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

“In Electrocardiology the electrical phenomena are always clears. What not always is clear are our interpretations about them”.
Andrés.

By Professor Bernard Belhassen MD
Affiliation: Professor of Cardiology, Sackler School of Medicine, Tel-Aviv University, Director, Cardiac Electrophysiology Laboratory, Sourasky Medical Center, Israel.

Prof. Bernard Belhassen brief biography

Cardiologist
Director, Cardiac Electrophysiology Laboratory Professor of Cardiology, Sackler School of Medicine, Tel-Aviv University. Prof. Belhassen graduated and completed his residency training in Cardiology during the years at Medical School, Faculte de Medecine de Paris VII, France. In 1978 he was appointed as Head of the Electrophysiology Laboratory. During 1983-1984 Prof. Belhassen completed the fellowship programs as a Visiting Professor of Cardiology, Hahnemann University, Philadelphia, USA and in 1988 as a Visiting Professor of Cardiology, Department of Cardiology, Hospital Broussais, Paris, France.
He is an author of over 200 medical publications in leading medical journals and over 230 lectures. He is active in professional societies: Israel Heart Society, French Society of Cardiology, North American Society of Pacing and Electrophysiology, Working Group on Cardiac Arrhythmias of the European Society of Cardiology.
ACADEMIC AND PROFESSIONAL AWARDS:
Grants:
1983 - William Fulbright Grant (U.S.A)
Prizes:
1984 - Israel Medical Association Award
1987 - Henry Neufeld Award, First Prize
1988 - Henry Neufeld Award, Second Prize
1990 - The Israeli-German Symposium on Clinical Cardiology Award
1997 - The First Michel Mirowski Prize
1998 - Henry Neufeld Award, First Prize
FIELD OF INTEREST:
Cardiac arrhythmias; clinical cardiac electrophysiology; diagnostic electrophysiological study; radiofrequency ablation (SVT, atrial flutter, WPW, VT), risk stratification of post-MI patients (do they need an ICD or not).

Congratulation dear BB for your fantastic trajectory. I'm very proud considered your fried.

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)**

Paciente femenino 58 años sana. Sin historia previa de cardiopatia. Ecocardiograma normal; test ergométrico con cámara gamma normal (estudio de perfusión miocárdica con talio 201)

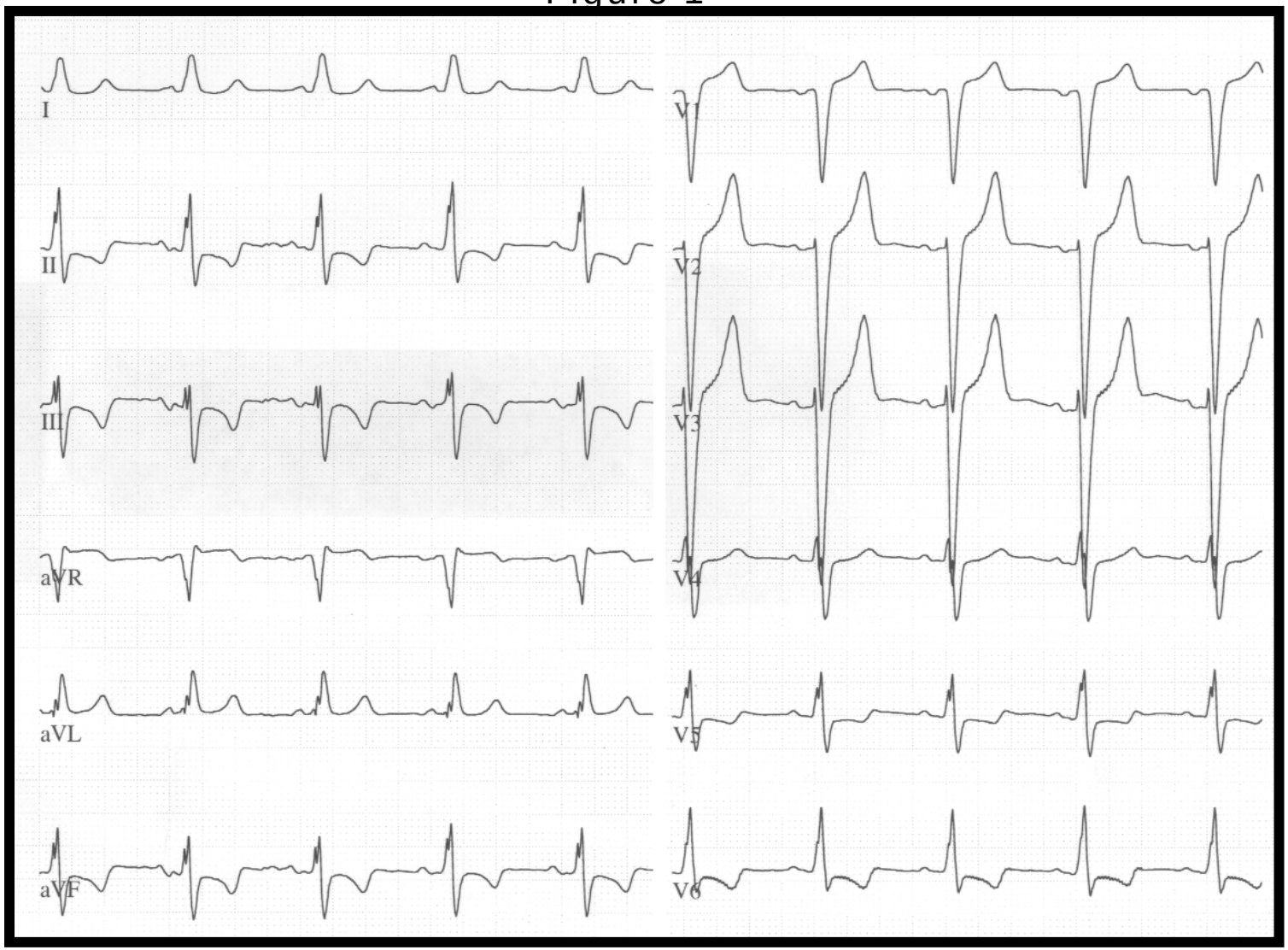
Todos lo siguientes ECGs fueron realizados durante la prueba de esfuerzo con talio (reposo y leve esfuerzo)

