Adolescente assintomático com fortes antecedentes de morte súbita em familiares jovens de primeiro grau

Asymptomatic adolescent with strong history of sudden death in young first-degree relatives

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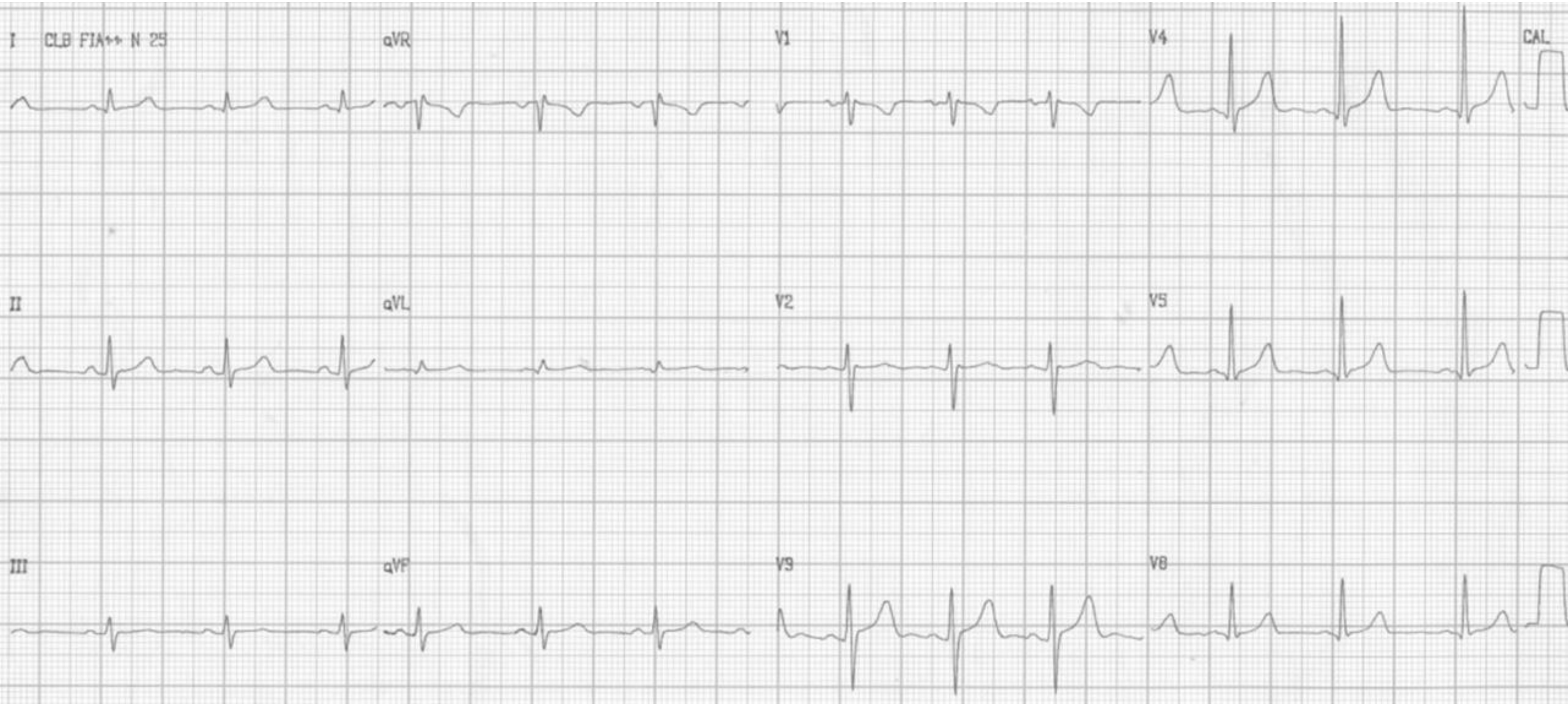
Bom dia maestro Andrés
Gostaria de ouvir a opinião dos colegas sobre este caso. Trata-se de um adolescente de 13 anos, assintomático (joga futebol) com importante história familiar de morte súbita(pai sofrera morte súbita aos 28 anos no banheiro, irmã aos 9 anos durante o sono e um irmão com 17 anos). Este último, foi realizada uma autopsia que revelou anomalia na artéria coronária direita(em anexo relatório do estudo).
ECO normal;
Holter normal.
Adjunto 2 ECGs.
Pergunta: Quais seriam os próximos passos adequados a serem seguidos num caso como este?
Um abraço
Raimundo Barbosa-Barros M.D. Fortaleza Brasil

English

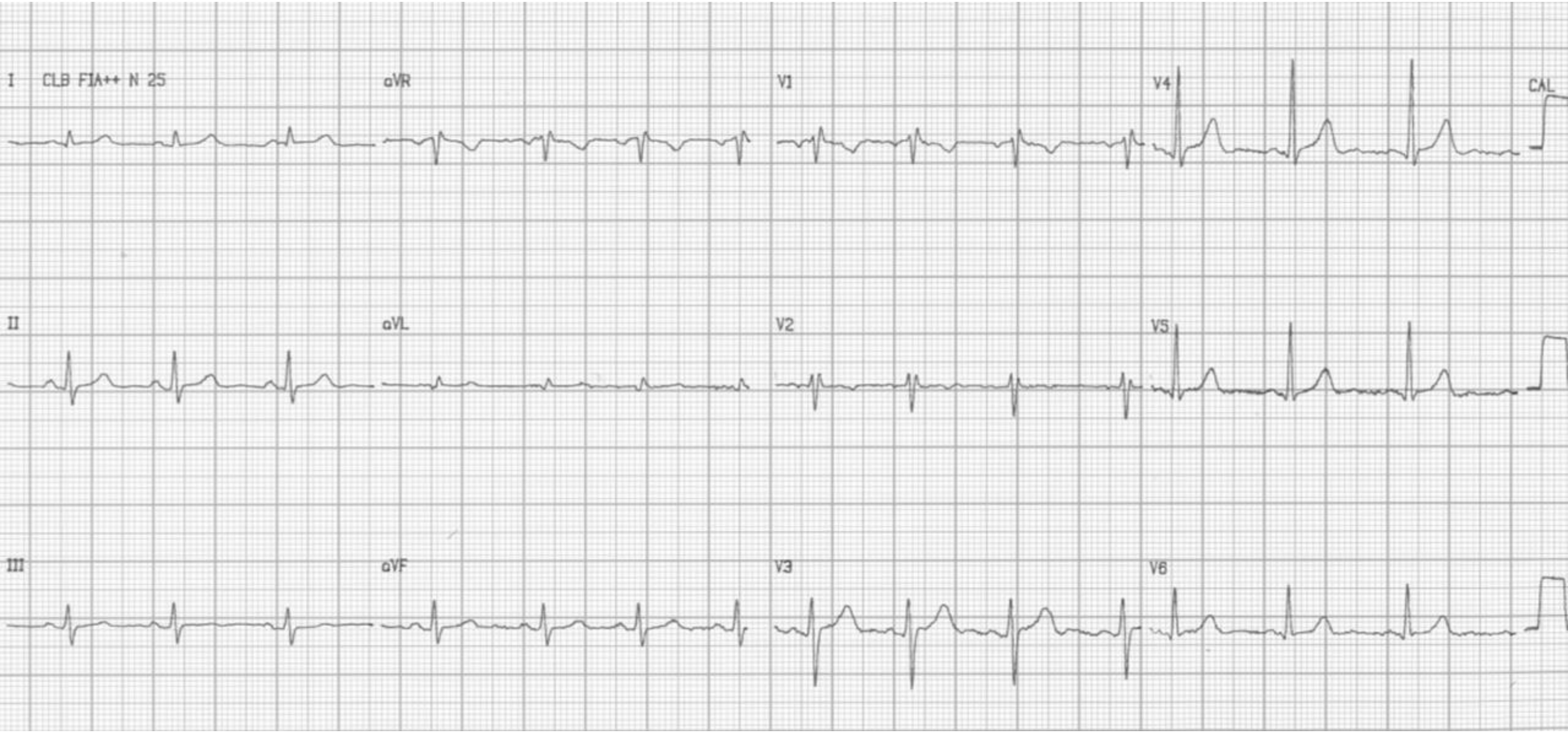
Good morning master Andrés
I would like to hear the opinion of colleagues on this case. This is a 13 year old, asymptomatic (playing football) with a strong family history of sudden death (father suffered sudden death at age 28 in bathroom, sister to 9 years during sleep and a brother aged 17). The latter, an autopsy was performed that showed abnormality in the right coronary artery (attached report of the study).
Normal ECO;
Normal Holter.
Deputy 2 ECGs.
Question: What would be the next appropriate to follow steps in a case like this?
a hug

Raimundo Barbosa-Barros M.D. Fortaleza Brazil

ECG-1 CONVENTIONAL 12-LEAD



ECG-2 MODIFIED PRECORDIAL LEADS: RIGHT PRECORDIAL LEADS AT HIGHER INTERCOSTAL SPACE POSITIONS: V_{1H}-V_{2H}-$V_{3H;}$



Prezados Edgardo. El Potro e Maestro The Fox e demais foristas: Não me impressiona padrão Brugada. A história é IMPRESSIONANTE para canalopatias como a família de SQTS ja discutida anteriormente em nosso Forum, mas o QT é normal nestes ECGs. A anomalia de coronária direita relatada (não veio o resultado da autópsia mas para causar morte súbita pensaria em tronco coronário único do Seio Aórtico Direito com AlCAPA - Coronária Esquerda com trajeto inter aórtico-pulmonar). O ECG com V1, V2 e V3 altas não muda muito o padrão para sugerir Brugada.- Javier com a palavra - exceto que evidencia melhor uma alteração no final de J/ST de V! que poderia configurar uma onda épsilon para ARVD

Amigos Pequena correção de pensamento: Não me impressiona padrão Brugada. A história de Morte Súbita É IMPRESSIONANTE para canalopatias como a família com SQTS já discutida anteriormente mas o QT é normal nestes ECGs,. A anomalia de coronária direita relatada (não veio o resultado da autópsia mas para causar morte súbita pensaria em ***Tronco coronário único do Seio Aórtico Direito ou Alcapa - Coronaria Esquerda com trajeto inter aórtico-pulmonar ou nascendo da pulmonar respectivamente).*** O ECG com V1, V2 e V3 altas não muda muito o padrão para sugerir Brugada.- Javier com a palavra - exceto que evidencia melhor uma alteração no final de J/ST de V!que poderia configurar uma onda Épsilon para ARVD

Adail Paixão Almeida MD Vitória da Conquista Bahia

English: Dear Edgardo, *El Potro(Andrés)* and Master The Fox(Raimundo) and other members of the Forum, It doesn't seem to me to be Brugada pattern. The history is IMPRESSIVE for channelopathies, such as the family of SQTS previously discussed in our Forum, but QT is normal in these ECGs. About the mentioned right coronary anomaly, I don't see the result of the autopsy, but to cause sudden cardiac death I would think of a single coronary trunk of the Right Aortic Sinus with ALCAPA – Left Coronary Artery with interaortic-pulmonary trajectory. The ECG with high V1, V2 and V3 does not change the pattern enough to suggest Brugada -Javier's words- unless there was better evidence of an alteration at the end of J/ST of the LV that may configure an epsilon wave for ARVD.

