Young Patients with Unknown Stroke and Little P Wave in ECG

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Summary
Here we report two young patients with atrial fibrillation/atrial flutter complicated with cardiogenic cerebral embolism. Electrophysiological study revealed a large area of low-voltage zone or area of electric silence in both sides of the atrium during restoration of sinus rhythm, and the echocardiogram showed loss of mechanical function of the atrium. The electrical-mechanical dysfunction of the atrium was considered to be the cause of embolic event in this type of patient who was “very low” stroke risk atrial fibrillation or atrial flutter. The idiopathic, fibrotic atrial cardiomyopathy may be underlying in these patients.

Key words: Atrial cardiomyopathy, Atrial fibrillation, Atrial tachyarrhythmia, Anticoagulation

Atrial fibrillation (AF) or atrial flutter (AFL) often complicates with cardiogenic cerebral embolism, which causes serious clinical sequela. The risk of cerebral embolism in AF/AFL patients has to date been systematically evaluated in several large scale studies, which show that an AF/AFL patient without any risk factors carries a very low incidence of stroke. Here we report two young patients with AF/AFL suffering from stroke, although neither of them had any stroke risk factors. These cases show the importance of atrial electric-mechanical function in the evaluation of risk of stroke and anticoagulation strategies for the atrial cardiomyopathy patients with AF/AFL.

Case Report

Case 1: A 30-year-old female was referred to our hospital for further evaluation because of recurrent episodes of palpitations and dizziness for six months. She had no cardiac disease history and the heart was otherwise normal, along with no familial history of lone AF. ECG showed paroxysmal AFL with variable atrioventricular conduction (Figure 1A) and the CT revealed an encephalomalacia of left parietal lobe. Transthoracic and transesophageal echocardiography demonstrated right atrium dilation, pulmonary hypertension with mild tricuspid regurgitation, normal ventricular size, and LVEF, without left atrium (LA) thrombus. After the successful abolishment of the AFL by cavotricuspid isthmus ablation, the patient presented a very small sinus P wave in ECG (Figure 1B). Accordingly, LA angiography revealed no marked contraction which was further confirmed by absence of A peak in echocardiography during the sinus rhythm (Figure 1C). Further intracardiac mapping revealed a large area of low-voltage zone (LVZ) in the right atrium (RA) free wall and LA anterior wall, along with both atrial appendages (Figure 1D), and also failed to be captured by pacing in these sites. Cardiac MRI indicated RA dilation with no structural and functional abnormalities in ventricles. The patient was discharged on instruction of rivaroxaban for life (15 mg once daily).

Case 2: A 30-year-old male was referred to our neurology department due to sudden onset of left limb weakness. He reported a history of cerebral infarction five years previously without any sequelae and complained of repeated palpitation for several months. In addition, he had no other comorbidity and no smoking or drinking history. There were also no first- or second-degree relatives with documented lone AF. Head CT showed new cerebral infarction in left temporal lobe and right temporal frontal lobe. ECG presented very low amplitude P waves in sinus rhythm (Figure 2B). Paroxysmal AF was recorded during an episode of palpitation (Figure 2A). Echocardiography revealed slightly dilated LA (anterior-posterior diameter 42 mm), mild to moderate mitral regurgitation, and absence of spectrum A peak of mitral flow velocity during sinus rhythm (Figure 2C). The cardiac MRI revealed no structural abnormalities. During the electroanatomical mapping (EnSite Velocity NavX), electric silence (AES) was detected in most areas of LA and RA (Figure 2D). Due to the high recurrence rate and potential risk of atrioventricular conduction block, catheter ablation was canceled. AF was terminated by direct current cardioversion and dabigatran (110 mg, twice daily) was recommended for life-term anticoagulation. During a 42-month follow-up, no recurrent stroke was identified.
Discussion

Although the CHA2DS2-VASc score provides a practicable guide for the evaluation of stroke risk for AF/AFL patients, it can only explain about 60% of the thromboembolic events. There must be other factors accounting for the stroke. The two cases presented here provide a specific insight into the role of the atrial electric-mechanical function in the pathogenesis of cardiac stroke in patients with AF/AFL. The two cases are differentiated from other AF patients by the extensive electrical silence in the atrium revealed by electroanatomical voltage mapping after the restoration of sinus rhythm. The loss of electrical activity may further result in prominent loss of atrial mechanical function, which can be confirmed by the echocardiogram. From this point of view, these two patients portended a significantly higher risk of thrombus formation in the atrium, although they would have been regarded as “very low risk” stroke patients due to a CHA2DS2-VASc score of “0.”