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

ECO normal; Teste ergométrico com tálio 201 normal.

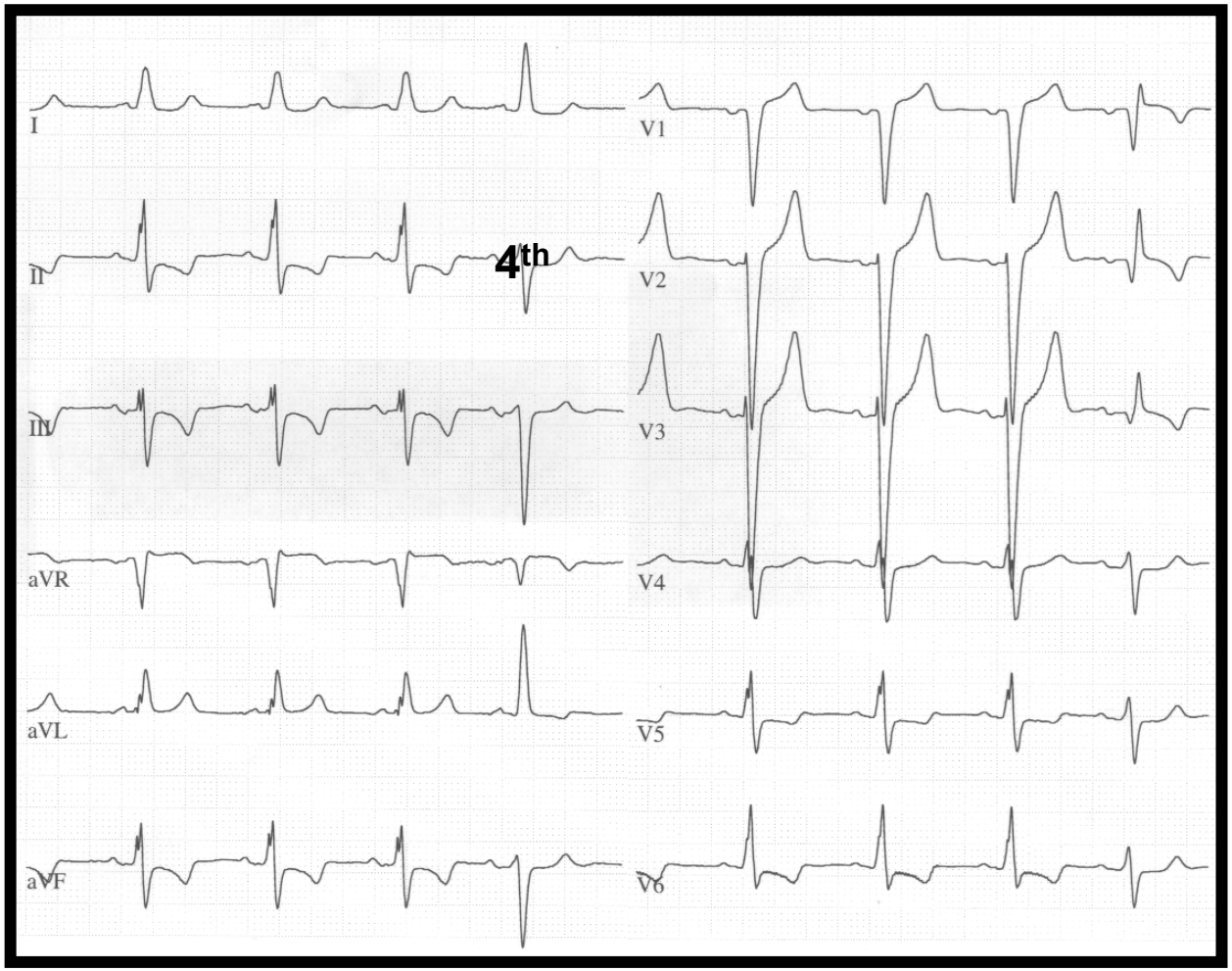
Todos os ECG a seguir foram realizados durante a prova de esforço con Tálio 201.

Figure 1



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

Figure 2



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).