Friends, A small change of mind: It doesn't seem to me to be Brugada pattern. The history is IMPRESSIVE for channelopathies, such as the family of SQTS previously discussed in our Forum, but QT is normal in these ECGs. About the mentioned right coronary anomaly, I don't see the result of the autopsy, but to cause sudden cardiac death I would think of a single coronary trunk of *the right aortic sinus or ALCAPA – Left Coronary with interaortic-pulmonary trajectory or originating in the pulmonary artery respectively*. The ECG with high V1, V2 and V3 does not change the pattern enough to suggest Brugada -Javier's words- unless there was better evidence of an alteration at the end of J/ST of the LV that may configure an epsilon wave for ARVD.

Warm regards,

Adail Paixão Almeida MD Vitória da Conquista Bahia Brazil

Spanish

Querido Raimundo, el ECG presenta en RS , con FC de 78 por minuto con eje eléctrico en + 80°. En V1 y V2 un patrón de rSR' con T negativa, no logro medir por la definición si presenta un aumento de la duración del QRS con respecto a V5 y V6. El intervalo QTc es normal. Frente a los fuertes antecedentes familiares positivos y MS en el sueño uno con este ECG sospecharía de un patrón de Brugada tipo I espontaneo asintomático, confirmaria la sospecha diagnostica ya que no encuentro retraso de las fuerzas finales en V5 y V6 que corroboren la presencia de BIRD, si no es por habito longilineo del paciente, y el Angulo de Chevalier que no logro medir por la escasa definición al aumentarlo, pero me impresiona positivo lo llego a medir en V1 y V2 en 67° y tambien en aVR. Obviamnete descartaria chagas. No tiene incidencia familar la asociación de malformaciones coronarias o al menos no esta descrito hasta el momento pero seria interesante previo a otras pruebas la realizacion de una ergometria, complementaria con ECO y observaria la derivacion V1 en el sueño si magnifica el patrón de Brugada o presenta bradicardias extremas. No encuentro motivos para RNM cardiaca pero no la descartaria si el eco es normal para descartar ARVD, seria un complemento que puede o no sumar a los diagnósticos diferenciales. Mi impresión es que se trata de un patrón de Brugada tipo I espontaneo, los demás estudios y la prueba de ajmalina que seria la prueba final para evidenciar con claridad si se trata de un Brugada o de una fenocopia. El estudio genetico no aportara a la estratificación de riesgo, si a confirmar el diagnostico y realizar screning familar. Hace poco una controversia de Viskin y Brugada restaba valor al estudio electrofisiologico para estraticar riesgo de MS. Si confirma el diagnostico y no se trata de una fenocopia (remitir a Adrian en este caso), se trata de un paciente asintomático. Alli se encontrara con el dilema de un Brugada asintomático con antecedentes familiares positivos. Si me pregunta no relazará deportes. Pero no me convence CDI profiláctico, a pesar de los antecedentes familiares, según las guias tendría que colocarle un CDI profiláctico, la opción seria evitar medicamentos que puedan bloquear los canales de Na y consultaría con Sami Viskin si lo considera un paciente que podría beneficiarse con quinidina, se que faltan estudios prospectivos que lo avalen pero los trabajos realizados por Sami nos dan una nueva herramienta para la prevención de MS en los pacientes con patrón de Brugada asintomático.

Un cordial saludo

Martín Ibarrola

English

Hello, dear Raimundo presents a patient in SR of 78 per minute, with electrical axis in +80°. In V1 and V2 a pattern of rSR’ with negative T. I cannot measure because of the definition, whether it presents an increase in QRS duration in regard to V5 and V6. QTc interval is normal. Faced with the strong positive familial background and SCD during sleep, I would suspect spontaneous asymptomatic Brugada type I with this ECG. I would confirm the diagnostic suspicion, since I don’t find delay in the final forces in V5 and V6 that would corroborate the presence of IRBBB. If not by the patient being asthenic and the Chevalier angle, I would be able to measure with the scant definition when enhanced, but it seems positive to me. I measure it in V1 and V2 in 67° and also in aVR. I would evidently rule out Chagas disease. There is no family incidence for the association of coronary malformations, or at least it has not been described to this moment; but it would be interesting before other tests to perform an ergometer test. I would complement it with ECHO and would observe in lead V1 in sleep if the Brugada pattern is magnified or if there are extreme bradycardias. I see no need for cardiac NMR, but I would not rule it out if the echo is normal, to rule out ARVD. It would be a supplement that may or may not add to the differential diagnosis. My impression is that this is spontaneous Brugada type I pattern. The other studies and ajmaline test would be the final test to clearly show whether it is Brugada or a phenocopy. The genetic study will not help in risk stratification, but it will help to confirm the diagnosis and to perform a family screening. A short while ago, a controversy by Viskin and Brugada detracted from the electrophysiology study to stratify the risk of SCD. If it confirms the diagnosis and it is not a phenocopy (submit to Adrian if so), it is an asymptomatic patient. Then you will find the dilemma of an asymptomatic Brugada patient with positive family history. If you ask me, he should not play sports. But I am not certain about a prophylactic ICD, in spite of the family history. According to guidelines, a prophylactic ICD should be implanted. The option would be to avoid medications that may block Na channels and I would consult with Sami Viskin whether he would consider this a patient that could benefit from quinidine. I know some prospective studies to support it are missing, but the work made by Sami is giving us a new tool to prevent SCD in patients with pattern of asymptomatic Brugada pattern.

Cordially,

Martín Ibarrola

Spanish

Querido Martin: Tu expresas ***"No tiene incidencia familar la asociación de malformaciones coronarias o al menos no esta descrito hasta el momento"*** Permíteme discordar un poco en relación a esto. El origen anómalo de las arterias coronarias se han descrito en hermanos(1). Brothers y col (2) señalan una mayor incidencia de orígenes coronarias anómalas asintomáticos en familiares de primer grado de pacientes con una coronaria anómala, planteando la cuestión de si el rastreamiento de los miembros de la familia deba ser considerado en todos los casos en los parientes asintomáticos.(2) Otra cosa que no entiendo es que expresas es lo siguiente: tu escribes textualmente:
"Frente a los fuertes antecedentes familiares positivos y MS en el sueño uno con este ECG sospecharía de un patrón de Brugada tipo 1 espontaneo asintomático" Que tenga fuertes antecedentes familiares de MS y que una de las muertes haya sido en familiar joven de primer grado durante el sueño son elementos compatibles con Brugada. Mas los 2 ECGs en ningún momento se ve el patrón tipo 1 ESPONTANEO. ¿Porque dices que sospecharías de un patrón Brugada tipo 1 espontaneo? O tiene o no tiene eso no se sospecha. Me temo que quisiste expresar alguna otra cosa y te salió esto. ¿Quisiste decir que harías prueba farmacológica para ver si se desenmascara? Espontaneo es cuando el patrón está presente sin la acción de drogas. En este caso en ninguno de los 2 ECGs esta presente el patrón tipo 1.

Andrés Ricardo **Pérez-Riera M.D.Ph.D.**

1. **Devanagondi R, Brenner J, Vricella L, Ravekes W. A tale of two brothers: anomalous coronary arteries in two siblings. *Pediatr Cardiol*. Jul 2008;29(4):816-9.**
2. **Brothers JA, Stephens P, Gaynor JW, Lorber R, Vricella LA, Paridon SM. Anomalous aortic origin of a coronary artery with an interarterial course: should family screening be routine?. *J Am Coll Cardiol*. May 27 2008;51(21):2062-4.**

English

Dear Martin,

You express, “The patient does not present familial incidence of association of coronary malformations or at least it has not been described to this moment.” Let me disagree with you a bit in regard to this. The anomalous source of the coronary arteries has been described in siblings(1). Brothers et al(2) point out a greater incidence of asymptomatic anomalous coronary origins in first-degree relatives of patients with anomalous coronary artery, raising the issue of whether tracking the members of a family should be considered in all cases of asymptomatic relatives(2).

Another thing I don’t understand is that you express the following, literally:

“Faced with the strong positive familial background and SCD during sleep, I would suspect spontaneous asymptomatic Brugada type I with this ECG”

That the patient has family history of SCD and that one of the deaths in a young first-degree relative occuring during sleep, are elements suggesting Brugada. Plus, in the 2 ECGs, at no time the SPONTANEOUS type 1 pattern is seen. Why do you say that you would suspect spontaneous type 1 Brugada pattern? He has it or not; that is not something you suspect about. I’m afraid that you meant to express something else and what came out is this incomprehensible nonsense. Did you mean to say that you would do a pharmacological test to see if it unmasks? It is spontaneous when the pattern is present without the action of drugs. In this case, in none of the 2 ECGs type 1 pattern is present.

Andrés Ricardo Pérez-Riera M.D.Ph.D.

Spanish: Queridos colegas Realmente el caso merece mucha atención y cuidado. Es un adolescente con pesados antecedentes familiares de muerte súbita en familiares jóvenes de primer grado (3 integrantes de la familia murieron súbitamente siendo que en uno la autopsia revelo origen anómala de la coronaria (ALCAPA) lo que nos obliga a realizar estudios de rastreamiento en forma obligatoria mismo que el adolescente sea asintomático y sus 2 ECG sean absolutamente normales. Realmente el trazado realizado con las precordiales derechas altas no tiene nada de patrón Brugada tipo 2, apenas un patrón trifásico normal con r final pequeña y de ángulo agudo inocente y el intervalo QT es normal tanto en precordiales derechas como izquierdas, asi como la duración del QRS. No se observa R prominente en aVR ni QRS fragmentado o Tpeak-Tend prolongado. La muerte de la hermana ocurriera durante el sueño lo que nos obliga a no descartarla posibilidad de mutación en el gen SCN5A sea Brugada o LQT3 oculto.

¿Cuales son los pasos que debemos dar en este caso concreto? **Propongo la realización de los siguientes exámenes complementarios:**

ECG de alta resolución("ECG de señales promediadas"): examen barato, no invasivo y de elevado poder preditivo en caso de Brugada. La presencia de potenciales tardíos (LPs) es de gran utilidad en la identificación de pacientes Brugada con alto riesgo. Mas todavía si en el centro de Raimundo se pudiera hacer LPs con variaciones circadianas. En un reciente trabajo, 25 voluntarios sanos (controles) fueron comparados con pacientes brugada.Los pacientes con SBr, presentaron LPs con periodicidad circadiana apreciable asi como aumento en duración filtrada QRS (fQRS) y la duración de la señal de terminal de baja amplitud <40 mV (LAS40) aumentaron, mientras raíz cuadrada de los 40ms terminales fQRS (RMS40) disminuyó durante la noche en comparación con el día. Los voluntarios no mostraron esta periodicidad tal circadiana.(**Yoshioka K, et al. Circ J. 2013;77(3):610-8**) Si el ECG-AR resultara normal sin LPs se haría acompañamiento clínico. Si LPs están presentes sugiero prueba farmacológica con ajamlina en ambiente apropiado. Los criterios de positividad en el ECG de señal promediada son:

Root Mean Square (RMS): La amplitud media de los 40 ms finales del complejo QRS, filtrados < 25microvolts. VN: > 25 microvoltios (μV).

Amplitud de la señal baja (LAS): El componente terminal de amplitud baja del complejo con una amplitud de menos de 40 mV excede 40 milisegundos. Duración total de las señales eléctricas de baja amplitud superior a 40 mV hasta el final del complejo QRS filtrado. Valor normal: inferior a 40 μV si se utilizan de 25 a 250Hz filtros y menores de 35 años si se utilizan filtros de 40 a 250Hz.

QRSD: Duración total del complejo QRS filtrado en ausencia de bloqueo de rama (QRSD) > 114 ms (o 120 ms).

