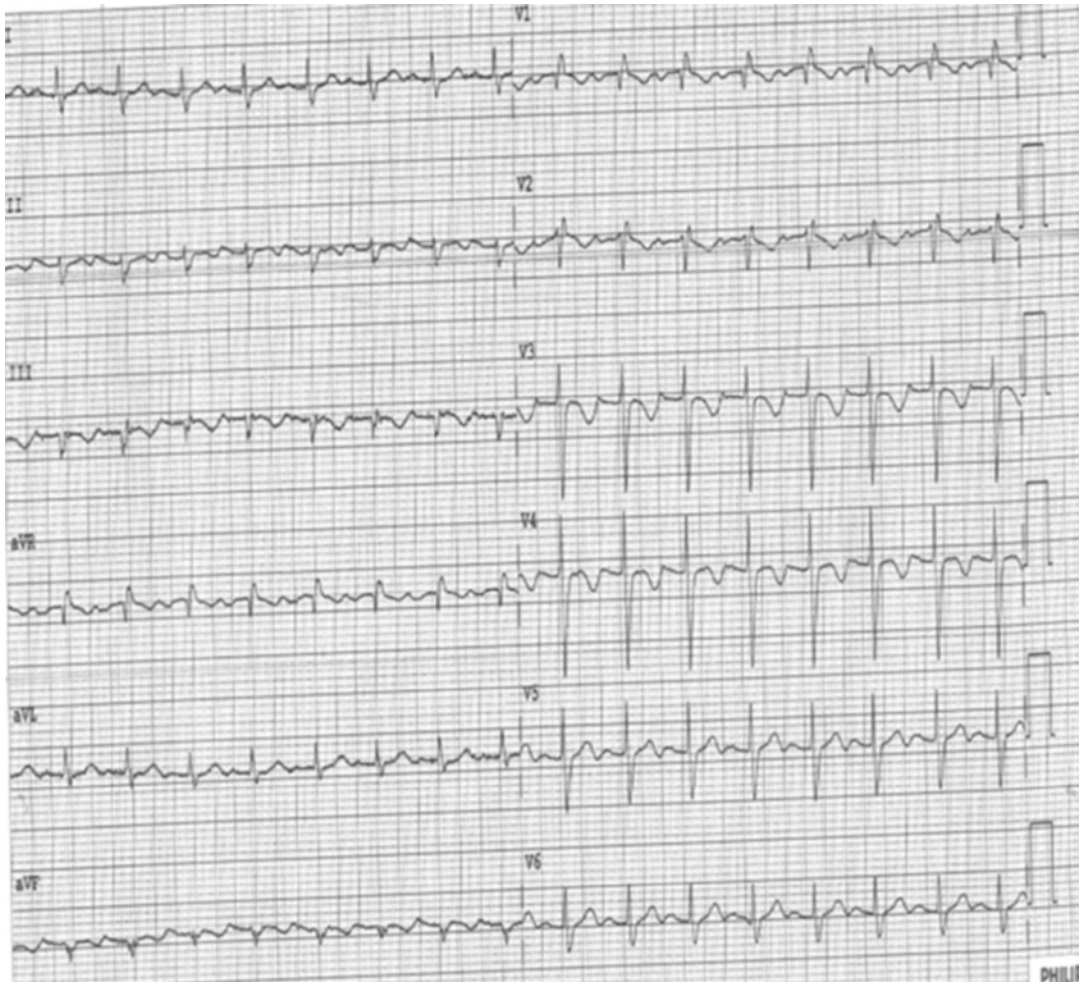

Fig. 15.3 12-lead ECG: acute pulmonary embolism

RBBB. There are evident Q waves in leads III and VF, negative T waves in the inferior and in the precordial leads until V4 and S wave in I (typical S1/Q3 sign).

15.3.1.1 Diagnosis

A pulmonary embolism could be suspected.

The diagnosis was confirmed by CT angiography that showed filling defects of thromboembolic nature in the main branches of pulmonary arteries that confirmed a massive pulmonary embolism causing an acute right ventricle overload whose signs are indirectly visible in this ECG.

15.3.2 From ECG to Clinic

This ECG is therefore consistent with an acute pulmonary embolism.

The 'S1Q3T3' typical pattern of pulmonary embolism was described for the first time in 1935 by McGinn and White [14]. There is S wave in I; the Q waves are followed by a negative T in III. This pattern is however not highly specific, because Q waves and negative T waves in III can also be observed in patients who had an inferior myocardial infarction. However, in the latter, a Q wave usually is present also in lead II. Also a sinus tachycardia could be another sensitive but poorly specific electrocardiographic index in favour of a

pulmonary embolism. In the case of inferior myocardial infarction, it is most likely to observe normal heart rate or even bradycardia because of possible SA or AV node involvement [15].

Other ECG clues suggestive of pulmonary embolism are:

- New onset of incomplete/complete RBBB and ST-segment elevation and positive T waves in the right precordial lead, especially V1 [16].
- Negative T waves in the precordial leads. These could be present also during acute coronary syndromes; however the differential diagnosis is possible by looking for specular (mirror) signs in the peripheral leads that are absent in pulmonary embolisms. Moreover, a subsequent T normalization could also be a sign of partial thrombus lysis after the acute pulmonary event [17].
- Clockwise rotation on the longitudinal axis and low voltage in the limb leads are not specific signs of pulmonary embolism, since they could be present in other conditions like COPD, pneumothorax, emphysema, pleural or pericardial effusion, obesity, infiltrative cardiomyopathies, constrictive pericarditis, hypothermia and hypothyroidism [18].
- Pulmonary P waves (high P waves whose voltage >0.25 mV in at least one of the inferior leads) that are usually due to right atrial enlargement secondary to pressure overload [19].
- Right axis deviation that may be a consequence of right ventricle dilation could be present together with new-onset atrial arrhythmias like atrial fibrillation or atrial flutter [20].

15.4 Case No. 4

An 80-year-old woman was admitted to the ER for sudden loss of consciousness while she was in the bathroom.

Cardiovascular risk factors are arterial hypertension, type II diabetes mellitus and dyslipidaemia.

She had no any previous cardiovascular events.

Glasgow Coma Scale at the arrival was 9; PA is 150/90 mmHg.

A brain CT scan was performed that showed a subarachnoid haemorrhage due to rupture of an intracranial aneurysm.

A 12-lead ECG was recorded (Fig. 15.4).

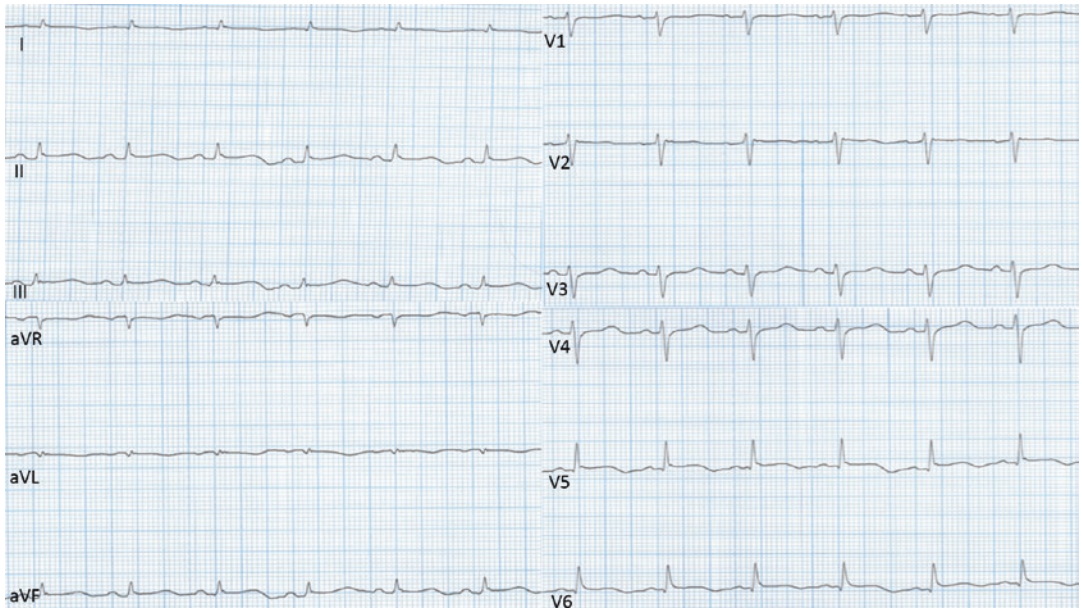

Fig. 15.4 12-lead ECG: Takotsubo syndrome in patient with subarachnoid haemorrhage

15.4.1 ECG Analysis

She had a regular RR interval with a heart rate of 90 bpm (RR 680 ms). Each QRS is preceded by a positive P wave in leads II, negative in VR and biphasic in V1. It is a sinus rhythm.

The P-wave maximum amplitude is 0.20 mV with 80 ms length. P-wave axis is +60°.

PQ interval is 160 ms. QRS is 80 ms. QRS axis is +60° (isoelectric VL).

There is ST-segment elevation of 1 mm in leads I and VF and of 1.5 mm in leads II, III and V5–V6. QT interval is 400 ms and QTc 489 ms.

The routine laboratory tests showed elevated Tn I (0.16 ng/mL).

15.4.1.1 Diagnosis

Because of these ECG patterns, we should consider several different clinical conditions for differential diagnosis:

- Myocardial disease:
  - Acute coronary syndromes with ST-segment elevation
  - Coronary spasm
  - Stress cardiomyopathy (Takotsubo syndrome)
  - Myocarditis, pericarditis and myopericarditis
- Valvular heart disease such as severe aortic stenosis or severe aortic regurgitation
- Aortic disease such as aortic dissection
- Acute cerebrovascular disease

15.4.2 From ECG to Clinic

Electrocardiographic changes are reported frequently after acute strokes.

In particular, subarachnoid haemorrhage (SAH) may be accomplished with a variety of electrocardiographic abnormalities, some of which are not easily distinguishable from those seen during an episode of severe myocardial ischemia and/or infarction [21]. ECG abnormalities in patients with SAH were firstly reported in 1947 [22], but the prevalence, characteristics and prognostic significances of those have still not been fully explored. The reported prevalence of ECG modifications in patients with SAH ranges from 27% to 100% [23].

The most common stroke-associated ECG patterns are T-wave abnormalities, prolonged QTc interval and ensuing arrhythmias, but other alterations such as ensuing new Q wave, ST-segment depression or elevation and prominent U wave may also occur. The electrocardiographic spectrum seems to be related to the type of cerebrovascular disease and its localization [24].

The echocardiography of this patient showed apical and mid-left ventricular dilatation and severe reduction of systolic global function because of complete akinesia of the apical and mid-segments and compensatory basal hyperkinesia. The ejection fraction measured with Simpson's biplane method was 30%. The patient had a normal pericardium and aorta and no significant valvular disease.

Those echocardiographic patterns showing wall motion abnormalities (mid-apical akinesia with compensatory basal hyperkinesia also known as 'apical ballooning') are quite typical for stress cardiomyopathy (Takotsubo-like), but also an acute myocardial infarction or a coronary spasm cannot be excluded without going to coronary angiography.

The ECG evolution in the following days was in favour of a Takotsubo syndrome. Deep and negative T waves ensued together with a marked QTc prolongation (figure below). Those patterns completely reversed to normal in few days (Fig. 15.5).

We observed also a progressive reduction until normalization of cardiac biomarkers (maximum values of troponin I was 6 ng/ml), and finally there was a progressive recovery of the contractile function at echo.

At a first presentation, a history of physical or emotional stress (in this case SAH) accomplished with modest ECG alterations and a modest plasma level of cardiac biomarker elevation, together with a contrasting severity of ventricular dysfunction, could suggest the diagnosis of Takotsubo cardiomyopathy [25]. ECG changes in this syndrome include ST-segment elevation, the evolution of marked anterior T-wave inversion and QT interval prolongation. These features all appear to solve in few days [26–28].

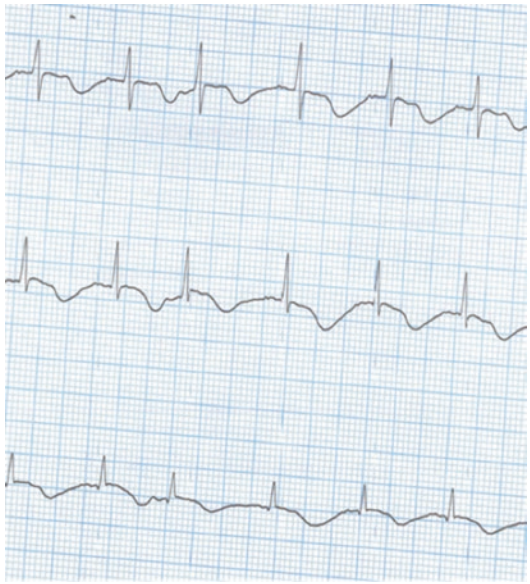

Fig. 15.5 Detail of repolarization pattern

The diagnosis of Takotsubo syndrome has been confirmed in this case by finding normal coronary arteries without any sign of spasm at coronary catheterization. Many authors have already described an association between Takotsubo syndrome and SAH [29] and other neurological conditions such as epilepsy, electroconvulsive therapy, head injury, stroke and anxiety or depression.

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Pacemaker Stimulation Criticism at ECG

16

Paolo Bonelli, Giorgio Guidotti, Enrico Paolini, and Giulio Spinucci

Cardiac implantable electronic devices' (CIEDs) numbers have grown up worldwide over the last years [1]. At the same time, functions and algorithms' complexity implementation also expanded. It will be therefore more and more frequent for the clinician to deal with pacemaker (PM) ECGs and unusual device behaviors, particularly when they mimic pseudo-malfunctions. In this chapter, we present some examples of challenging electrocardiograms, aiming to show how the clinician, just by analyzing the ECG, could reach or at least suspect the correct diagnosis.

16.1 Case 1

An 82-year-old man with a history of systemic hypertension and previous dual-chamber PM implantation for second-degree atrioventricular (AV) block was referred to our clinic with a suspected PM malfunction. The patient was asymptomatic. ECG is shown in Fig. 16.1a, b.

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16.1.1 ECG Analysis

The ECG shows a regularly irregular rhythm with recurrence of long RR intervals. The average ventricular rate is 95 bpm when RR is regular. At first glance, there is no visible spike, while the P waves have one morphology; PP intervals are regular. P waves are positive in leads I and II and negative in aVR with normal morphology, length, and axis (±0°). They are sinus node beats.

Most of the QRS complexes are clearly preceded by a P wave with a constant PR interval of 160 ms. These QRS are wide (120 ms) with a left bundle branch block morphology (broad R wave in leads I and aVL and a deep S wave in lead V1) and small left axis deviation (−15°). Other wide QRS complexes, with a different morphology (LBBB with inferiorly oriented axis), come after the long RR intervals. These last QRS are preceded by a P wave with a long PR interval of 400 ms. ST segment and T waves which follow the two QRS types have an abnormal orientation. QT/QTc intervals are normal (350 ms and 440 ms, respectively).

This ECG shows therefore normal sinus rhythm with heart rate of 95 bpm.

