

CASE REPORT:
APPARENTLY HEALTHY WOMAN WITH DORMOTROPIC UNUSUAL
ECG MODIFICATIONS DURING STRESS TESTING

By Professor Bernard Belhassen MD

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CASE REPORT/ PRESENTACIÓN DE CASO/ RELATO DE CASO

- 58-asymptomatic healthy woman
 - No previous cardiac history
 - Normal echocardiogram
 - Thallium test: normal
 - All following ECG tracings were obtained during Thallium test (rest + mild exercise)
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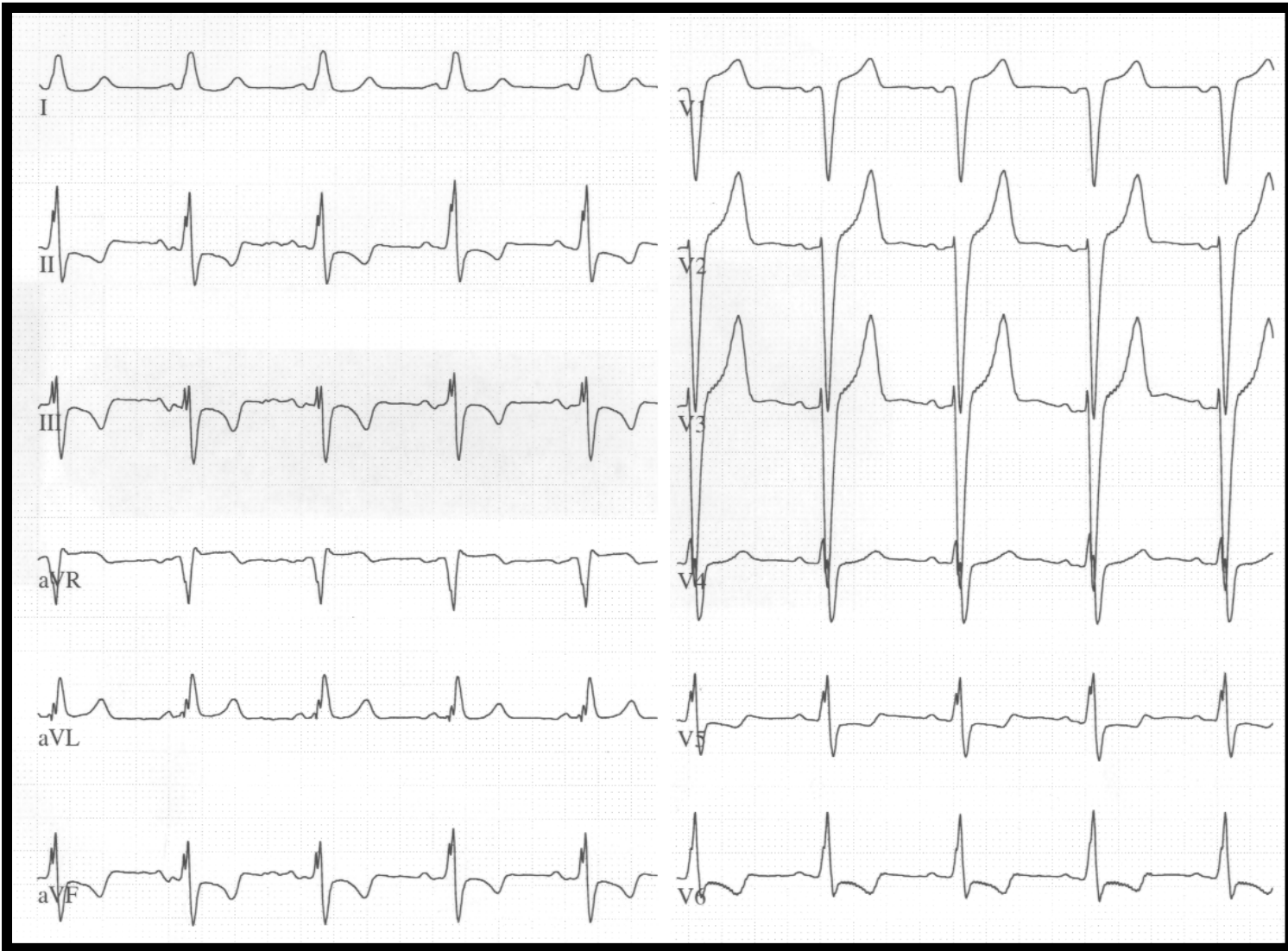
Paciente femenino 58 años sana. Sin historia previa de cardiopatía. Ecocardiograma normal; test ergométrico con cámara gamma normal (estudio de perfusión miocárdica con talio 201)

Todos lo siguientes ECGs fueron realizados durante la prueba de esfuerzo con talio (reposo y leve esfuerzo)