Teste de esfuerzo: también puede tener algún valor en caso de Brugada y en otras canalopatías sin cardiopatía estructural La prueba de esfuerzo o ergometría pueden revelar mejora repolarización durante el esfuerzo, como consecuencia de los aumentos del tono adrenérgico y la consecuente disminución del tono vagal, ya que la fase 1 canal Ito1 se vuelve menos prominente durante altas frecuencias cardiacas, lo que lleva a una disminución en el la elevación del punto J y del segmento ST, y menor incidencia de arritmias ventriculares. En la fase de recuperación, cuando el tono vagal aumenta la elevación del ST, se hace más evidente lo que se podría simular una corriente de lesión subepicárdica, (3) El aumento en la elevación del segmento ST durante la recuperación es especifico de los pacientes Brugada y puede ser un preditor de pobre pronóstico en especial

English
Dear colleagues,
Indeed the case deserves plenty of attention and caution. The patient is a teenager with strong family history of sudden cardiac death in young first-degree relatives (3 members of the family died suddenly, with one of them revealing in autopsy anomalous origin of the coronary artery (ALCAPA)), which leads us obligatorily to perform screening studies, even if the teenager is asymptomatic and his 2 ECGs are absolutely normal. Indeed, the tracing made with high right precordial leads presents no indication of type 2 Brugada pattern; just a normal triphasic pattern with final small r and innocent acute angle and QT interval is normal both in right and left precordial leads, as well as QRS duration. Prominent R is not observed in aVR, and neither fragmented QRS or prolonged Tpeak-Tend. The death of his sister occurred during sleep, which leads us not to rule out the possibility of mutation in the SCN5A gene, whether Brugada or concealed LQT3.
What are the steps to follow in this particular case? **I propose performing the following supplementary tests:**
High resolution ECG (signal-averaged ECG): cheap, noninvasive test, and with a high predictive power in case of Brugada. The presence of late potentials (LPs) is very useful to identify Brugada patients in high risk. All the more so, if in Raimundo's center LPs could be detected with circadian variations. In a recent paper, 25 healthy volunteers (controls) were compared with Brugada patients. The patients with BrS presented LPs with evident circadian periodicity, as well as increase in filtered QRS duration (fQRS) and duration of terminal signal of low amplitude <40 mV (LAS40); while the square root of the terminal fQRS 40 ms (RMS40) decreased during the night in comparison with the day. The volunteers did not show this circadian periodicity (**Yoshioka K, et al. Circ J. 2013;77(3):610-8**). If AS-ECG is normal and without LPs, clinical accompaniment should be done. If LPs are present, I suggest pharmacological test with ajmaline in a proper environment. Positivity criteria in SA-ECG are:
Root mean square (RMS): The average amplitude of the final QRS complex 40 ms, filtered <25 microvolts. Normal value: >25 microvolts (μV)
Low amplitude signal (LAS): The terminal component of low amplitude of the complex with an amplitude of less than 40 mV exceeds 40 milliseconds. Total duration of the electrical signals of low amplitude above 40 mV until the final filtered QRS complex. Normal value: less than 40 μV if 50 to 250 Hz filters are used and younger than 35 years of age if filters of 40 to 250 Hz are used.
QRSD: Total duration of the filtered QRS complex in absence of branch block (QRSD) > 114 ms (or 120 ms).
Stress test: It may also have some value in case of Brugada and in other channelopathies without structural heart disease. The stress test or ergometry may reveal repolarization improvement during strain, as a consequence of the increases in adrenergic tone and the subsequent decrease of vagal tone, since phase 1 of the Ito1 channel becomes less prominent during high heart rates, which leads to a decrease in J point and ST segment elevation, and less incidence of ventricular arrhythmias. In the recovery phase, when vagal tone increases ST elevation, what may resemble a subepicardial lesion current becomes more evident(3). The increase in ST segment elevation during recovery is specific of Brugada patients and may be a predictor of poor prognosis, especially in patients with syncope or asymptomatic(4).

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Transthoracic Doppler echo: It would be useful to confirm the absence or not of structural heart disease and besides, it is relevant if we were facing a concealed form of ALCAPA, which after childhood, may present normal ECG. Echo and Doppler images show in case of asymptomatic coronary anomaly: (1) direct signs: abnormal coronary ostium originating in the pulmonary trunk with retrograde flow of coronary artery, and (2) indirect signs: abundant intercoronary septal collateral arteries with anterograde flow (ARCAPA) or retrograde flow (ALCAPA) and dilatation of contralateral coronary artery(2). As Raimundo commented, the Echo was normal, and we suggest repeating the method now searching for this. As I expressed recently, the value of routine tracking in ALCAPA relatives(5), as in this case, has been proposed.

In case of doubt, CT angiogram and NMR allow the diagnosis and noninvasive characterization of this pathology conclusively, which I also propose for this case. Finally, I think the following is essential:

Electrocardiographic and genetic screening of probands and all the members of the family that may eventually shed some light.

1) Standard testing with ECG under resting or exercise conditions is unlikely to provide clinical evidence of myocardial ischemia and would not be reliable as screening tests in large athletic populations,(1)
2) premonitory cardiac symptoms not uncommonly occurred shortly before sudden death (typically associated with anomalous left main coronary artery), suggesting that a history of exertional syncope or chest pain requires exclusion of this anomaly.
3) The electrocardiographically (ECG)-gated multi-detector row computed tomography (CT) allows accurate and noninvasive depiction of coronary artery anomalies of origin, course, and termination. Multi-detector row CT is superior to conventional angiography in delineating the ostial origin and proximal path of an anomalous coronary artery.(2)

Andrés Ricardo Pérez-Riera M.D.Ph.D.

1. **Basso C, Maron BJ, Corrado D, Thiene G. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. J Am Coll Cardiol. 2000 May;35(6):1493-501.**
2. **Kim SY, Seo JB, Do KH, Heo JN, Lee JS, Song JW, Choe YH, Kim TH, Yong HS, Choi SI, Song KS, Lim TH. Coronary artery anomalies: classification and ECG-gated multi-detector row CT findings with angiographic correlation. Radiographics. 2006 Mar-Apr;26(2):317-33.**

Theoretical considerations of Coronary Artery Anomalies with emphasis on electro-vectorcardiographic aspects

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Coronary Artery Anomalies

There are three types: Anomalies of the origin, anomalies of the course and anomalies of termination

Anomalies of the origin

Anomalous Left Coronary Artery from the Pulmonary Artery: Bland White-Garland Syndrome

Other denominations: ALCAPA syndrome: English acronym for Anomalous origin of the Left Coronary Artery arising from the Pulmonary Artery.

This rare entity was first described in 1866, but represents one of the most common causes of myocardial ischemia in infants and if left untreated results in a high mortality rate. Bland, White and Garland described the first clinical description in conjunction with autopsy findings in 1933, **(1)** so the anomaly is also called Bland-White-Garland syndrome. Fontana and Edwards reported a series of 58 postmortem specimens that demonstrated that most patients had died at a young age **(2)**.

Epidemiology

Congenital coronary artery anomalies are seen in 0.6-1 % of adult patients undergoing coronary angiography **(3)**. The entity is a rare, congenital cardiac anomaly accounting for 0.2-1.2% of the general population and cause 12% of sudden cardiac deaths related to sports and 1.2% of deaths not related to sports**(4)**, approximately 0.25-0.5% of all congenital heart disease or 4 per 1,000 of all congenital heart diseases**(5)**.

ALCAPA occurs in approximately 1/300 000 live births or 0.5% of children with congenital heart disease. The mortality of untreated ALCAPA has been estimated to range from 35% to greater than 85% in the first year of life **(6; 7)**. Of the carriers of the BWG syndrome, only 10% reach an adult age **(8)**.

ALCAPA is not associated with any syndromes or noncardiac conditions.

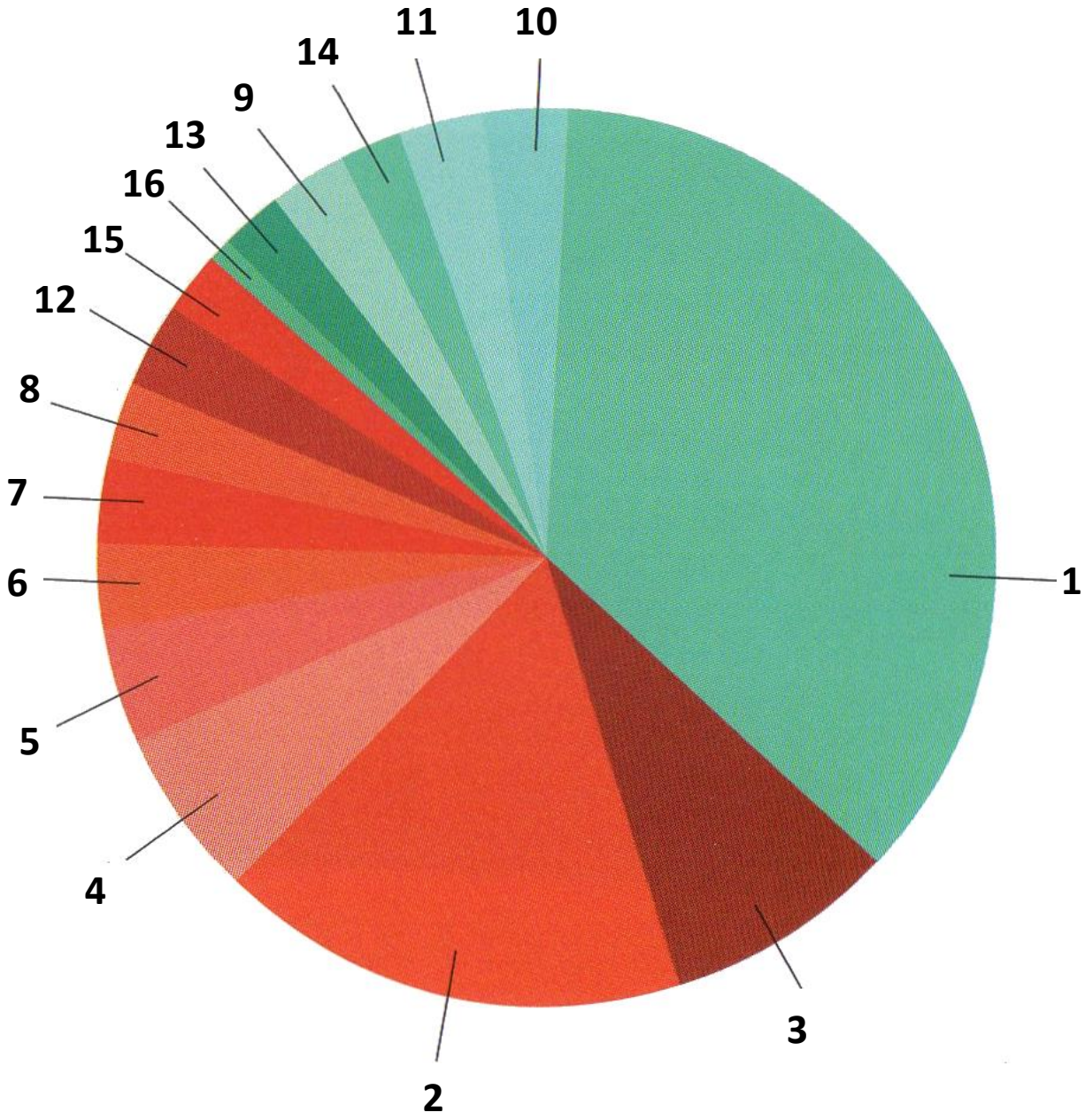
Coronary anomalies are important cause of sudden cardiac death (SCD) among young competitive athletes (< 35 years old). SCD is the leading cause of mortality among young athletes with an incidence of 1-2 per 100,000 athletes per annum **(9)**. The annual risk of sudden cardiac death in athletes (both young and masters) ranges between 5 and 10 per 1,000,000**(10)**. **Figure 1**

Embryological causes

The anomaly may be the result of: 1) Abnormal tronco-conal separation between the aorta and pulmonary artery; 2) Persistence of pulmonary sinus of Valvsalva along with aortic sinus of Valsalva, which spring from coronary arteries. Persistence of the pulmonary buds together with involution of the aortic buds that eventually form the coronary arteries.