The QRS coming after a normal PR interval has a morphology that is not consistent either with a RV apical pacing, which is usually associated with a broader QRS and more leftward axis deviation (QS complex in all inferior leads, positive QRS in aVR lead), or with a right ven-

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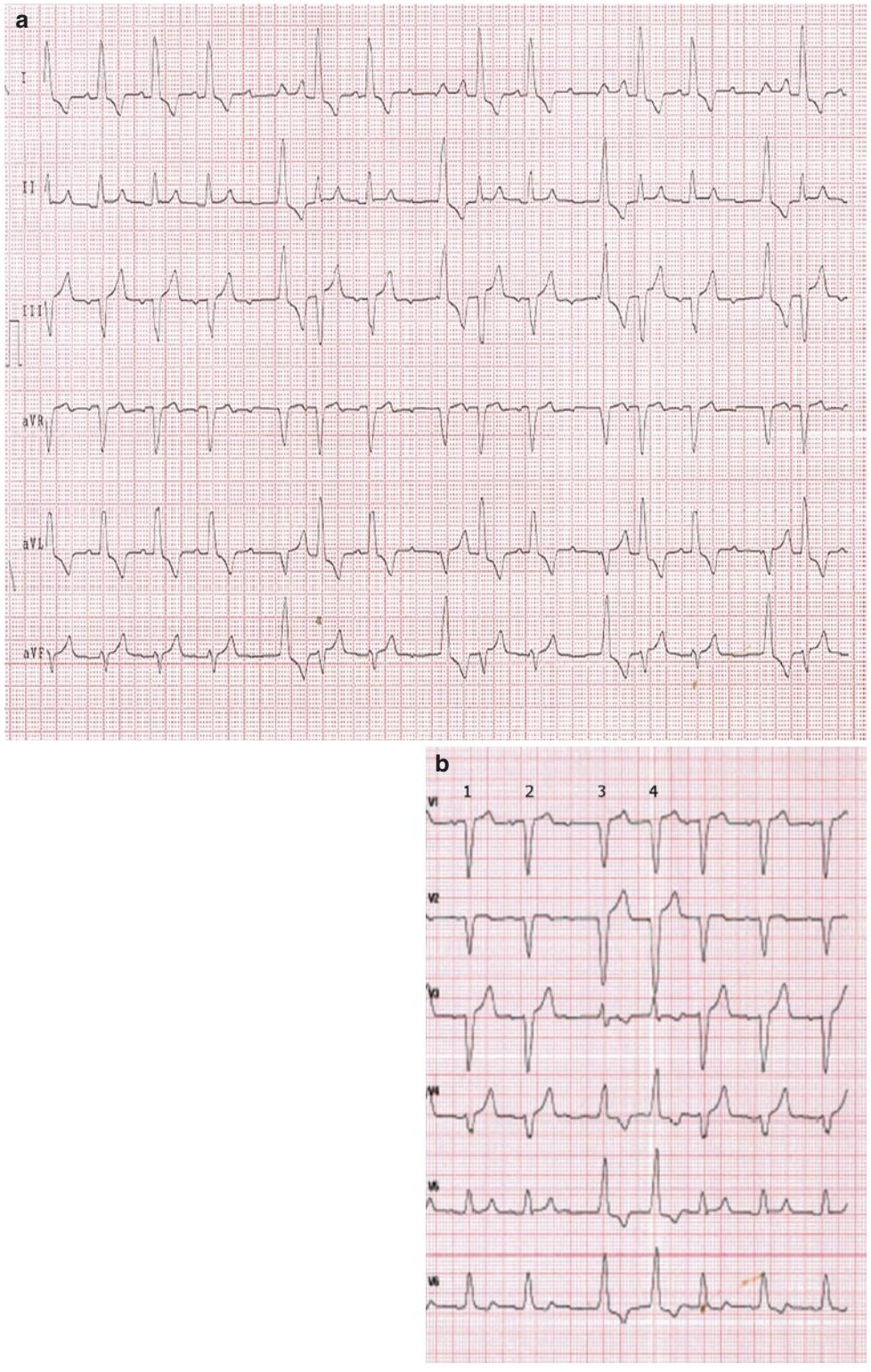


Fig. 16.1 (**a**) Case 1 ECG: limb leads. (**b**) Case 1 ECG: chest leads (not simultaneously recorded)

tricular septal pacing (usually heralded by an inferiorly oriented axis). QRS coming after the long PR are consistent with a RVOT septal pacing (QR in I and QS in aVL). These QRS are also wide (120 ms), but their axis is downward (near +75°). The regular association of these QRS with P waves makes unlikely the hypothesis of escape junctional beats. Indeed, there is a barely visible "spike" before the QRS in lead III. The sudden increase of PR interval which ends with a paced ventricular beat is diagnostic for a Mobitz second-degree AV block. This type of AV block is characterized by a single P wave which fails to be conducted to the ventricles without a previous progressive increase of PR interval.

As can be seen in Fig. 16.2, the PM delivers a paced beat after a delay of 400 ms.

This behavior can be explained in two different ways:

– AV delay interval is kept fixed at 400 ms after sensed P wave (it should be a too long and nonoptimal programmed interval, rarely used today), or, alternatively, the PM is following an AV interval extension algorithm to maintain a spontaneous AV conduction as long as possible. Finally, the higher QRS amplitude after every ventricular paced beat reflects simply a longer diastolic filling.
– PM interrogation revealed that an AV hysteresis algorithm was running with an AV delay extension programmed up to 400 ms to promote intrinsic AV conduction. When AV block occurs, PM continues to apply the extended AV delay for up to five cycles (in Fig. 16.1b, beats 3 and 4 are paced ones, and P wave merged with the preceding T wave can be seen 400 ms before beat 4), and if intrinsic conduction doesn't resume, it switches back to the nominal AV delay.

In conclusion, the tracing shows a normally functioning PM.

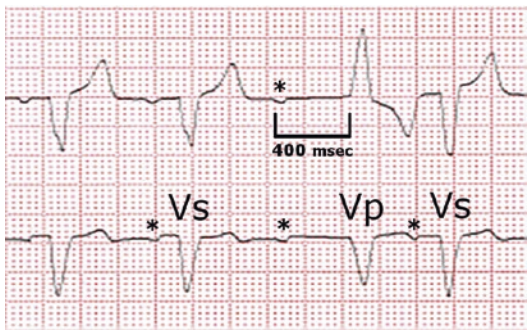


Fig. 16.2 Detail of the Fig. 16.1a. Ventricular sensed beat (V_s). Ventricular paced beat (V_p). P wave (asterisk)

16.1.2 Strategies to Reduce Ventricular Pacing

The adverse effects of pacing from the right ventricle apex have been documented in several studies [2]. Algorithms to reduce as much as possible the unnecessary RV stimulation have been developed for a dual-chamber PM. Any ECG reader must keep in mind this caveat.

Basically, there are two main algorithm families: one that relies on a periodic AV interval prolongation, called AV hysteresis, and the other that automatically switches between DDD and AAI mode [3].

More in detail, there are three types of AV interval hysteresis [4]:

- *AV hysteresis*: in its simplest form, it refers to the base AV paced interval lengthening, by a programmable amount of time, after a ventricular sensed beat. This longer AV interval remains unchanged until the resumption of ventricular pacing.
- *AV repetitive hysteresis*: unlike simple AV hysteresis, after the loss of spontaneous conduction, it keeps the extended AV paced interval for a programmed number of cycles.
- *AV search hysteresis*: it works by periodically extending the short base AV paced interval in order to detect the presence of spontaneous AV conduction.

In the most recent PM, these distinct features are usually combined in a single AV hysteresis "package."

Observing a longer and intermittent AV delay may therefore help to rule out a malfunction, even without the aid of a programmer.

Conversely, in AAI-DDD mode, the PM works by pacing in AAI(R) mode as much as possible and switching back to DDD mode in case of no ventricular sensed event.

In this latter case, a single not conducted P wave (e.g., as in second-degree AV block type 1) is allowed. Obviously, when a higher degree of AV block occurs, the device reverts to dual-chamber pacing until the resumption of the spontaneous AV conduction.

By paying attention to Holter ECG recordings, it is so not uncommon to find single non-conducted P waves even in normal PM function: a fairly reliable clue to PM proper function is the observation of ventricular paced event with an unusually short AV delay after each "dropped" atrial beat [5].

A big help is coming from the knowledge of the normal PM algorithms.

16.2 Case 2

A 1-year-old male underwent temporary epicardial single-chamber AAI-PM implantation for a rare diagnosis of sick sinus syndrome (SSS). During hospital stay, being scheduled for surgical tonsillectomy, he was moved to another ward of our hospital and maintained under continuous ECG monitoring. The monitor indeed recorded the following ECG tracing (Fig. 16.3) by which a suspicion of PM malfunctioning was raised. Our little patient was totally asymptomatic.

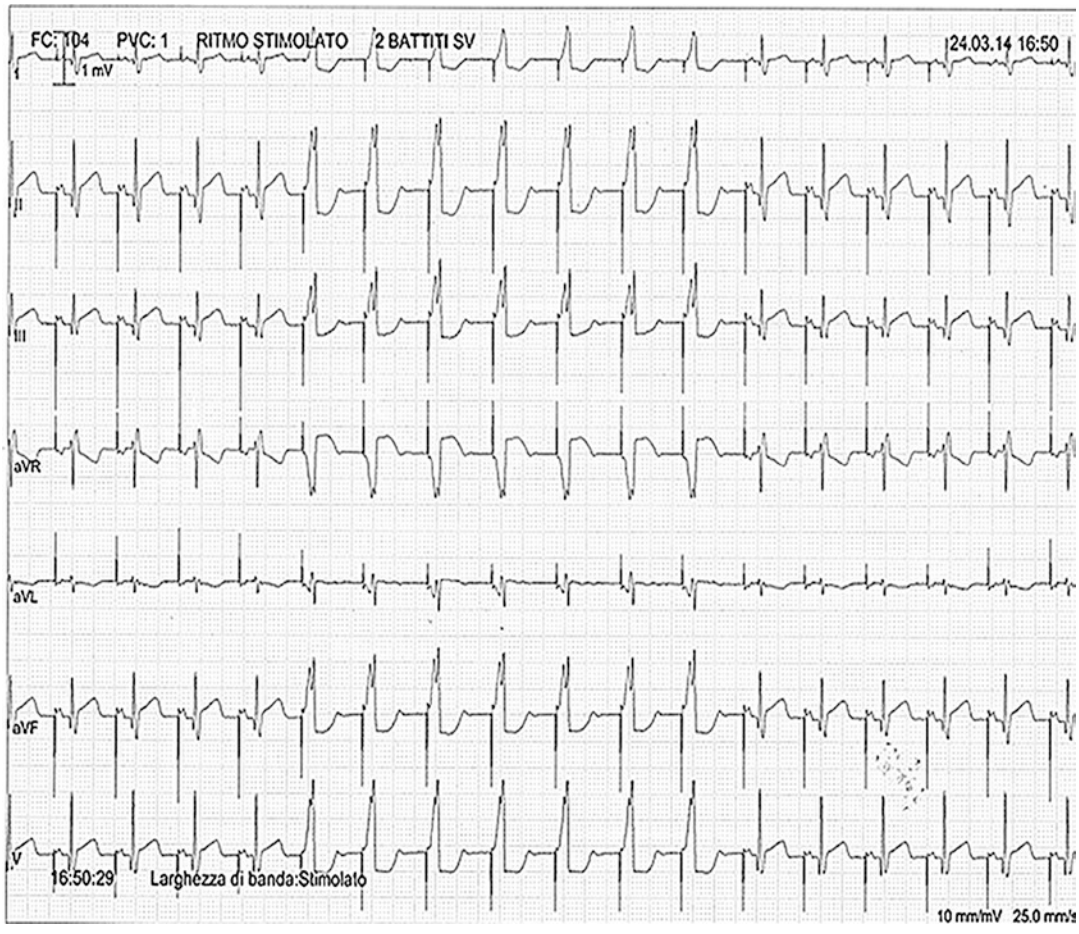


Fig. 16.3 Case 2 12-lead ECG

16.2.1 ECG Analysis

The ECG shows a regular rhythm at 100 bpm. There are two different QRS morphologies: one preceded by a paced P wave and one without it. Even though PM-induced, P waves retain a normal morphology. When P waves are visible, AV conduction is normal (PR segment is 120 ms); intraventricular conduction is also normal (QRS duration of 90 ms) with a QRS axis of +75°. T waves match with QRS axis and they appear quite normal. QT segment duration is 320 ms and QTc is 410 ms. QRS complex morphology preceded by P waves is consistent with the young age of the patient with a physiological right ventricular predominance (narrow S waves in inferior leads and R in aVR). The other QRS morphology, visible in the middle section of the ECG, is quite different, despite a similar axis orientation. These QRS complexes are closely preceded by PM spikes; they are wide (about 120 ms duration) without any distinct P wave before. There is a slurring in the starting part of QRS, which could represent a hidden P wave. The repolarization pattern after the wider QRS complexes is also different from the one of the narrow QRS.

This ECG could have enlightened the pacemaker malfunction. The first rhythm (narrow QRS preceded by paced P waves), visible at the beginning and at the end of the tracing, is consistent with a normally functioning AAI-PM in a patient with a normal AV conduction. The peculiarity, represented by the second QRS morphology, is debatable.

Heart rate is virtually constant, suggesting that PM spikes are always capturing myocardium. Second, P waves may be hidden in the ascending QRS branch. A similar P/QRS fusion may be found in ventricular preexcitation. This patient has been always asymptomatic, and neither ECG signs of preexcitation (*Δ wave*) nor tachycardia episodes were previously recorded.

An EP study performed before the PM implantation did confirm SSS with normal AV conduction. Last but not least, a temporary PM malpositioning and/or inappropriate PM setting should be ruled out. The chest X-ray confirmed a correct PM lead position. At interrogation, his mother said to have inadvertently turned the temporary PM voltage knob, bringing it back immediately. The transient rise of PM current output, due to the tiny dimensions of the patient's heart, led to the simultaneous capture of both atrial and ventricular myocardia, thus changing the QRS morphology. *In this case*, *the final diagnosis was a pseudo-malfunctioning of temporary AAI-PM*, *mimicking lead dislocation*.

16.2.2 Temporary Cardiac Pacing Pitfalls

Ventricular preexcitation in infants is a well-known cause of wide QRS and short PR intervals, but it should not be overlooked [6]. Familiar anamnesis may greatly help the clinician. Children's ECG screening is growing in clinical practice [7]; however more studies are expected in this field to clarify its real clinical advantages. Temporary PM lead malpositions are not so uncommon, especially in the emergency settings [8]. When examining a patient with an epicardial PM, a possible malposition (either of leads or of the generator) should be always considered [9].

When suspected, checking the device is the first choice. Sensing and pacing thresholds should be regularly tested (preferably with daily controls) while waiting for permanent implant [10]. It has to evaluate the underlying spontaneous heart rhythm, simply by lowering pacing rate. Also the current output must be selected in order to avoid capture of neighbor structures and the phrenic nerve stimulation, especially with an epicardial temporary PM.

When a suspicion of malposition has been raised, a chest X-ray is advisable. Furthermore, even if it could appear superficial and taken for granted, the lock mode must always be set on. This simple measure could prevent some errors and troubleshooting coming from patient's (or parents') inadvertent PM manipulation. Finally, in order to prevent other forms of pseudo-malfunctions, it is important to neutralize static electricity from the patients.

It is also recommended that all healthcare professionals involved in patients' care discharge any static electricity by touching a large conductive metal before touching the patient, cables, leads, or the PM per se. These attentions must be followed because pacing leads provide a low-impedance way to the heart [11].

16.3 Case 3

A 76-year-old male with a clinical history of dual-chamber PM implantation for paroxysmal third-degree AV block came to control. He was also dyslipidemic, had systemic hypertension, and reported dizziness at an outpatient visit. After the analysis of surface ECG (Fig. 16.4), he was referred to our clinic with a suspicion of PM malfunction.

16.3.1 ECG Analysis (see Fig. 16.5)

16.3.1.1 P Wave and Rhythm

There is an irregular rhythm, with no clear evidence of P waves. Before some narrow QRS complexes, we can appreciate an A_p spike, but the distance of A_p spike to QRS interval is not constant. As first assumption, that could be due to intrinsic AV node conduction variability. A flat P wave is not rare in paced patients.