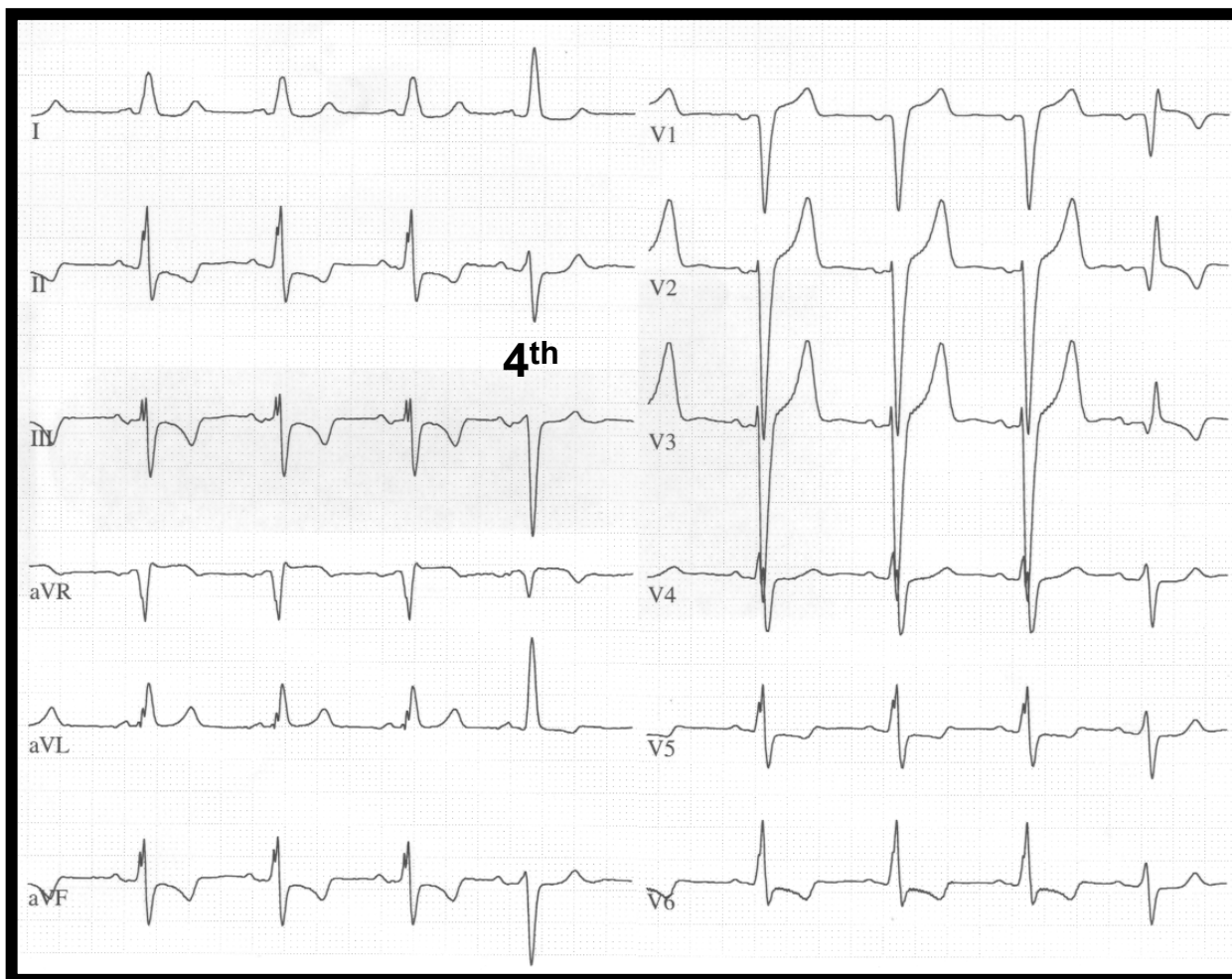
Paciente do sexo fememenino, 58 anos sadia. Sem história prévia de cardiopatía.

ECO normal; Teste ergométrico com tálio 201 normal.

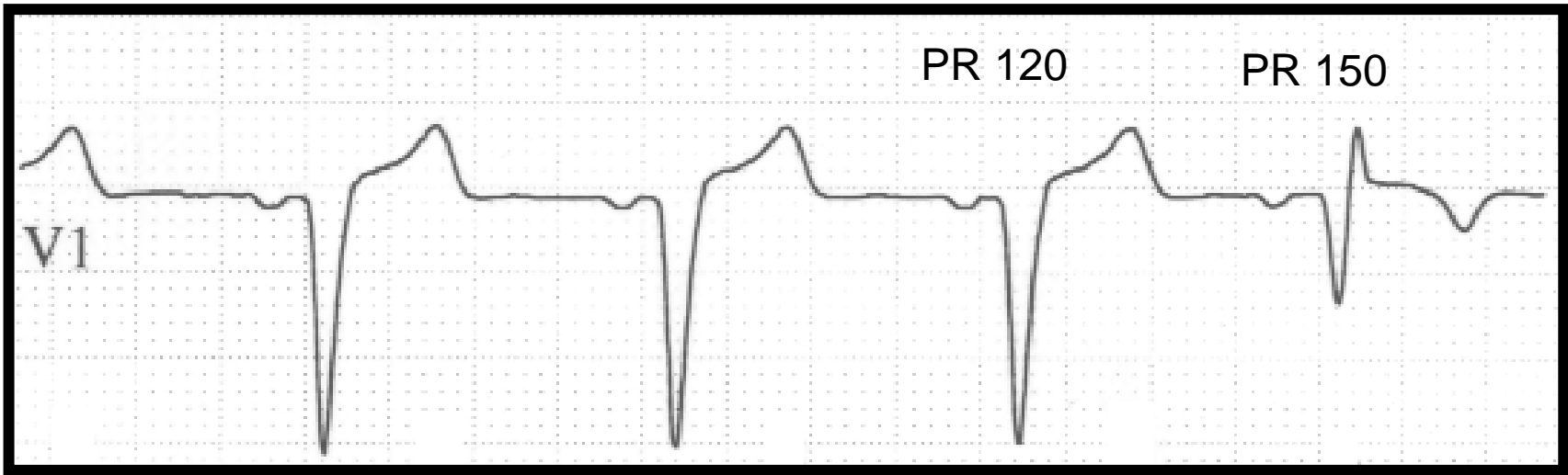
Todos os ECG a seguir foram realizados durante a prova de esforço con Tálio 201.