These two cases were sporadic. Also, no obvious virus infection events could be detected. Genetic disorder underlying the substrate of atrial tachyarrhythmia in such young patients may be taken into consideration. Previous studies have identified multiple genetic determinants for familial AF (i.e., GATA6, KCNQ1, SCN1B, KCNA5, or KCNE3); functional deficiency of these genes predisposes them to the progression of AF. Substantial evidence has also demonstrated the familial aggregation of AF and the correlation between the risk of AF and the youngest rela-
Figure 2. Electrocardiograms and electrophysiologic study for case 2. A: Patient suffers from repeated palpitation and paroxysmal AF recorded by ECG. B: ECG presents little P waves in V1 lead during sinus rhythm. C: Absence of spectrum A peak is recorded by echocardiography. D: Three-dimensional voltage mapping exhibits AES/LVZ in most areas of RA and LA.

tive age of onset. This highlights the critical role of genetic factors in the pathogenesis of AF. Nonetheless, these two young patients had no family history of early onset atrial tachyarrhythmia, and regrettfully the genetic test was not performed. Therefore, the exact etiology of the two cases remains unknown and further investigation with genetic mapping is needed to identify the possible chromosomal location.

A previous study has delineated a group of patients with unexplained scar-related atrial arrhythmias characterized by extensive fibrosis in atrial myocardium without age-related comorbidities or underlying cardiovascular disease, and with rare ventricular involvement. In that study, no clue of genetic or acquired disease could be found. It was confirmed that those patients may be cases of a specific subtype of atrial cardiomyopathy named idiopathic, fibrotic atrial cardiomyopathy.

Atrial cardiomyopathy is defined as a series of clinically-relevant symptoms caused by any complex of structural or functional abnormality of atria, according to the EHRA/HRS/APHRS/SOLAECE expert consensus. Fibrotic remodeling is the most important pathophysiological basis for development of atrial cardiomyopathy and may possibly account for atrial arrhythmia. Accumulating evidence has demonstrated a causal relationship between fibrosis and atrial tachyarrhythmia, particularly “lone” AF with no concomitant conditions. Importantly, even curative catheter ablation of atrial arrhythmia could not retard the progression of fibrotic remodeling, indicating that the atrial fibrosis is not the consequence of coexisting atrial arrhythmias but the progression of atrial cardiomyopathy per se. The patients in the afore-mentioned study demonstrated similar clinical characterization but more advanced atrial scaring compared with those cases reported in the study. In terms of this, we proposed that the pathological change of atrial cardiomyopathy is the main cause of these catastrophic events.

The underlying fibrotic remodeling not only predisposes the atrium to develop complex cardiac arrhythmias, but also impairs atrial contractility and compliance, and even leads to atrial standstill. These abnormalities may be clearly associated with cardiac dysfunction and, more importantly, increased risk of thromboembolic events. Here we provided the representative cases demonstrating...
the consequence of impaired atrial contractility caused by absence of electrical activity: both cases suffered from ischemic stroke before anticoagulation. It is noted that during sinus rhythm, there was no atrial contractility, which was demonstrated by no A peak in echocardiogram. This study has therefore provided the rationale for lifelong anticoagulation in this type of patient even the CHA2DS2-VASc score of “0.” The lower amplitude or disappearance of the P wave during the sinus rhythm may be a diagnosis clue for the loss of atrial electrical activity in such a patient.

Thus, early identification of atrial cardiomyopathy is of great importance, and low amplitude P wave in ECG may independently predict the pathological changes of atria and can also be a major risk factor for stroke.

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Disclosures
Conflicts of interest: The authors declare no conflicts of interest.

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