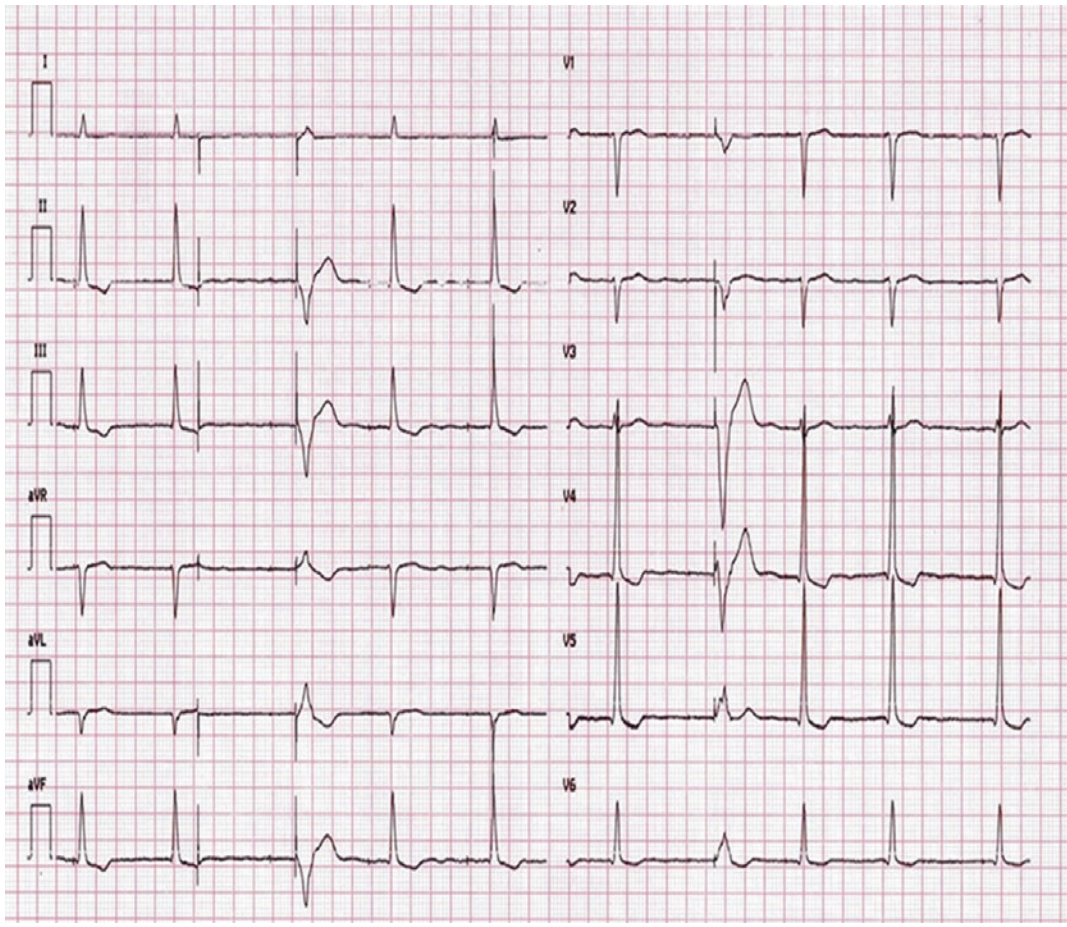


Fig. 16.4 Case 3 12-lead ECG

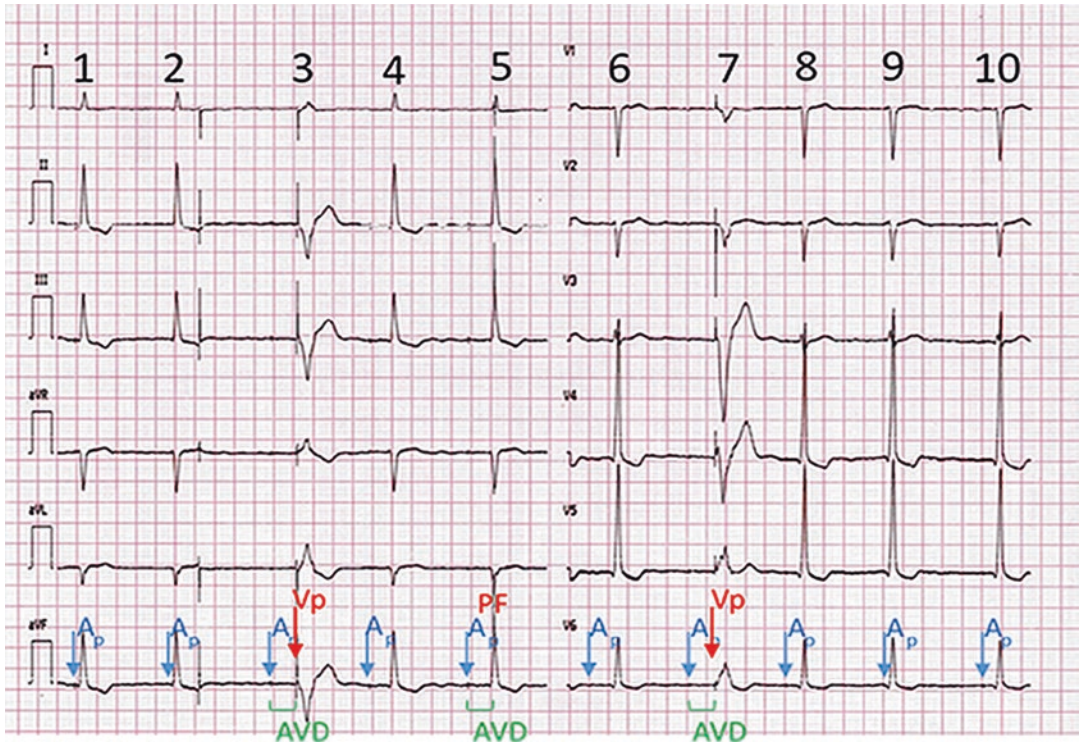


Fig. 16.5 Case 3 ECG with notations. AV delay (AVD). Atrial paced beat (A_p). Ventricular paced beat (V_p)

16.3.1.2 QRS Complexes and V_p Spike

The majority of QRS complexes (1st, 2nd, 4th, 6th, 8th, 9th, 10th) are narrow and spontaneously conducted, with a normal axis (+75°) and normal transition phase.

Instead the 3rd and 7th QRS are wide, clearly paced ventricular complexes, with a left axis deviation (−75°) and LBBB morphology; they are consistent with right ventricular apical pacing.

The 5th QRS is a pseudofusion complex, created by a ventricular spike which interferes with the spontaneous QRS, but the stimulus cannot depolarize the ventricles because it falls in the ventricular effective refractory period (ERP).

The 2nd QRS is followed by a V_p spike, which falls in the middle of the T wave.

The patient had a new-onset atrial fibrillation, and the device did not switch from DDD to VVI mode because of atrial fibrillation undersensing. Indeed, the PM worked on DDD with the programmed lower rate (LR) of 60 bpm and an AV delay (AVD) of 260 ms that could be appreciated with a close look at the 3rd and 7th beats.

Because of atrial fibrillation, not any clear P wave was visible after the atrial spikes (3rd and 4th beat).

By looking at the 2nd intrinsic ventricular complex, we notice a ventricular spike falling on the T wave (i.e., "spike-on-T" phenomenon), an event which at first glance might be related to R-wave undersensing. The spike does not capture the ventricular myocardium because it falls within the ventricular effective refractory period (ERP). However, if we look at the 5th ventricular complex, we notice another particular event, a spike superimposed to the QRS complex (i.e., a pseudofusion beat).

Both phenomena are due to an inappropriate pacing mode during AF (and not to R wave undersensing due some kind of lead malfunction).

The spike-on-T phenomenon after the 2nd QRS is explained by the R wave falling in the post-atrial ventricular blanking (PAVB), which is a predefined time interval after every atrial stimulus. If an intrinsic R wave falls soon after an atrial stimulus, within the PAVB, that R wave is not sensed by the device that consequently will

deliver a ventricular stimulus after a programmed delay from the atrial stimulus (i.e., AVD).

The 5th QRS ventricular pseudofusion instead is due to the late occurrence of the intrinsic QRS after the atrial stimulus. The device cannot sense the intrinsic R wave within the AVD; therefore it delivers an "inappropriate" ventricular spike that results in pseudofusion.

16.3.2 Automatic Mode Switching and Refractory Periods

The dizziness experienced by the patient was not due therefore to a PM loss of capture as hypothesized after the first ECG glance but was related to the new-onset atrial fibrillation.

In this case, the PM malfunction is indeed due to atrial fibrillation undersensing.

In this case, the cause-effect chain of events is:

Atrial fibrillation undersensing

Lack of switch to VVI mode

Persistence of undue AV DDD sequential pacing

16.3.2.1 Deficit of Atrial Fibrillation Sensing

One of the best-known electrophysiological patterns of AF is secondary to micro reentrant circuits that chaotically depolarize groups of myocytes. This pattern of activations reduces the amplitude of atrial signals. When AF waves fall below the programmed sensing threshold, the consequence will be atrial undersensing.

16.3.2.2 Lack of Switch to VVI Mode

Automatic mode switch (AMS) is a programmable function that provides automatic change of pacing mode from an atrioventricular (AV) synchronous one to one without atrial tracking in response to supraventricular tachyarrhythmias, to avoid nonphysiologically high rates during DDD(R) pacing.

If an atrial tachyarrhythmia is undersensed, the device cannot switch from AV sequential (i.e., DDD) to single-chamber pacing (i.e., VVI or VVIR).

This is the reason for the A_p spike seen in our surface ECG that is useless atrial pacing during AF.

16.3.2.3 Persistence of Undue AV Sequential Pacing

In dual-chamber pacing, a ventricular stimulus ensues after the AVD if no intrinsic ventricular complex is sensed within the same AVD.

As already explained, the persistence of inappropriate AV sequential pacing accounts for phenomena such as "spike on T" (2nd complex) and pseudofusion (5th complex).

What About the Pseudo-malfunction?

A PM refractory period is the time interval after a sensed or paced event during which any sensed event cannot initiate actions or counters.

Sensed events during a blanking period may be ignored completely; on the other end, they may be taken into account by the device only to initiate particular algorithms (e.g., mode switching with high atrial rates) [12]. Blanking periods are usually less than 100 ms long and are useful to prevent detrimental cross talk, far field, or inhibition of pacing [12].

PAVB (post-atrial ventricular blanking) is a short interval (<60 ms) that switches off sensing in the ventricular channel immediately after atrial pacing (but not sensing). It prevents the ventricular channel from inappropriately sensing the atrial pacing stimulus. If the PAVB period is too long, ventricular premature beats, which occur early after A_p, may not be sensed, and a ventricular pacing stimulus could be delivered onto the T-wave portion of the PVC, with the potential to trigger ventricular tachyarrhythmias [12]. The spontaneous 2nd beat falls inside the PAVB, so the PM ignores it and after 260 ms (i.e., after the AVD) emits a ventricular stimulus that does not capture the myocardium because it falls within ventricular ERP.

16.4 How to Approach a PM ECG

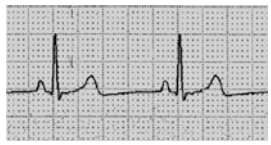
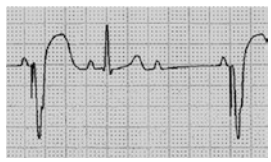
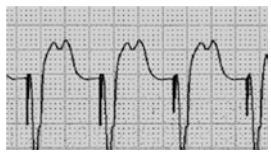
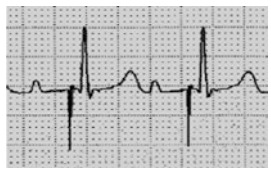
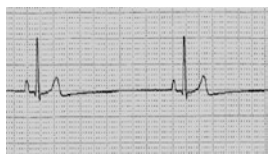
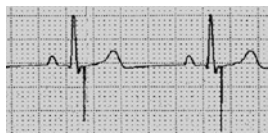
A simple step reading method for PM ECGs, especially useful in the emergency department in the suspicion of PM, can be suggested:

- *Step 1: Spike identification* (see Case #1 for an example). Modern digital electrocardiographs have low-pass filters that sometimes make the bipolar pacing spike very difficult to recognize, which is a high-frequency signal, and filter setting changing is required. Conversely, unipolar pacing artifacts are much higher in amplitude, and filters usually do not have to be turned off to unmask them.
- *Step 2: Rate assessment*. As in non-paced electrocardiogram, heart rate assessment is crucial: both in paced and non-paced rhythm, too slow rate almost always suggests a pace malfunction problem (remember that PMs are rarely programmed at rates lower than 40 bpm), while a too fast-paced rate is often the sign of a normal response to an accelerated atrial activity. A properly working PM normally should not have sinus pause or asystolic periods. There are however some exceptions. As discussed in Case #1, modern devices are often programmed to minimize ventricular pacing burden, switching from AAI to DDD mode usually when an AV block ensues. When this occurs, however, more or less long pacing pauses could be observed, depending on the particular type of algorithm implemented by the manufacturer. RR intervals longer than 3 s should never occur; otherwise a pacing failure should be considered.
- *Step 3: Evaluation of a pacing stimulus response*. It is of utmost importance to ensure that P or QRS waves follow a paced spike, because this indicates enough energy to overcome the stimulation threshold: if this does not occur, then failure to capture has to be suspected. A meaningful exception to this rule is when a pacing spike occurs later after a spontaneous cardiac chamber depolarization; this is a special beat, named "pseudofusion," and absolutely it does not represent PM malfunction. Atrial capture can often be difficult to see in a standard ECG (e.g., see Case #3), with a higher ECG voltage recording of a special help.
- *Step 4: Assessment of pacing spike timing*. A spike constantly and randomly falling without stimulating the chamber means that the PM isn't sensing myocardial depolarization and thus it is failing to sense the native rhythm (e.g., see Case #3).
- *Step 5: Pseudo-malfunctions*: if any doubts about possible device malfunction remain, a pseudo-malfunction should be ruled out as the possible cause of an anomalous ECG strip. Pseudo-malfunctions are defined as unusual, unexpected, and eccentric ECG findings (see Case #2 for a hint regarding these latter features). They appear to be secondary to device malfunctions, but they are instead a normal behavior pattern (see Table 16.1 for a list of most common pseudo-malfunctions) [13].

Table 16.1 Pseudo-malfunction categories (please note this list is not exhaustive) [13, 14]

Rate changes (most common)	Rate response	PM adjusts pacing rate to match metabolic demand
	Rate drop response	PM paces at higher rate to avoid abrupt rate lowering during cardioinhibitory syncope
	Rate hysteresis	PM allows intrinsic heart activity below the lower rate
	Mode switching	PM switches between tracking to non-tracking mode if atrial arrhythmias sensed
	Automatic pacing threshold measurement	Typically at the same hour every day
	Active device intervention algorithms	PM tries to prevent or stop atrial tachyarrhythmias
AV interval and refractory periods	AV interval hysteresis and rate-adaptive AV delay	See Sect. 16.1 for details The rate-adaptive AV delay function mimics physiologic response of the PR interval to heart rate changing
	Functional undersensing	See Sect. 16.3 for an example
	Safety pacing	PM paces ventricular chambers after a very short AV interval following an atrial paced event (it is designed to prevent inhibition due to cross talk)
Mode change	Mode switching	See Sect. 16.1.2
	Mode reversion	PM could operate in less expensive modes in case of battery depletion

Table 16.2 PM Troubleshooting [15]

	Differential diagnoses	Action
Non-paced rhythm: rate >60 bpm 	1. Normal device function: consider rate hysteresis if rate between 50 and 60 bpm	Apply magnet: asynchronous pacing and capture should appear at the magnetic rate
Paced rhythm: rate too slow 	1. Failure to capture/pace 2. Oversensing 3. Programming error (e.g., VVI mode and 2:1 AV block)	PM interrogation
Paced rhythm rate too fast 	1. PM tracks sinus or atrial tachycardia 2. PM-mediated tachycardia (usually ended by the device itself) 3. Sensor-induced tachycardia (rate-adaptive pacing) 4. Special features (e.g., atrial pacing for preventing atrial fibrillation)	Apply magnet: termination points out normal pacer behavior
Failure to capture 	1. Lead disconnection, break, or displacement 2. Battery depletion 3. Exit block (increased stimulation threshold at electrode attachment site) 4. Patient issues (electrolytes, drugs, AMI)	PM interrogation
Failure to pace (no spike and low rate) 	1. Hardware issues 2. Oversensing (electrical signals are inappropriately sensed as cardiac activity)	PM interrogation
Failure to sense 	1. Hardware issues 2. Low amplitudes of intracardiac voltages	PM interrogation

- A list of differential diagnoses to consider when facing some of the most common PM mulfunctions encountered in clinical practice and how to deal with them is presented in Table 16.2.

