Histology of Sudden Death in Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia

To the Editor:

In a recent issue of Circulation, Tabib et al. reported the largest ever published series of sudden cardiac deaths caused by arrhythmogenic right ventricular cardiomyopathy (ARVC/D).

The authors addressed the controversial issue of the histologic definition of ARVC/D. Fatty replacement of the right ventricular myocardium is the salient feature in ARVC/D. “Fatty” and “fibrofatty” patterns have been distinguished, depending on the presence of additional fibrosis. Morphometric investigations performed by Burke et al. suggested that fatty and fibrofatty patterns represented 2 distinct entities. We agree with Tabib et al. that disorganization or isolation of myocardial cells within fat is necessary for the diagnosis, pure fat characterizing a different entity.

A second point of controversy is the astonishing wide range, from 5% up to 80% of cases, in which lymphocytic infiltrates have been reported. Different methods of quantification of lymphocytes may explain this range. We follow the opinion of the group of Padoua considering that presence of a small number of lymphocytes may be significant. A mild lymphocytic infiltrate can be arrhythmogenic as suggested by our recent observation of increased C-reactive protein levels, which are associated with arrhythmogenic right ventricular tachycardia in ARVD and not ARVC.

Myocarditis may also explain replacement fibrosis in some patients with a hypertrophied heart. This feature is more frequently observed in males than in females, because of the protective effect of female hormones on infection (S. Hüber, personal communication, 1996). We also agree with Tabib et al. that the presence of lymphocytes is an “aggravating factor.” In our understanding of the disease, inflammation explains the bimodal nature of left ventricular ejection fraction in the most severe forms of ARVC.

In the Tabib et al. study, almost 70% of hearts had abnormal conduction tissue. To our knowledge, no other studies have reported such a finding. All cardiovascular pathologists are aware of the difficulty in interpreting findings involving the conduction tissue. Lesions of the conduction tissue are often overestimated. Two examples are illustrated in this paper. In our opinion, the microphotographs are not convincing because no low-magnification view has been provided to prove location of fibrosis/adipocytes. In our clinical experience involving >200 ARVC patients, ventricular arrhythmias are frequent, and atrioventricular block is rare. Pacemakers have been implanted in 12 patients because of bradycardias that were mostly attributed to therapeutics used to control tachycardias. In this context, we would like to have further expert opinions from both clinical and pathology teams, to make sure that findings reported in this paper are relevant.

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Response

We thank Drs Fontaine and Fornes for their comments. We appreciate their agreement about the importance of disorganization and isolation of myocardial fibers within fat as key elements to distinguish arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) from fatty replacement. It is difficult to infer the role of lymphocyte infiltration in ARVC/D, and our study does not bring any new elements to that issue.

On the contrary, one of the novel findings of our study is certainly the observation of frequent infiltration of conductive tissue by fibrosis (54%), adipose tissue (8%) or both (6%) in hearts of individuals who had unexpected sudden death associated with ARVC/D. It is impossible to compare this high prevalence with previous studies because conduction tissue was never systematically scrutinized in ARVC/D. We have seen conduction tissue with adipose infiltration and/or fibrosis in numerous ARVC/D cases as convincing evidence of conduction tissue alteration.

Fontaine and Fornes raised an interesting point: how can conductive tissue infiltration in ARVC/D be so prevalent (~70%) when atrioventricular (AV) block is so rare? In our series, among the 6 rare patients who had an ECG recording before death, 1 had an AV block. Moreover, among the 50 patients with ARVC/D whose cases were followed in our department, 2 have a pacemaker for complete AV block. A third patient who suffered from ventricular tachycardia had documented infranodal block. Thus, AV block is not so infrequent (about 6%) and appears as the tip of the iceberg of the conduction tissue involvement. Clinicians should be aware of the risk of AV block during antiarrhythmic drug prescription. Furthermore, our observations support the view that an invasive electrophysiologic study is recommended to detect hidden intracardiac conduction disturbances when antiarrhythmic drugs are indicated.

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