PÓS-OPERATÓRIO TARDÍO DE CARDIOPATIA CONGÊNITA EM CRIANÇA SINDRÔMICA

LATE POSTOPERATIVE CONGENITAL HEART DEFECTS IN SYNDROMIC CHILD

Andrés Ricardo Pérez-Riera
Encarregado do setor de eletro-vetorcardiografia. Disciplina de Cardiologia – Faculdade de Medicina do ABC - Fundação do ABC – Santo André – SP - Brasil
Fones: Celular 84693388 – Consultório: 56212390 – Residencial: 5044-6243.
riera@uol.com.br

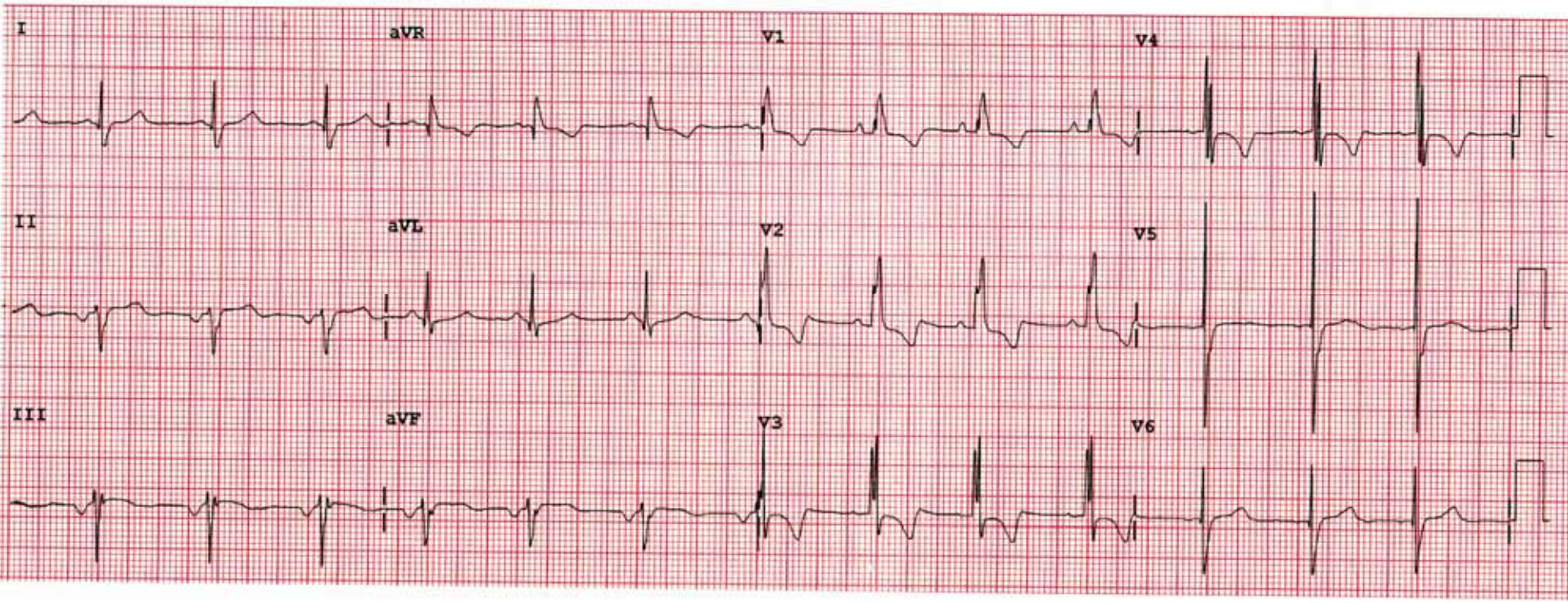
Male, interracial boy (Asian father and Caucasian mother). Currently 8 years and 3 months old (born on Jan. 26, 2002).
Late post-operative period for cardiac surgery due to congenital heart disease.
When he was an infant, his karyotype was studied and it resulted normal.
When four months of age, he presented feverish symptoms by unkown origin, associated to cardiac murmur. Repeated tests of hemoculture and uroculture resulted negative. The clinical examination and the echocardiogram back then, diagnosed a large atrial septal defect, associated to pulmonary stenosis in a moderate degree and left pulmonary artery stenosis. Surgery was indicated, which was performed on June 3, 2003 (atrioseptoplasty and pulmonary valve commissurotomy). The post-operative period evolved with symptoms of heart failure and mediastinitis, which lead to treatment with drugs and re-suturing the sternum. After the fourth day, he evolved favorably and he was discharged.
Physical examination:
Low ponderal development, and with a low height for his age (17 kg/1.10 m), syndromic facies: hypertelorism, antimongoloid slant, strabismus, flat and pointy nose, low-set and posteriorized ears, and low posterior line of hair (in the nape). Webbed neck. Superior pectum carinatum and inferior pectus excavatum. Bilateral scar of the surgery of bilateral cryptorchydism.
Cubitus valgus.
Auscultation: ejection systolic murmur and click ++/+++ along the superior left border of the sternum. Mild diastolic murmur ++ in the left superior border of the sternum. Hypophonic P2 (pulmonary component of the second heart sound).

Questions:
1. What is the likely clinical diagnosis?
1. What is the electro-vectorcardiographic diagnosis?