Usually, is an isolated cardiac anomaly but, rarelly, has been described with patent ductus arteriosus, ventricular septal defect(VSD), tetralogy of Fallot, coarctation of the aorta and scimitar syndrome **(11)**.

Figure 1 - Distribution of cardiovascular sudden deaths among young athletes



1. Hypertrophic cardiomyopathy (HCM) 36%
2. Coronary anomalies 17%
3. Left ventricular hypertrophy possible HCM 8%
4. Myocardits 6%
5. Arrythmogenic right ventricular cardiomyopathy / dysplasia 4%
6. Mitral valve prolapse 3%
7. Myocardial bridges 3%
8. Coronary artery diseases 3%
9. Channelopaties 3%
10. Normal heart 3%
11. Others 3%
12. Aortic stenosis 3%
13. Aortic rupture 2%
14. Others congenital heart disease 2%
15. Dilated cardiomyopathy 2%
16. Sarcoidosis 1%

Pathophysiology

Anomalies does not present prenatally because of the favorable fetal physiology that includes equivalent pressures in the pulmonary artery(PA) and aorta(Ao) secondary to a nonrestrictive patent ductus arteriosus, and relatively equivalent oxygen concentrations due to parallel circulations. This results in normal myocardial perfusion and, therefore, no stimulus for collateral vessel formation between the right and left coronary artery systems is present. Shortly after birth, as the circulation becomes one in series, PA pressure and resistance decrease, as does oxygen content of pulmonary blood flow. This results in the left ventricular myocardium being perfused by relatively desaturated blood under low pressure, leading to myocardial ischemia. Initially, myocardial ischemia is transient, occurring during periods of increased myocardial demands, such as when the infant is feeding and crying. Further increases in myocardial oxygen consumption lead to myocardial infarction of the anterolateral left ventricular (LV) free wall. This often causes mitral valve papillary muscle dysfunction and variable degrees of mitral insufficiency.
Collateral circulation between the right and left coronary systems ensues. Left coronary artery flow reverses and enters the pulmonic trunk due to the low pulmonary vascular resistance (coronary steal phenomena). As a result, LV myocardium remains underperfused. Consequently, the combination of LV dysfunction and significant mitral valve insufficiency leads to congestive heart failure (CHF) in the young infant. Inadequate myocardial perfusion likely causes significant chest pain and these symptoms of myocardial ischemia may be misinterpreted as routine infantile colic **(12)**.

Mortality/Morbidity

Left untreated, the mortality rate in the first year of life is 90% secondary to myocardial ischemia or infarction and mitral valve insufficiency leading to CHF. Sudden death may occur because of inadequate collateral circulation between the left and right coronary artery systems.
It is not considered an inheritable congenital cardiac defect.
Approximately 85% of patients present with clinical symptoms of CHF within the first 1-2 months of life. In unusual cases, the clinical presentation with symptoms of myocardial ischemia may be delayed into early childhood. Rarely, a patient may stabilize following infarction and present with mitral valve regurgitation later in childhood or even adulthood.

Normal Features of the Coronary Anatomy in Humans

Feature	Range
LAD indicates left anterior descending artery; Cx, circumflex artery; RCA, right coronary artery; RV, right ventricular; OM, obtuse marginal artery; and LV, left ventricular.	
No. of ostia	2 to 4
Location	right and left anterior sinuses (upper midsection)
Proximal orientation	45° to 90° off the aortic wall
Proximal common stem or trunk	only left (LAD and Cx)
Proximal course	direct, from ostium to destination
Mid-course	extramural (subepicardial)
Branches	adequate for the dependent myocardium
Essential territories	RCA (RV free wall), LAD (anteroseptal), OM (LV free wall)
Termination	capillary bed

Rational Classification of Coronary Anomalies

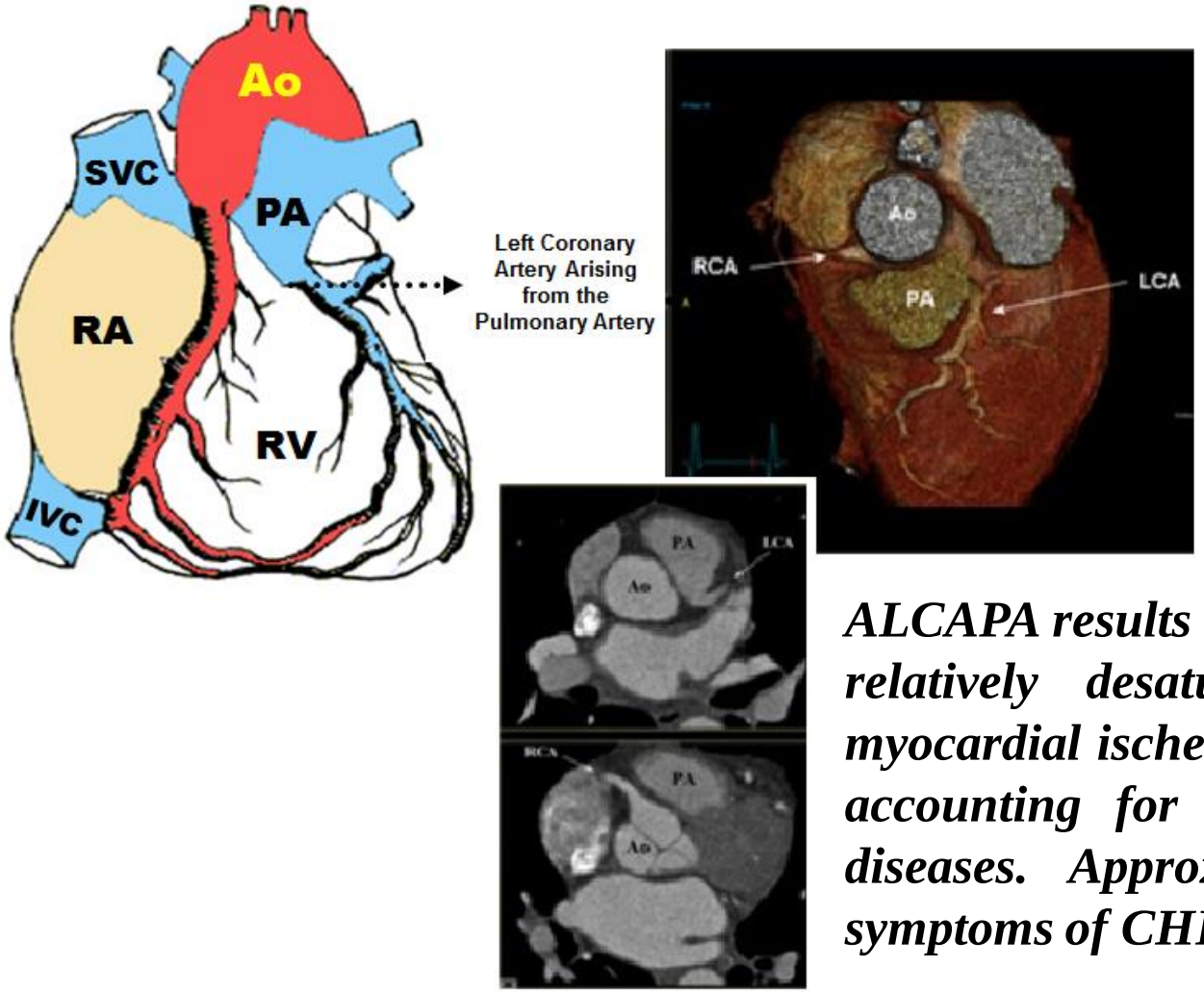
I - Anomalies of the origin

1. Anomalous origin of the Left Coronary Artery arising from the Pulmonary Artery. (ALCAPA)
2. Anomalous origins of the left main coronary artery from(ALMCA)
3. Anomalous origins the right coronary artery from the left sinus of Valsalva (ARCA)
4. Single coronary artery
5. Origin from “non-coronary cusp”

II - Anomalies of the course
    1. Myocardial bridging
    2. Duplication

III - Anomalies of termination
    1. Coronary artery fistula
    2. Extracardiac termination

Figure 2 - ALCAPA: Anomalous origin of the Left Coronary Artery arising from the Pulmonary Artery



ALCAPA results in the left ventricular myocardium being perfused by relatively desaturated blood under low pressure, leading to myocardial ischemia. ALCAPA is a rare, congenital cardiac anomaly accounting for approximately 0.25-0.5% of all congenital heart diseases. Approximately 85% of patients present with clinical symptoms of CHF within the first 1-2 months of life.