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17 Pitfalls and Errors of the ECG and Monitoring Systems Recording

Paolo Bonelli, Irene Giannini, and Giorgio Guidotti

17.1 Case 1

A 40-year-old female was admitted to our emergency department because of faintness and palpitations. A typical atrioventricular nodal reentrant tachycardia *(AVNRT, see Chap. 5 for more details on supraventricular tachycardias)* was diagnosed at the first ECG, and the patient was admitted to our clinic for radio-frequency (RF) ablation. Her previous medical history was negative, and she denied main cardiovascular risk factors. A standard evaluation was performed at admission (e.g., physical examination, echocardio, etc.), and also a rest ECG was recorded while the patient was asymptomatic (Fig. 17.1a, b): *"bad news coming from a first glance?"*

17.1.1 ECG Analysis

The ECG shows regular rhythm at 83 beats/min. Every QRS complex is preceded by a P wave. P wave morphology is normal (positive in II and negative in VR) with normal axis and duration (*see Chap. 1 for more information on P wave*). Atrioventricular (AV) conduction is normal (PR segment of 160 ms); intraventricular conduction is also normal (QRS duration of 90 ms) with normal QRS axis (+75°). R wave progression is normal in the precordial leads. QT segment (measured in II, *see Chap. 13*) is 360 ms, and QTc is 426 ms. There are diffuse waves within PR, ST, and T waves. There is a PR segment depression in almost all leads, except in I and VL where it appears elevated. ST segment is diffusely elevated (also in VR), except in I and VL where it is depressed. T wave is biphasic in the most part of the leads with a positive predominant component in all leads. In leads I, VL, and III, T waves have an uncommon sinusoidal pattern. It is difficult to identify the TP segment since the isoelectric line is hard to find.

17.1.1.1 "Bad News Coming from a First Glance?"

We have a regular rhythm with normal P axis and a P wave preceding a normal QRS. It is a sinus rhythm.

A PR segment depression could be pathognomonic of acute pericarditis associated with diffuse ST segment elevation and a reciprocal PR elevation and ST depression in VR [1].

Another important possible diagnosis to evaluate is acute coronary syndrome. Also in that case, there is an ST elevation (*see Chap. 9 for detailed information*). An ST elevation in this ECG is clearly present in inferior leads (III > VF > II), thus potentially suggesting the right coronary artery involvement. Posterior wall is eventually not affected since V1 and V2 don't have the

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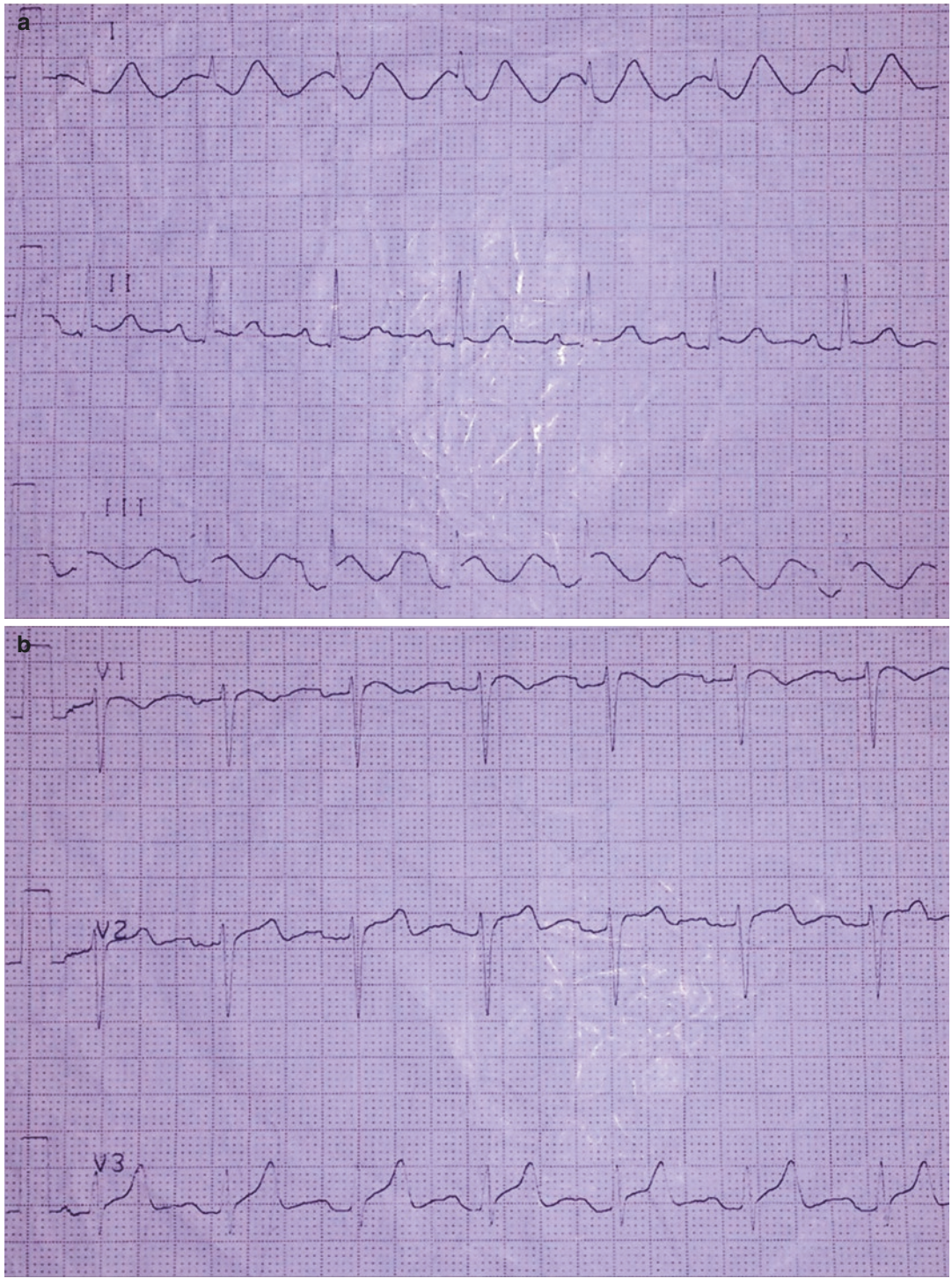

Fig. 17.1 (**a**) Peripheral leads. (**b**) Precordial leads

typical pattern. ST is also depressed in I and VL. Could we consider this as a possible sign of reciprocity?

The patients remained always asymptomatic. She didn't suffer from chest pain, swelling, fatigue, palpitations, or other cardiological symptoms. No pericardial rubs were present. Blood samples did not show any cardiac myocardial necrosis nor inflammation marker elevation. She didn't refer any flu-like syndrome before admission.

Finally a 2D echocardiogram was performed and resulted to be normal with normal ejection fraction and not any sign of pericardial fluid accumulation.

Other possible causes to rule out in this trace are ionic imbalances and specific drug effects. However, no ionic imbalances were detected, and not any drug was taken by the patient before admission.

After repeating the ECG a couple of minutes later, we simply realized that some of the electrodes were not correctly positioned on the skin with consequent poor contact.

17.1.1.2 This Was Thus Just an Artifact!

A similar problem did come 2 years after the above described case in another patient (Fig. 17.2a).

We have a regular rhythm. All the QRS are preceded by P waves with normal axis and duration (clearly positive in II–III and VF and negative in VR). It is a sinus rhythm.

Also in this case, PR segment is depressed in I and III; ST segment elevated in I–III and VL with a biphasic T waves. There is a similar sinusoidal pattern as seen in Fig. 17.1a, b. We must observe lead II and the precordial leads. In lead II the trace is clean and shows a normal sinus rhythm with a quite normal ECG. Even in this case, after a careful electrodes repositioning, everything returned to normal (Fig. 17.2b).

When you observe a sinusoidal isoelectric line strange pattern, check electrodes first!

17.1.2 Artifact Interpretation

Misplaced leads and electrodes malpositioning are surely the most common causes of artifacts in the 12-lead ECG. P and QRS axis and morphology in I and VR are essential in this analysis. "Patient motion" may also cause artifacts sometimes simulating even a ventricular tachycardia (VT, see below) or an atrial tachycardia (like atrial flutter). Sometimes (see Table 17.1) when the patches are overdue or the amount of gel is not sufficient, the "electrical skin contact" may not be optimal. This brings impedance instability and leads to sharp or slow waves with different morphologies and amplitudes. The isoelectric line is affected and could become sinusoidal. The skin must be correctly prepared before each ECG recording; that must be shaved and cleaned with isopropyl alcohol in order to remove lipids and impurities.

17.2 Case 2

This electrocardiogram of a 75-year-old patient (Fig. 17.3) comes from a bedside prolonged monitoring system. The patient was admitted for investigating a possible ischemic heart disease after a syncope.

17.2.1 ECG Analysis

In the chest leads (right part), the rhythm is regular at 75 bpm. P waves are visible, and they precede each QRS with a prolonged PR interval of 260 ms, consistent with a first-degree AV block. QRS duration is 100 ms and has an incomplete right bundle branch delay (R wave in V1). There are no evident repolarization abnormalities, and QT/QTc intervals are normal (380/420 ms).

In the limb leads (left part), there is a run of beats with wide QRS with very sharp initial upslope.

This run has a warm-up phase and very high rate of 300 bpm before ending after polymorphic

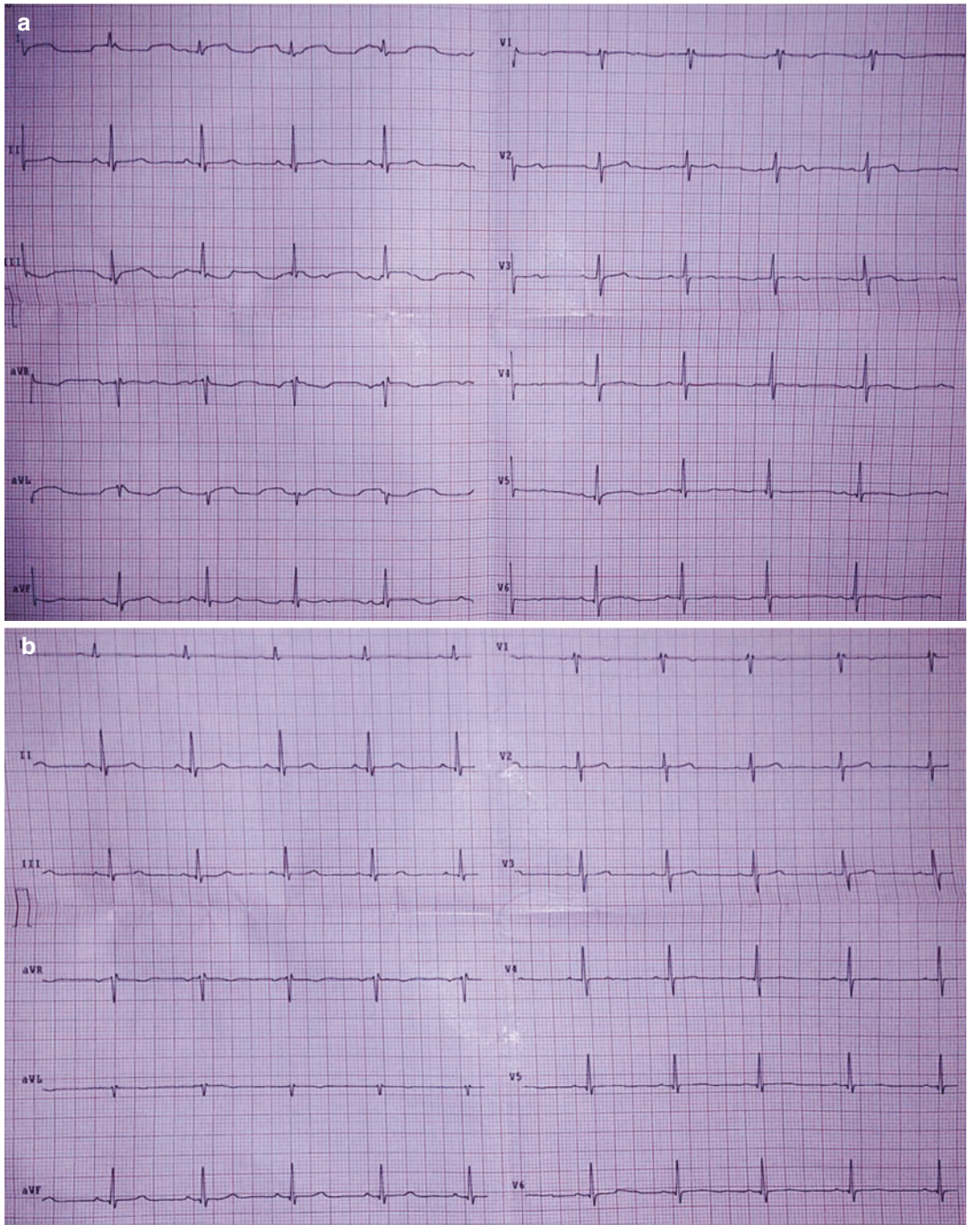

Fig. 17.2 (**a**) Typical ECG artifacts due to not properly sticked patches. (**b**) After patches repositioning

beats. The last two QRS are narrow and simulate the sinus origin; they have an indeterminate axis.

17.2.1.1 This Is a Pseudo Non-sustained VT

Diagnosis may be simple by comparing the peripheral and the chest leads (notably lead I). That ECG pattern could be particularly challenging when having a single lead in a bed monitoring system.

Table 17.1 Schematic subdivision of possible artifacts sources

Internal (physiological)	• *Patient motion*: does not allow electronic filtration (large swings, usually by stretching the epidermis) • *Muscular activity*: allows electronic filtration (small spikes)
External (not physiological)	• *Electromagnetic interference* (widely isoelectric line): light fixtures, electrocautery, electrical devices in the room • Cable and electrode malfunction, insuffficient amount of electrode gel, fractured wires, inappropriate filter settings, loose connections, misplaced leads, accumulation of static energy

There are few features that may help in the differential diagnosis: the baseline trace movement before and after the "tachycardia episode," the too sharp slopes of the terminal parts of the pseudo-ventricular tachycardia compared to the slower slopes of a true ventricular tachycardia, and, at last, the too fast rate (up to 300 bpm); that is unusual in a VT.

17.2.2 Artifact Interpretation

Huang et al. suggested a diagnostic algorithm for pseudo-VT caused by a tremor-induced artifact [2, 3]:

1. *Sinus sign*: one of the frontal leads (I, II, or III) shows normal P waves, QRS complexes, and T waves if one of the upper limbs is free of tremor or movement.
2. *Notch sign*: intersection of the native complex with the artifact creates visible notches and that the notch-to-notch intervals can be compared with the RR intervals of the underlying rhythm (*see asterisk on* Fig. 17.3 *for an example*).

