Reviewer's report

Title: Cardiac involvement in beagle-based canine X-linked muscular dystrophy in Japan (CXMDJ): electrocardiographic, echocardiographic, and morphologic studies

Version: 2 Date: 28 August 2006

Reviewer: Luca Ferasin

Reviewer's report:

General
This is an interesting paper, which describes clinical, electrocardiographic and echocardiographic evaluations in a group of beagle-based X-linked muscular dystrophy dogs produced in Japan (CXMDj).

The paper may potentially add a valuable contribution in the field of suitable animal model for the study of Duchenne muscular dystrophy (DMD). However, there are some important questions that the Authors should address before considering this manuscript publishable in BMC Cardiovascular Disorders.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1) Although the hypothesis of the study is relatively clear, the purpose should be explained in further detail. The Authors state that a valid animal model is already available (GRMD) but “dogs are large”. Do the Authors propose a different animal model because GRMD are more expensive to breed and maintain? Are there significant advantages in animal housing or welfare? Are Beagle-based dogs easier to examine?

2) The Authors should also explain in detail the ECG recording technique used in this study. It is well documented that body position affects QRS morphology in dogs (Rishniw et al [2002] JVIM 16:69) and variations in recumbency may have been responsible for the observed changes. Furthermore, at the end of the subheading “Clinical profiles of CXMD”, the Authors state that a dog “ran about wildly” during routine ECG and the “ECG monitor showed an idioventricular rhythm”. How could the ECG be recorded while the dog was running? Were these dogs permanently instrumented?

3) On multiple occasions, the Authors state that both PQ and PR intervals were measured. It is my understanding that PQ and PR intervals are the same thing (time between the onset of atrial depolarisation [P wave] and the onset of ventricular depolarization [QRS complex], and it is measured from the beginning of the P wave to the first deflection of the QRS complex, whether this be a Q wave or an R wave) (Meek & Morris [2002] BMJ 324:470)

4) The negative correlation between heart rate and PQ (PR) interval has been clearly demonstrated in normal Beagle dogs (Hanton & Rabemampianina [2006] Lab Animals 40:123) and it may be attributed to a parasympathetic input at the level of the AV node. The Authors should acknowledge the already available information.

5) The Authors state that the Q/R ratio continuously increased from 6 to 21 months. However, this does not appear obvious from the data presented in figure 1C, where affected dogs presented a higher ratio but not clearly increasing over time (especially in lead aVF).

6) The echocardiographic changes in figure 3B are convincing (increased echogenicity in the left ventricular posterior wall); however, the claimed hypokinesia in III-302MA, 21m is a subjective evaluation. Moreover, 27.3% fractional shortening is lower than that recorded in the other dogs in this study, but it can still be considered a normal value from a clinical point of view.

7) It is my understanding that the Q wave represents the early depolarization of the interventricular septum and right ventricular subendocardium. Therefore, I find it difficult to believe that a fibrotic lesion of the posterobasal region of the left ventricle may cause deep Q waves. Altered ionic currents described by Perloff et al (ref n. 17) seem to explain this phenomenon more convincingly.

8) I would imagine that data were not normally distributed. If so, the median (±SE) may add useful
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1) Cephalic vein of a forefoot sounds redundant (cephalic vein is only on the forelimb)

2) Some paragraphs in the “Result” section report (or repeat) the description of the method. They should be moved to the “Methods” section or be removed.

Discretionary Revisions (which the author can choose to ignore)

1) I would suggest to change the phrase “from 2-month old” into ‘from 2-months of age”
2) I would suggest to change the phrase “almost comparable” instead of “roughly comparable”
3) In “Methods”, the subheading “electrocardiography” sounds rather confusing and should be rewritten.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:
'I declare that I have no competing interests'