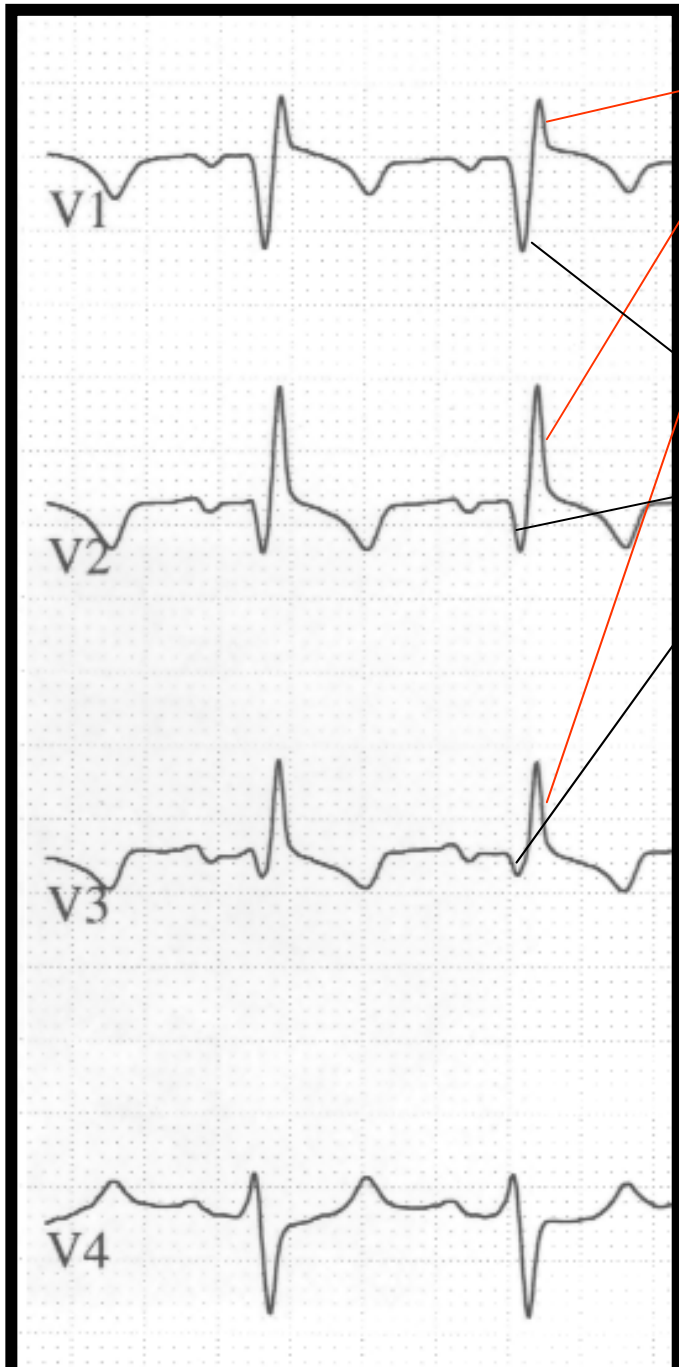


**Sinus rhythm, HR:75bpm, PR 120ms, QRS axis: 0° ; QRSd:110ms, T wave: -55° to front
Incomplete LBBB.**



The four first beats maintain the same pattern of the first ECG: PR= 120ms and incomplete LBBB pattern. The fourth beat has a PR=150ms, LAFB pattern on FP and LSFB pattern on precordial leads: bifascicular left bundle branch block (LAFB+LSFB).



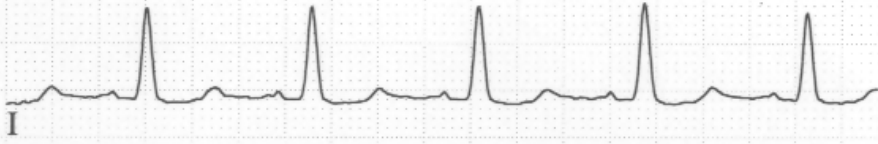


The final R wave in right precordial leads V_1 - V_3 is not broad. It is clearly very narrow



PSEUDO RBBB

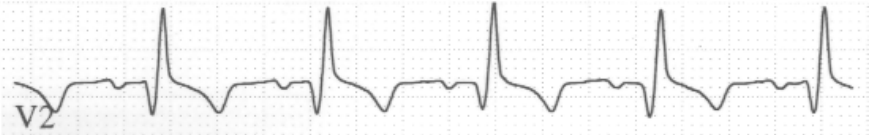
The initial ventricular activation is processed by the only nonblocked divisions: the Left Posterior Fascicle (LPF). Since the LPF heading backward and leftward causes the appearance of initial q or Q wave in right and/ or intermediary precordial leads.



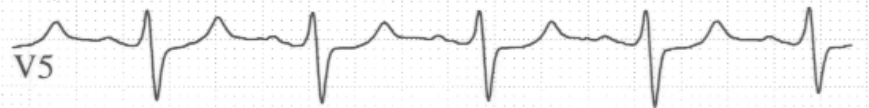
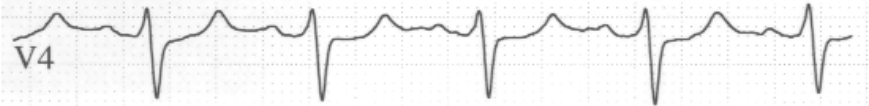
Absence of initial q wave on left leads: LSFB