Figure 3

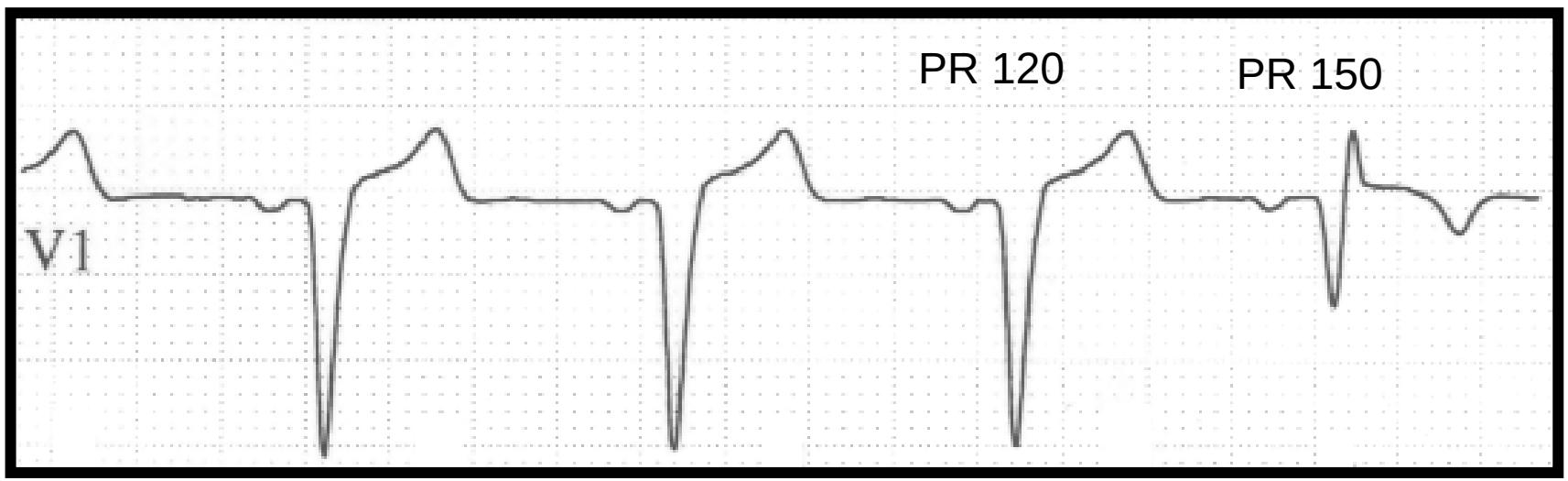
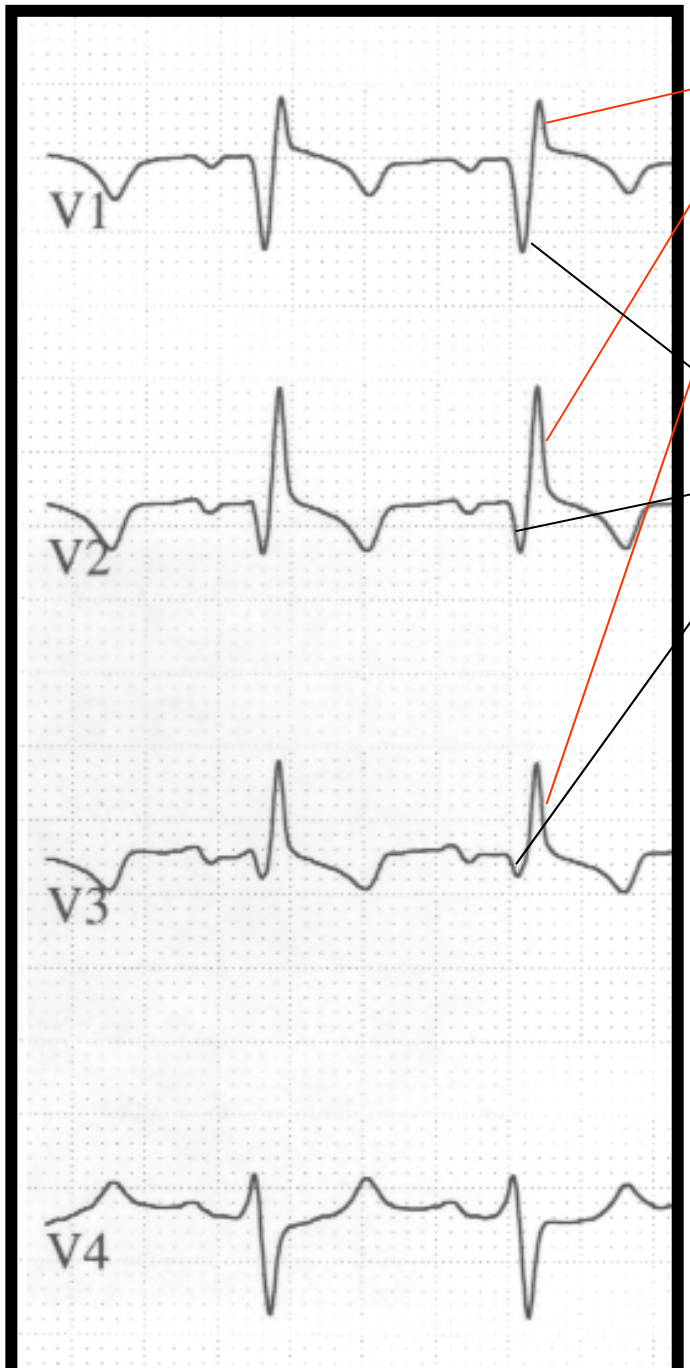


Figure 4



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.