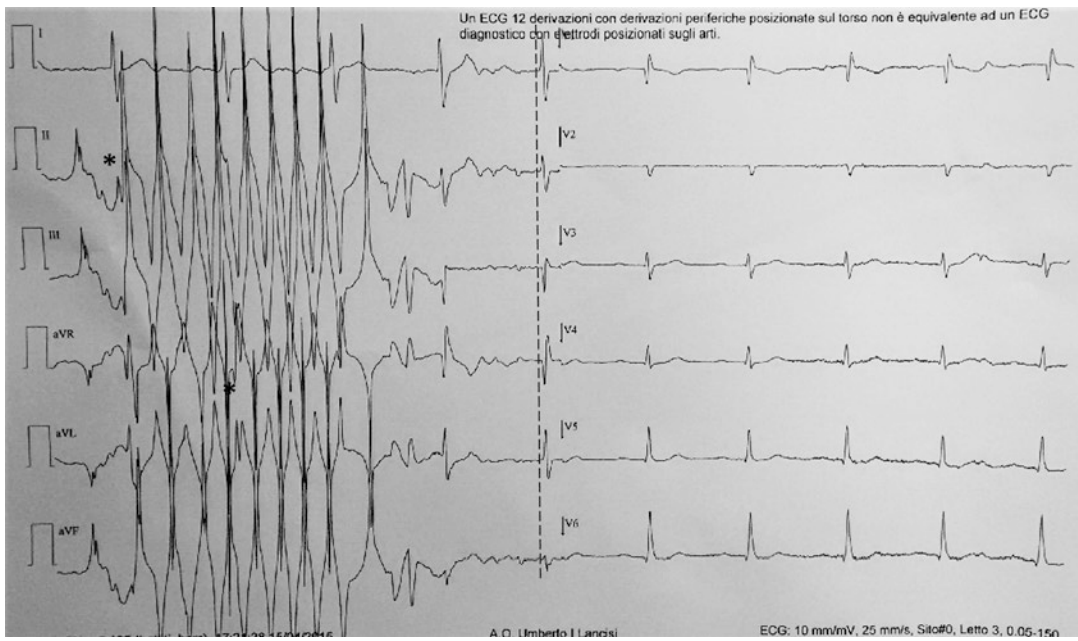

Fig. 17.3 Pseudo-VT

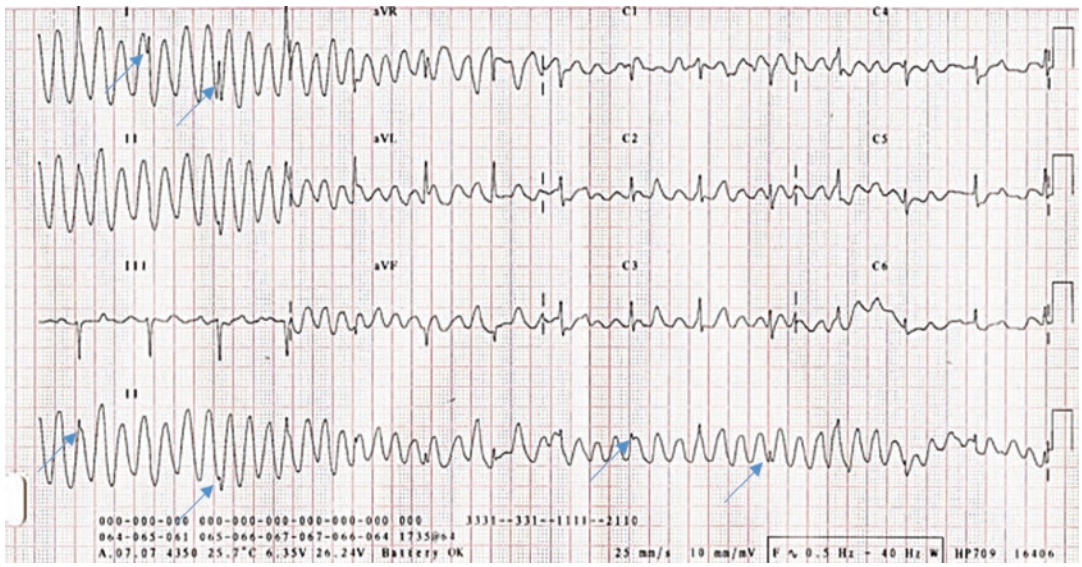

Fig. 17.4 Pseudo-VT with spike sign (reprinted with Springer permission from "Pseudo ventricular tachycardia: a case report" DOI: 10.1007/s11845-009-0387-4)

3. *Spike sign*: tiny "spikes" can be seen among the pseudo-ventricular tachycardia complexes, indicating the presence of real QRS complexes. In the ECG of Fig. 17.4, the limb leads, except lead III, show a rapid and irregular rhythm with a rate of up to 300 bpm. The QRS complexes show marked variability in amplitude, interval, morphology, and axis, resembling a torsades de pointes arrhythmia. On careful examination of the 12-lead ECG, it is obvious that this is a fake VT because lead III is spared and narrow QRS can be seen at regular intervals in the chest leads. Also, the diagnosis is aided by observing these tiny "spikes" (pointed by arrows on the figure), which are narrow QRS merged in the larger deflections falling exactly with the QRS of the other lead (dotted line).

17.3 Case 3

T. F., 51 years, previously implanted (*Jan 2017*) with a loop recorder for lightheadedness episodes and a family history of sudden cardiac death, is currently hospitalized in a near hospital because of ischemic left frontotemporal stroke. He came to our attention, with the suspect of a cardioembolic origin of the clinical event, and the loop recorder was interrogated.

There were many episodes classified as atrial fibrillation, but just at first glance something was wrong. See the trace below (Fig. 17.5).

17.3.1 ECG Analysis

The rhythm is clearly irregular, but an evident P wave precedes each QRS. In this short strip, PP intervals are different in duration: the PP interval after the pause is longer than the preceding one, and the pause is shorter than twice of the PP interval before the pause. P waves, QRS complexes, and T waves are reconstructed by the device and may be affected by individual chest variation and implant position.

The evidence of a P wave excludes atrial fibrillation. A possible interpretation could be therefore a sinus arrhythmia in a young subject enhanced by night vagal tone, but the presence of a II degree sinoatrial block with a Wenckebach phenomenon should also be considered in the differential diagnosis. Supraventricular bigeminism caused by a perisinusoidal focus can be excluded

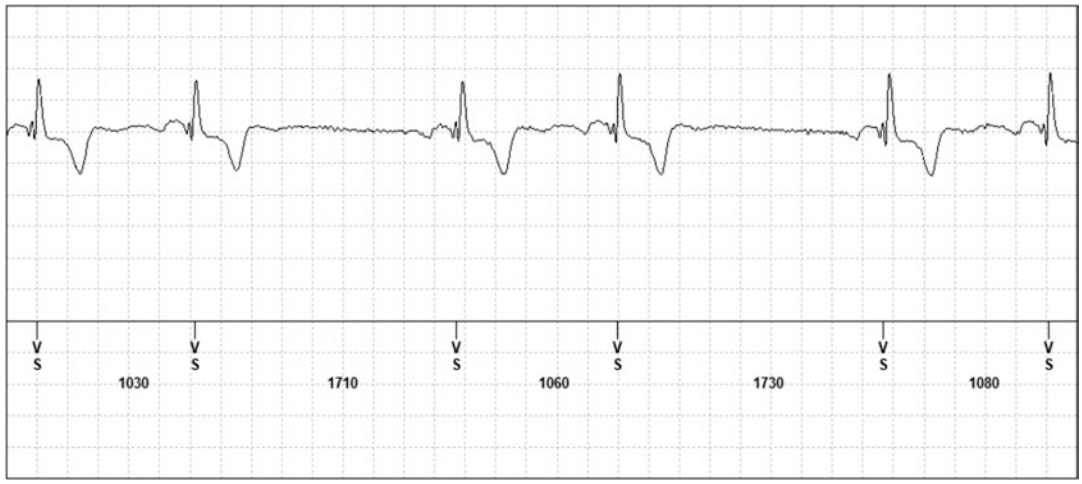

Fig. 17.5 Loop recorder trace

because of an extremely variable coupling interval during the all recording.

17.3.2 Artifacts Interpretation

The hallmark of atrial fibrillation interpretation is an irregularly irregular ventricular rhythm.

First-generation loop recorders discriminate atrial fibrillation occurrence on RR interval variation in a period of 2 min, and then the difference in consecutive RR intervals is reported in Lorenz diagram [4].

Other devices are endowed with exclusion algorithms that ignore ectopic beats and avoid atrial fibrillation misdiagnosis [5]. Another algorithm searches a P wave between two R waves combined with the previous mentioned methods [6]. The "smart atrial fibrillation detection" signs research evolution in this field, leading to about 50% false-positive reduction and preserving the 99.1% diagnostic sensibility [6]. Trademarks have obtained a high-quality signal in their devices which permits to distinguish artifacts (noise) from genuine ECG signals.

This is the result of multiple electrodes analysis and multiple vectors reconstruction leading to a reliable arrhythmia detection [7, 8]. Modern implantable devices record high-amplitude waves with a stable sensing, even in breathing tests or in body position changes, that it is of main importance for a precise ECG interpretation [9]. A main challenge for clinicians is to find reliable algorithms in implantable cardiac monitors that diagnose atrial fibrillation and quantify its burden [10]. The correct interpretation of this ECG trace avoided the initiation of an unnecessary anticoagulation therapy.

17.4 From ECG to Diagnosis

Artifacts are common during ECG monitoring in several clinical settings (e.g., ambulatory 12-lead ECG, telemetry during hospitalization, loop recorder devices, etc.). Despite ECG monitoring systems are widely used in common clinical practice, little is written in literature about possible pitfalls and errors. Pitfalls and errors are also more often present in emergency department where it could be much more dangerous, leading to wrong diagnosis and treatment [11]. There have been suggested two large categories of artifact sources in order to easily solve possible pitfalls: *internal and external artifacts sources* (Table 17.1) [12, 13].

One interesting algorithm was also proposed, by Baranchuk and colleague, to avoid misleading interpretations and systematically and carefully examine ECG traces: *R E V E R S E* (Table 17.2) [12].

Table 17.2 Reverse algorithm (modified from Baranchuk A. et al. [12])

	Finding of interest	Meaning
R	R wave is positive in lead a VR (P wave also positive)	Possible reversal of left arm and right arm electrodes
E	Extreme axis deviation: QRS axis between +180° and −90° (negative R wave in lead I, positive R wave in AVF)	Possible reversal of left arm and right arm electrodes
V	Very low (<0.1 mV) amplitude in an isolated limb lead (isolated "flat" lead)	Possible reversal of right leg and left arm or right arm electrodes
E	Exchanged amplitude of the P waves (P wave in lead I greater than in lead II)	Possible reversal of left arm and left leg electrodes
R	R wave abnormal progression in the precordial leads (predominant R wave in V1, predominant S wave in V6)	Possible reversal of precordial electrodes (V1 through V6)
S	Suspect dextrocardia (negative P waves in lead I)	Possible left arm-right arm electrode reversal
E	Eliminate noise and interference (artifact mimicking tachycardias or ST-T changes)	

Stop patient's tremors and match ECG with clinical findings. A very simple and effective technique to solve diagnostic dilemmas particularly on the suspicion of a wide QRS tachycardia is to mark the RR intervals preceding the false arrhythmia and extend the marks to the underlying spontaneous QRS hidden within the wide deflections.

The ECG monitoring systems changed the physicians' way to operate. These devices allow a complete rhythm monitoring but sometimes need a specific interpretation skills. An incorrect analysis could be inherent to the monitoring system itself. That is only a tool in the physician hands, not the opposite. A mere acquiescence of the "machine diagnosis" could be harmful by directing medical efforts toward incorrect strategies. Clinical practice should guide more and more the engineer research in solving the unmet issues, overcoming pitfalls of the traces interpretation. We must always treat patients and not their ECG.

Special thanks to Dr. Enrico Rita for the support on this chapter

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Check for updates

18 Basic Paediatric ECG Interpretation Principles

Silvia Cesini, Mirko Beltrame, Simone D'Agostino, Agnese Fioranelli, and Roberto Ricciotti

18.1 Case 1

A 13-year-old male went to paediatrician for fatigue and palpitation during effort.

A 12-lead ECG was recorded (Fig. 18.1).

18.1.1 ECG Analysis

In Fig. 18.1 there is a narrow complex tachycardia, with a mean heart rate of 200–250 bpm. The RR intervals are not regular. P waves are not clearly recognizable. The rhythm is therefore atrial fibrillation.

The mean QRS axis in the frontal plane is −30° (LAH).

A clockwise rotation is also present in the horizontal plan. The frontal plane initial QRS vector (Q wave), which represents the septal activation, is directed to the left and superiorly in the frontal plane and leftwards and slightly anteriorly in the horizontal plan.

The right precordial lead V1 has a QS pattern, while V6 has an RS morphology. The right precordial leads V2–V4 have an RS morphology. There is therefore an inversion of the normal precordial pattern.

A QS pattern is also present in III and VF.

QRS duration is 80 ms.

ST segment is almost isoelectric, and T waves are positive in all the peripheral leads except for VR and VL and isodiphasic in lead I. T waves are also positive in all precordial leads.

The T vector is directed anteriorly, inferiorly and slightly leftwards (+85°). The magnitude of T wave voltage is 1.3 mV in V2, while it is 0.3 mV in V6.

The main ECG elements to the correct diagnosis are the inversion of the normal precordial pattern with Q waves in right precordial leads; QS or QRS pattern in II, III and VF; left axis deviation and positive T waves in all precordial leads.

These signs are a typical pattern of a corrected transposition of the great arteries (CTGA) [1].

The clinical diagnosis was confirmed at 2D echocardiography (Fig. 18.2).

Amiodarone iv (5 mg/kg) was administrated with return to sinus rhythm within 2 h (Fig. 18.3).

18.1.2 From ECG to the Pathology

- *Septal activation*. Ventricular depolarization normally starts from the septal endocardial surface, generating a vector-directed anteriorly and rightwards. In the CTGA the ventricular

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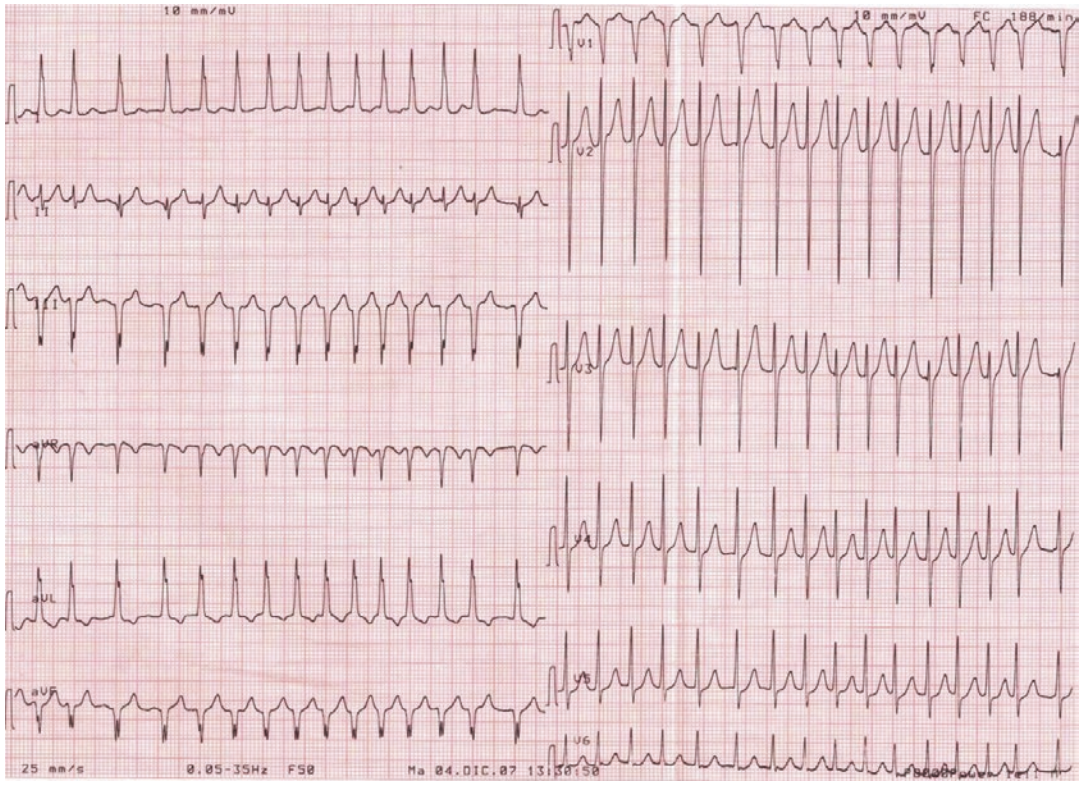

Fig. 18.1 Case 1 12-lead ECG

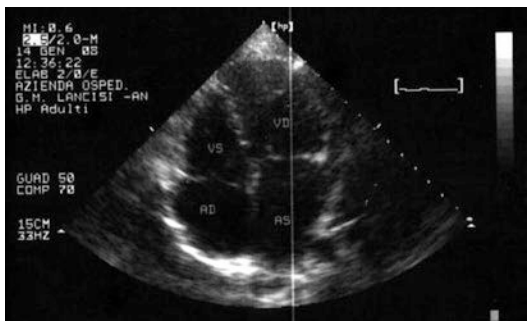

Fig. 18.2 Echocardiography

activation starts instead from the anatomical left side of the septum, which is located at the right because of the ventricular inversion that characterizes this pathology. The resulting vector is oriented leftwards, anteriorly and almost always superiorly. That is the reason why the physiologic Q waves in the left precordial leads and in VL and I are not present; on the contrary they are in the right precordial leads. There is inversion of the normal precordial QR pattern [1–3].