Extreme left axis deviation: LAFB

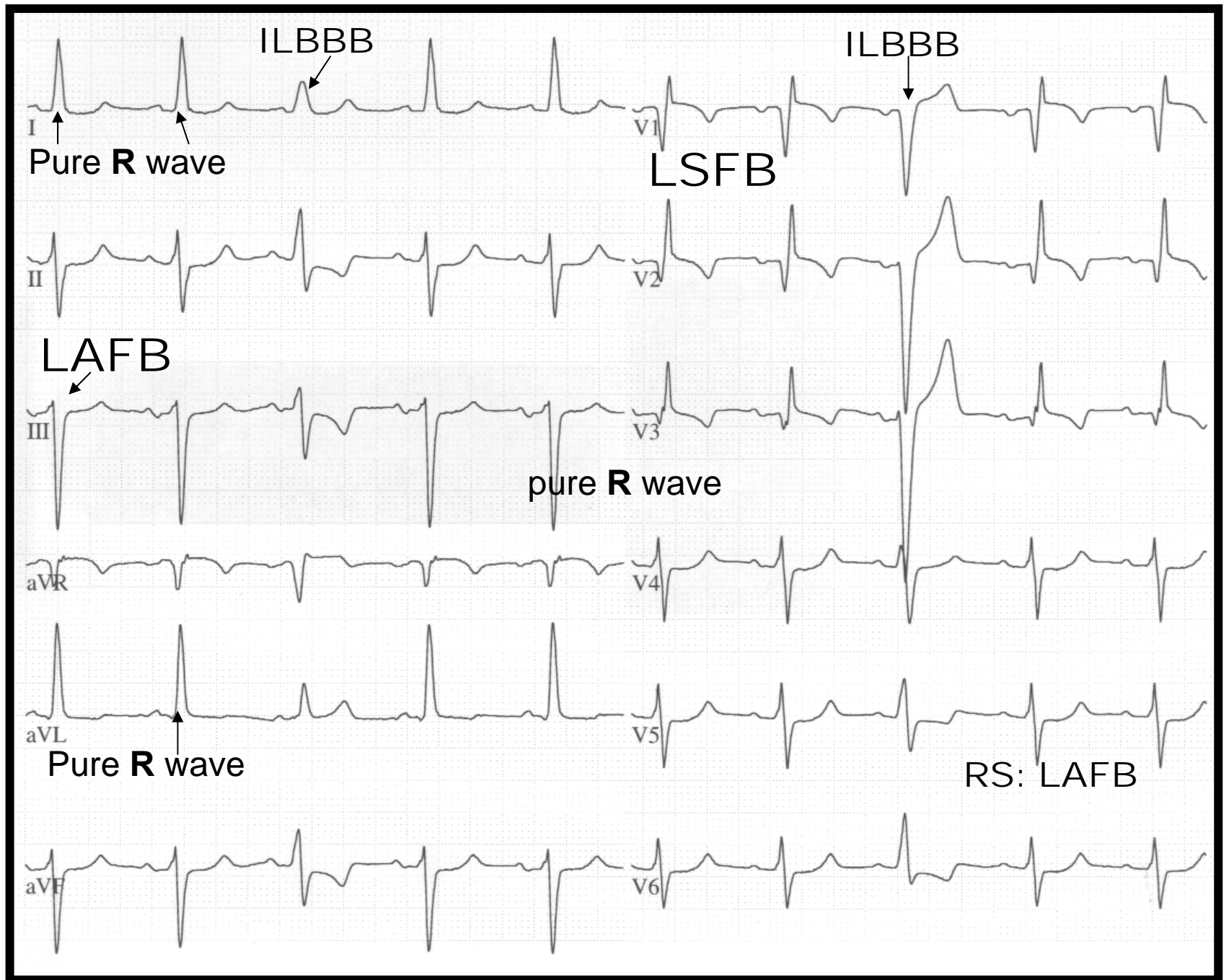


QR/qR pattern from V₁ to V₃: LSFB



Absence of initial q wave on left leads: LSFB





QUESTIONS/PREGUNTAS/PERGUNTAS

- RBBB, LBBB
 - Mechanism
 - Treatment (permanent pacemaker?)
- Inverted T waves mechanism
 - in V1-V3 (during RBBB)
 - in inferolateral leads (during LBBB)
- Old anteroseptal MI ?

BRD, BRI

Mecanismo?

Tratamiento: marcapaso permanente?

Ondas T invertidas en V1 a V3 durante el BRD. Mecanismo?

Ondas T negativas em pared infero-lateral durante el BCRI

Infarto antiguo antero-septal?

BRD, BRE

Mecanismo?

Tratamiento marca-passos definitivo?

Ondas T invertidas de V1 a V2 durante o BRD Mecanismo?

Ondas T invertida em parede ínfero-lateral durante o BRE

Infarto antiguo antero-septal?

Colleagues opinion

Hi Very interesting case Prof Belhassen, thanks.

Let me try:

1. When PR is short, it conducts with LBBB, thus we hit the antegrade refractory period of the left bundle and it is conducting "preferently" by the right bundle.
2. When PR prolongs, QRS gets narrower and with RBBB morphology.
3. The fact that QRS narrows but PR prolongs, strongly suggest "equal delay in both branches", also know as "pseudo-supernormal conduction" (see Josephson et al.).
4. However, this case is interesting because the left bundle recovers, the PR prolongs but now delayed conduction through the right bundle occurs.

There is no doubt that the distal conduction is sick in both branches.

I am ready to learn from others.

One more addition: when it conducts with RBBB morphology it also presents LAFB, indicating that the left posterior fascicle has recovered, thus, LBBB is not complete but functional.

Best

AB BestAdrian Baranchuk

PS: Plese allow to guide potential readers to a recent paper published in PACE by our group called "Grouped beats: What's the mechanism?" (see advanced papers)

Hola

Muy interesante el caso Prof Belhassen, gracias.