Figure 5

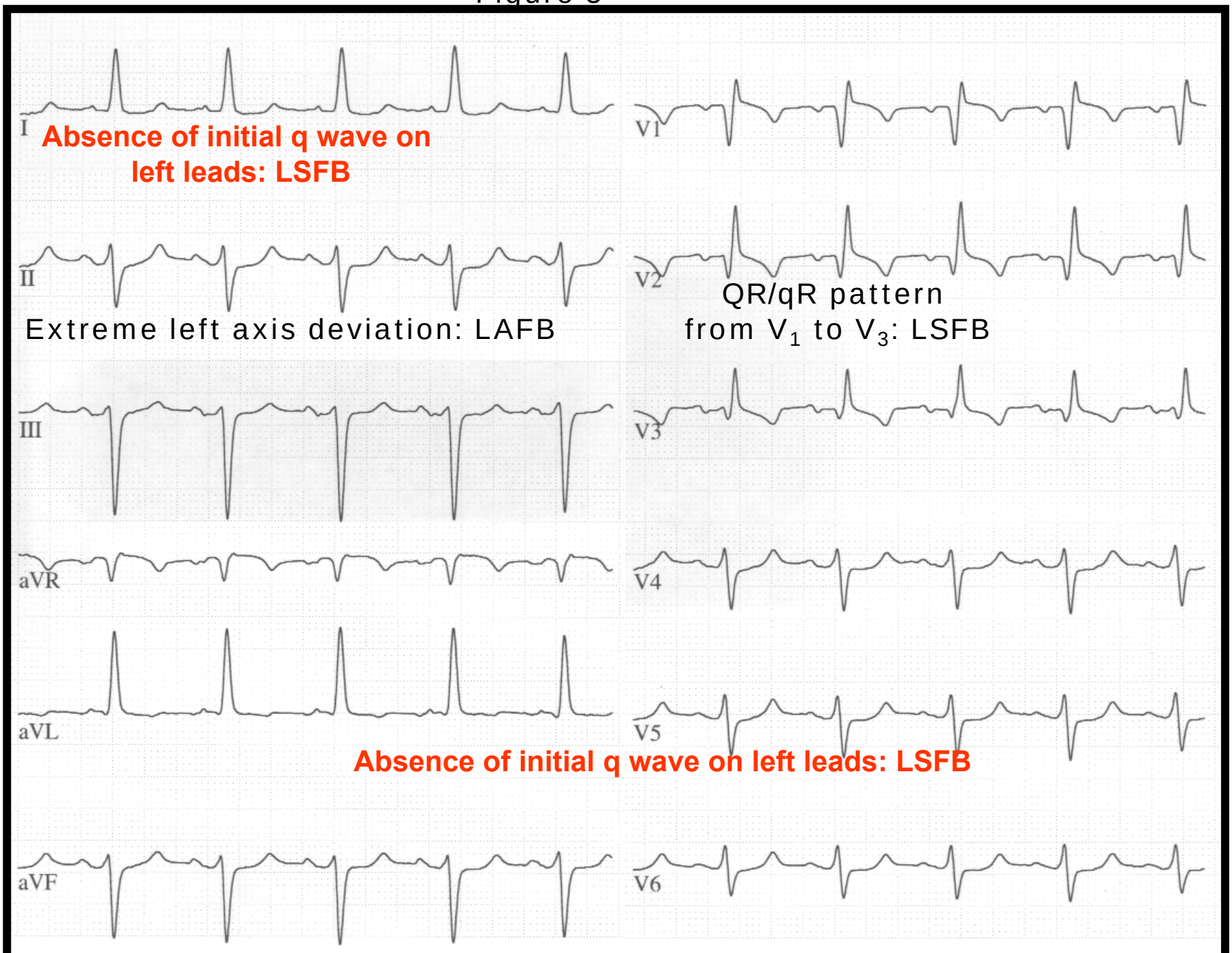
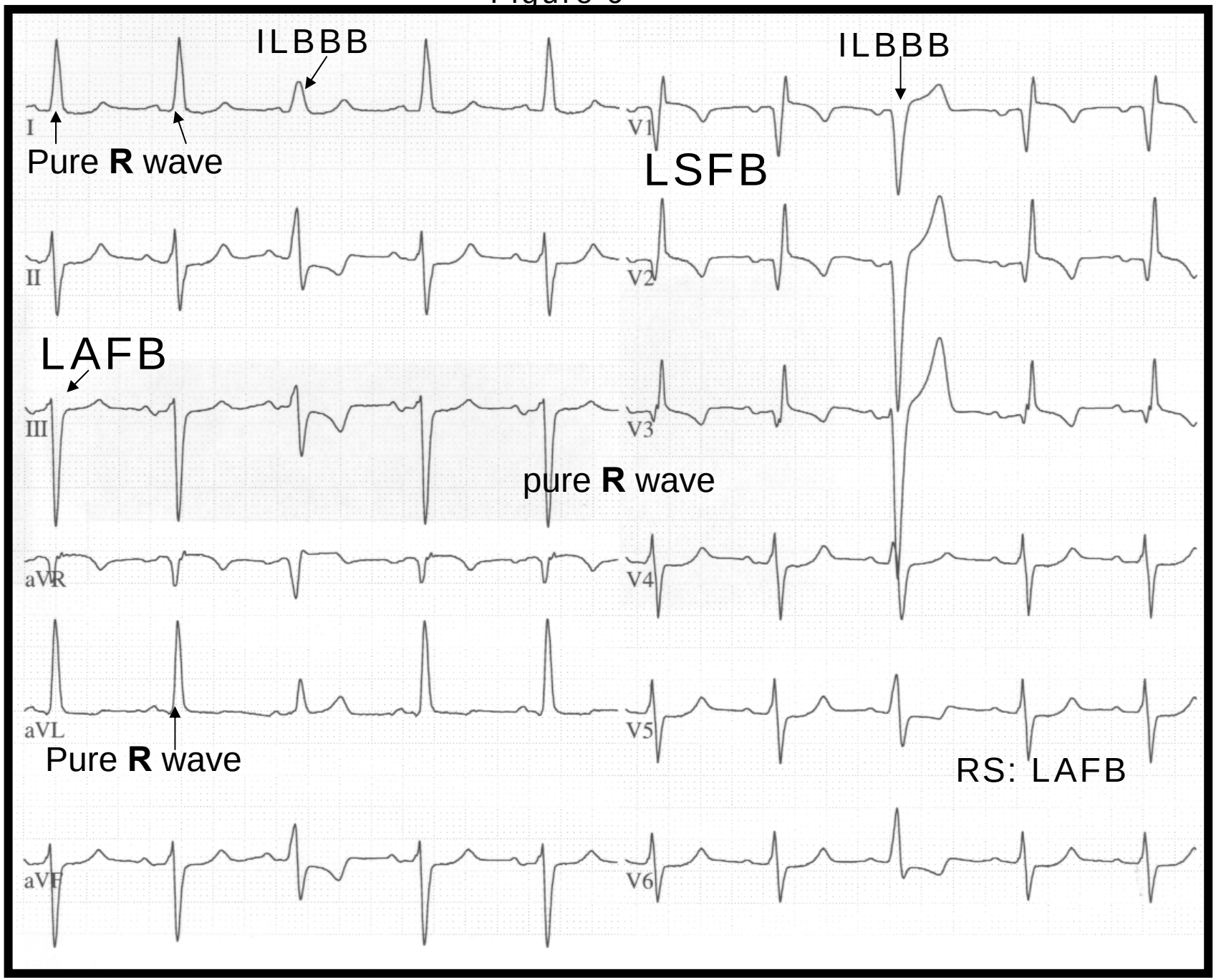