- *QRS axis*. QRS axis is typically left and superiorly oriented. Leads III and VF usually have a QR or QS morphology, because of the orientation of the septal vector. Left deviation of the axis is also secondary to overload of the left-sided systemic ventricle due to a usual tricuspid insufficiency. An ECG pattern suggestive of systemic ventricular hypertrophy (left-sided right ventricle) with strain may be present [4].
- *T waves* are positive in all precordial leads in more than 80% of patients, because of the anterior direction of T axis; also T wave magnitude voltages are usually higher in the right leads. The T loop anterior orientation is probably due to the position of the venosus ventricle (morphologically the left ventricle), which plays an important role in the determination of the orientation of the T loop [3].

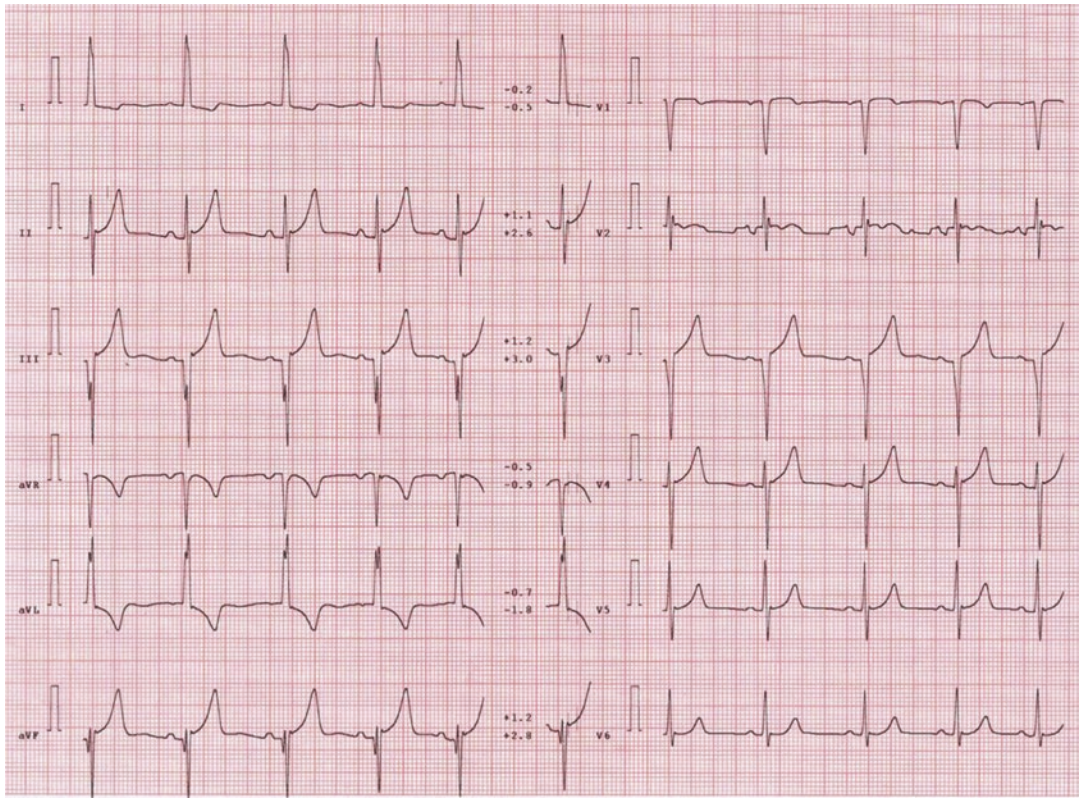

Fig. 18.3 Case 1 12-lead ECG after infusion of amiodarone iv

- *Rhythm disturbance*. AV blocks and atrial arrhythmias are frequent. The AV nodal tissue in patients with CTGA is abnormal and potentially unstable [2].

Congenitally corrected transposition of the great arteries is a rare defect representing approximately 0.5% of all congenital heart disease. CTGA is characterized by the combination of atrioventricular (AV) discordance and ventriculoarterial (VA) discordance, usually accompanied by other cardiovascular malformations [5–7].

There is usually normal drainage of the systemic and pulmonary veins to the right and left atrium, respectively.

Left atrium connects to the morphological right ventricle via the tricuspid valve. The right ventricle in turn connects to the aorta supplying the systemic circulation. The right atrium connects to the morphological left ventricle via the mitral valve. This ventricle supplies the pulmonary circulation via the pulmonary artery. The ventricles are most commonly side by side.

Associated malformations may include interventricular communications, obstructions of the outlet from the morphologically left ventricle and anomalies of the tricuspid valve.

The *clinical presentation* and age of onset are variable and largely based on the associated malformations. Patient with isolated CTGA could be asymptomatic and may be referred to cardiologist because of bradycardia. At clinical examination, it is usually audible, a single loud second heart sound and a heart murmur.

In the rare cases where there are no associated malformations, CTGA may be diagnosed late in life due to symptoms related to systemic right ventricular dysfunction or complete heart block [8]. Diagnosis is commonly made on clinical signs and echocardiography.

Magnetic resonance imaging and catheterization could be performed for better anatomic definition. Surgical management consists of repairing of the associated malformations or redirection of the systemic circulation and pulmonary venous return with the double arterial switch approach [7].

Prognosis depends on the associated malformations and on the timing and approach to palliative surgical care.

18.2 Case 2

ECG in Fig. 18.4 belongs to a 1-day-old male patient born at 40th week +4 days with urgent

c-section for prenatal detection of a tachyarrhythmia. At birth, he showed clinical signs of heart failure.

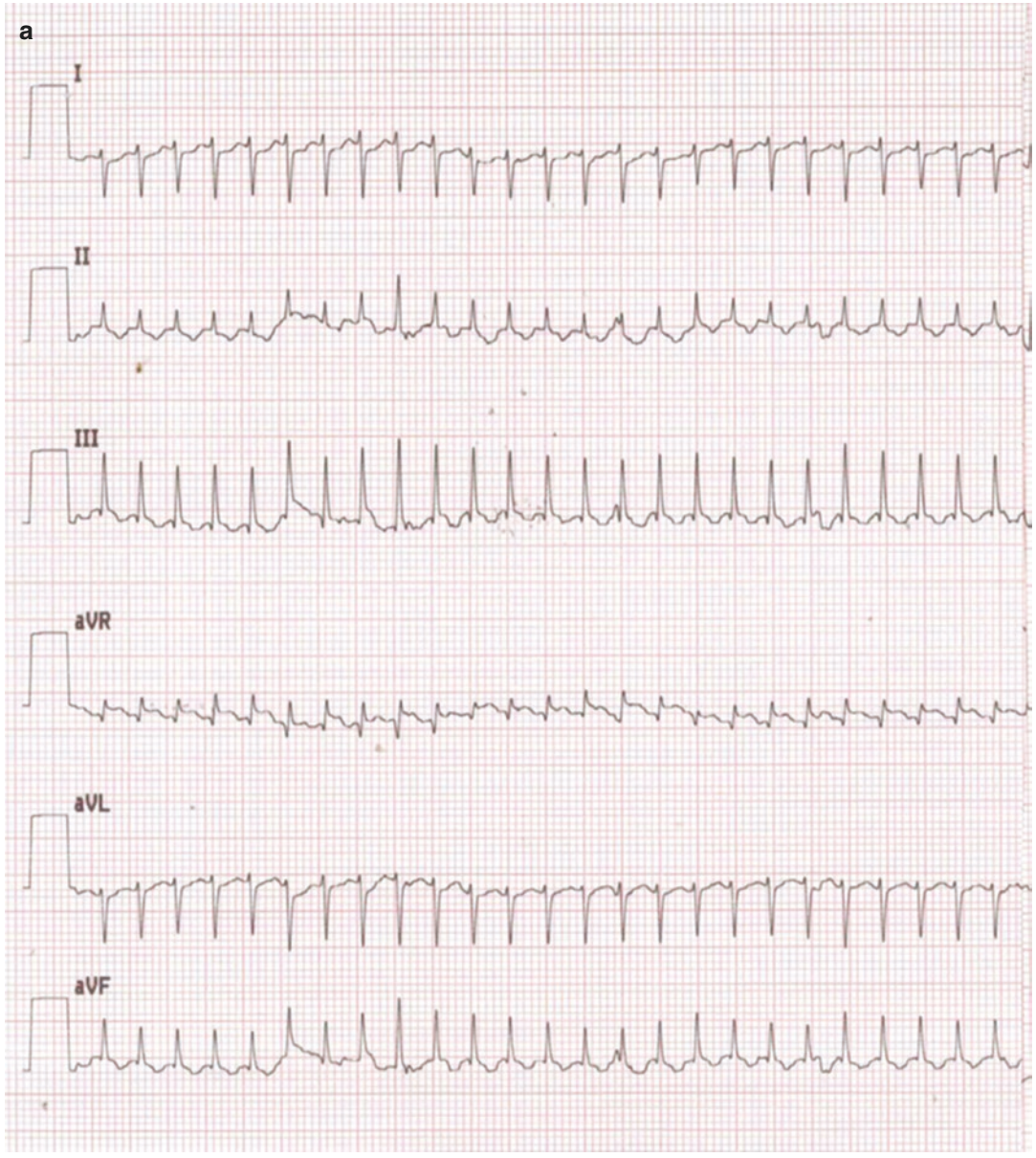

Fig. 18.4 (**a**, **b**) Case 2 12-lead ECG (during tachycardia)

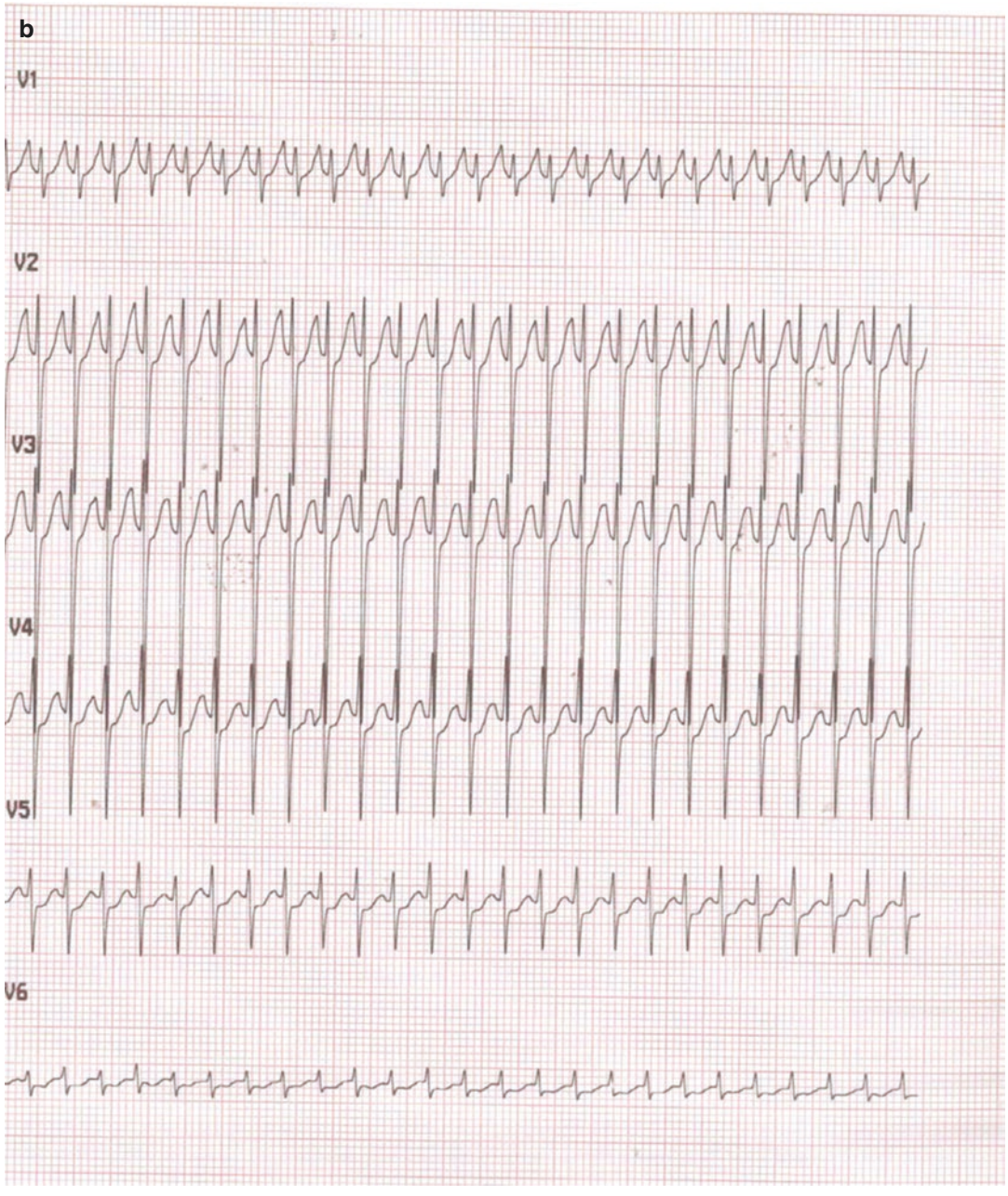

Fig. 18.4 (continued)

18.2.1 ECG Analysis

The ECG shows a narrow complex tachycardia with a mean heart rate of 300 bpm. The RR intervals are regular (200 ms).

We cannot observe definite P waves preceding the QRS complexes in any lead. In the peripheral leads and in V1, notches are visible inside the proximal branch of T waves. These notches can be compatible with a P wave. If these are P waves, the RP lasts about 100 ms. In that case there is also a constant relationship between QRS and P with a 1:1 conduction.

QRS axis in the frontal plane is oriented rightwards and inferiorly (+120°). QRS length is 60 ms. There is ST depression in anterolateral

leads; T waves are negative in inferior leads. These repolarization patterns are secondary to tachycardia.

This is a case of supraventricular tachyarrhythmia with regular RR intervals. But what is the mechanism?

Possible different diagnoses are:

- *Atrial flutter*. In this type of arrhythmia, atrial rate is usually 300–350 bpm; therefore it could be an atrial flutter with 1:1 conduction. Typically F waves are visible before QRS complexes, and irregular RR intervals due to AV conduction variability (2:1; 3:1) are also usually present. Thus atrial flutter is a possible mechanism.
- *Atrial tachycardia*. Generally, in this arrhythmia atrial rate is <200 bpm, and P waves are recorded before the QRS complexes. For these reasons that is an unlikely diagnosis.
- *Junctional tachycardia (JT)*. That is unlikely because of the long RP interval and the high heart rate. Usual automatic tachycardias in the infant have a lower heart rate (200–220 bpm), and P waves should be visible before or immediately after the QRS complexes.
- *Atrioventricular node re-entry tachycardia (AVNRT)*. This option cannot be completely excluded, but an attent analysis of P waves and RP interval lengths does not lead towards that direction. In the present case, RP interval is 100 ms, while typically in AVNRT RP interval is shorter than 70 ms. Another important element is the axis of retrograde P wave that in AVNRT is usually directed towards −90°.
- *Atrioventricular re-entry tachycardia (AVRT)*. Typically in this type of re-entrant tachycardia, there is a retrograde P wave following the R wave with a long RP interval (>70 ms). P axis varies in relation to the accessory pathway location [9].

  In the present ECG, P waves are visible within the T waves with an RP interval longer than 70 ms, but we can't define exactly the P axis because the waves are not well visible. This RP interval of 100 ms is therefore suggestive for an AVRT.

After ineffective carotid sinus massage and adenosine iv, a propafenone iv bolus (2 mg/kg/5 min infusion) was administrated with prompt return to sinus rhythm (Fig. 18.5).

The ECG in Fig. 18.5 shows the sinus rhythm; there are regular RR intervals (440 ms); heart rate is 140 bpm. P wave is positive in leads I, VL, II, III and VF and negative in VR. P axis is +45° (normally oriented). PR interval is only 80 ms, and there is a clear delta wave that is positive in V1–V5 and negative in the inferior leads. Delta wave axis is thus directed leftwards and superiorly. QRS duration is 80 ms, with an axis of −120°. QRS transition (R/S >1) in precordial leads is in V1. Ventricular repolarization is normal. QT interval is 280 ms and QTc 428 ms.

This ECG shows therefore a sinus rhythm with evidence of ventricular pre-excitation due to an accessory pathway located in the left posterior septal region (delta axis in left superior quadrant; QRS transition in V1). AVRT diagnosis was confirmed, and the initial possible atrial flutter hypothesis was rejected.