Voy a tratar de explicar:

1. Cuando PR es corto, se lleva a cabo con BRI, por lo que dimos el período refractario anterógrado de la rama izquierda y se está llevando a cabo "preferentemente" por la rama derecha.
2. Cuando se prolonga el PR, el QRS se estrecha y la morfología es de BRD.
3. El hecho de que QRS estrecho, pero prolonga la PR, sugieren fuertemente "retardo igual en ambas ramas", también conocido como "pseudo-supernormal conducción" (véase Josephson et al.).
4. Sin embargo, este caso es interesante porque la rama izquierda se recupera, el PR se prolonga, pero ahora se produce el retraso de la conducción a través de la rama derecha.

No hay duda de que la conducción distal está enferma en ambas ramas. Estoy dispuesto a aprender de los demás.

Una adición más: cuando se lleva a cabo con morfología de BRD también presenta LAFB, lo que indica que el fascículo posterior izquierdo se ha recuperado, por lo tanto, el BRI no está completa, pero funcional.mejor

AB

mejor

Adrian Baranchuk

PS: Plese permiten guiar a los lectores potenciales de un reciente artículo publicado en el PACE por nuestro grupo llamado "beats agrupados: ¿Cuál es el mecanismo?" (véanse los documentos avanzados)

Queridos amigos,

Coincido con Adrian en que ambas ramas estan enfermas. Me llama la atención que cuando se acelera la frecuencia cardíaca "mejora la conducción intraventricular". En la historia clínica no se menciona antecedentes de taquicardias supraventriculares pero quizás la prolongación del PR se deba a salto de conducción AV por doble vía nodal.

Un abrazo.

José Estepo

Dear friends,

I agree with Adrian that both branches are sick. It strikes me that when it increases heart rate "improves intraventricular conduction." The case history does not mention a history of supraventricular tachycardia but perhaps the PR prolongation is due to hopping AV conduction consequence of dual nodal pathway.

A hug.

José

Dear Andres: This apparently normal lady may or may not be completely normal. There are so many subclinical conditions that cannot be diagnosed by routine tests.

The P wave is notched and wide (120 ms), the conduction degeneration may have affected left atrium.

It is possible this is a slow rate dependant divisional LBBB. With the rate is increased slightly, left posterior fascicular blockage is improved a little bit thus we see LAFB pattern in limb leads, and if so that may have altered the activation sequence.

I don't see the RECD in this case thus I'm not so convinced about RBBB.

I would look forward to hearing the explanation of the Q wave and ST-T changes in V1-3 changes during Ex.

Thanks much,

**Li Zhang MD ldlzhang@gmail.com Director, Cardiovascular Outcomes Research
Main Line Health Heart CenterLankenau Hospital Associate Professor Lankenau Institute for
Medical Research 558 MOB East100 Lancaster Avenue Wynnewood, PA 19096U.S.A.Tel:
610-645-2694Cell: 484-222-1876**

Caro Andres: Esta senhora de aparência normal, pode ou não pode ser completamente normal. Existem muitas condições sub-clínicas que não podem ser diagnosticada por exames de rotina.

A onda P é entalhada e larga (120 ms), a degeneração de condução pode ter afetado átrio esquerdo. É possível que este seja um BRE divisional bradicárdico dependente. Com a FC aumentada ligeiramente, o bloqueio fascicular posterior esquerdo é melhorado um pouco assim vemos padrão LAFB nas derivações dos membros, e se assim que pode estar alterada a seqüência de ativação. Não vejo atraso final de condução neste caso, portanto, eu não estou convencida sobre a existência de BRD. Estou ansiosa para ouvir a explicação da onda Q e as mudanças do ST-T mudanças de V1-3. Muito obrigada

Li

Dear Andrés,

These ECG tracings are most amazing! I will try to come up with a reasonable interpretation. My first comment, however, is that an asymptomatic 58 y.o. woman with no cardiac history and a normal echocardiogram probably shouldn't have to undergo a thallium stress test. The first ECG a heart rate of approximately 75 bpm shows an atypical LBBB with primary T wave changes in the infero-lateral leads. During low-level exercise as the heart rate accelerates the LBBB disappears and a slightly longer PR interval appears. Therefore, I suspect that the LBBB is a bradycardia-dependent or phase 4 rate-related LBBB. I usually see phase 4 block at a much slower heart rate, however. At the faster heart rate (~85 bpm) and longer PR interval the ECG shows left anterior fascicular block in the frontal plane with a somewhat atypical RBBB in the precordial leads. To me this suggests a tachycardia-dependent or phase 3 rate-related bifascicular block. The last ECG with slightly slower HR shows several beats with the return of LBBB morphology. The more prolonged PR during the slightly faster HR indicates that there is probably underlying conduction slowing in the AV junction or (more likely) in the left bundle branch. I don't have a good explanation for the primary T wave changes in the resting ECG based on the limited clinical information provided. Also, the Q-waves in V1-3 are unexplained. Perhaps this has something to do with slowed conduction (phase 3 block) in the septal fascicle of the left bundle branches. The etiology of these conduction disorders in the absence of coronary disease or underlying cardiomyopathy is probably hereditary and related to primary degeneration of the conduction system (Lenegre disease, SCN5A mutation). She will eventually need a pacemaker, but as she is still asymptomatic, this can be postponed for now. Periodic ECG monitoring will be an important component in her follow-up. As always I await the comments from our colleagues.

Regards, Frank Yanowitz, Frank MD Professor of Medicine University of Utah School of Medicine Medical Director, ECG Department LDS Hospital Salt Lake City, Utah 8th Ave. and C Street Salt Lake City, Utah 84143 USA

Estimado Andrés: Estos trazados ECG son increíbles! Voy a tratar de llegar a una interpretación razonable. Mi primer comentario, sin embargo, es que en una mujer de 58 años asintomática y sin antecedentes cardiacos y un ecocardiograma normal probablemente no debería haberse sometido a una prueba de esfuerzo con talio.