I
Absence of initial q wave on left leads: LSFB
II
Extreme left axis deviation: LAFB
III
aVR
aVL
aVF
V1
V2
QR/qR pattern from V_1 to V_3: LSFB
V3
V4
V5
Absence of initial q wave on left leads: LSFB
V6

Figure 6


ILBBB
ILBBB
I
V1
Pure **R** wave
LSFB
II
V2
LAFB
III
V3
pure **R** wave
aVR
V4
aVL
V5
Pure **R** wave
RS: LAFB
aVF
V6

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?
Tratamento marca-passos definitivo?
Ondas T ineritdas de V1 a V2 durante o BRD Mecanismo?
Ondas T invertida em parede ínfero-lateral durante o BRE
Infarto antigo 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 MedicineUniversity of Utah School of MedicineMedical Director, ECG DepartmentLDS Hospital Salt Lake City, Utah 8th Ave. and C StreetSalt 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 58a 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 alteracion primaria de la onda T en pared infero-lateral. Durante bajo nivel de ejercicio el BRI desaparece y el intervalo PR se hace mas 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 mas 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 mas prolongado durante el discreto aumento da FC indica que probablemente hay un enlentecimiento en al unión AV o mas 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 estas 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 intevalo PR se prolonga con el patrón de BRD. Estos hayazgos son patognomónicos de enfermedad del sistema de conducción infranodal descripto 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 muestan HV prolongado y deben ser tratados com implante de marcapaso permanente. El ECO normal y el talio elimina la posibilidad de enfermedad coronaria o isquemia.

