Brugada syndrome masked by complete left bundle branch block

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Brugada syndrome is a genetic disorder that affects the electrical activity of the heart. It is characterized by ST-segment elevations in the right precordial leads and right bundle branch morphology on ECG.[1] These ECG changes are present in the absence of other causes of ST elevation or right bundle branch block morphology such as structural heart disease, ischemia, pacing or electrolyte disturbances.[2] Clinical presentation varies between patients; it can range from asymptomatic changes seen on ECG to syncope, ventricular arrhythmias, and sudden cardiac death. [3]So far, three types of ECG repolarization patterns have been identified (type 1, type 2, and type 3).[4] Type 1 pattern is diagnostic of Brugada syndrome whereas types 2 and 3 are considered suggestive.[5] According to the 2016 consensus conference of J-wave syndromes, the diagnosis of Brugada syndrome can only be made by finding a type 1 repolarization pattern. A type

1 pattern can either be spontaneous or unmasked by fever or medications. If it has been unmasked by either, then further evidence of patient clinical history, family history, or genetic testing should be present to fulfill a score of 3.5 or higher according to the Shanghai Scoring System.[6 7] The Shanghai Scoring System does not include imaging; hence, even if changes in the right ventricle are found on cardiac MRI, they play no role in the diagnosis. [7]In patients presenting with a non-type 1 pattern, a sodium channel blocker challenge is frequently used to unmask the type 1 pattern. Unmasking this pattern allows for diagnosis of Brugada syndrome which has a big impact on prognosis and management options. In some patients, an initial flecainide challenge test may be negative due to the variable sensitivity of this test. Some studies have shown that repeating the test may increase sensitivity, but, with increased risk of adverse drug effects. Prasad et al. showed that in patients with high clinical suspicion, family history of sudden cardiac death could serve as an indicator to repeat the flecainide test.[5 8 9]

Several possible risk factors, that might predispose individuals to have a more severe presentation, have been identified. These include male gender, history of syncope, spontaneous type 1 pattern, family history of Brugada syndrome, and loss-of-function mutations in the SCN5A gene (which codes the alpha subunit of the cardiac sodium channel).[10] Patients with SCN5A mutations tend to have earlier onset of symptoms, more noticeable electrophysiological defects (such as sick sinus syndrome and AV blocks), and increased risk of major arrhythmic events especially in Asian and Caucasian populations.[11] High-risk patients are susceptible to sudden cardiac death; therefore, risk stratification helps in patient selection for Implantable Cardioverter Defibrillator placement.[12 13]

In their article, Eduardo et al. presented the case of a 48-year-old lady who was initially diagnosed with Brugada syndrome after having a type 1 pattern on ECG. During follow-up, the patient's ECG changed and showed a complete left bundle branch block instead of the typical type 1 pattern. Molecular studies showed the novel SCN5A p.1449Y>H variant and subsequent functional analysis showed a nonfunctional mutated membrane channel. SCN5A mutation can cause Brugada syndrome and conduction system abnormality as described in this lady. This variant generated minimal sodium currents. Such major decrease in current magnitude is associated with high penetrance as seen in the cases in this study. Although, during close follow-up, these patients did not have severe symptoms.[14] What is most significant is that the authors presented a patient with Brugada syndrome who subsequently developed findings of complete left bundle branch block on ECG, making the diagnosis challenging due to masking of the type 1 pattern. This opens further discussion about diagnosis of the syndrome and potential maneuvers or procedures that would help unmask type 1 pattern under heart block. Since diagnosis can only be made by witnessing this pattern, this presents us a possibility where a diagnosis would be missed in such patients. SCN5A is the most common gene associated with this syndrome, accounting for around 20%. However, patient presentation varies widely with different mutations affecting channel function differently. In this case, the p.1449Y>H variant showed high penetrance and channel dysfunction despite relatively non-severe symptoms in patients affected. However, further observation is warranted to assess progression of the disease and the incidence of major arrhythmogenic events with aging and subsequent fibrosis. Further research is required to investigate the role of genetic studies in risk stratification and projecting patient clinical course depending on the presence of specific gene mutations/variants.

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