El primer ECG tiene una FC de ≈ 75 lpm patrón de BRI atípico con alteración primaria de la onda T en pared infero-lateral. Durante bajo nivel de ejercicio el BRI desaparece y el intervalo PR se hace más largo. Por lo tanto, sospecho que el BRI es bradicardico-dependiente o en fase 4. Usualmente los bloqueos de fase 4 ocurren con FCs mucho menores. Con FC más rápidas (~ 85 lpm) y el intervalo PR más largo aparece LAFB en el PF con un BRD un poco atípico en las derivaciones precordiales. Para mí, esto sugiere un bloqueo en fase 3 relacionado con bloqueo bifascicular.

El último ECG con FC un poco más lenta muestra varios latidos con el regreso de la morfología de BRI. El PR más prolongado durante el discreto aumento de FC indica que probablemente hay un enlentecimiento en la unión AV o más probablemente en la rama izquierda. No tengo una buena explicación para las T primarias en el ECG de base en reposo por las limitadas informaciones clínicas proporcionadas. Además, la onda Q en V1-3 son inexplicables. Quizá esto tenga algo que ver con conducción lenta (bloqueo en fase 3) en el fascículo septal de la rama a izquierda.

La etiología de estos trastornos de la conducción en la ausencia de enfermedad coronaria o miocardiopatía subyacente es, probablemente, hereditaria y relacionada con la degeneración primaria del sistema de conducción o enfermedad de Lenegre por mutación en el gen SCN5A. Con el tiempo se va a necesitar un marcapasos, pero en cuando ella se encuentre asintomática, esto puede ser pospuesto por ahora. Periódica monitorización del ECG será un componente importante en su seguimiento.

Como siempre espero los comentarios de nuestros colegas.

Saludos,

Frank

Interesting sequence.

There is LBBB pattern that alternates with a RBBB and LAFB pattern at the same rate and the PR interval lengthens with RBBB pattern. This finding is pathgnomonic of infranodal conduction system disease as described by Lepeshkin. The deep q waves in V1 and V2 are most likely due to alterations in the initial forces (directed right and inferior) due to the associated Left Ant fascicle block pattern seen with RBBB. These patients always show a prolonged H-V and should be treated with a permanent pacemaker. The normal Echo and Thallium R/O infarction or ischemia.

Prof. Melvin M Scheinman,

Department of Cardiac Electrophysiology, University of California San Francisco, San Francisco, California, USA. scheinman@medicine.ucsf.edu

Professor of Medicine.

Interesante secuencia Hay un patrón de BRI que alterna con el padrón de BRD y LAFB con la misma frecuencia cardiaca y el intervalo PR se prolonga con el patrón de BRD. Estos hayazgos son patognomónicos de enfermedad del sistema de conducción infranodal descrito por Lepeshkin,

La onda Q profunda en V1 y V2 es mas probablemente ocasionada por alteración en la dirección del primer vector dirigido para abajo y a la izquierda consecuencia de la asociación de LAFB con BRD. Estos pacientes siempre muestran HV prolongado y deben ser tratados con implante de marcapaso permanente. El ECO normal y el talio elimina la posibilidad de enfermedad coronaria o isquemia.

Queridos amigos del forum discutire el difícil y enigmático caso de una mujer de 50 años durante el estudio de ergometría. Antes de todo quiero explicar quien es el maestro Profe Bernard, es el padre de la electrofisiología moderna en Israel, típico representante de la electrofisiología francesa, y basta leer las innumerables contribuciones en la gran literatura cardiológica. Para describir a este extraordinario profesional me llevaría varias páginas. Pero lo importante ahora es descifrar este caso casi imposible fenómeno electrocardiográfico.

Lo primero que llama la atención es una mujer relativamente joven, asintomática, y con un eco normal, y un mapeo isotópico sin signos de alteración en la perfusión miocárdica.

Desde el punto de vista fisiológico, la paciente no eleva la frecuencia, en lo mínimo, y esto es un signo de gran gravedad, tampoco sabemos si aumentó la presión arterial.

En el primer ECG hay una alteración en la conducción intraventricular que parece un bloqueo de rama izquierda, pero no es el clásico.

Vemos un notch inicial en DII, DIII, AVF, y V5, V6. Q/S en DIII y ST-T invertidas en estas derivaciones.

También llama la atención la presencia de S en V5, V6, no común en un bloqueo izquierdo troncular.

En esta etapa diría sin tomar en cuenta los datos negativos de la función cardíaca, y pensaría que el ventrículo izquierdo existe un fenómeno fibrotico inicial inferoposterior lateral con alta sospecha de isquemia inferolateral.

Debo acentuar que no hay alteración en la conducción atrial y en el complejo nodal.

En el segundo ECG aparece en forma intermedia y sin aumentar la frecuencia sinusal, latidos sinusales con signos de desviación del eje a la izquierda (LAH) y con S, S en AVL, y complejos similares a bloqueos de rama derecha pero sin R; en aVR, y las S, S en V5, V6 son menos de 60 ms, elevando la sospecha de que no es un típico RBBB, pero las ondas Q en V1 a V3, sugieren un infarto anteroseptal, o severa fibrosis del septo.

El último trazado muestra una imagen persistente con imagen semejante a un bloqueo bilateral bundle branch block.

Para mí esta señora sufre de un proceso fibrotico intracardiaco, que podría ser sarcoidosis o amiloidosis primaria o Fabry disease.

Para decidir este drama hace falta un MRI, donde se podrá descubrir una enfermedad infiltrativa que produce una severa enfermedad fibrotica cardíaca.