Dear friend, I will tried to analyze the rare case presented by professor Bernard Belhassen, about this outstanding cardiology, who is consider by all of us, as the father of modern electrophysiology in Israel, is a long history, which will take a few pages. This is a 58 years asymptomatic female, with normal echocardiogram and no signs of myocardial perfusion disturbances, but a severe intraventricular conduction delay. From the physiological point of view, no increased heart rate during the effort test was seen, suggesting a severe cardiac dysfunction. The ECG's pattern suggest bilateral bundle branch block, because an a intermittent LBBB and RBBB. The first ECG shows a LBBB-like pattern, but the initial vector in II ,II, aVF V_5 and V^6 with ST-T depression are non frequent finding in troncular LBBB. This pattern suggests a probably severe chronic early depolarization defect in the inferoposterior lateral wall, most probably to a fibrotic process. Also the S waves in V_5,V_6 are unusual in troncular LBBB.
The next ECG shows an intermittent pattern similar to a RBBB + LAFB. The deep S wave in III suggests basal LVH. The RBBB pattern has some diagnosis difficulties because a non wide second R in aVR and wide S waves in V_5 ,V_6 were seen, and is well known that these waves, per definition, must be over 60ms. The Q waves in V_1 ,V_2, and V_3 indicate a chronic fibrotic process in the right and left septum frequently due to an old infarction or a infiltrative disease in the LV. My impression is that the patient suffers a intraventricular fibrotic disease to an infiltrative disease such a sarcoidosis primary amiloidosis or Fabre disease. inducing a severe pattern of Lenègre mechanism is important to rule out, that these diseases have medical cure. I think that most important method for rule out these diseases is to perform a MRI study, which can provide information of tissue diffentiation, and a full left and right venticular hemodynamic recording and coronary study as well, this a young patient that have the possibility of more than 30 years survival. I don't think that pacemaker can help, because this is most probably a non conducting big branches disease My best regard of all our friends , and probably can impaired her clinical situation. Samuel Sclarovsky

Queridos amigos del forum discutire el dificil y enigmatico mujer de 50 anios durante ergometria
Antes de todo quiero explicar quien es el maestro Profe Bernard , es el padre de la electrofisiologia moderna en Israel ,tipico represenrante de la electrofisiologia francesa, y basta leer . las inumerables conrtibuciones en la gran literatura cardiologica,. Para describir a a este extraordinario profesional . me llevaria varias paginas
Pero lo importante ahora es descifrar . este caso casi imposible fenomeno electrocardiografico
Lo primero que llama la atencion es mujer relativamente joven asintomatica ,y con eco normal , y mapeo isoitopico sin signos se alteracion en la perfusion miocardica
Desde punta de vista fisiologico .la paciente no eleva la frecuencia , en lo minimo, y esto es un signo de gran gravedad , tampoco sabemos si aumento la presion arterial
En el primer ECG hay una alteracion en la conduccion intraventricular .que parece un bloqueo de rama izqueirda , pero no es el clasico
Vemos un notch incial en DII ,DIII ,AVF , Y V5 ,V6 . Q/S in DIII . y ST -T invertidas en estas derivaciones
Tambien llama la atencion la presencia de S en v5 .v6, no comun en bloqueo izquierdo troncular
En esta etapa diria sin tomar en cuenta los datos negativos de la funcion cardiaca , y pensaria que el ventriculo izquierdo existe un fenomeno fibrotico inicial inferoposterior lateral con alta sospecha de isquemia inferolateral
Debo acentuar que no hay alteracion en la conduccion atrial y en el complejo nodal
En el segundo ECG aprece en forma intermedia y sin aumentar la frecuencia sinusal , latidos sinusales con signos de desviacion del eje a la izquierda (LAH) y con S,S en AVL , y complejos de 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 tipico RBBB, pero las ondas Q in V1 a V3, sugieren un infarto anteroseptal , o severa fibrosis del septo
EL ultimo trazado , muestra una imagen persistente con imagen senejante a bilateral bundle branch block
Para mi esta seniora sufre de un proceso fibrotico intracardiaco ,que podria ser sarcoidosis o amiloidosis primaria o Fabre desease
para decidir este drama hace falta un MRI, donde se podra descubrir enfermead infiltrativa que produce severa enfermedad fibrotica cardiaca
Por ahora no poner pacemaker porque los cambios no parecen ser un blqueo bilateral intermitente de LBBB y RBBB Estas 3 enfermedades infiltrtivas tienen CURA MEDICA
Este caso es verdaderamente para pensarlo mucho tiempo pero tambien hay que realizar un estudio hemodinamico completo , medir las presiones diastlicas derechas e izquierdas y coronariografia
Hay que tener todos los datos posibles de esta joven mujer, para poder ayudarla a seguir viviendo, en la mejor epoca de la mujer que tiene mas de un tercio de vida por delante
no poner pacemaker y se termino el problema y a otra cosa
y buscar la etiologia de este estado fibrotico cardiaco
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: 0º; 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 -45º). 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 $\mathbf{1_{AM}}$ dependent of left septal fascicle (LSF). Concomitantly, on precordial leads LSFB is manifested by **QR/qR** pattern from V_1 to V_3. 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 V_1-V_3 is 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 V_5-V_6 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 V_1 and V_2 precordial leads and the initial q wave of the left precordial leads: from V4 through V6 or V_5-V_6. **The anteromedial vector (1_{AM}) directed to front and rightward is absent in this case.**

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

About the concept expressed here by the colleague Adrian Baranchuk of "equal delay in both branches", proposed by Josephson, I think it should be tested by BB in the electrophysiology lab. This mechanism presents a differential diagnosis with blocks dependent on phases 3 and 4, which Professor Yanowitz proposed. This mechanism does NOT explain PR prolongation when QRS is narrower. The idea of the mechanism postulated by Josephson and shown in the PACE Journal by Adrian (only case published), is the following.