Few days later another 12-lead ECG (Fig. 18.6) was recorded:

Sinus rhythm with heart rate 110 bpm. P wave axis is normal. PR interval is 160 ms. Delta waves are not visible anymore. QRS length is 70 ms; QRS axis is 120°. Ventricular repolarization is normal. QT interval is 340 ms with a QTc of

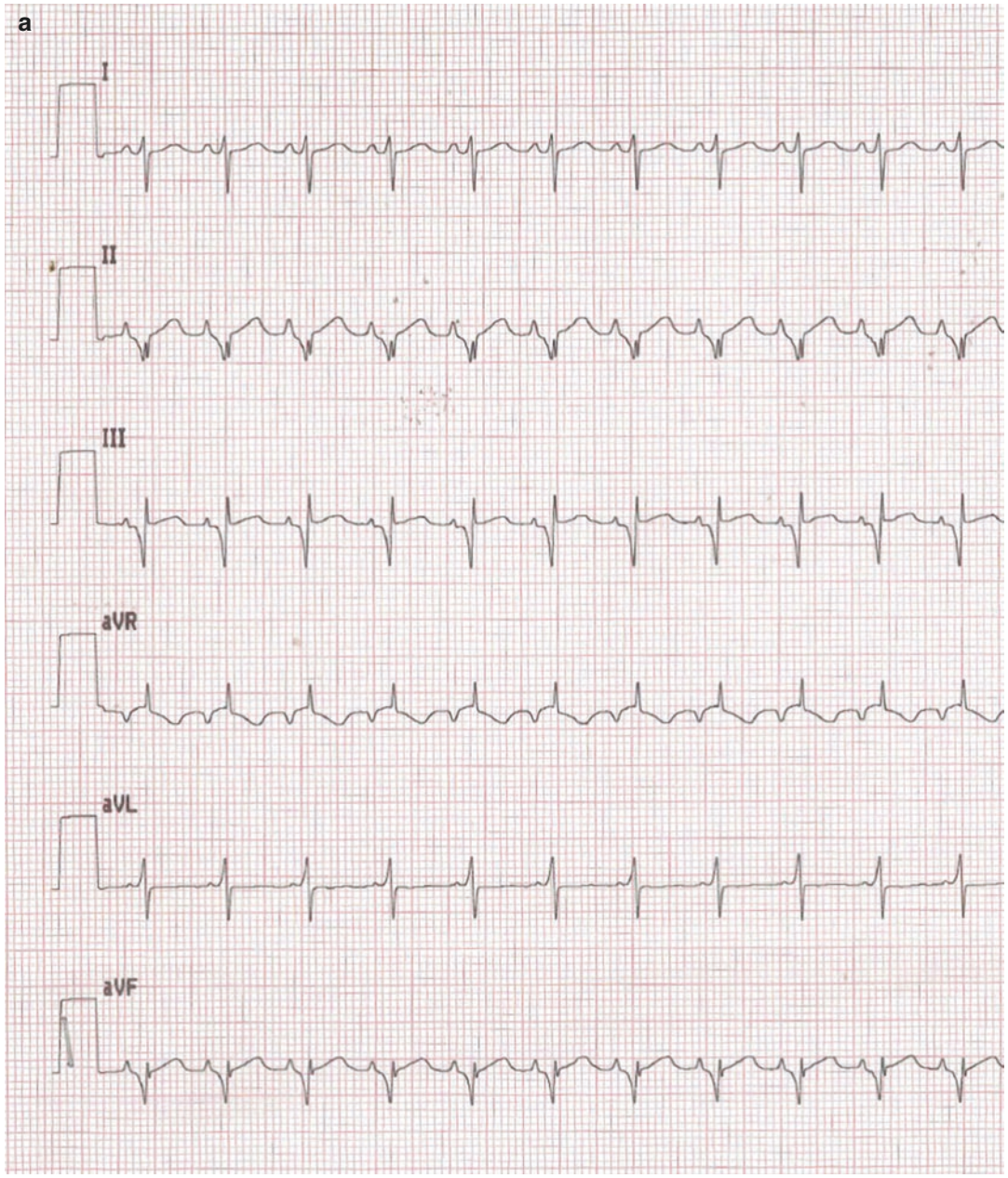

Fig. 18.5 (**a**, **b**) Case 2 12-lead ECG after infusion of propafenone iv

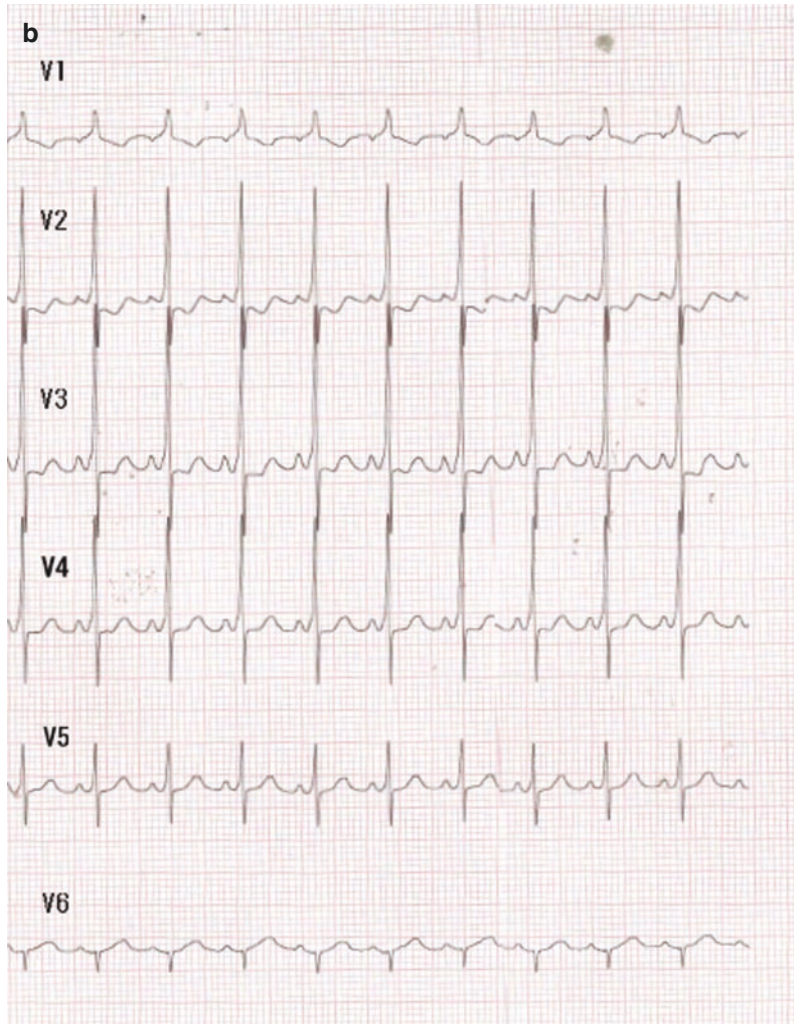

Fig. 18.5 (continued)

460 ms (longer compared to the previous recording).

This is a sinus rhythm with no evidence of ventricular pre-excitation. This is a case of intermittent pre-excitation.

18.2.2 From ECG to the Pathology

Supraventricular tachycardias are relatively common in infants with an incidence of 1:1000 [9]. The vast majority of SVT are due to accessory pathways (WPW syndrome). At 1–2 years of age, more than half of the pathways spontaneously regress, and the SVT become no more inducible.

The autonomic cholinergic innervation prevalence during early life might enhance conduction velocity via bypass tracts and generates AVRT. Later, after 2 years of age, the adrenergic autonomic innervation emergence may decrease the frequency of arrhythmias.

Chronic treatment is based on Class I antiarrhythmic drugs.

A transoesophageal electrophysiological study may be performed, at the beginning of treatment, when the drug steady state is reached, to test the oral drug prophylactic efficacy.

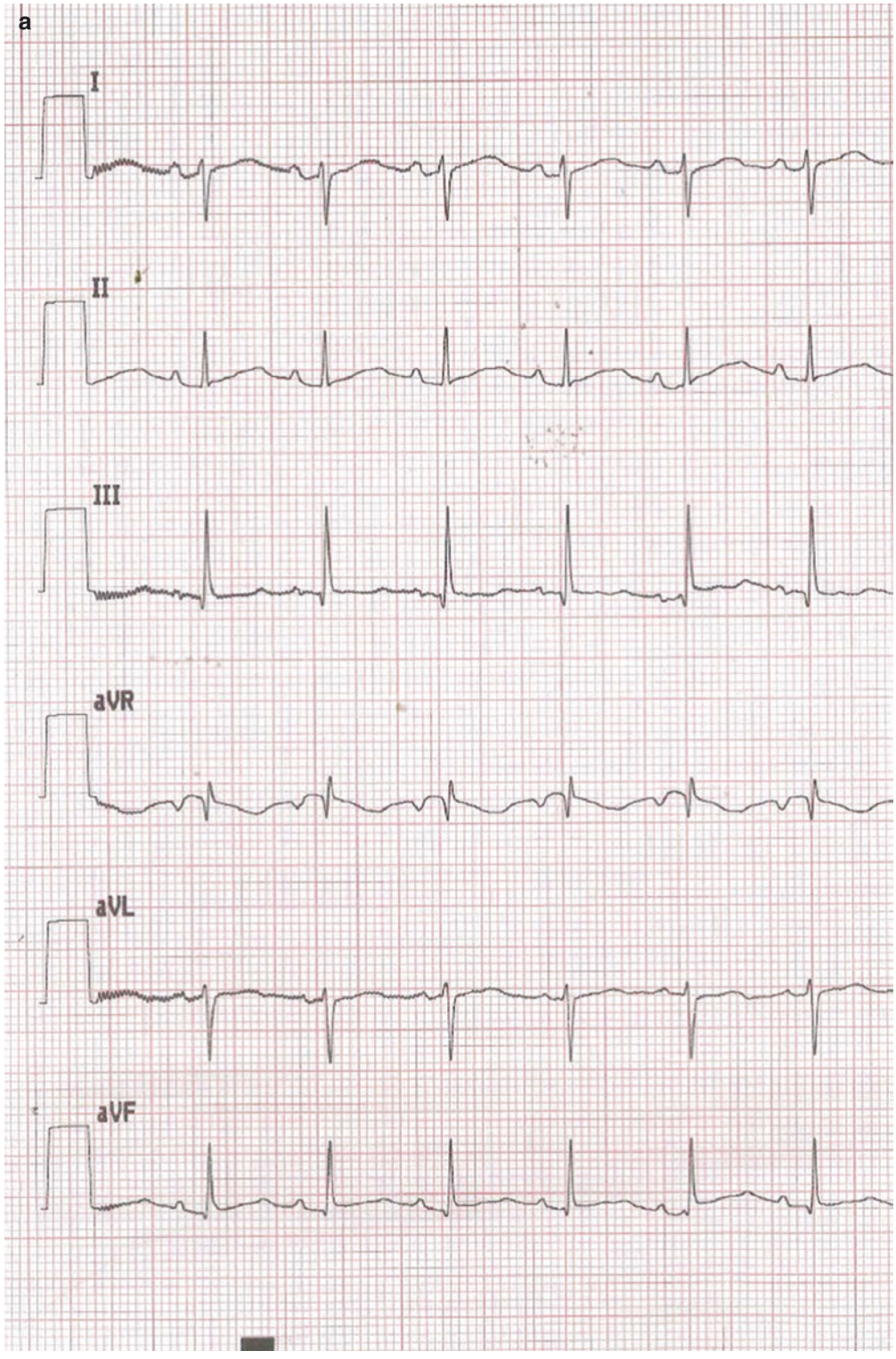

Fig. 18.6 (**a**, **b**) Case 2 12-lead ECG, few days later

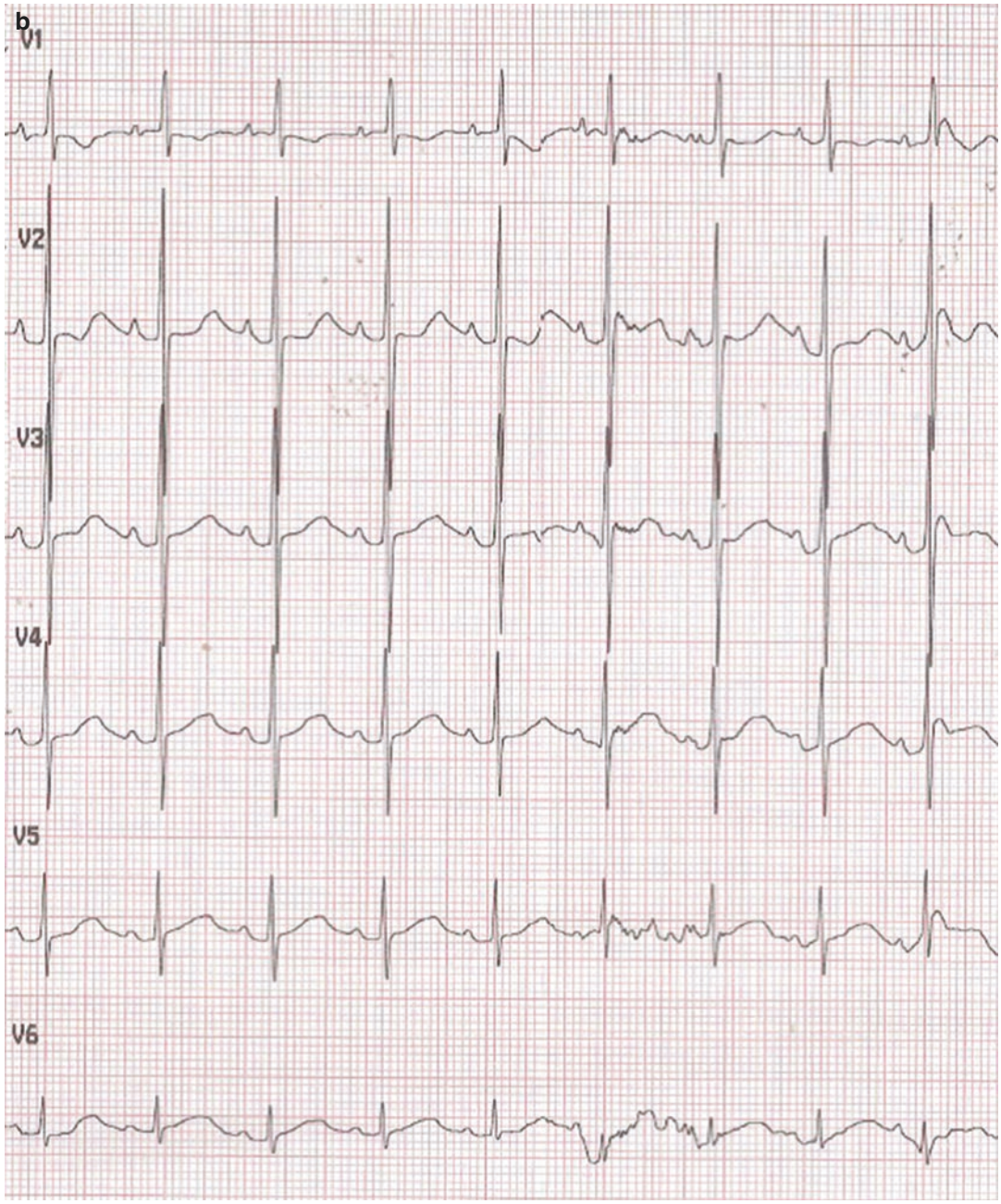

Fig. 18.6 (continued)

A prophylactic treatment must be continued for the following years, until transcatheter ablation that is usually indicated at adult age [10].

18.3 Case 3

A 6-month-old male patient referred to physician for dyspnoea and fatigue.

18.3.1 ECG Analysis

A standard 12-lead ECG was performed (Fig. 18.7): the rhythm is sinus, with 135 bpm.

P wave is positive in all leads while negative in VR. P axis is normal. P waves have high voltage in I, II and VF. PR is 80 ms. The QRS axis is −30°. QRS length is 60 ms.

There is an incomplete right bundle branch block (RR morphology in V1) and a left anterior fascicular hemiblock (QRS in I and VL; RS in III and VF). T wave is negative in leads V1-V2-V3. QTc is 440 ms.

A normal ECG recorded at 6 months of age had a heart rate between 105 and 180 bpm.