Por ahora no poner pacemaker porque los cambios no parecen ser un bloqueo bilateral intermitente de LBBB y RBBB. Estas 3 enfermedades infiltrativas tienen cura médica.

Este caso es verdaderamente difícil para pensarlo mucho tiempo pero también hay que realizar un estudio hemodinámico completo, medir las presiones diastólicas derechas e izquierdas y coronariografía.

Hay que tener todos los datos posibles de esta joven mujer, para poder ayudarla a seguir viviendo, en la mejor época de la vida que tiene más de un tercio de vida por delante.

No poner pacemaker y se terminó el problema y a otra cosa.

Y buscar la etiología de este estado fibrotico cardíaco.

Un fraternal abrazo.

Samuel Sclarovsky

Presenta BCRI con HVI mas bloqueo AV de primer grado. en las derivaciones V1,V2,V3 se observa infarto con BRD. QRS de duración mayor de 120ms PR prolongado.v1 bloqueo AV y BRD mas infarto de la cara anterior del ventrículo izquierdo. Tiene en conclusión un bloqueo bifascicular. IMA inferolateral y requiere uso de marcapaso.

Gregorio Maslivar

Andrés Ricardo Pérez-Riera Analysis

First ECG: Sinus rhythm, HR:75bpm, PRi = 120ms, QRS axis: 0°; QRSd:115ms, T wave: -55°FP and to front in HP. **Conclusion:** Incomplete LBBB (LBBB pattern and QRS<120ms).

Second ECG: The first four beats maintain the same pattern of the first ECG: PR interval = 120ms and QRS with **incomplete** LBBB pattern (QRS duration =115ms <120ms).

The fourth beat prolong minimally the PR interval (PRi = 150ms) and the frontal plane shows an extreme left axis QRS deviation (QRS axis is near -45°). Differently of classical LAFB, the QRS pattern in I and aVL show a pure **R** wave (not **qR** as observed a isolated **LAFB**). This phenomena is consequence of absence of first vector **1_{AM}** dependent of left septal fascicle (LSF). Concomitantly, on precordial leads LSFB is manifested by **QR/qR** pattern from V₁ to V₃. The initial ventricular activation is processed by the only nonblocked divisions: the left posterior fascicle (LPF). Since the LPF heading backward and leftward causes the appearance of initial q or Q wave in right and/ or intermediary precordial leads. Additionally, the final **R** wave in right precordial leads V₁-V₃ is very narrow (Li observation). A truly RBBB has a broad or wide final R' or R wave. This is a **pseudo RBBB**. Finally, the absence of initial **q** wave on left precordial leads V₅-V₆ and I an aVL is indicative of absence of the first vector(1_{AM} vector) which corresponds to the activation of the middle third or the left septal surface, always heading to the front in horizontal plane (HP), usually heading to the right (85% of the cases), thus originating the r or R wave of V₁ and V₂ precordial leads and the initial q wave of the left precordial leads: from V₄ through V₆ or V₅-V₆. **The anteromedial vector (1_{AM}) directed to front and rightward is absent in this case.**

Conclusion: bifascicular left bundle branch block (**LAFB + LSFB**).

Theoretical explanation: In 1970, Dr. Dirk Durren et al from Amsterdam, The Netherlands, demonstrated in a classical manuscript using 870 intramural terminals in isolated human hearts, that three endocardial areas are synchronously excited from 0 to 5 ms after the start of left ventricle (LV) activity potential

excited from 0 to 5 ms after the start of LV activity potential. To obtain information concerning the time course and instantaneous distribution of the excitatory process of the normal human heart, the authors studied on isolated human hearts from seven individuals who died from various cerebral conditions, but who had no history of cardiac disease. The first LV areas excited were:

1. High on the anterior paraseptal wall just below the attachment of the anterolateral papilar muscle (ALPM) where the left anterior fascicle (LAF) ends;
2. Central on the left surface of the IVS where the left septal fascicle (LSF) ends. Septal activation started in the middle third of the left side of the IVS, somewhat anteriorly and the lower third at the junction of the IVS and posterior wall. The normally functioning LSF, the left middle septum surface and the inferior two-thirds of the septum originate the first vector, vector 1 or first anteromedial (1_{AM}) vector and left inferior two-thirds of the IVS (second vector or vector of the inferior $2/3$ of IVS)
3. Posterior paraseptal about one third of the distance from the apex to the base near the base of posteromedial papilar muscle (PMPM) where the left posterior fascicle LPF ends. The posterobasal area is the last part of the LV to activate. In the present case report this is the only fascicle without block, consequently the only manifested ant the initial 10ms of ventricular activation.

A definite diagnosis of the bilateral bundle branch block on ECG can be made only if both left and pseudo right bundle branch block patterns appear in the same patient, accompanied by consistent changes of the PR interval duration. This is the present case report. There are many signs which made an A-V conduction disturbance due to bilateral bundle branch block, rather than to block in the A-V node or the common bundle, probable. Several types of "atypical right bundle branch block" (or pseudo RBBB) patterns appear to be caused by a combination of block of the a part of the left branch (modified from 1;2). If this patient has not structural heart disease or CAD the most probable diagnosis is the progressive dromotropic disorders of the His Purkinje system or "Lenègre disease". Two entities, called Progressive Cardiac Conduction Defects (PCCD), are grouped together as primary conduction diseases (Lev-Lenègre). Both Lenègre disease—known as "primary" PCCD³—as well as the secondary mechanic lesion—sclerosis of the left "cardiac skeleton" or Lev disease⁴—usually cause LBBB or RBBB, frequently associated with fascicular blocks. Occasionally, they develop into more advanced degrees of block with a potential to cause SCD due to total AV block, to the extent that they represent **the most important cause of pacemaker implantation in the first world: 0.15 per 1,000 inhabitants a year**. The same mutation in novel single SCN5A missense mutation can lead either to Brugada syndrome or to an PCCD. Modifier gene(s) may influence the phenotypic consequences of a SCN5A mutation. A G-to-T mutation at position 4372 was identified by direct sequencing and was predicted to change a glycine for an arginine (G1406R) between the DIII-S5 and DIII-S6 domain of the Na⁺ channel protein⁵