With short PR there is ILBBB and when QRS is narrower (goes to LAFB +/- LSFB), the PR is prolonged. Why? Does this mean that the patient is worse or better? Normally, we would say better, because QRS is narrower; however, when it does it at the expense of prolonging PR it is because distal conduction slows down simultaneously in the two branches, so it generates a conduction delay in the AV node, which manifests in ECG as prolonged PR.

Incredibly, "equal delay in both branches" described by Josephson, has NEVER been published as a report, until this case of the great Adrian. For this reason I think that if BB, that if Belhassen noticed it with EPS, it will be published for sure.

This patient should be taken to the lab, and phase-dependent block should be ruled out (the mechanism postulated by Yanowitz). It would be fantastic, because it would be the first time that this is proven.

In the book by Josephson, the explanation along with EPS is clear. I did the same protocol, but for some reason, I could not reproduce it.

Search "equal delay in both branches" in Google, and you will find Josephson's mechanism.

1. Baranchuk A, Miranda R, Rana J, Michael KA. Grouped Beats: What's the Mechanism? Pacing Clin Electrophysiol. 2011 Jul 28. doi: 10.1111/j.1540-8159.2011.03175.x. [Epub ahead of print]

El concepto aqui expresado por el colega Adrian Baranchuk de "equal delay in both branches" postulado por Josephson me parece que deberia ser testado por BB en su laboratorio de eletrofisiologia. Este mecanismo presenta diagnostico diferencial con los bloqueos fases 3 y 4 dependientes que postulara el Profesor Yanowitz. Este mecanismo NO explica la prolongacion del PR cuando el QRS es mas angosto. La idea del mecanismo postulado por Josephson y mostrado en la revista PACE por Adrian(unico caso publicado) es la siguiente:

Con PR corto tiene ILBBB y cuando el QRS se angosta (pasa a LAFB +- LSFB) el PR se alarga. Porque? Eso queire decir que el paciente esta peor o mejor?

Normalmente diriamos que mejor porque el QRS se angosta, sin embargo, cuando lo hace a expensas de prolongar el PR es porque la conduccino distal se enlentece simultaneamente en las dos ramas, por lo tanto genera un retraso de conduccion en el nodo AV que se manifeista en el ECG como PR prolongado.

Increiblemente, el Equal delay in Both branches descripto por Josephson, NO se ha publicado como case report NUNCA hasta este caso del genial Adrian.

Por eso creo que si BB que si Belhassen lo pesco con EEF tiene una publicacion segura.

lleva esta pte al laboratorio y pude descartar bloqueo fase dependiente (el mecanismo que postula Yanowitz) seria fantástico porque seria la primera vez que se demuestra esto.

En el libro de josephson, esa clara la explicacion junto al EEF. Hice el mismo protocolo, pero por algun motivo no lo pide reporoducir.

Procuren en el Google "equal delay in both branches" que encontrarn el mecanismo de Josephson.

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" PCCD[3] —as well as the secondary mechanic lesion—sclerosis of the left "cardiac skeleton” or Lev disease[4] —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 protein[5]

1. **Lepeschkin 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 196437:742.**
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
Pathology	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	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.	Absent.
Age	Younger	Older

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 arrhthymia
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.

Familial cardiac conduction defects belong to the group of inherited arrhythmias and can be classified under the broad heading of ``familial disorders affecting impulse propagation and cardiac conduction''. Patients can be asymptomatic or present with palpitations or occasionally symptoms of hemodynamic disorder, i.e. dizziness, syncope, heart failure, sudden cardiac death. Patients are often well aware of the onset and offset of intermittent tachyarrhythmias. Genetic studies of families with inherited cardiac rhythm disturbances led to the establishment of a molecular basis for arrhythmogenesis disorders. Both autosomal dominant and autosomal recessive transmissions have been described. More recently, mutations in the CSX/NKX2-5 (cardiac-specific homeo box), LMNA A/C (lamin), SNC5A (sodium channel, voltage-gated, type V, alpha subunit), PRKAG2 (protein kinase, AMP-activated, non catalytic, gamma-2) genes have been described, widening the large family of genes causing cardiac conduction defects. Etiology has not been elucidated yet. Most electrocardiographic disturbances are explained by developmental failure, abnormal anatomy, cardiac electrical instability, aberration in autonomic regulation of cardiac conduction or direct substance infiltration of the atrio-ventricular conduction system. The reported frequency can vary from 6 per 100,000,000 in the atrio-ventricular block of second degree to 4.1 per million in the incomplete inter-ventricular block, and 6.3 per million in the atrio-ventricular block of first degree. Diagnosis is suggested by characteristic symptoms. Standard 12-lead ECG and 24-hour ambulatory ECG monitoring confirm the diagnosis.