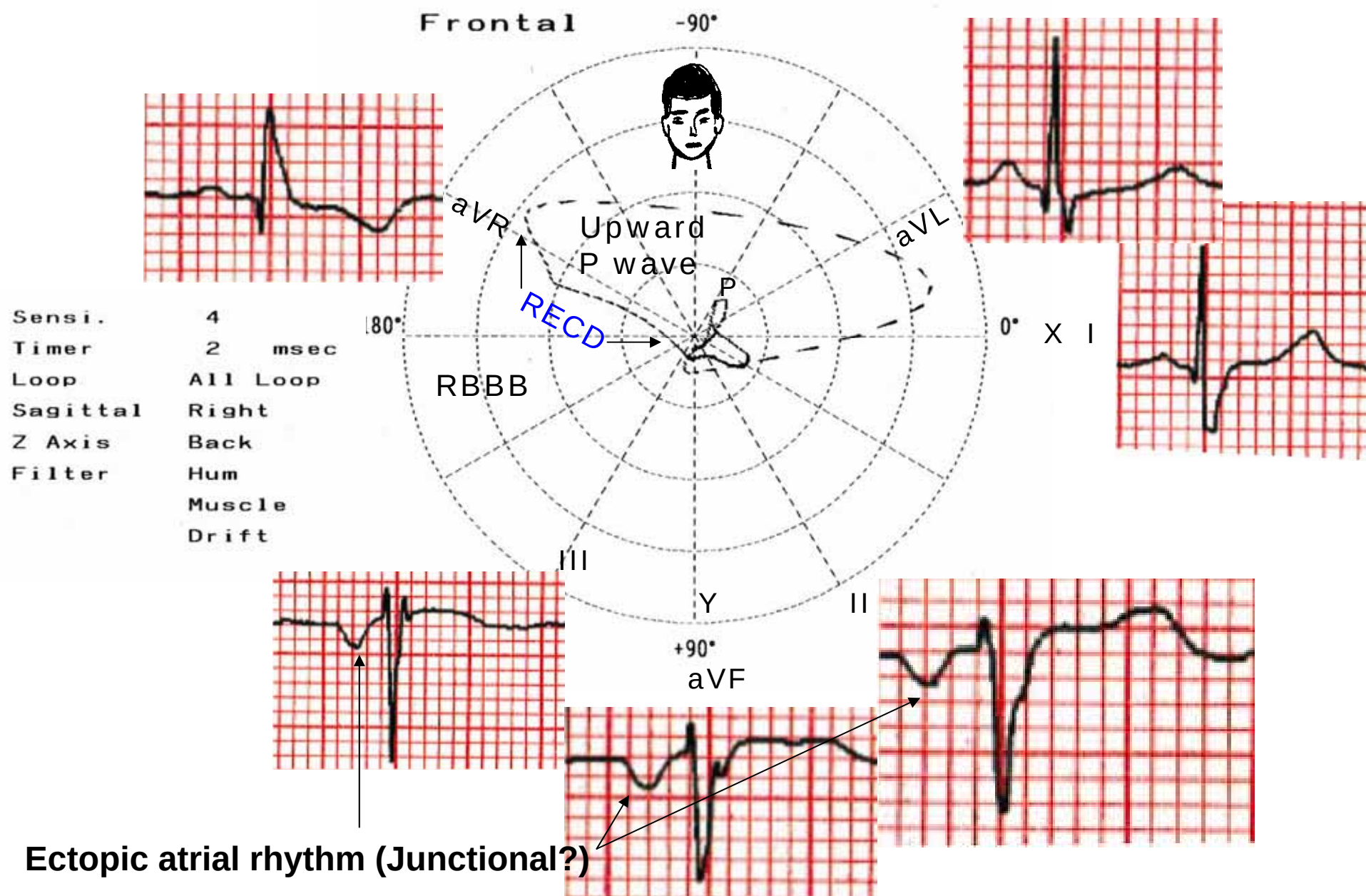
Criança do sexo masculino, inter-racial (pai asiático e mãe caucasiana). atualmente com oito anos e três meses de idade, (nascido no dia 26/01/2002).
Pós-operatório tardio de cirurgia cardíaca por cardiopatia congênita.
Quando lactente estudado cariótipo que resultou normal.
Com quatro meses de vida apresentou quadro febril de origem desconhecido associada ao sopro cardíaco. Repetidos exames de hemocultura e urocultura resultaram negativos.
O exame clínico e de ecocardiograma na oportunidade diagnosticaram grande comunicação interatrial associada à estenose pulmonar de grau moderado y estenose da artéria pulmonar esquerda. Indicada cirurgia que ocorreu no dia 03/06/03 (atrioseptoplastia e comissurotomia da válvula pulmonar.). O pós-operatório evoluiu com quadro de insuficiência cardíaca e mediastinite que motivou tratamento com drogas e re-sutura do esternocom dreno. Após o quarto dia evolui favoravelmente e teve alta.
Exame físico:
Baixo desenvolvimento ponderal e de estatura para idade, (17kg/1.10m) face sindrómica: hipertelorismo, pálpebras com inclinação anti-mongoloide, estrabismo, nariz achatada com uma ponte, orelhas posteriorizadas de implantação baixa, linha posterior dos cabelos de implantação baixa (na nuca) . Pescoço alado.
Tórax: Pectum carinatum superior e pectus excavatum inferior y escoliose.
Cicatriz bilatereal de cirurgia de criptorquidia. Cúbitus valgus.
Ausculta: clique e sopro sistólico de ejeção++/+++ junto a borda esquerda superior do esterno. Sopro diastólico suave ++ na borda superior esquerda do esterno. P_2 (componente pulmonar da segunda bulha) hipofonética.

