Reviewer's report

Title: Synchronous cardiac arrest in monozygotic twins with hypertrophic cardiomyopathy - Is sudden cardiac death genetically pre-programmed?

Version: 2 Date: 18 December 2014

Reviewer: Imke Christiaans

Reviewer's report:

This report nicely illustrates a case of phenotypic overlap in a monozygotic HCM twin. Such a case with synchronous cardiac arrest has not been published before for as far as I know.

Minor essential revisions

1) In both abstract and discussion it is mentioned that incidence of cardiac arrest in monozygotic twins is not known. Indeed it is not known, but should we expect it is any different from the incidence in non-twin HCM patients? Or do the authors mean that they have not heard of such an event in monozygotic twins, then do not use the term incidence and described it is not known from literature (as I happen to known cases, although not synchronous).

2) I do not see any additional value of the first sentence of the third paragraph in the discussion section “While LGE in cardiac MRI...”. Can the authors explain why they mention this? Not one of the twin brothers has had an MRI.

3) On what basis was concluded that these men were monozygotic twins?

Major revisions

1) In the discussion section the authors mention that the patient’s twin brother did not meet any of the established criteria for ICD insertion. May I remind the authors that both in the patient and the deceased twin brother risk stratification was incomplete, and that risk stratification (exercise test and Holter recording) is advised to be repeated on a yearly basis. It can therefore not be said that risk stratification did not demonstrate an increased risk, just that it was not performed according to the guidelines (which might have cost a life....).

2) I do not understand why the authors mention on an underlying genetic factor responsible for timing of ventricular arrhythmias in a subset of patients with HCM (they mention this three times: abstract, discussion, and conclusion). If so I would like to have more information on why they think this could be the case here. Such a genetic factor seems very unlikely to me in this specific case. As monozygotic twins they already share the HCM causing mutation. We know that such mutations are associated with an extremely variable phenotype within families. An additional genetic factor most likely would also have been inherited from one of the parents, would it not have caused cardiac arrest in that parent or in another sibling? Perhaps not because it was transmitted by the parent not carrying the HCM mutation. If such a genetic factor would exist we would expect
more reports of synchronous cardiac arrests in siblings/relatives in literature. I do not know this from literature and from my own experience with several hundreds of HCM families. We do know that a double mutations (on different alleles or in different genes) cause a more severe phenotype with earlier disease penetrance, more hypertrophy, and a higher risk of SCD. Why should an additional genetic timing factor be more likely than just coincidence? They are monozygotic and this is the VF is the only disease characteristic they have in common. Other parameters like LVH were different.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.