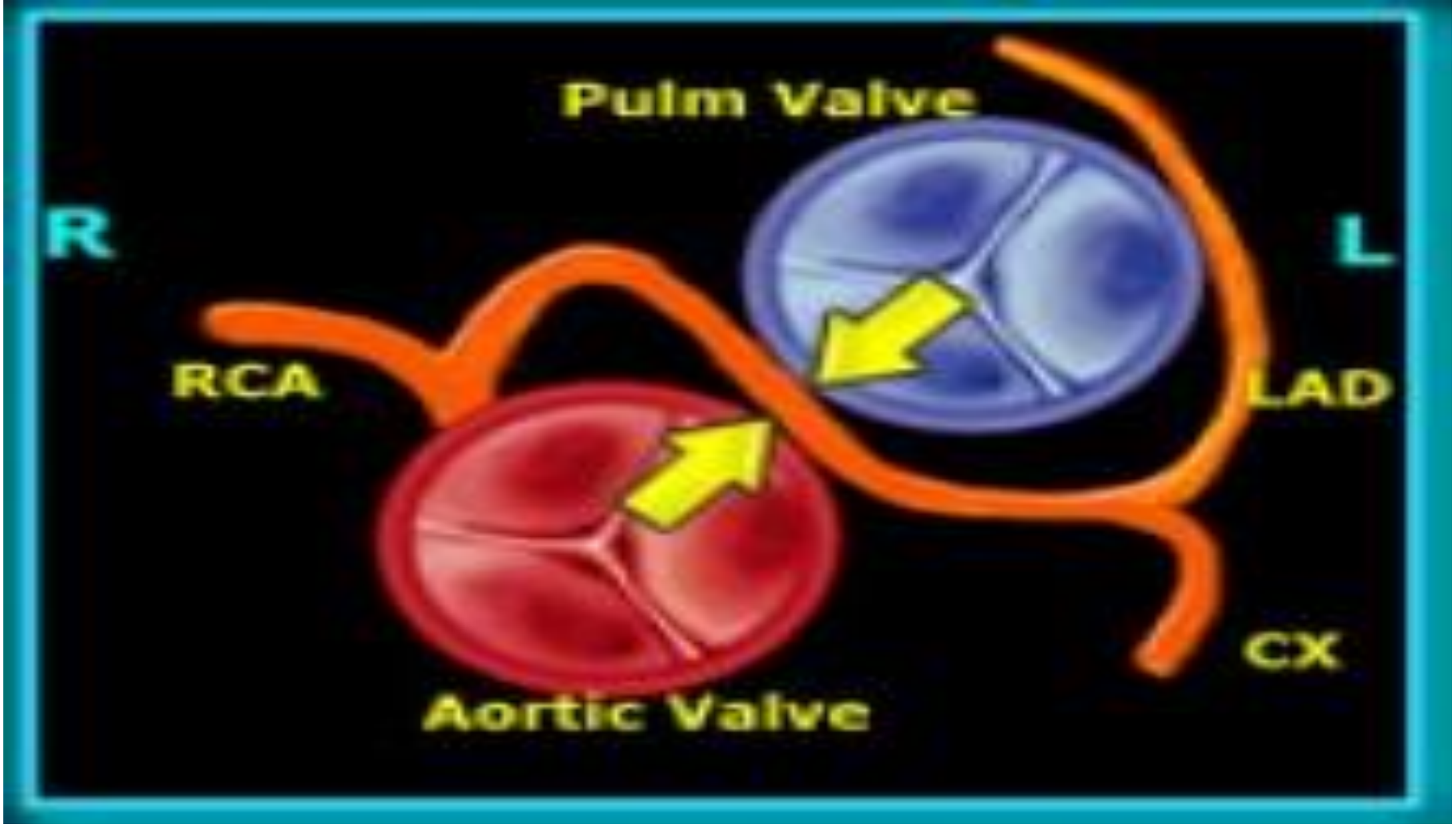
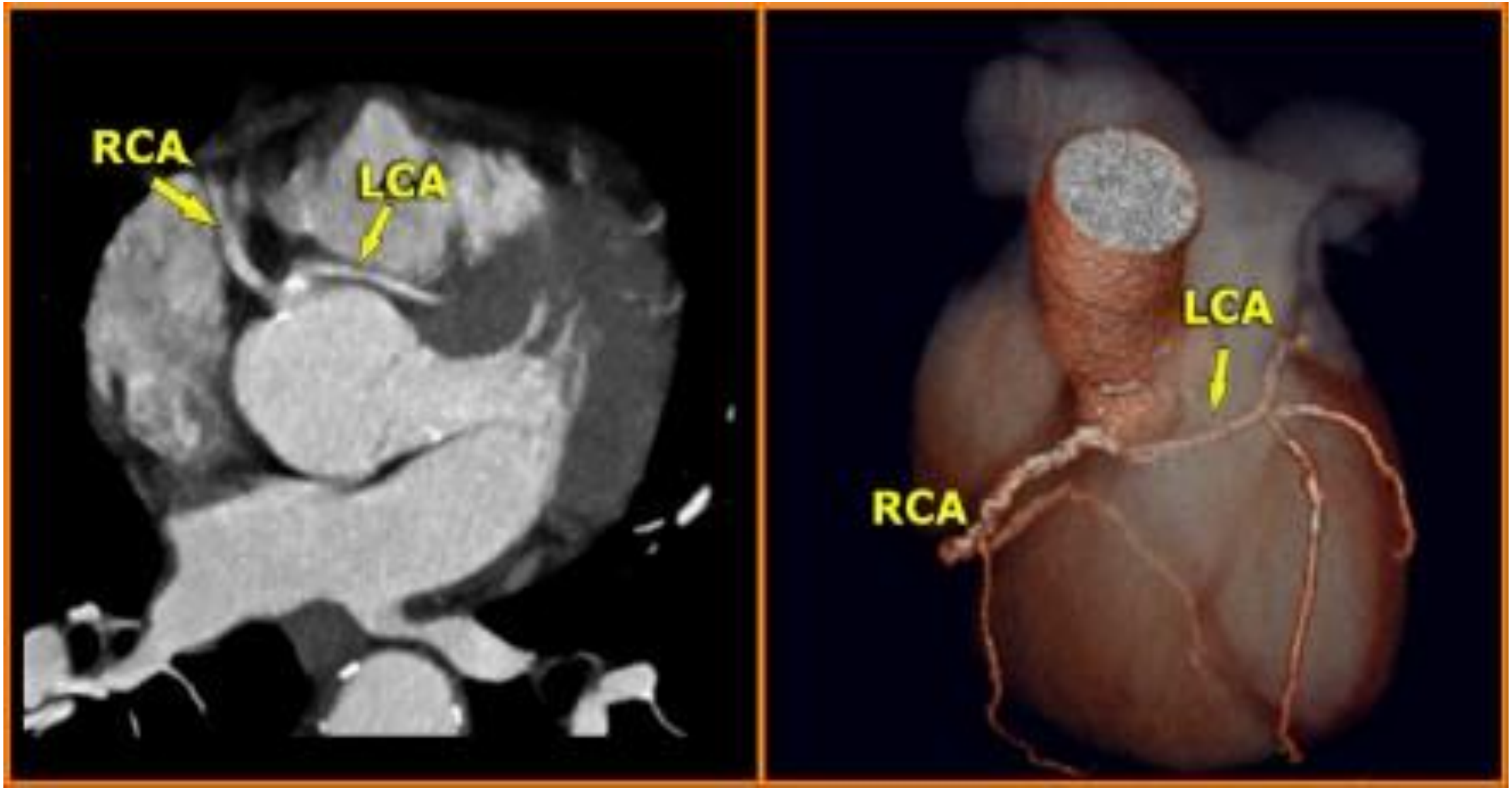


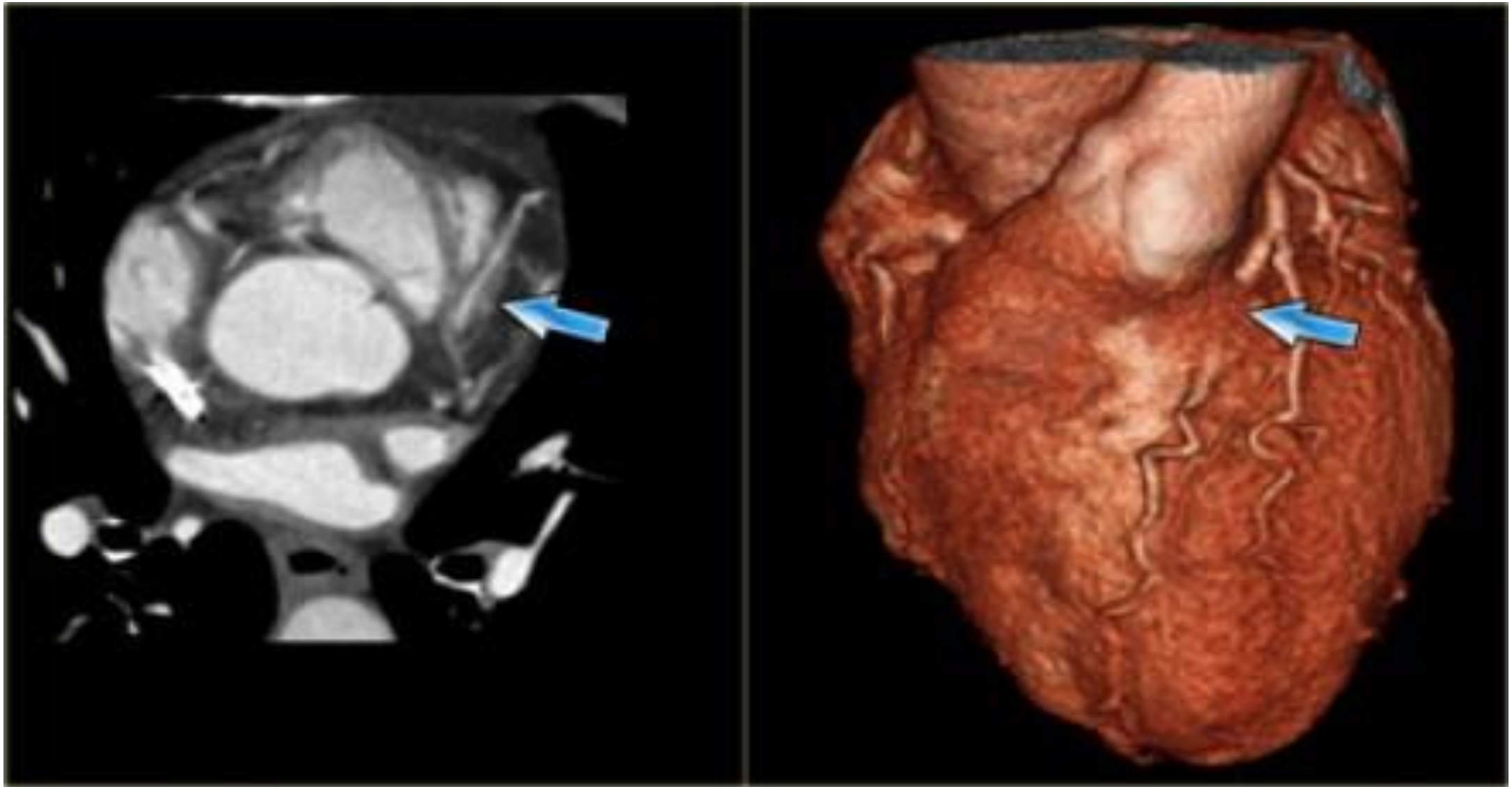
Figure 3 - The upper illustration is the most common and clinically significant coronary anomaly. There is an anomalous origin of the LCA from the right sinus of Valsalva and the LCA courses between the aorta and pulmonary artery. This interarterial course can lead to compression of the LCA (yellow arrows) resulting in myocardial ischemia.

Figure 4 - Interarterial LCA



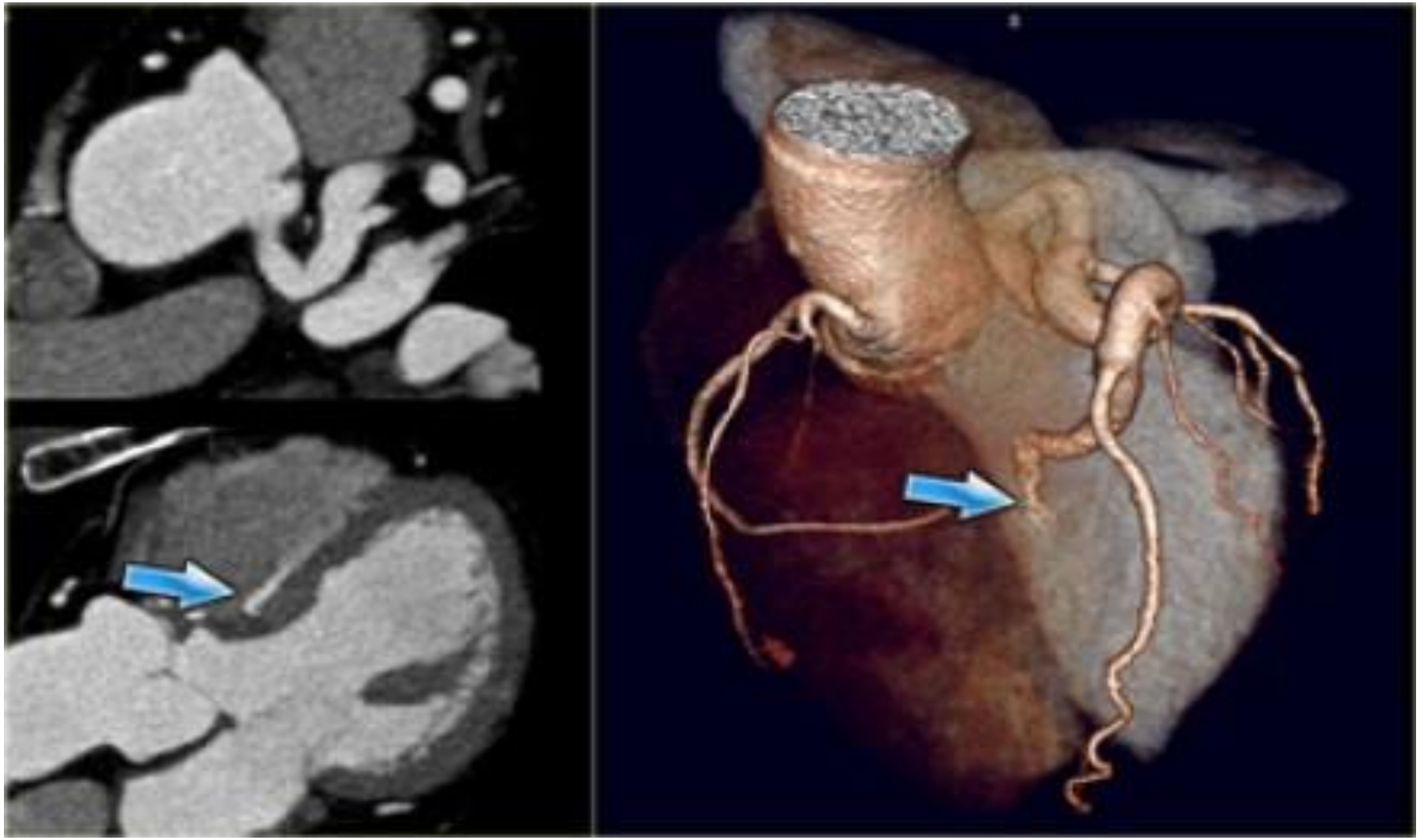
Anomalous origin of the left coronary artery form the right coronary sinus of Valsalva and coursing between the aorta and pulmonary artery. Sudden cardiac death and the presence of cardiac ischaemia is frequently observed in these patients.