Perguntas:
1. **Qual o provável diagnóstico clínico?**
2. **Qual o diagnóstico eletrovetorcardiográfico?**

Name: IHMK Date: Mach 29/2011 Age: 8yo Height: 1.10m Weight: 17Kg

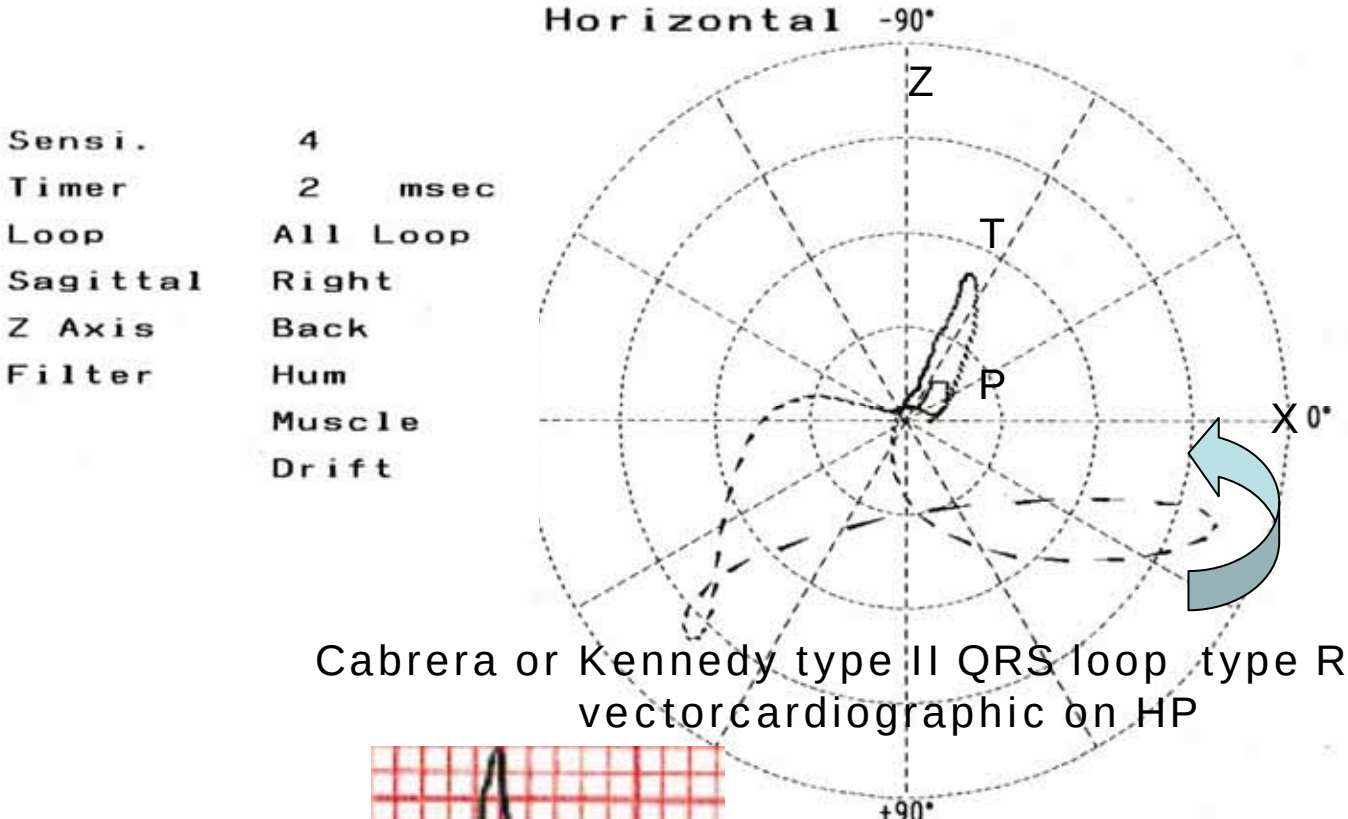


ECG/VCG CORRELATION ON FRONTAL PLANE



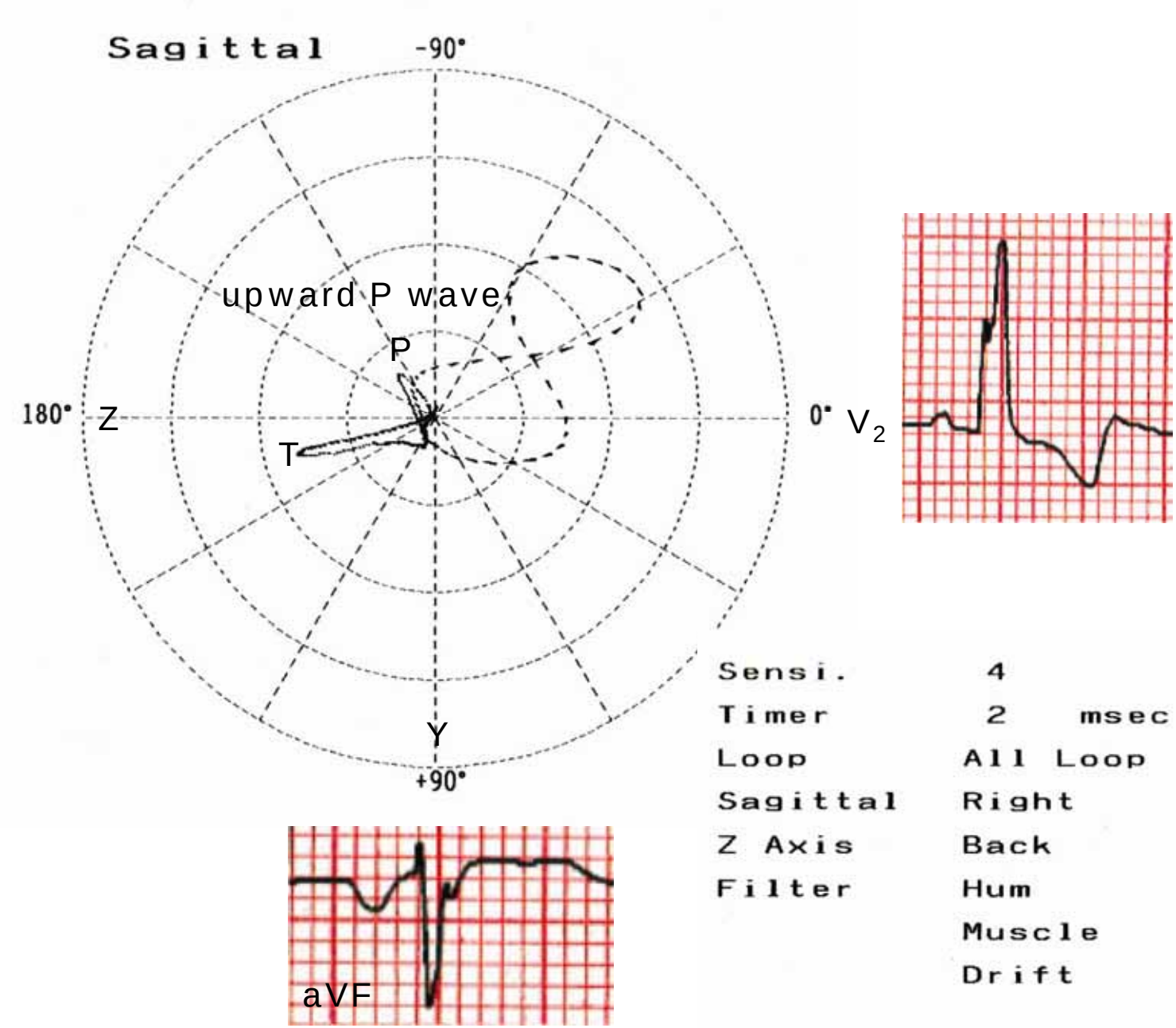
Ectopic atrial rhythm (Junctional?)

