

**Brugada Phenocopy Emerging as a New Concept. Response****Fenocopia de Brugada: surgimiento de un nuevo concepto. Respuesta****To the Editor,**

The authors appreciate the interest in the case report we published in *Revista Española de Cardiología* concerning the observation of the Brugada electrocardiographic (ECG) pattern in a patient with hyperkalemia.<sup>1</sup> We likewise welcome the introduction of the concept of phenocopy, an expression with which our finding is compatible.<sup>2,3</sup> We also consider it opportune to stress that both the latest consensus on ECG diagnosis of Brugada syndrome and the introduction of the term *phenocopy* are more recent than the online publication of our case report in 2011.<sup>2-4</sup> The definitions of the ECG patterns that are typical of Brugada syndrome and those that mimic this syndrome in the presence of serum electrolyte disturbances were introduced subsequent to our publication.

It is important to highlight reasons for attributing the changes observed in the ECG to hyperkalemia rather than to the acidosis and hyponatremia also observed in our patient. Reports of Brugada phenocopy associated with hyponatremia and acidosis have described the development of pseudo J waves in the QRS complex and ST segment depression in leads other than right precordial leads. These are precisely the features that differentiate this ECG pattern from type 1 Brugada pattern.<sup>5,6</sup> Other possible causes (hyperglycemia, drugs, fever, and myocardial ischemia) were ruled out in the case discussed in our report.

We appreciate any contribution that aids in the understanding of the mechanisms involved in the induction of ECG patterns mimicking Brugada syndrome (phenocopies) and other patterns, such as early repolarization, which can also be associated with the risk of sudden cardiac death.<sup>7</sup>

Finally, we agree with Dr. Anselm on the importance of performing a challenge test with flecainide to rule out Brugada syndrome. Until the prognosis of patients presenting with

Brugada phenocopy has been established, it is advisable to perform pharmacological challenge tests and, if appropriate, to induce ventricular arrhythmias by means of an electrophysiological study.

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**REFERENCES**

1. Recasens L, Meroño O, Ribas N. Hiperpotasemia simulando un síndrome de Brugada. *Rev Esp Cardiol.* 2013;66:309.
2. Baranchuk A, Nguyen T, Ryu MH, Femenía F, Zareba W, Wilde AA, et al. Brugada phenocopy: new terminology and proposed classification. *Ann Noninvasive Electrocardiol.* 2012;17:299-314.
3. Anselm DD, Baranchuk A. Brugada phenocopy: redefinition and updated classification. *Am J Cardiol.* 2013;111:453.
4. Bayés de Luna A, Brugada J, Baranchuk A, Borggrefe M, Breithardt G, Goldwasser D, et al. Current electrocardiographic criteria for diagnosis of Brugada pattern: a consensus report. *J Electrocardiol.* 2012;45:433-42.
5. Tamene A, Sattiraju S, Wang K, Benditt DG. Brugada-like electrocardiography pattern induced by severe hyponatremia. *Europace.* 2010;12:905-7.
6. Kovacic JC, Kuchar DL. Brugada pattern electrocardiographic changes associated with profound electrolyte disturbance. *Pacing Clin Electrophysiol.* 2004;27:1020-3.
7. Junttila MJ, Sager SJ, Tikkanen JT, Anttonen O, Huikuri HV, Myerburg RJ. Clinical significance of variants of J-points and J-waves: early repolarization patterns and risk. *Eur Heart J.* 2012;22:2639-43.

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**RASopathies: From Noonan to LEOPARD Syndrome****RASopatías: del síndrome de Noonan al síndrome LEOPARD****To the Editor,**

We have read with interest the article recently published by Carcavilla et al.<sup>1</sup> titled "LEOPARD Syndrome: A Variant of Noonan Syndrome Strongly Associated With Hypertrophic Cardiomyopathy." However, we would like to add some comments that we find interesting.

LEOPARD syndrome (LS) (OMIM 151100) and Noonan syndrome (NS) (OMIM 163950) are two disorders that are part of a newly classified family of autosomal dominant syndromes termed "RASopathies", which are caused by germline mutations in components of the RAS-MAPK (mitogen-activated protein kinases) signal transduction pathway<sup>2</sup> that is involved in the regulation of normal cell proliferation, survival, and differentiation.

Although the diagnosis of LS is made on clinical grounds by observation of key features, none of which is pathognomonic, to provide a valid overview on symptoms and features of LS we should not overestimate the reports published in the pre-molecular era, because these cohorts may consist of heterogeneous diseases. In fact, in early childhood the phenotype of LS can be typical of NS;

however, with age other characteristic features of LS, including lentigines, hypertrophic cardiomyopathy (HCM), and hearing loss, may appear. For this reason, anomalies observed in molecularly confirmed cases should be regarded as more reliable.

Genetically, both syndromes share mutations in the *PTPN11* (protein-tyrosine phosphatase, non-receptor type 11) gene on chromosome 12q24, as they are heterozygous missense mutations in *PTPN11* observed in up to 90% and 50% of LS and NS cases, respectively. Similarly, mutations in the *RAF1* (v-Raf-1 murine leukemia viral oncogene homolog 1) gene on chromosome 3p25.2 and mutation in the *BRAF* (v-Raf murine sarcoma viral oncogene homolog B1) gene on chromosome 7q34 are also seen. However, the point mutations identified in *PTPN11* that are associated with NS are distinct from those associated with LS and therefore with different biochemical properties: gain-of-function mutations in *PTPN11* are more frequent in NS patients<sup>3,4</sup> while a loss-of-function or dominant-negative mutations in *PTPN11* are more prevalent in patients with LS.<sup>5,6</sup> These gain-of-function and loss-of-function mutations may explain the differences in phenotypes between these two syndromes.

Although it is not included in the LEOPARD acronym, HCM is the most frequent anomaly observed, representing a potentially life-threatening problem in these patients. HCM, which is generally