Usually QRS axis is vertical; in the precordial leads, there are higher R waves in V6 than in V1, because of a gradual increase of R voltage in the left precordial leads, compared to the neonatal ECG. The R/S ratio in V1 is 1.5 on average. Negative T waves in right precordial leads are to be considered a normal pattern.

In this case, therefore, the atypical elements are left QRS axis deviation, presence of an incomplete right bundle branch block and indirect signs of a right atrial enlargement.

Possible different diagnoses are therefore:

- *Tricuspid atresia*. It is a congenital disease, characterized by right atrial enlargement with left QRS axis deviation. Axis deviation is caused by stretching of the anterior fascicular branch, secondary to left ventricular dilatation and hypertrophy, since the ventricle must support both pulmonary and systemic circulations. The absence of the right ventricular forces (therefore predominantly negative QRS in right precordial leads) is due to the right ventricular hypoplasia. In the current ECG, there are prominent R waves in right precordial leads and little R waves in V5–V6, so this is not quite typical for that pathology [1].
- *Atrioventricular canal defect*. In patients with AVCD, the most characteristic electrocardiographic findings are leftwards and superior QRS axis deviation, caused by posterior displacement of the atrioventricular node and His bundle [11]; right atrial enlargement due to shunting from the left atrium to right atrium; prolongation of PR interval in some patients with atrial enlargement; and increase conduction time [12]. RV

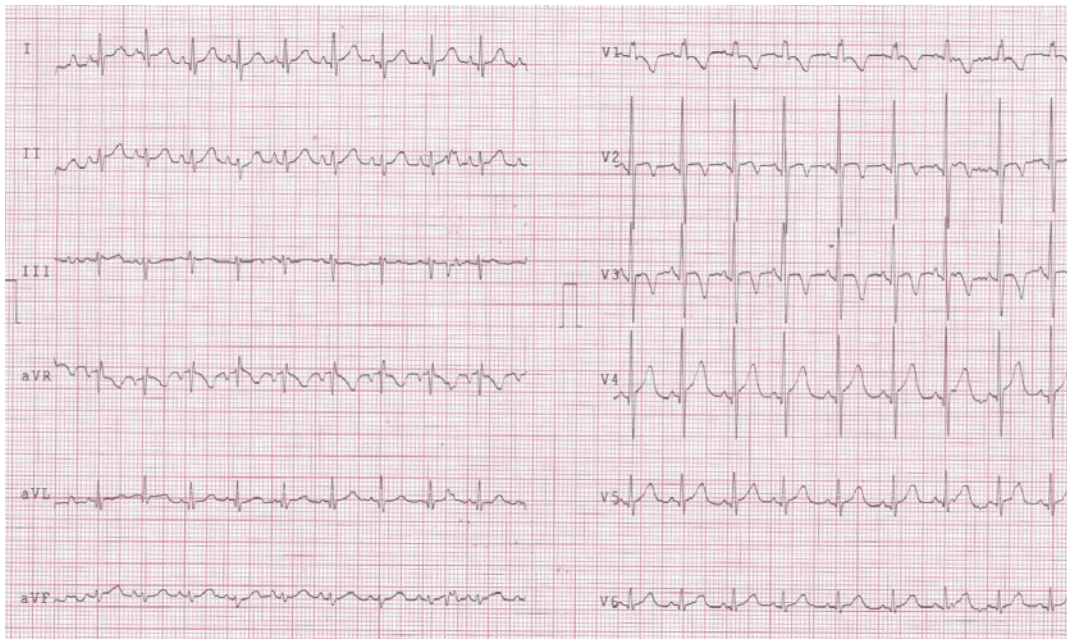

Fig. 18.7 Case 3 12-lead ECG

volume or pressure overload reflected as an rsR' pattern in the right precordial leads (incomplete right bundle branch block) is also usually present.
Based on ECG characteristics, the diagnosis of atrioventricular canal defect is therefore the most likely in this case.

At 2D echo the diagnosis of partial AV canal was confirmed.

18.3.2 From ECG to the Pathology

AV canal defects account for about 4–5% of congenital heart defects with a reported prevalence of 0.3–0.4 per 1000 live births [13, 14].

There is a strong association between AV canal defects and trisomy 21 (also referred to as Down syndrome), with a 40–50% risk of Down syndrome in new-born in whom an AV canal defect is detected [15]. Non-syndromic AV canal defects appear to be associated with maternal diabetes and obesity [16].

AV canal defects are classified into two forms: complete and partial.

- Complete atrioventricular canal is characterized by an ostium primum atrial septal defect, a common atrioventricular valve and ventricular septum defect.
- Partial AV canal consists of atrial septal defect (ostium primum) but without a direct intraventricular communication. Furthermore, anterior leaflet of the mitral valve typically is cleft. There is left-to-right shunting through atrial septal defect; this causes volume overload of the right atrium and ventricle and pulmonary overcirculation. However pulmonary artery pressures are usually normal to mildly elevated.

Symptoms may remain minimal until adulthood, when a reduced LV compliance leads to increase interatrial shunting and potential heart failure [17]. Some patients may have symptoms related to excess pulmonary blood flow, especially during exertion, such as shortness of breath, and they could present atrial fibrillation because of a right atrial enlargement or a mitral regurgitation. Asymptomatic patients may be identified during a routine physical examination because of the ECG pattern. A left axis deviation of QRS above −30°, usually together with a right bundle branch block, appears to be suggestive of AVC. Echocardiography is key examination for the final correct diagnosis.

18.4 Case 4

This previously healthy 8-month-old male was admitted to ER because of hypotension and asthenia. He presented signs and symptoms of heart failure.

18.4.1 ECG Analysis

The ECG (Fig. 18.8) shows a wide QRS tachycardia. Heart rate is 215 bpm. RR intervals are regular (RR 280 ms). P waves are clearly visible in all leads especially in I, after the 1st and 9th QRS complex inside T waves and immediately before the 13th complex. There is therefore an atrioventricular dissociation since it does not exist any correlation between P waves and QRS complexes.

QRS duration is 100 ms. QRS axis is about −60° (left deviation). QRS morphology has a right bundle branch block (monophasic R in V1).

The QRS complexes in the precordial leads were not concordant; RS complexes are visible in V5–V6.

In lead V1 the QRS has a monophasic R morphology and in V6 an RS morphology.

The initial diagnosis was mistaken for a paroxysmal atrial tachycardia with Wolff-Parkinson-White syndrome, because of the bizarre QRS complexes with a shape very similar to delta wave.

Transoesophageal electrical recording was performed mainly for diagnostic reason; then firstly adenosine (suspicion of an aberrant supraventricular tachycardia) and then vera-

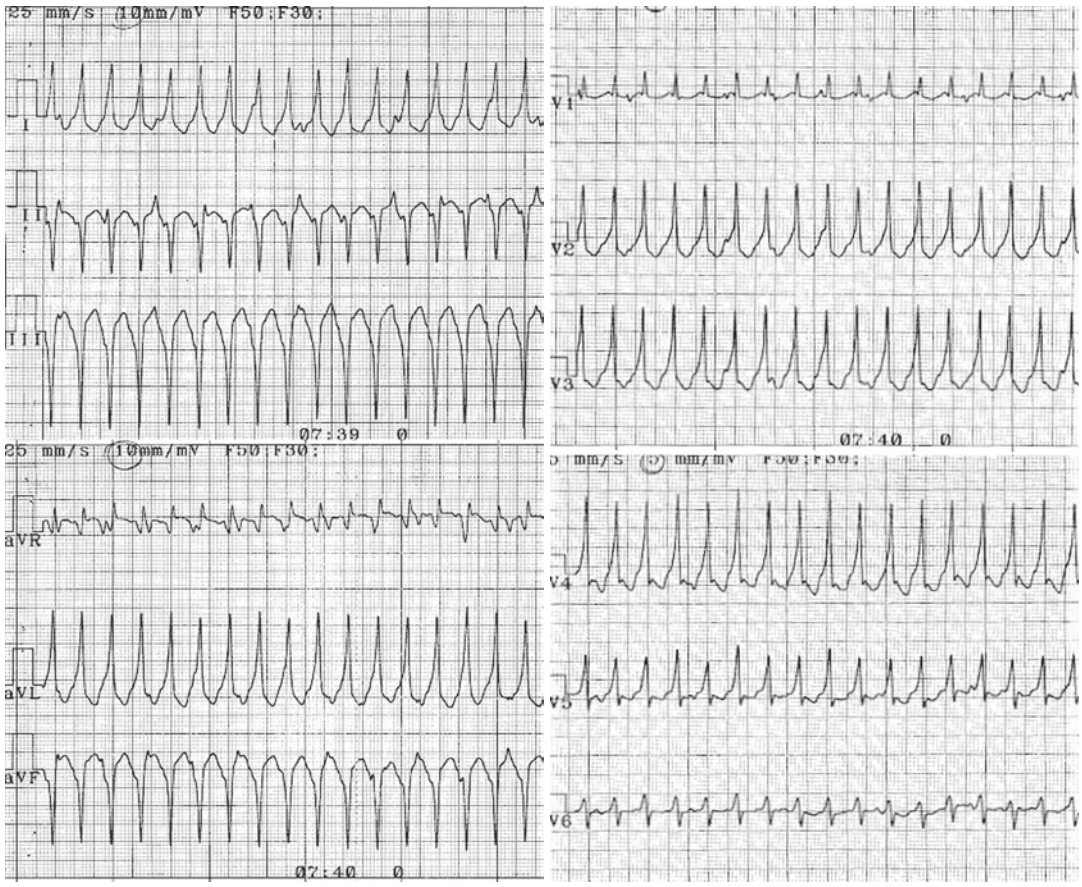

Fig. 18.8 Case 4 12-lead ECG (*speed*: 25 mm/s; *calibration*: 10 mm/mV in peripheral leads, 5 mm/mV in precordial leads)

pamil (suspicion of an idiopathic left ventricular tachycardia for the right bundle branch block and left axis deviation pattern) were injected. The tachycardia did not respond to medical therapy, and therefore an electrical cardioversion was performed that also failed to restore a stable sinus rhythm.

Administration of iv amiodarone was lastly successful: the rhythm instability decreased from constant VT to runs of non-sustained ventricular tachycardia (VT) with evidence of fusion beats (Fig. 18.9).

A retrospective ECG analysis underlines the presence of an atrioventricular dissociation during tachycardia (Fig. 18.10).

The electrical cardioversion failure suggested that the electrophysiological mechanism was likely to be automatism more than re-entry.

Heart failure was thus secondary to the constant high heart rate, and it regressed completely after tachycardia resolution.

Nuclear cardiac magnetic resonance showed in the left ventricle a non-compacted area, localized mostly in the inferior ventricular wall. This site corresponds to the origin of tachycardia as suggested by the bundle branch block configuration on the surface ECG and the negative QRS in inferior leads.

At 5 years of age, in washout from prophylactic therapy (at first amiodarone was given for a few months and nadolol later), he underwent an electrophysiological ventricular stimulation that showed ventricular stability. Now he is under treatment with angiotensin-converting enzyme inhibitors because of left ventricle's mild dilatation and remodelling, with still a normal systolic function.

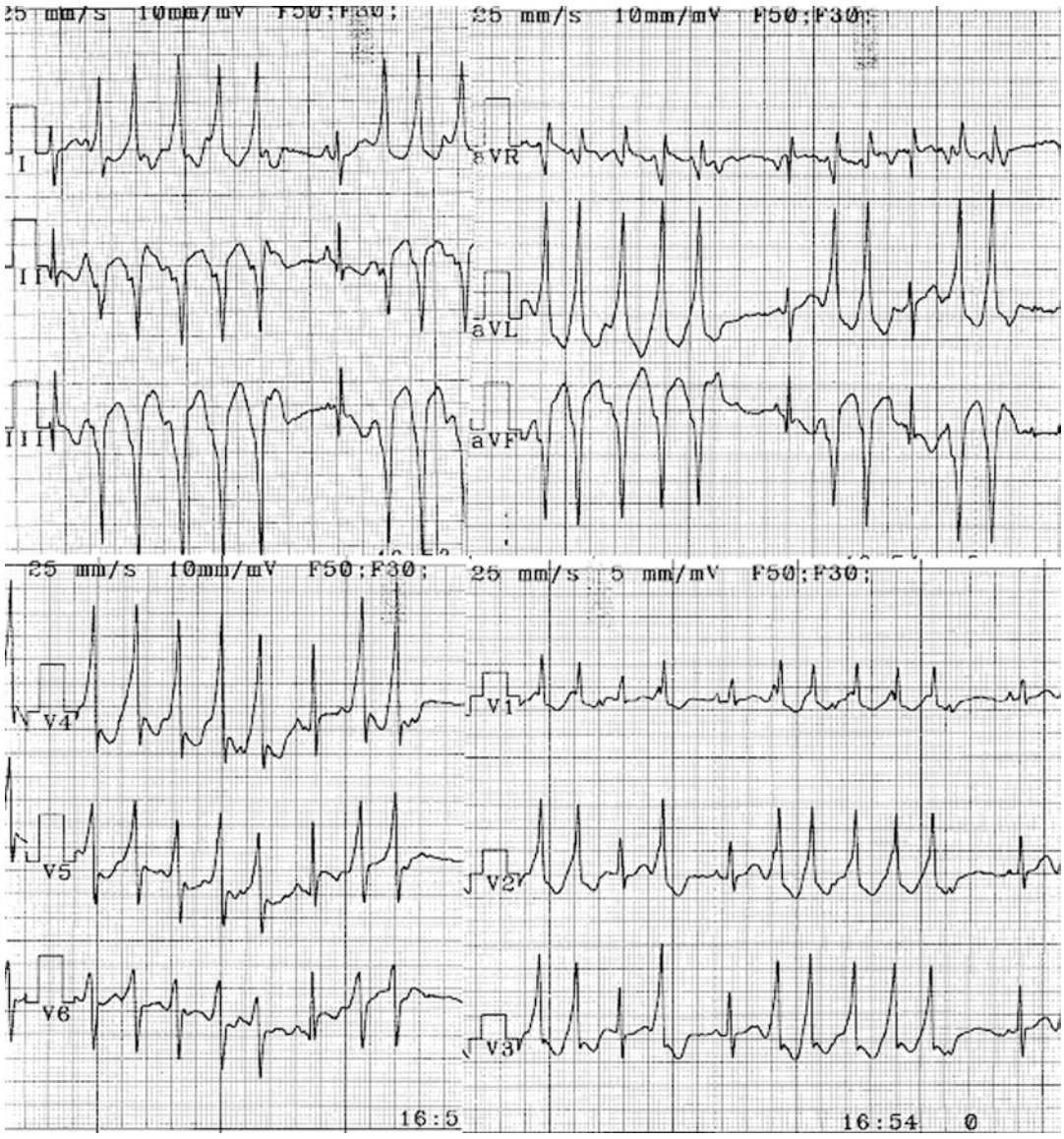

Fig. 18.9 Case 4 12-lead ECG after amiodarone iv infusion

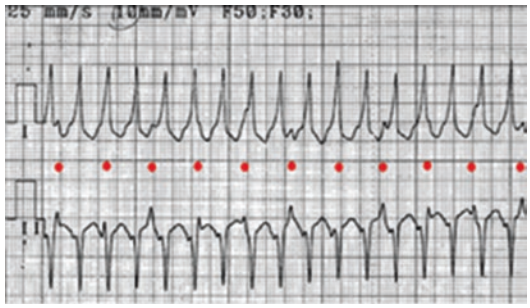

Fig. 18.10 Evidence of atrioventricular dissociation (red points mark dissociated P waves)

The patient did not have any clinical VT recurrence, and there was not any progression of the myocardial disease. Nowadays, at 10 years of age, he is fully asymptomatic.

18.4.2 From ECG to Pathology

Ventricular tachycardia is rare in children.

There are just few case reports in the first year of life.

The most frequent forms of VT in infancy are idiopathic VTs, catecholaminergic polymorphic VTs and VTs secondary to congenital heart disease, myocarditis, cardiomyopathy and heart tumours.

Early VT onset in infancy with a monomorphic morphology has usually a successful spontaneous arrhythmia resolution during growth [18].

Proper diagnosis and a correct treatment may contribute to improving the outcome.

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