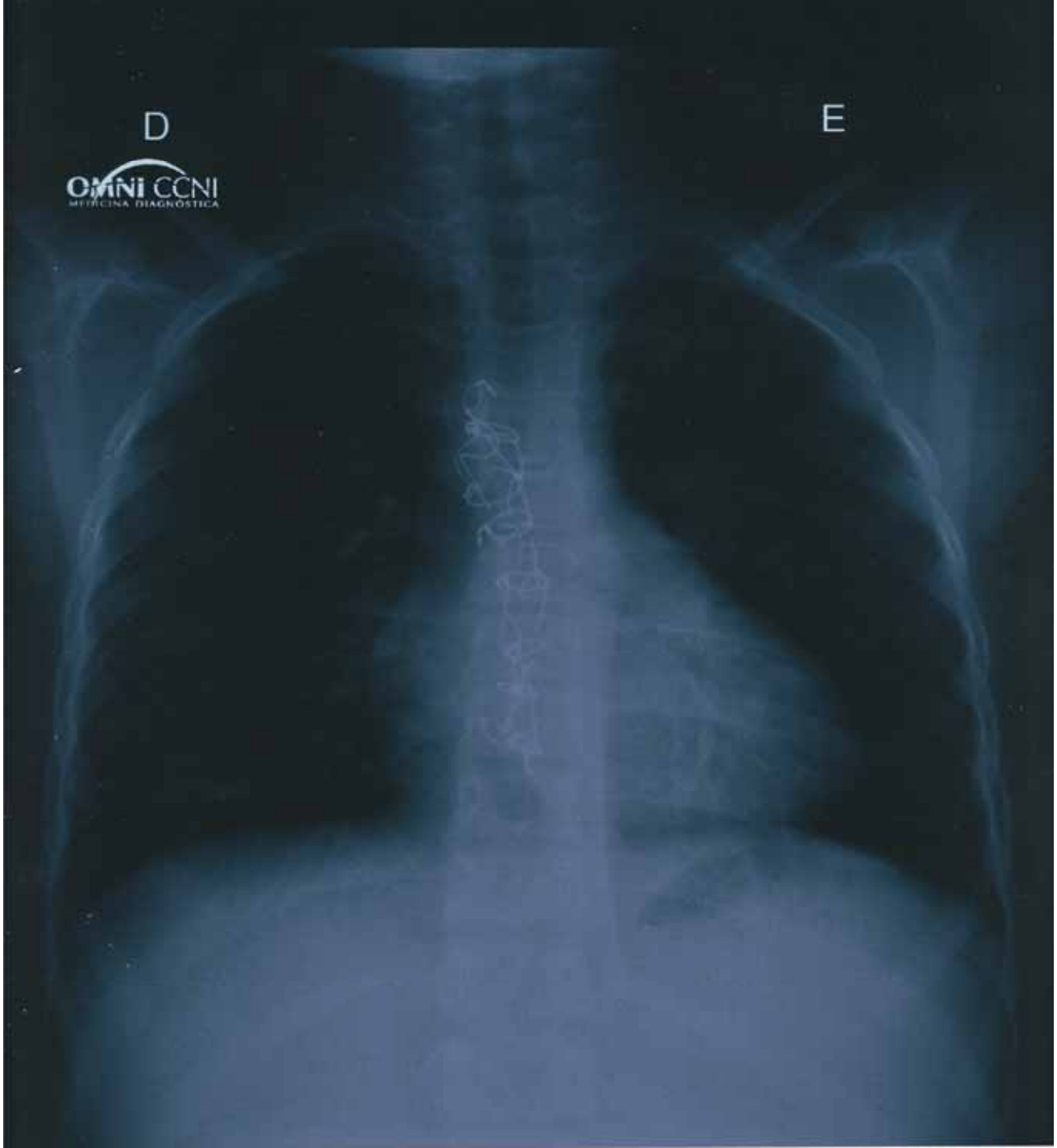
ECG/VCG CORRELATION HORIZONTAL PLANE

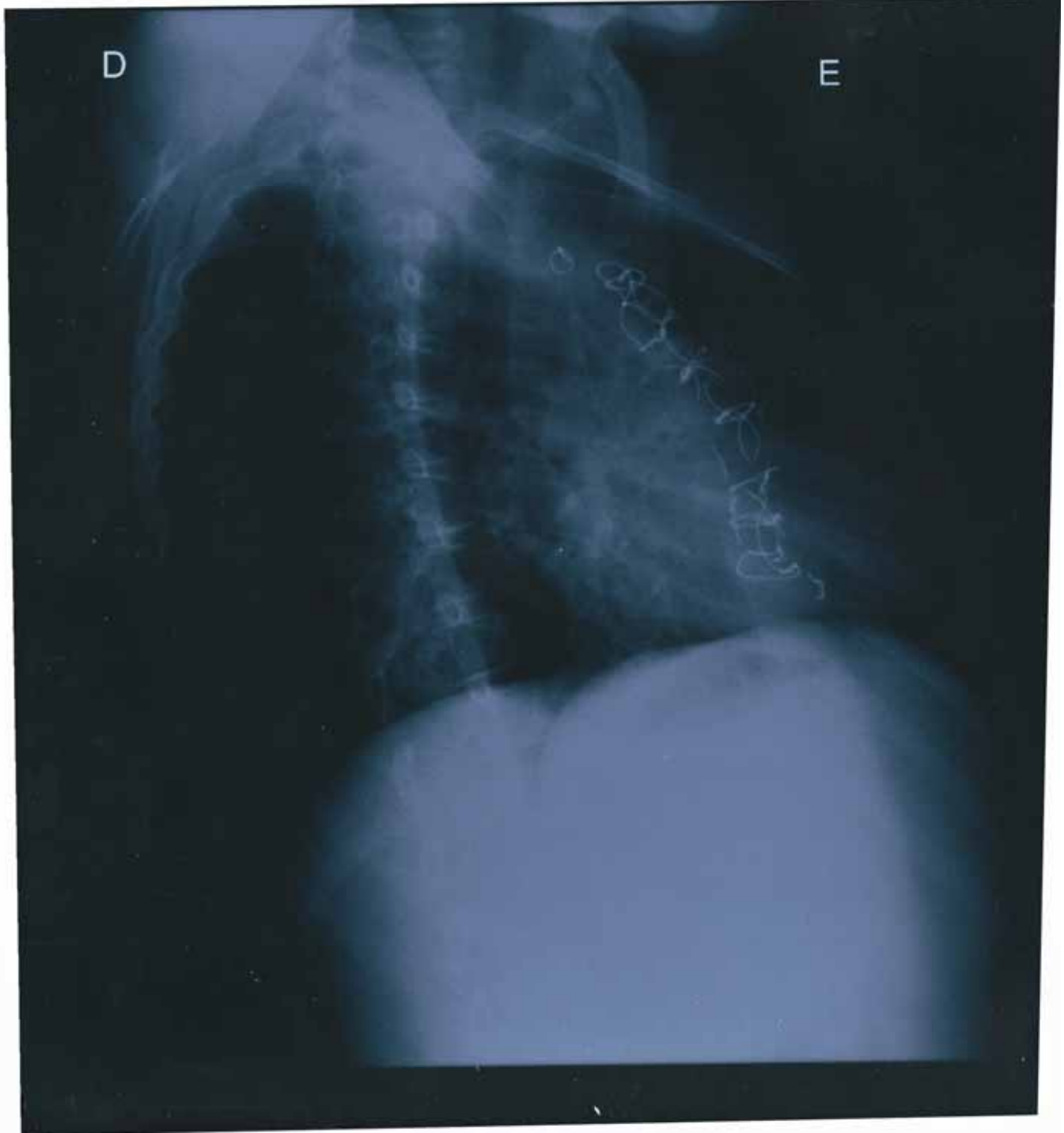


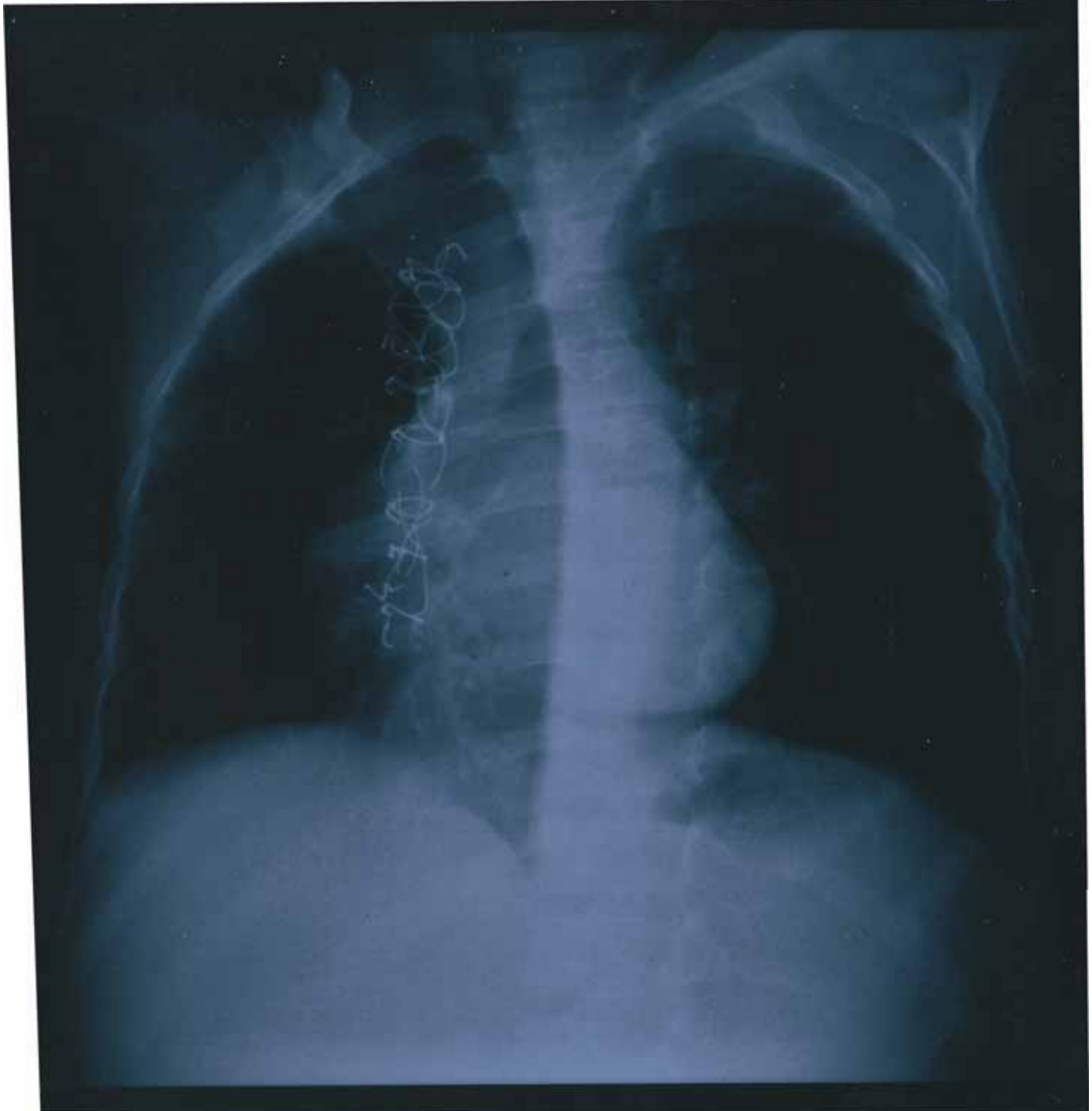
Cabrera or Kennedy type II QRS loop type RBBB vectorcardiographic on HP

