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EDITORIAL

Cardioembolic stroke in cardiac amyloidosis: the real challenge lies beyond heart rhythm

Vasilios Giampatzis[1,2], Beatrice Musumeci [3], and Giacomo Tini [3]*

[1]Cardiology Department, General Hospital of Kavala, Kavala, Greece; [2]Emergency Department, General Hospital of Kavala, Kavala, Greece; and [3]Cardiology, Azienda Ospedaliera Universitaria Sant'Andrea, Dipartimento di Medicina Clinica e Molecolare, Sapienza University of Rome, Rome, Italy

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This editorial refers to 'Use of transoesophageal echocardiography to detect and manage atrial thrombi in light-chain cardiac amyloidosis: a case report', by T.Q. Dang and S. Van Hoang. https://doi.org/10.1093/ehjcre/ytad076.

Cardiac involvement in light-chain amyloidosis (light-chain cardiac amyloidosis, AL-CA) may be found in up to 50–70% of cases.[1] Cardiovascular complications of AL-CA include heart failure, brady- or tachyarrhythmias, and thromboembolic events,[1,2] with the prevalence of the latter ranging from 6% to 33%.[3]

The recently published manuscript by Dang and Hoang[4] describes the case of a 51-year-old male with a recent supposed diagnosis of hypertrophic cardiomyopathy who presented at the emergency department with acute ischaemic stroke (IS), without previous history nor detection during hospitalization of atrial fibrillation (AF). The subsequent work-up led to the final diagnosis of AL-CA.

One first important clinical point derived from this case report is the need for careful evaluation for cardioembolic causes of IS. A high clinical suspicion for the presence of CA, especially when typical 'red flags' are present, is particularly important, as an IS may even be the first clinical manifestation of AL-CA.[5–7] Light-chain cardiac amyloidosis and CA in general should thus be kept in mind in the differential diagnostic pathway of cardiogenic causes of IS.

Another important point raised by the authors is the need for rigorous assessment for intracardiac thrombi in the case of thromboembolic events in the context of AL-CA. This diagnostic evaluation should be performed independently of the presence of normal sinus rhythm. In fact, previous cohort studies have highlighted the high prevalence of intracardial thrombi in CA, detected by echocardiography and cardiac magnetic resonance (CMR) imaging, as well as the greater thrombotic risk in the subtype of AL-CA.[8,9] Despite the absence of documented AF in this case, the authors handled the case appropriately by performing transoesophageal echocardiography (TEE) to investigate for intracardiac thrombi.

Increasing evidence supports the multifactorial nature of arterial thromboembolism and intracardiac thrombi formation in CA.[10,11] Various cardiac factors such as blood stasis and altered haemodynamics, focal endocardial damage from amyloid deposits, and ischaemic-induced mural thrombosis could act synergically and promote thrombi formation in CA.[5,11] Besides, various other extracardiac factors, such as the hypercoagulable state from the circulating paraproteins and the frequent occurrence of nephrotic syndrome (as in this case), contribute to the even higher thrombotic risk in AL-CA.[3,11] Accordingly, the cardioembolic risk in AL-CA is high irrespectively of sinus rhythm.

Moreover, increased atrial stiffness and abnormal atrial mechanics due to atrial remodelling and dysfunction (i.e. atrial myopathy) are common in AL-CA.[12] Indeed, the transthoracic echocardiography (TTE) and TEE indices in the recently published case report confirm the presence of atrial myopathy. Previous studies have shown the prognostic value of atrial dysfunction (in terms of mortality, but not of cardioembolic events), estimated with TEE and CMR indices, in AL-CA independently of left atrium size.[13,14]

Nevertheless, it should be kept in mind that AF and other atrial arrhythmias have a high prevalence in CA.[2] These arrhythmias may be underdetected, and a thorough and periodic rhythm monitoring in all patients with CA with sinus rhythm should be performed.

The high risk of cardioembolic events in AL-CA despite sinus rhythm poses an important challenge for the management of these patients. Whom, when, and how to initiate anticoagulation remain open questions. One previous study reported the association of CHA2DS2-VASc ≥ 3 with thromboembolism in patients with CA with sinus rhythm[10] but this was not confirmed in a following study.[15] However, the first included patients with both AL-CA and transthyretin CA,[11] while the latter only patients with trasthyretin CA.[16] As the authors of the recently published case report suggested that the creation of a reliable risk stratification tool irrespective of baseline heart rhythm will likely require various TTE and TEE indices of atrial (dys) function, along with appropriate demographic and clinical data. Such a tool could provide information on the need for further advanced imaging or for the initiation of anticoagulant treatment in such patients.

The role of advanced imaging in the investigation of thromboembolic events in patients with CA is undisputed. This case report emphasizes the need for TEE implementation after negative or inconclusive initial TTE examination. The diagnostic value of cardiac computed tomography and/or CMR for the detection of intracardiac thrombi is also well recognized.[9,16] These imaging modalities could greatly contribute to thrombi detection in CA after thromboembolic events or even to the investigation of asymptomatic patients with CA with presumed high thrombotic risk.

* Corresponding author: Tel: +39 06 33775584, Email: giacomo.tinimelato@uniroma1.it

Finally, there is few evidence on the comparative efficacy between non-vitamin K antagonist (NOACs) and vitamin K antagonist (VKAs) oral anticoagulants in the setting of thromboembolic protection in AL-CA. Recent studies emphasized a similar efficacy of VKAs and NOACs in reduction of thrombotic complications in CA.[15,17,18] However, the analyses of these studies were performed exclusively[15,17] or mainly[18] on patients with transthyretin CA with AF. Of note, few studies showed that even therapeutic anticoagulation may not be sufficient enough to prevent thromboembolic events and intracardiac thrombi in patients with CA with atrial arrythmia or AF.[10,19]

The subpopulation of patients with AL-CA in sinus rhythm complicated with acute IS or intracardiac thrombi is understudied. Indeed, these patients have been included only in some case reports with different anticoagulation regimes and outcomes.[5–7,20] The choice of NOAC for the patient of Dang and Hoang proved to be effective in thrombi resolution and secondary prevention of cardioembolic events at follow-up. To date, no formal recommendations exist for the duration of anticoagulation treatment in these cases. Taking into account the irreversible signs of atrial dysfunction (low emptying velocities) and the spontaneous echo contrast in follow-up TEE, the decision for lifelong oral anticoagulant treatment may have correctly been taken in this case. In fact, long-term anticoagulation might be the optimal treatment plan for patients with AL-CA due to their high thrombotic risk, irrespective of the presence of atrial arrhythmia or the transient resolution of intracardiac thrombi. However, AL-CA is also associated with a high bleeding risk due to amyloid vasculopathy, X-factor deficiencies, and concomitant liver and/or renal involvement.[3] Consequently, more studies are needed in this complex population on the appropriate time of initiation, the type, as well as the duration of anticoagulation treatment balancing always the risk/benefit ratio in each individual case.

Lead author biography

Giacomo Tini is Assistant Professor in Cardiology at Sapienza, University of Rome.

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Data availability

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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