Figure 5 - Myocardial bridges



Myocardial bridging is most commonly observed of the LAD. The depth of the vessel under the myocardium is more important that the length of the myocardial bridging. There is debate, whether some of these myocardial bridges are hemodynamically significant.

Figure 6 – Coronary fistula



On the image, we see a large LAD giving rise to a large septal branch that terminates in the right ventricle (blue arrow).*Pictures from Robin Smithuisand Tineke Willems Radiology department of the Rijnland Hospital Leiderdorp and the University Medical Centre Groningen, the Netherlands.*

Clinical manifestations

As most of the patients are asymptomatic, the diagnosis is usually made post-mortem, and as the risk of SCD is high, aggressive surgical treatment is indicated, in association to close follow up (13). The clinical diagnosis of ALCAPA is still a challenge for pediatricians and pediatric cardiologists **(14).** The clinical and pathomorphological aspects may be grouped in 2 types (15): the infantile and adult types

The infantile type is observed in absence of enough collateral circulation, which explains the bad prognosis in natural history in patients without intervention and pattern of myocardial infarction in ECG. The entity should be suspected in infants in the face of unexplained cardiomegaly **(16)**.

The ALCAPA syndrome may result in myocardial infarction, heart failure and possibly death during the early infantile period **(17)**. In this type, two subtypes stand out:

Severe symptoms with death before a year. Symptoms of anomalous left coronary artery in an infant include:

Crying or sweating during feeding

Pale skin, poor feeding, rapid breathing, sweating, symptoms of pain or distress in the baby (often mistaken for colic)

Symptoms can appear within the first 2 months of the baby's life.

-Early disease followed by improvement.

Signs of ALCAPA include:

Arrhytymias

Cardiomegaly

Pansistolic murmur in mitral focus consequence of anterior mitral valve prolapse secondary to papillary muscle rupture, severe mitral valve regurgitation, as well as an anterior myocardial wall hypokinesis**(18)**. Sometimes it is necessary mitral valve repair or mitral valve replacement.

Tachycardia consequence of heart failure.

Adult type: characterized by absence of early symptoms. Late presentation of abnormal origin of coronary artery from the pulmonary artery (ALCAPA) is uncommon compared with early presentation, which usually induces extended myocardial necrosis and severe heart failure. The late presentation is characterized by abundant development of intercoronary collaterals resulting in mild and rare symptoms, but nevertheless can cause sudden cardiac death. In this case, collateral circulation is present appropriately or almost, with normal or almost normal ECG. In this context, coronary insufficiency usually manifests with strain, which explains sudden deaths in young athletes.

ALCAPA: ELECTROCARDIOGRAM CHARACTERISTICS

The electrocardiogram is the most helpful resource in clinical diagnosis, especially in symptomatic infants, and the VCG is useful not only for the diagnosis, but also for the follow up from the prognostic point of view. In children and in adutls, the ECG/VCG may be normal or almost normal **(19)** nevertheless, two elements characterize the ECG in this entity: pattern of myocardial infarction and pattern of LVH.

Rhythm: Sinus. There may be recurrent atrial fibrillation. A tendency to severe arrhythmias has been described, post-acute infarction and physical strain, which results in arrhythmic sudden cardiac death. SCD may occur during the practice of exercises in adolescents **(20)**. Saeed et al **(21)** postulate the possibility of SCD by polymorphic VT secondary to reperfusion. In pediatric patients, VT/VF was associated to a high rate of mortality (approximately 80%) in patients with recent or remote MI **(22)** frequent sinus tachycardia in cases with heart failure.

P wave: normal in most cases. In the presence of left ventricular failure with increase in *LV end diastolic pressure* or mitral failure by ischemia or anterolateral papillary muscle infarction, it may originate electrocardiographic pattern of LAE. In infants, sweating and dyspnea secondary to dilated cardiomyopathy are described, secondary to anomalous origin of coronary artery **(23)**.

SÂQRS: it may be normal; however, there are cases –particularly in adults- with a tendency to extreme shift to the left. The cause of the shift is controversial. It has been proposed that it may be the consequence of selective hypertrophy of the LV posterobasal wall without irrigation involvement (irrigated by the right coronary artery).
The anterior and lateral walls, irrigated by the left coronary artery, are thin and possibly fibrotic.

Electrical position: usually horizontal.

LVE pattern: it is found at all ages. It so consequence of replication of myocytes, predisposed by chronic hypoxia. More observed in adults.

QRS duration: there usually is mild increase for the age, not reaching values compatible to block. The average in children younger than one year old, is 70 ms, and in older, 90 ms.

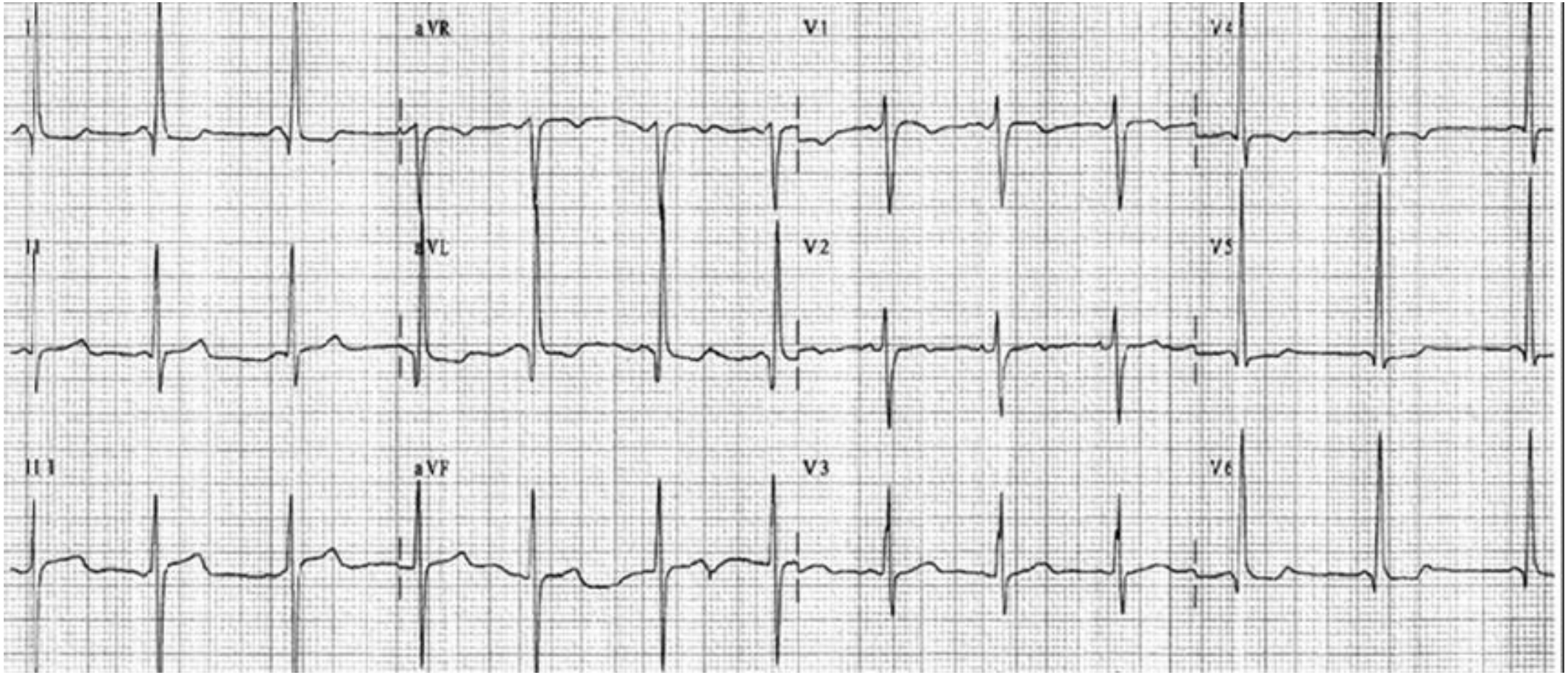
Deep S waves from V_1 to V_3: this sign should be due to RV postero-basal hypertrophy, which increases the negative component of QRS complexes located in the anterior opposite region (V1 to V3) (resulting in deeper S waves in antero-septal wall rS complexes: V1 to V3).
Amputation of R waves in V_2 and V_3.
Pattern of myocardial infarction: present in the cases where collateral circulation from the right coronary artery is insufficient (90% of the cases). More frequent in infants.
Q waves of necrosis: present in 88.8% of the cases **(24)** frequently in the anterior, antero-septal, antero-apical or antero-lateral (apico-lateral) wall: V5, V6, DI and aVL, mainly in infants. They are characteristically deeper, but not wide. Q wave with depth ≥ 3 mm and ≥ 30 ms with QR pattern in at least 1 of the following leads: DI, aVL, and from V5 to V7, and absence of Q wave in inferior wall leads, which is considered typical and highly sensitive **(22)**. Prominent Q wave in lateral leads is considered characteristic **(25)**.
The most frequent cause of deep Q-waves in children (≥,0.4 mV in 3 consecutive leads or in one of the leads I, aVL, V4, V5 and V6) is volume-overload of the LV (35%) and left axis deviation (33,3%). Looking for the various heart diseases, 30% of the children with deep Q-waves have a ventricular septal defect(23,3%), endocardial cushion defect(10,8%), patent ductus arteriosus(3,3%), Bland-White-Garland syndrome (1,6%) and hypertrophic cardiomyopathy(17,5%)**(26)**.
Ventricular repolarization: frequent ST segment elevation in the acute phase of infarction or later, possibly related to the formation of a ventricular aneurysm, accompanied by ischemic T waves. The appearance of an unexpected ST segment elevation during a surgical act of a different nature has been described. In the cases in which this atypical electrocardiographic manifestation occurs during elective surgery for other causes, the authors advise ruling out the possibility of the presence of anomalous origin of the coronary artery**(27)**.
The three components of coronary insufficiency: Q of necrosis, ST of lesion and T of ischemia. T wave inversion is more frequent in DI (94%), aVL,V5 and V6.
QT and QTc interval: QTc interval prolongation has been described, which returns to normal levels after surgical correction **(28)**.
Ventricular arrhythmias: in athletes, potentially fatal ventricular arrhythmias generally occur as a consequence of structural heart disease, as hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, and the different forms of anomalous origin of coronary arteries **(29)**.
Three pathophysiologic mechanisms have been proposed to explain the origin of ventricular arrhythmias:

Local ischemia caused by short circuit;
Reentry circuit that originates in the peripheral region of the area involved by necrosis;
Electrical instability secondary to endocardial fibrosis **(30)**.