ECG/VCG CORRELATION RIGHT SAGITTAL PLANE




D
E
OMNI CCNI
MEDICINA DIAGNÓSTICA


D
E



COLEAGUES OPINIONS

OPINIÃO DOS COLEGAS

Sindrome de Noonan. Herencia autosomica dominante. ECG: HBAI -Hemibloqueo anterior izquierdo- (BDASI -bloqueo diviosnal anterosuperior izquierdo- , BCRD -bloqueo completo de rama derecha-).

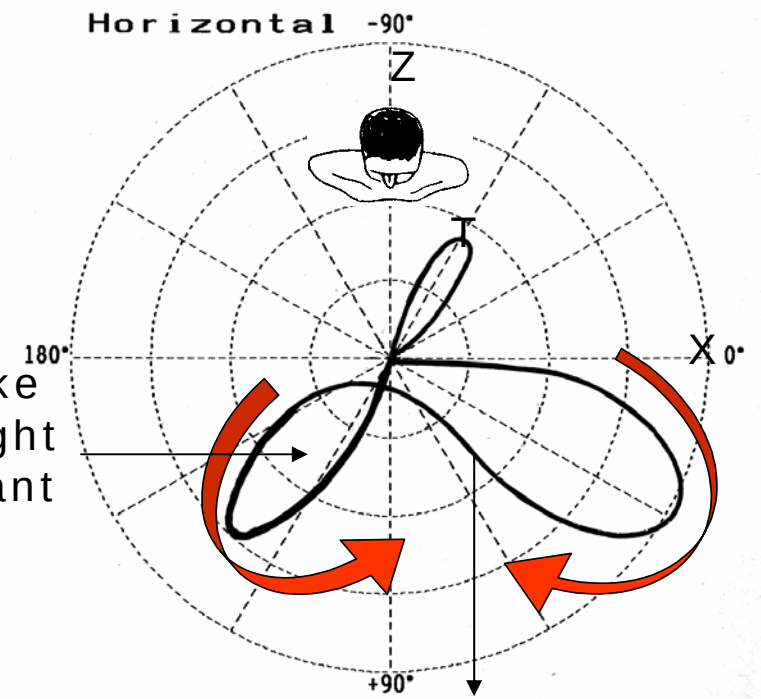
Eduardo Quiñones

Noonan syndrome. Autosomal dominant inheritance.
ECG Left Anterior Fascicular block + Right Bundle branch Block