1. Lipeschkin E. THE ELECTROCARDIOGRAPHIC DIAGNOSIS OF BILATERAL BUNDLE BRANCH BLOCK IN RELATION TO HEART BLOCK. *Prog Cardiovasc Dis.* 1964 Mar;6:445-471.
2. LENEGRE J. ETIOLOGY AND PATHOLOGY OF BILATERAL BUNDLE BRANCH BLOCK IN RELATION TO COMPLETE HEART BLOCK. *Prog Cardiovasc Dis.* 1964 Mar;6:409-44.
3. Lenègre J. The pathology of complete atrioventricular block. *Progr Cardiovasc Dis* 1964; 6:317-323
4. Lev M. Anatomic basis of atrioventricular block. *Am J Med* 1964;37:742.
5. Kyndt F, Probst V, Potet F, et. al. Novel SCN5A Mutation Leading Either to Isolated Cardiac Conduction Defect or Brugada Syndrome in a Large French Family. *Circulation* 2001; 104: 3081-3086

BRUGADA SYNDROME AND LENÈGRE DISEASE

Tan et al ¹ identified a single mutation in five affected family members; this mutation results in the substitution of cysteine 514 for glycine (G514C) in the channel protein. Biophysical characterization of the mutant channel shows that there are abnormalities in voltage-dependent 'gating' behaviour that can be partially corrected by dexamethasone, consistent with the salutary effects of glucocorticoids on the clinical phenotype. Computational analysis predicts that the gating defects of G514C selectively slow myocardial conduction, but do not provoke the rapid cardiac arrhythmias associated previously with SCN5A mutations. Two allelic heterozygotic mutations with Brugada syndrome, located in the alpha subunit of the Na⁺ channel in the SCN5A gene, what has been clinically translated into AV block. They are the result of the substitution of the serine amino acid by glycine (G298S) in the domain of the I S5-S6 loop, and asparagine by aspartic acid within the S3 of the IV domain (D1595N). Both mutations prevent fast inactivation, reduce sodium channel density, and accentuate the slow component of inactivation. This combination causes a decrease in conduction velocity and leads to AV block.

A mutation was identified, which causes intraventricular dromotropic disorder secondary to substitution of the cysteine amino acid by glycine (G514C) in the Na⁺ proteic fast channel

In Brugada syndrome, the PR interval and the HV of the electrogram are prolonged in nearly 50% of cases. HV can reach a duration of approximately twice its maximal normal limit.

Lenègre disease should not continue to be classified as an idiopathic progressive disease of the His-Purkinje system. It should be called a Progressive Cardiac Conduction Defect or PCCD. It has been identified as a disease of the Na⁺ fast channel or channelopathy by mutation in the SCN5A gene, and as allele of Brugada syndrome with a different phenotypic expression, in a similar fashion to the LQT3 variant of the hereditary-familial LQTS. The same missense mutation in the SCN5A gene can cause both phenotypes: Brugada disease and Lenègre disease.

1. **Tan HL, Bink-Boelkens MT, Bezzina CR, et al. A sodium-channel mutation causes Isolated cardiac conduction disease. Nature 2001; 409:1043-1047.**

DIFFERENCES BETWEEN LENÈGRE AND LEV DISEASE

	LENÈGRE DISEASE	LEV DISEASE
Pathologic anatomy	Progressive sclerosis of the intraventricular His-Purkinje conduction system.	Mechanical progressive fibrosis of the left “cardiac skeleton.” Calcification of the mitral valve ring, fibrous central body, membranous part of the aorta base, apex muscular septum, and direct Hissian system and anterosuperior fascicle of the left branch.
Etiology	Allelic heterozygotic mutation with Brugada syndrome located in the alpha subunit of the sodium channel in the SCN5A gene.	Idiopathic. Mechanical acceleration of the aging process.
Identified genetic defect	<ol style="list-style-type: none"> 1) Substitution of the serine amino acid by glycine (G298S) in the domain of the I S5-S6 loop. 2) Substitution of asparagine by aspartic acid within the IV domain of S3 (D1595N). 3) Substitution of 514 cysteine by glycine (G514C). 4) Substitution of glycine by threonine in the 4372 position and glycine by arginine (G1405R) between the DIII-S5 domains of the sodium channel. 	No.

Disorders of the Cardiac Sodium Channel Gene SCN5A

VENTRICULAR ARRHYTHMIA AND SUDDEN DEATH

Congenital LQTS type 3

Brugada Syndrome type 1

Idiopathic ventricular fibrillation

Sudden Unexplained Nocturnal Death Syndrome

Sudden Infant Death Syndrome

IMPAIRED CARDIAC CONDUCTION

Progressive Cardiac Conduction System Disease(Lenègre)

Congenital Sick Sinus Syndrome

Atrial Standstill

LATENT ARRHYTHMIA SUSCEPTIBILITY

Drug-induced long-QT syndrome

Arrhythmia susceptibility in African Americans (S103Y)

OTHER

Mixed phenotypes or overlap syndromes

Dilated cardiomyopathy with arrhythmia

Atrial fibrillation

My Proposal Approach: **Definitive Pacemaker implantation. Severe intraventricular conduction disease.**

Class I (ACC/AHA Guidelines for implantable permanent pacing. Level of evidence B.

We are waiting for the
definitive Professor' BB
diagnosis