Reviewer's report

Title: Ovarian dysfunction and FMR1 alleles in a large Italian family with POF and FRAXA disorders: Case report

Version: 1 Date: 7 November 2006

Reviewer: Anna Murray

Reviewer's report:

General
This is an interesting case report of a family in which the POF phenotype and an FMR1 premutation are segregating. There is one case of POF which doesn't segregate with a premutation and is therefore attributed to an alternative cause. POF has a relatively high population frequency at 1%, and it is therefore not surprising that cases of POF unrelated to the FMR1 premutation will be found in fragile X families. The strength of the paper is in the large number of individuals studied within one family and the correlation between genotypic and phenotypic data. The emphasis should be on why the premutation has such a variable effect in carriers, eg. premutation size and X inactivation ratio.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. It is not clear which patient is the proband in this family. Figure 1 indicates IV-7 as the proband, but the Results & Discussion section suggests that the male with fragile X syndrome is the proband.
2. The last paragraph does not seem to fit the data, as in this family an FMR1 premutation did not predict the age of menopause.

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. Page 4, 3rd para - not clear which individuals are being discussed when using family relationship, it would be much clearer to use the individual ID.
2. 'pre-puberal' - should be 'pre-pubertal'
3. DNA extraction method - more details and/or reference should be given.
4. Results & Discussion, para 2 - it is very well established that premutations are very unstable when maternally transmitted, however I think the authors could discuss the transmissions from individual II-6. It is very unusual for a repeat of 200 to stay within the premutation range during female transmission and apparent repeat contractions are also rare.
5. The term 'the POF' should not be used, should use 'the girl with POF' for example.
6. Discrepancies between text and figure - II-2 genotype is 31/100 in text 31/60 in figure and III-5 is 24/200 in the text and 24/100 in figure.
7. Berry-Kravis reference is not numbered or on reference list.

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential 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 I have no competing interests