FINAL CONCLUSIONS

ECG/VCG diagnosis

1. **Ectopic atrial rhythm (Junctional?) P negative wave in inferior leads and positive in superior frontal leads aVR and aVL**
2. **Extreme superior axis deviation on FP. SÂQRS located on top right quadrant (QRS -100º) on "Northeast quadrant"**
3. **Left Anterior Fascicular Block (LAFB)**
4. **Complete Right Bundle Branch Block(CRBBB)**
5. **Cabrera or Kennedy type II QRS loop type RBBB vectorcardiographic on HP**
6. **Signals of Right Ventricular Hypertrophy in presence of CRBBB figure**



Moderate RVH + CRBBB

Final finger-like Appendix on right anterior quadrant

Cabrera or Kennedy type II VCG type RBBB

Afferent limb to front of orthogonal X line

Clinical diagnosis: Noonan Syndrome

Noonan Syndrome (NS) is a relatively common autosomal dominant congenital disorder considered to be a type of dwarfism, that affects both males and females equally :550. It used to be referred to as the male version of Turner's syndrom (and is still sometimes described in this way);[however, the genetic causes of Noonan syndrome and Turner syndrome are distinct. The principal features include congenital heart defect (typically), short stature, learning problems, pectus excavatum, impaired blood clotting, and a characteristic configuration of facial features including a webbed neck and a flat nose bridge. The syndrome is named after Dr. Jacqueline Noonan.

It is believed that between approximately 1 in 1,000 and 1 in 2,500 children worldwide are born with NS.

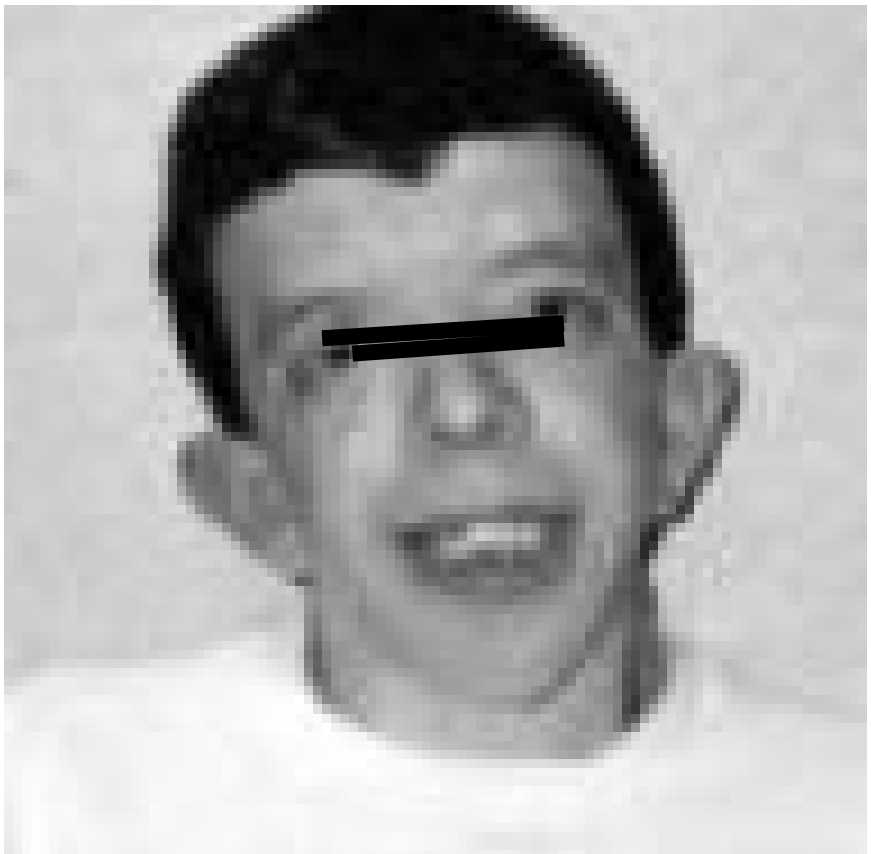
Noonan syndrome was first recognized as a unique entity in 1963 when Noonan and Ehmke described a series of patients with unusual facies and multiple malformations, including congenital heart disease. These patients were previously thought to have a form of Turner syndrome, with which Noonan syndrome shares numerous clinical features. The observation that patients with Noonan syndrome have normal karyotypes was important in allowing the distinction to be made between the Turner and Noonan syndromes.

The cardinal features of Noonan syndrome include unusual facies (ie, hypertelorism, down-slanting eyes, webbed neck), congenital heart disease (in 50%), short stature, and chest deformity. Approximately 25% of individuals with Noonan syndrome have mental retardation. Bleeding diathesis is present in as many as half of all patients with Noonan syndrome. Skeletal, neurologic, genitourinary, lymphatic, eye, and skin findings may be present to varying degrees.

It is one of the most common genetic syndromes associated with congenital heart disease, similar in frequency to Down syndrome. However, the range and severity of features can vary greatly in patients with NS. Therefore, the syndrome is not always identified at an early age.

Recurrence in siblings and apparent transmission from parent to child has long suggested a genetic defect with autosomal dominant inheritance and variable expression. A person with NS has up to a 50% chance of transmitting it to a child. The fact that an affected parent is not always identified for children with NS suggests several possibilities:manifestations are variably expressed and could be so subtle as to go unrecognized (variable expressivity) a high proportion of cases represent new, sporadic mutations or

Noonan syndrome is heterogeneous, comprising more than one similar condition of differing cause, some not inherited.