Treatment is based on antiarrhythmic drugs, pharmacological and/or electrical cardioversion in case of tachyarrhythmic episodes and on pacemaker implantation in the case of bradiarrhythmic episodes or sever dromotrohic diseorders. Cardiac conduction defects and their pattern of inheritance are listed

A. Familial primary dysrhythmias

Name	Pattern of inheritance	Locus
Long QT syndrome	**Autosomal dominant** **Autosomal recessive**	**11p15.5 ;7q35-36 ;3p21-24; 4q25-27;21q22** **11p15.5; 21q22**
Familial ventricular tachycardia	**Autosomal dominant**	**3p21-p23**
Brugada syndrome	**Autosomal dominant**	**3p21-p23**
Familial total atrial standstill	**Autosomal dominant**	
Sinus node dysfunction	**Autosomal dominant**	Connexin 40 gene polymorphism. Susceptibility gene, MYH6, encoding the alpha heavy chain subunit of cardiac myosin. A missense variant in this gene, c.2161C>T, results in the conceptual amino acid substitution p.Arg721Trp, has an allelic frequency of 0.38% in Icelanders and associates with **SSS**
Wolff-Parkinson-White syndrome	**Autosomal dominant**	**7q3;19p12-q13**
Familial atrioventricular block	**Autosomal dominant**	**19q13.2-q13.3**

Definitive Diagnosis: Professor Bernard Belhassen

Preliminary remarks:

The case of this woman was brought to my attention by a cardiologist who performed Thallium study and was surprised by the ECG changes recorded during the study.
My interpretation of the case below is only presumptive taking in account that electrophysiologic study, exercise test and coronary angiography were not performed. However, based on the lack of any previous history of cardiac disease and the normality of the echocardiogram and Thallium study (both were specially looked for any LV contraction abnormality) we can assume that we were actually dealing with *Primary Conduction Electrical Disturbances* of the Lenegre type.
This interpretation will rely on the standard classification of intraventricular conduction disturbances (RBBB, LBBB, LAH, LPH) without discussing the possibility that some IVCD may be related to His bundle lesions in the setting of longitudinal His bundle dissociation.
The ECG recordings presented hereunder were continuous and obtained during Thallium study using IV dipyridamole within a # 7 minute period.

Comment on the ECG tracings

Figure 1: Baseline recording (before IV dipyridamole): Regular sinus rhythm CL 800msec (75/min): PR 150msec; QRS 120msec; LBBB; negative T waves in infero-lateral leads that seem to be "primary changes"; S waves in V5-V6.
Figure 2: Tracing recorded about 1 min later after the first dose of dipyridamole. Following 3 sinus beats with LBBB (CL 800msec), a slightly premature sinus beat (PP 740msec) is conducted with a pattern of "RBBB" + LAH + suspected additional proximal LBBB (lack of q wave in lead I that is unusual for standard LAH).The QRS duration of the "RBBB" complexes is 120msec. The PR associated with the "RBBB" pattern is unchanged as compared to the one conducting with LBBB pattern if we look to lead aVF where the onset of QRS is clear-cut. In contrast the PR seems shorter and to increase by 30msec if looking to lead V1 (also see Figure 3).

Figure 3: shows an amplification of the same tracings in V1 and AVF with various PR measurements..
Figure 4: tracing recording about 5 min after slide 2: sinus rhythm CL 710msec (84/min) with QRS suggesting "RBBB" + LAH + proximal LBBB. ECG pattern suggesting old anteroseptal MI. Note minimal ST elevation in V1-V3 and obvious negative T waves in V1-V3.
Figure 5: shows amplification of V1-V4 leads suggesting an old anteroseptal MI.
Figure 6: tracing recording about 1 min after slide 2: regular sinus rhythm CL 780msec (76/min), The first and last 2 complexes are of the "RBBB" type similar to those previously described; the 3rd complex is of the "LBBB" type similar to that previously described.

Mechanism of conduction disturbances: we are in presence of multiple intraventricular conduction disturbances that are either rate-related or intermittent, known as "bilateral bundle branch block". In the absence of His bundle activity recording, it is impossible to establish the activation time at each of the bundle. Taking in account the fact that the PR interval does not significantly change (when measured at a ECG paper speed of 25mm/sec), it seems that both bundles exhibit first degree conduction disturbances and similar conduction times, that may explain that the QRS duration during both LBBB and RBBB is only 120msec. I have no explanation why the "RBBB" pattern is not obvious on the aVR lead (as it is usual).

Mechanism of T wave abnormalities: I believe that the T wave abnormalities present in inferolateral leads (in presence of LBBB) and in anteroseptal leads (in presence of RBBB) are due to a memory phenomenon. The fact that both RBBB and LBBB complexes are observed within a short period of time (7 min during the Thallium test) at very similar rates suggest that they are also present during many hours during a 24-hour period. At my best knowledge, anteroseptal T changes following disappearance of LBBB (intermittent or rate-dependent LBBB) is a well-known entity. In contrast inferolateral T changes following disappearance of LAH is less known.

Old anteroseptal MI? As outlined previously, this patient with no previous cardiac history had a normal LV function as attested by very careful examination of the apex during echocardiography and radionucleide angiography. The pattern of "anteroseptal MI" very likely result from the LAH as it has been previously reported in the literature.

Management: Pacemaker implantation is usually recommended for such patients, even for the asymptomatic ones mainly based on the belief that these patients are at risk for future occurrence of second or third degree infranodal AV block. This also was our policy. We should, however, recognize that the long term prognosis of some of these patients may not be so bad since development of second degree AV block may take time and only be revealed by an effort related 2:1 infranodal block rather than by a paroxysmal syncopal complete infranodal block.

A fraternal hug to all!