Sudden Cardiac Death Due To IgG4-Related Disease

To the Editor—We read with interest the recently published case report by Patel et al.1 describing a patient who died suddenly and for whom immunohistochemistry of the autopsy sample demonstrated marked immunoglobulin G4 (IgG4)–positive lymphocytic infiltration in the coronary artery wall and other organs, including the kidney, pancreas, and lymph nodes.

Coronary artery involvement of IgG4-related disease has been demonstrated in several previous case reports: coronary artery luminal narrowing, presumably of an atherosclerotic nature, may occur at the site of a coronary artery surrounded by thickened or tumefactive adventitia with IgG4–positive lymphocytic infiltration,2 as in the case described by Patel et al.1 On the other hand, several case reports have demonstrated only mild coronary artery luminal narrowing, regardless of the marked adventitial IgG4–positive cell infiltration.3,4

The condition that was documented by Patel et al might be termed IgG4-related coronary artery disease; on the other hand, it should be noted that there have been no specific criteria for diagnosing IgG4–related coronary artery disease or IgG4–related cardiac disease until now. Histologic findings are an important and indispensable requirement for the diagnosis of IgG4–related diseases; however, there are several organs, such as the pancreas, in which IgG4–related disease does exist but for which the acquisition of antemortem tissue is difficult and/or impractical. Diagnostic criteria for IgG4–related disease in such organs are advocated; however, diagnostic criteria for IgG4–related cardiovascular disease have not been defined as yet.

According to a previous report by Tanigawa et al,2 and the report by Patel et al,1 there is no doubt that the cardiovascular system is a target of the multiorgan involvement of IgG4–related disease, and IgG4–related coronary artery disease may lead to a fatal outcome. On the other hand, considering that IgG4 may counteract the overactivated inflammatory process and that the severe IgG4–related pericoronary phenomenon is not necessarily accompanied by coronary artery stenosis or occlusion, we may need to further assess whether IgG4–related pathological conditions enhanced or, in reverse, ameliorated the coronary artery luminal stenosis and occlusion observed in their case. It is possible that the IgG4–positive cell infiltrate in the pericoronary artery may have, conversely, reduced the severity of the coronary artery disease. Nevertheless, whether IgG4–positive lymphocytic infiltrates promote or suppress coronary artery disease, such a histology, or elevated serum IgG4, may indicate a higher possibility of the presence of coronary artery lesions.

In terms of the role of IgG4–positive lymphocytes in coronary atherogenesis, it would be of relevance to determine whether the thickened intima was positive for infiltration of such cells in the case of Patel et al.1 In general, B and T cells may reside in adventitial regions, but T cells (but not B cells), as well as monocytes/macrophages, infiltrate the inflamed intimal lesions.5 Although Patel et al demonstrated immunostaining of the wall of a coronary artery, we would be interested in IgG4 staining in specific parts of the coronary artery wall, including the adventitia, media, and intima, and would welcome comment on this point from the authors. We think that the case report by Patel et al has two important messages: first, coronary artery involvement can occur as a component of multiorgan IgG4–related disease; and second, IgG4–related coronary artery disease may be associated with a sudden fatal outcome, although whether IgG4–positive lymphocytes promote the coronary artery atherosclerotic process remains unclear.

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In Reply.—We thank Drs Ishizaka, Tanigawa, and Suzuki for their interest in our recent article describing a case of sudden cardiac death in a man with concomitant coronary artery disease and IgG4–related disease (IgG4–RD).1 The authors raise several concerns, and we thank them for the opportunity to further explain our findings. First, the authors of the letter state, “The condition that was documented by Patel et al might be termed IgG4–related coronary artery disease.” In contrast, we have described our findings as “coronary artery involvement by IgG4–related disease.” This distinction is crucial because no conclusion can be drawn about the biological relationship between the fibrosis with infiltration by IgG4–positive lymphocytes and the coronary artery atherosclerosis. The authors go on to say that “…we may need to further assess whether IgG4–related pathological conditions had enhanced or, in reverse, ameliorated the coronary artery luminal stenosis and occlusion observed in their case.” We interpreted the findings in our case as “…fatal outcome due to sudden cardiac death in a patient with IgG4–RD.”1 To clarify, we believe that this patient exhibited 2 distinct processes that simultaneously involved the coronary arteries. Indeed, it would be difficult to make any claims about whether a causal relationship between the processes of IgG4–RD and atherogenesis even exists. Instead, the inflammation and sclerosis, in combination with concomitant atherosclerotic disease, resulted in severe stenosis of the coronary arteries. Two of the coronary arteries were further occluded by thrombosis, leading to cardiac hypoperfusion and sudden cardiac death.