Type	OMIM	Gene	Description
NS1	163950	PTPN11	In most of the families with multiple affected members, NS maps to chromosome 12q24.1. In 2001, it was reported that approximately half of a group of patients with Noonan syndrome carried a mutation of the *PTPN11* gene at that location, which encodes protein tyrosine phosphatase SHP-2.[1] The SHP2 protein is a component of several intracellular signal transduction pathways involved in embryonic development that modulate cell division, differentiation, and migration, including that mediated by the epidermal growth factor receptor. The latter pathway is important in the formation of the cardiac semilunar valves.Chromosomal abnormalities, such as a duplication of chromosome region 12q24 encompassing gene *PTPN11* can result in an apparent Noonan syndrome[2].
NS2	605275	unknown (autosomal recessive) 6	
NS3	609942	KRAS	Additional mutations in KRAS[3] genes have been reported to cause Noonan syndrome in a smaller percentage of individuals with the syndrome.
NS4	610733	SOS1	It has recently been shown that activating mutations in SOS1 also give rise to NS[4]. Shp2 and SOS1 both have roles as positive regulators of the Ras/MAP kinase pathway suggesting that dysregulation of this pathway may play a major role in the genesis of this syndrome[5].
NS5	611553	RAF1	Additional mutations in *RAF1*[6] genes have been reported to cause Noonan syndrome in a smaller percentage of individuals with the syndrome.

1. **Tartaglia M, Mehler EL, Goldberg R, *et al* (2001). "Mutations in PTPN11, encoding the protein tyrosine phosphatase SHP-2, cause Noonan syndrome". *Nat. Genet.* 29: 465–8.**
2. **Shchelochkov OA, Patel A, Weissenberger GM, et al. Duplication of chromosome band 12q24.11q24.23 results in apparent Noonan syndrome. Am J Med Genet A. 2008 Apr 15;146A(8):1042-8.**
3. **Schubbert S, Zenker M, Rowe SL, *et al* (2006). "Germline KRAS mutations cause Noonan syndrome". *Nat. Genet.* 38: 331–336.**
4. **Roberts AE, Araki T, Swanson KD, *et al* (2007). "Germline gain-of-function mutations in SOS1 cause Noonan syndrome". *Nat. Genet.* 39 : 70–74.**
5. **Bentires-Alj M, Kontaridis MI, Neel BG (2006). "Stops along the RAS pathway in human genetic disease". *Nat. Med.* 12: 283–285.**
6. **Razzaque MA, Nishizawa T, Komoike Y, *et al* (2007). "Germline gain-of-function mutations in *RAF1* cause Noonan syndrome". *Nat. Genet.* 39 (8): 1013–7.**

Heart: 2/3 of patients have one of the following heart defects

Pulmonary Valvular Stenosis: 50%
Atrial septa defect: 10%
Ventricular septal defect (less common)
Cardiomyopathy

Gastrointestinal System: anorexia, forceful vomiting, swallowing difficulties

Genito-urinary system: Cryptorchidism (undescended testicles)

Lymphatic system: Posterior cervical hygroma (webbed neck) Lymphedema (build-up of body fluid due to poor functioning of the lymphatic system)

Developmental: clumsiness, poor coordination, motor delay, mental retardation *—(1/3 of patients have mild MR), learning disabilities, speech and language delays*

Musculoskeletal: Some patients suffer from severe joint pain or muscle pain often with no identifiable cause

Hematologic: Easy bruising, amegakaryocytic thrombocytopenia (low platelet count), blood clotting disorders, Von Willebrand disease, prolonged activated partial thromboplastin time, partial deficiency of Factor VIII:C, Factor XI:C, Factor XII:C and combined coagulation deficiencies

Neurological
Arnold-Chiari Malformation (Type 1) has been noted in some patients with Noonan Syndrome

Stature/Posture: Short stature, dwarfism, cervical (neck) spine fusion, scoliosis, Prominence of breast bone (pectus carinatum), depression of breast bone (pectus excavatum), joint contractures or tightness, or looseness, growth retardation, winging of the scapula, hypotonia (low muscle tone)

Head: Excess skin on the back of the neck, low hairline at the nape of the neck, large head, triangular face shape, broad forehead, short neck, webbed neck, posterior cervical, curly hair.

Eyes: Widely set eyes (hypertelorism) *—(95%), drooping of the eyelids (ptosis (eyelid)), epicanthal folds (extra fold of skin at the inner corner of the eye), proptosis (bulging eyes), refractive visual errors, Inward or outward turning of the eyes (strabismus), nystagmus - jerking movement of the eyes*

Nose: *Small, upturned nose*

Ears/hearing: Low set ears *—(over 90%), backward rotated ears —(over 90%), thick helix of ear (outer rim) —(over 90%)*, incomplete folding of ears, chronic otitis media (ear infections)

Mouth/speech: Deeply grooved philtrum (top lip line) *—(over 90%), micrognathia (undersized lower jaw), high arched palate, dental problems, articulation difficulties,* poor tongue control.

Limbs/extremities Bluntly ended fingers, Extra padding on fingers and toes, edema of the back of hands and tops of feet, cubitus valgus (elbow deformity: with abnormal turning-in).

Skin: Lymphedema (swelling of the extremities), keloids (scar hypertrophy), hyperkeratosis - overdevelopment of outer skin layer, pigmented nevi (birthmark)