Reviewer's report

**Title:** Transmission of HIV Infection from an Elite Controller to a Patient who Progressed to AIDS: a case report

**Version:** 3  **Date:** 8 March 2012

**Reviewer:** Klaus Korn

Which of the following best describes what type of case report this is?: An unexpected event in the course of observing or treating a patient

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: No

Is the anonymity of the patient protected?: Yes

Comments to authors:

The first three of my questions have been answered and they add some relevant information that was missing before.

The answer to the fourth question "How was sequencing accomplished in the male partner when "On at least eight separate occasions spanning this 10 year period, MM tested negative for HIV DNA by PCR."? What was different in the PCR method used to amplify for sequencing from the PCR method used in detection? The only difference I could notice is that for sequencing "total nucleic acids (both DNA and RNA)" were extracted, whereas for the detection attempts probably only DNA was extracted." however, is insufficient. Does the sentence "Roche used a nested PCR approach that involves 2 rounds of PCR amplification." mean that for the DNA detection with negative results on the eight
occasions only a single-round PCR was used? Furthermore, it is now stated that for this PCR testing separated PBMC were used. Was this also the starting material for the negative PCR tests? And the next sentence "Also, recent studies indicate that HIV DNA and RNA tests have comparably low sensitivities (~0.55) when the virus levels are very low (J Pediatr. 2012 Jan;160(1):6)." leaves me completely puzzled as to what this has to do with my question. Of course, if virus levels are low, the success rate of PCR amplification goes down, but this is true for either method.

Finally, the phylogenetic analysis presented by the authors in response to my fifth question does not give any new information, since it only shows that both sequences belong to clade C. A phylogenetic analysis capable of demonstrating that the two sequences are indeed epidemiologically linked would have to include the 20 or so most closely related sequences from e.g. the LANL database (ideally also some local sequences) and would need only one "outgroup" sequence from another clade like for example B.

The authors claim four lines of "primary evidence for this event" (i.e. transmission from an elite controller), which are "1) the medical history of MM involving probable exposure to HIV-1 infection, 2) the clinical history of FF, 3) the self-reported sexual histories of MM and FF and 4) comparisons of the HIV-1 sequences found in MM and FF". However, the evidence for transmission having occurred from an elite controller is basically "3) the self-reported sexual histories of MM and FF", since #1) and #2) provide evidence for the fact that MM is an elite controller and FF is not, but do not provide evidence for the transmission event itself. Therefore, a thorough phylogenetic analysis is in my opinion absolutely necessary to substantiate claim #4). It is clear that such a phylogenetic analysis can neither give information about the direction of the infection and can also not prove that the infection occurred directly between the two individuals. However, the critical issue in this case is not to demonstrate direct transmission, but to show unanimously that the two sequences are indeed epidemiologically linked. Counting only differences to a consensus sequence does not do that job.

**Quality of written English:** Acceptable

**Declaration of competing interests:**

'I declare that I have no competing interests'