There is a description in literature of paroxysmal AV block complicated with syncope, which requires permanent pacemaker implantation **(31)**.

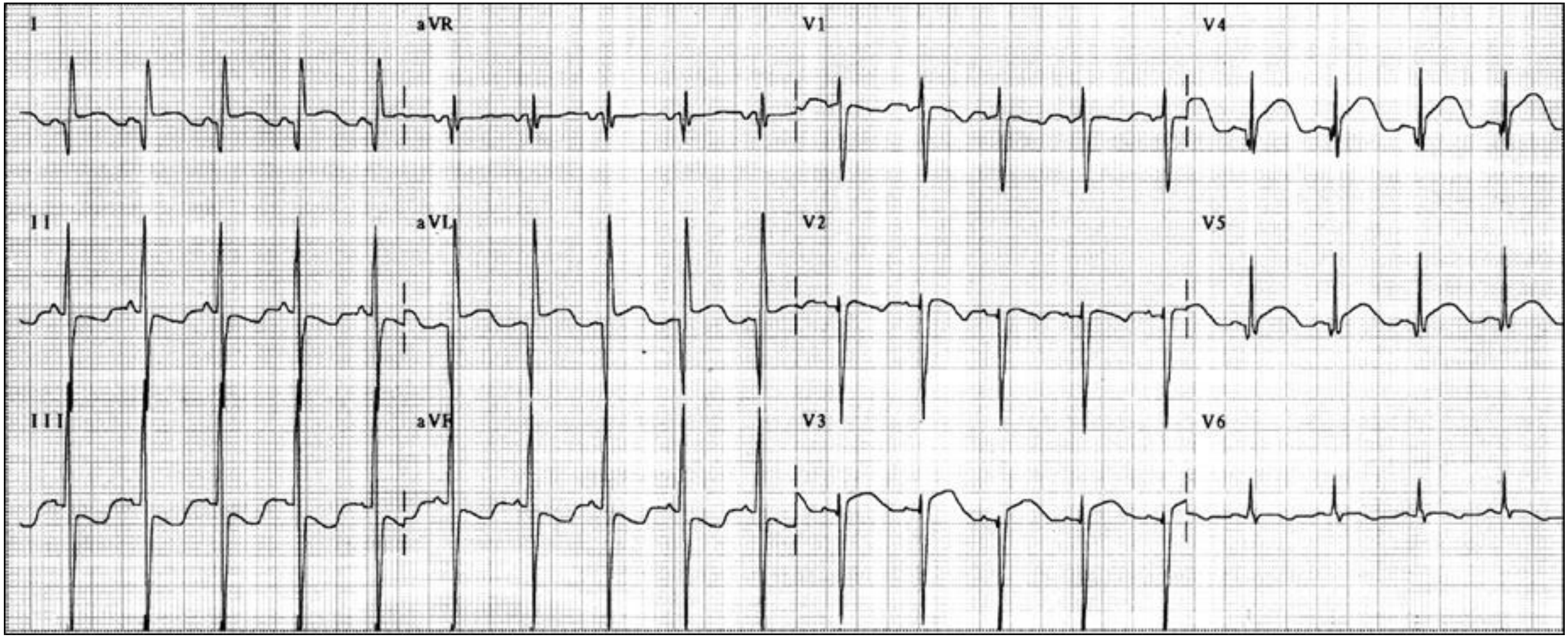
Electro-vectorcardiograms examples

Name: K.E.T. **Age:** 12 y.o. **Sex:** F**. Race:** W**. Date:** 09/17/2003 **Biotype: Medication in use:** Digoxin, Furosemide, Spironolactone



Clinical diagnosis: anomalous origin of left coronary artery that is born in the pulmonary artery.
ECG diagnosis: Rhythm: sinus; **Heart rate:** 76 bpm; **P wave:** SAP -25^0 forward; duration 100 ms; **PR:** 146 ms; **SAQRS:** near 0^0 shifted to the left (in this age range, in average is in $+55^0$ and it may vary between $+120^0$ and $+25^{0)}$; **QRS duration:** 104 ms: prolonged. The average duration of the QRS complex is 70 ms. The normal maximal limit is 90 ms until 12 years old and 100 ms until 16 years old; **QTc:** 408 ms.
CONCLUSION: LVE, volumetric or diastolic type. QR in DI, aVL and V6. The QR pattern in DI is found in more than 80% of the cases in DI and aVL. In this last lead, Q is usually greater than 50% of the voltage of R wave. In this age range, the average voltage of R wave in V_6 is 14 mm. Maximal 24 mm (our case: 21 mm).

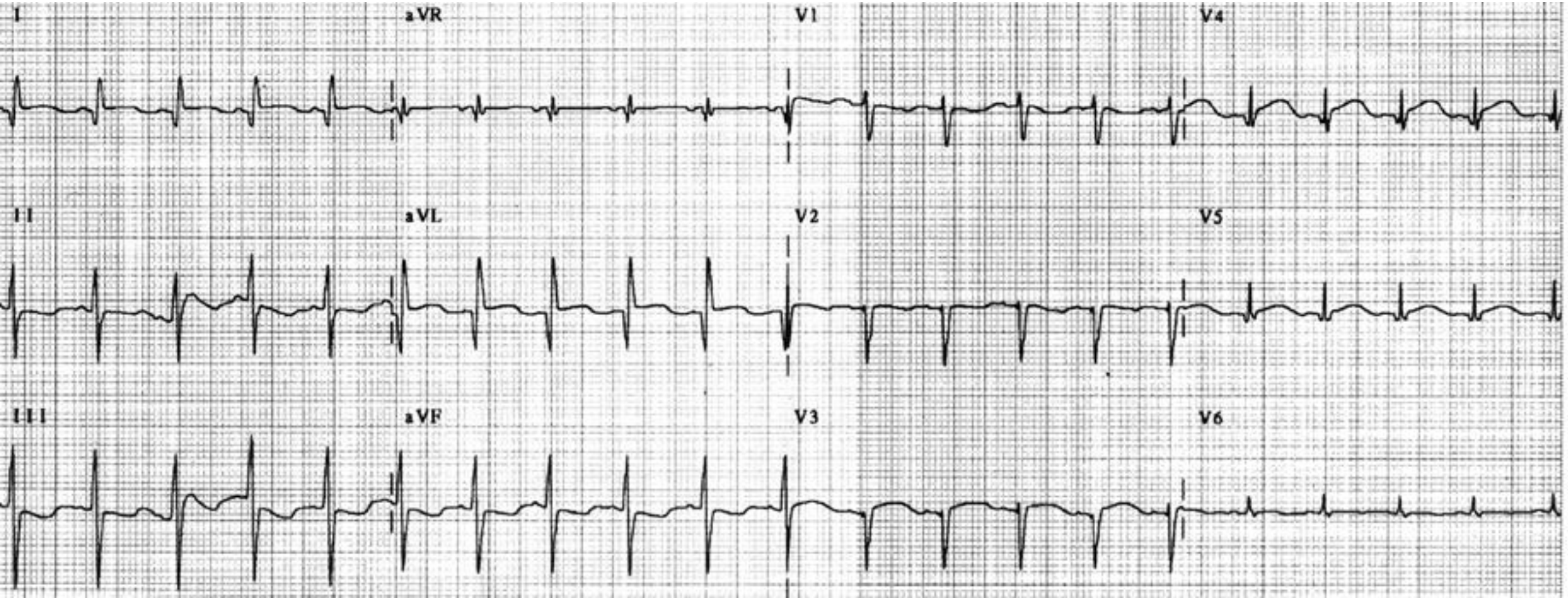
Name: G.A.A. **Age:** 2 months**. Sex:** M. **Race:** W**. Date:** 10/03/2001**. Weight:** 4 Kg. **Height:** 57 cm**. Biotype**: N. **Medication in use:** no use of medication. **Time:** 13:16:37



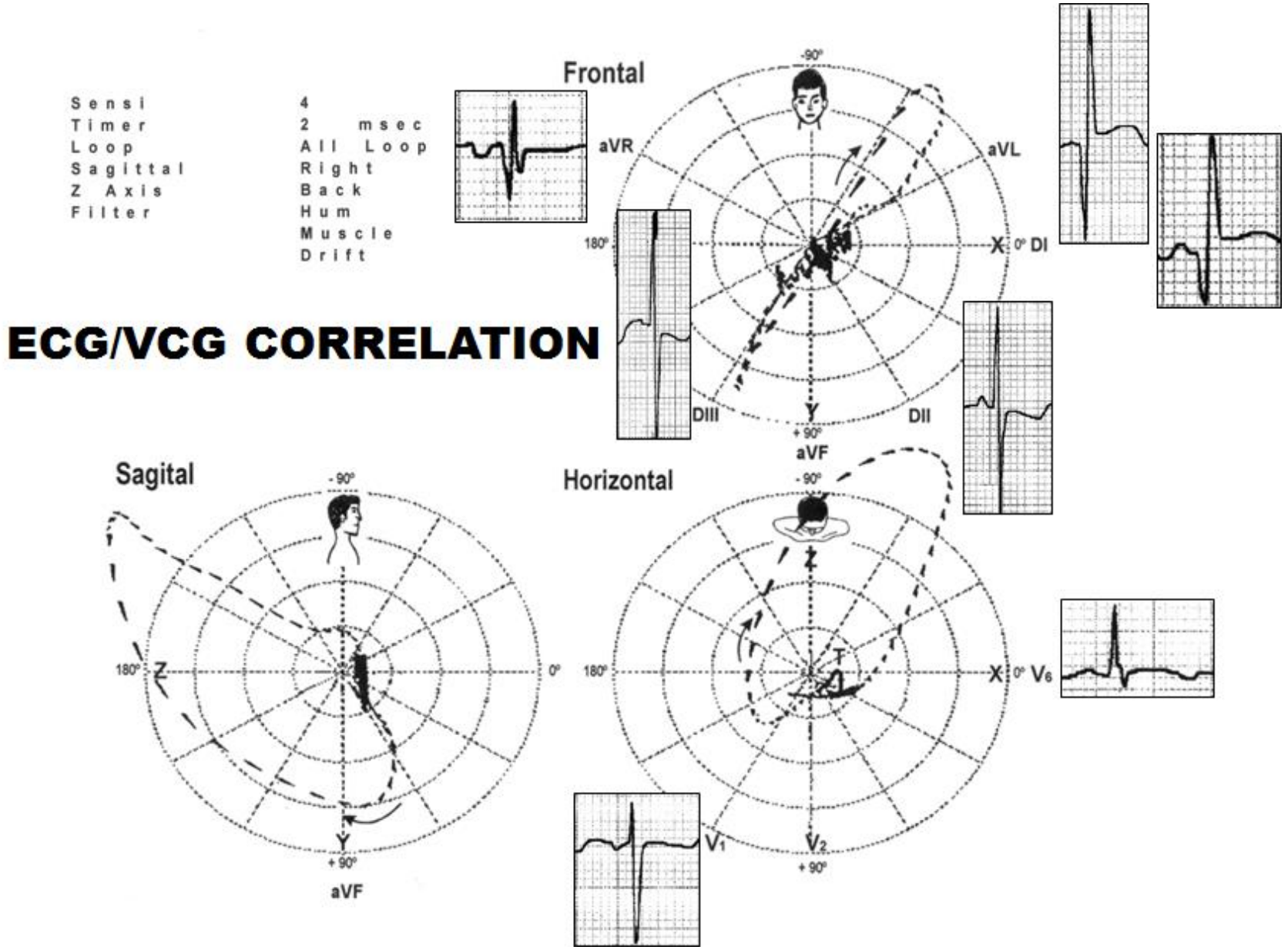
Clinical diagnosis: Successive ECGs of the same 2-month-old infant patient, in the acute phase, carrier of anomalous origin of the coronary artery.

Electrocardiographic diagnosis: LAE: increased duration (110 ms). In this age range, normal maximal duration of P 80 ms. Anteroapical MI (V_4 to V_6) and high lateral (I and aVL) or anterolateral MI: QR pattern in I (more than 80% of cases) or in I and aVL. In this last lead, Q is usually greater than 50% of the voltage of R. Q waves are characteristically deep, but not wide usually. Reversed progression of r voltage from V_1 to V_3 and R voltage in V_6 is decreased.

Name: G.A.A. **Age:** 2 months**. Sex:** M. **Race:** W**. Date:** 10/03/2001. **Weight:** 4 Kg. **Height:** 57 cm**. Biotype**: N. **Medication in use:** no use of medication. **Time:** 13:16:37

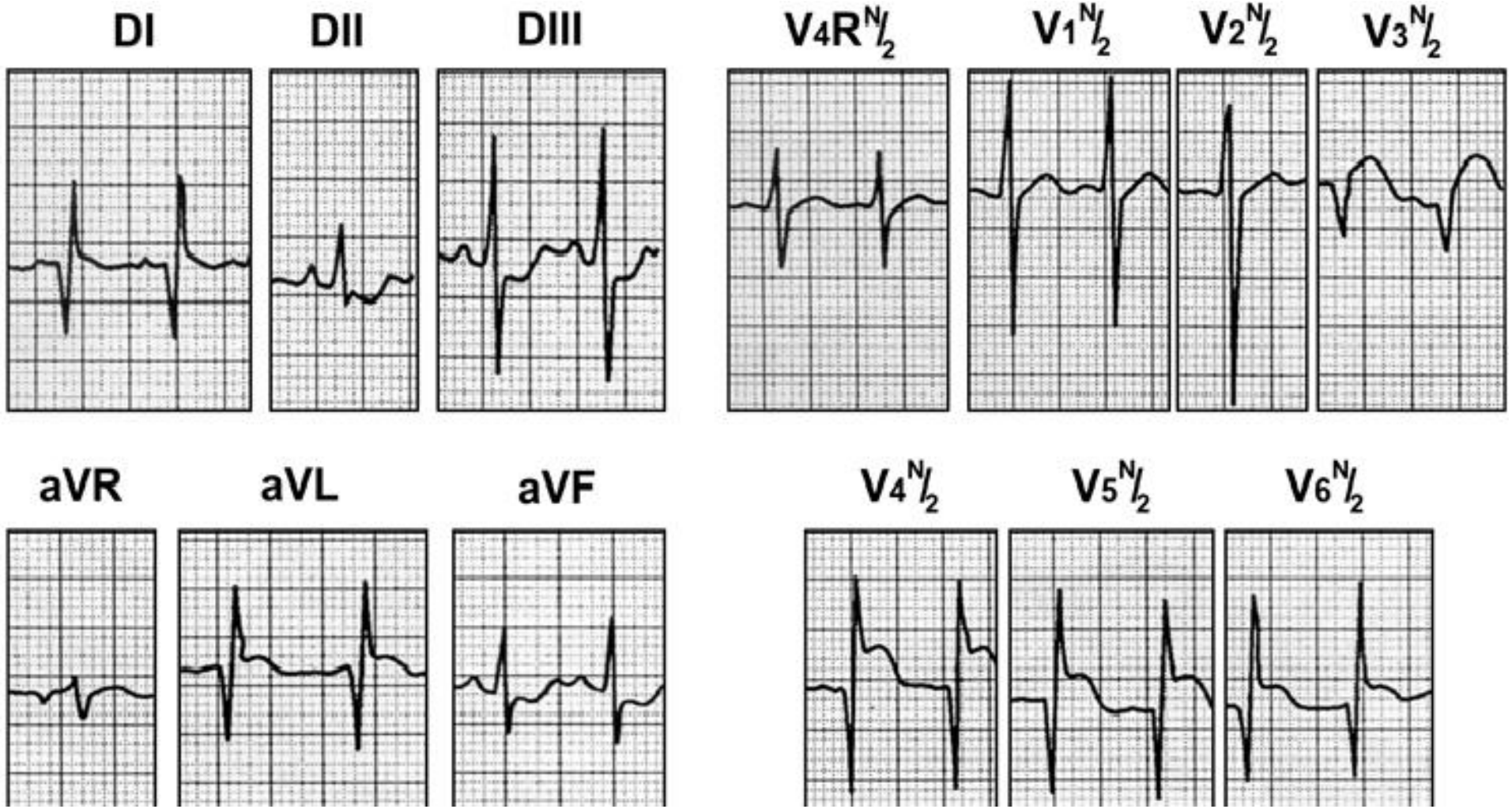


ECG/VCG correlation of a typical case, carrier of anomalous origin of coronary artery with anterolateral electrically MI.



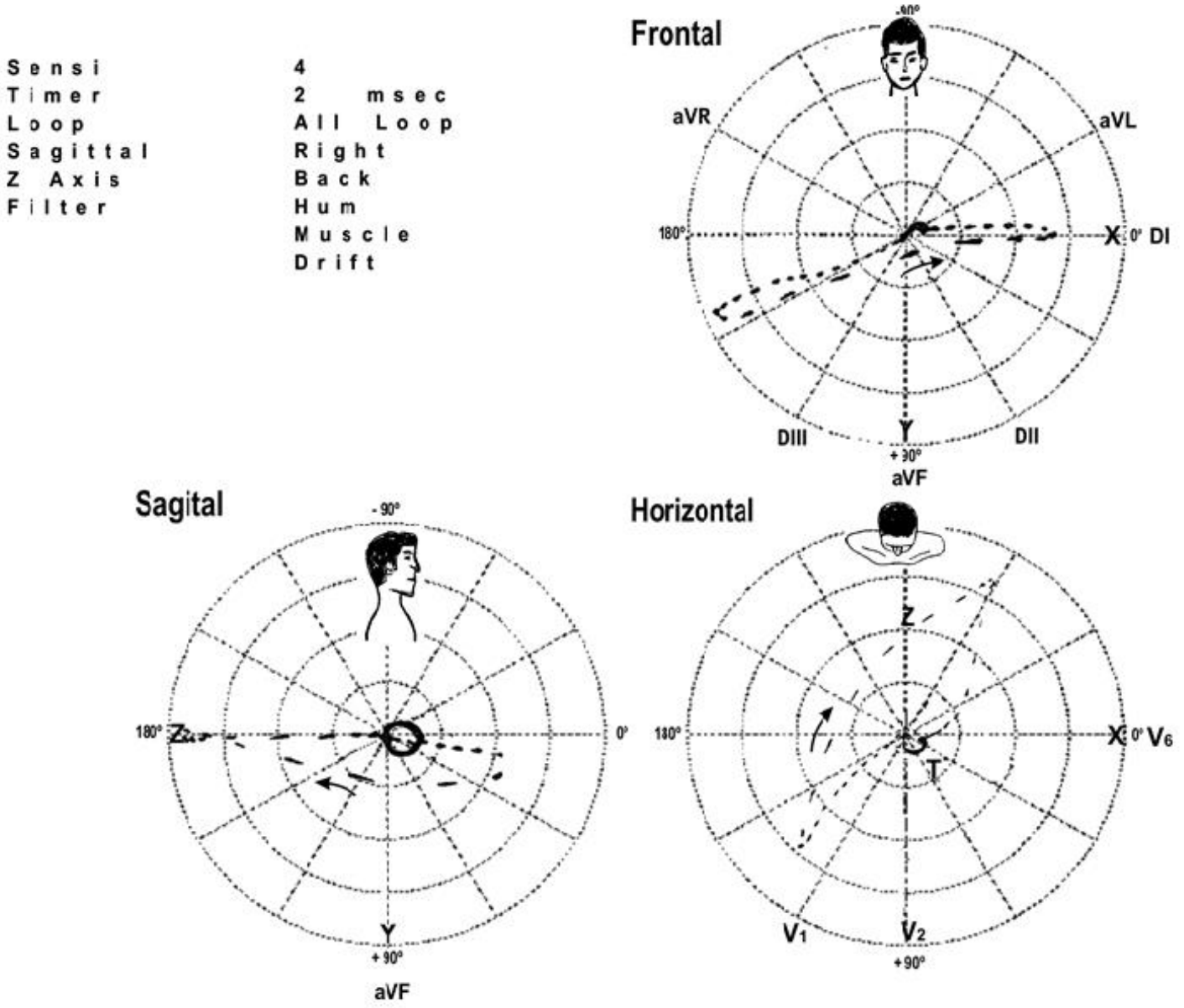
O FP deep and broad Q wave (Q > 40 ms) in high lateral leads aVL and I.
On Horizontal plane, the QRS loop displays an inverted rotation (clockwise).
QRS loop moved back on RSP.

Name: M. S. **Age:** 20 days**. Sex:** M. **Race:** Asian. **Date:** 08/04/2000. **Weight:** 2,900 gr. **Height:** 47 cm**.Biotype:** indefinite.



Clinical diagnosis: anomalous origin of the left coronary artery from PA.
Electrocardiographic diagnosis: Necrosis and subepicardial lesion in anterolateral (V3 to V6) and high lateral (I and aVL) walls. Characteristic QR pattern in I and aVL (present in more than 80% of the cases in this entity).
ECG and VCG of a newborn baby with 20 days of life, which display necrosis and anterolateral and high lateral subepicardial lesion, of a typical case of a carrier of anomalous origin of the coronary artery.

VECTORCARDIOGRAM



On Horizontal plane, the QRS loop displays an inverted rotation (clockwise). QRS displaced to right in both HP and FP.

Prognosis

Presently, the prognosis for patients with ALCAPA is dramatically improved as a result of both early diagnosis using echocardiography with color flow mapping and coronarygraphy. improvements in surgical techniques, including myocardial preservation. Echocardiography and Doppler imaging evidenced: (1) direct signs: the abnormal coronary ostium arising from the pulmonary trunk with retrograde coronary artery flow and (2) indirect signs: abundant intercoronary septal collaterals with anterograde flow (ARCAPA) or retrograde flow (ALCAPA) and dilatation of the controlateral normally originated coronary artery. Surgical repair has good long-term results with low mortality and reintervention rates. The majority of mitral regurgitation is functional and will improve with reperfusion, but structural mitral valve abnormalities should be repaired at the time of surgery **(32)**. Although most congenital coronary artery anomalies are clinically silent, they may be associated with severe symptoms in children. Recognition of potentially serious anomalies such as ALCAPA syndrome is mandatory so that early surgical treatment can be prescribed.

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