Reviewer’s report

Title: Type I Gaucher disease with exophthalmos and pulmonary arteriovenous malformation: A more severe clinical variant?

Version: 1 Date: 28 December 2004

Reviewer: Deborah Elstein

Reviewer’s report:

General

Comments on paper entitled “Type I Gaucher disease with exophthalmos and pulmonary arteriovenous malformation: A more severe clinical variant?” by Chen et al.

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

This case report is quite interesting, although I find it problematic that the authors want to consider it a “variant”: not every patient with a heretofore-unrecognized genotype and/or phenotype will necessarily be a new variant. Therefore my first recommendation is to modify the title.

My second recommendation is to remind the authors that there is no justification for the use of “Gaucher patients” or the like: these are individuals or patients with Gaucher disease, and should not be dehumanized by virtue of a genetic disorder.

And my third general comment is that the references are sometimes less good choices (e.g. reference 1 should not be a specific manuscript about pulmonary involvement but rather some textbook citation) or slightly out-dated (reference 11) or inappropriate (reference 5).

Whereas choice of references may appear a trite consideration, the Discussion hinges on understanding the current literature, and this brings me to my final general comment: I believe that the case presented is remarkable because it highlights both the good and less good aspects of response to enzyme replacement therapy. Indeed, the eye problem improved with enzyme therapy, and hence one may posit that this complication is an expression of Gaucher disease (or this genotype), although it is the first such report and neither of the index case’s sisters with the same genotype have this complication.

However, the index patient suffered from pulmonary disease that was probably secondary to more severe Gaucher disease including severe liver involvement, i.e. hepatopulmonary syndrome and pulmonary hypertension (as described in reference 3). She developed pulmonary hypertension with clubbing of the fingers despite having no evidence of lung/alveolar infiltration. Whereas the younger sister with lung disease improved with enzyme therapy, the index case developed restrictive lung disease and worsening pulmonary hypertension within two years of advent of enzyme therapy. Therefore one interpretation could be enzyme-induced pulmonary hypertension and then a possible strategy would be withdrawal from enzyme therapy. The authors cite an early reference (#15) that implicates this mechanism, but fail to discuss their findings in light of more current papers (by Elstein and/or Mistry) that specifically hone in on this finding. Hence, I would suggest the authors consider these issues in a revision.

Minor comments include: the Discussion about Gaucher-related bone disease is also affected by the lack of appropriate referencing since it is rather well accepted that early splenectomy (and even partial splenectomy) induces bone disease, but I wonder if this is even relevant since bone disease
is an unpredictable finding whereas the liver involvement is sufficient to implicate severe disease.

Similarly, I wonder what to make of the discussion of genotype-phenotype correlation when in fact neither of the index case’s two sisters with the same genotype has either the ocular nor the pulmonary finding.

Finally, the Discussion should be compartmentalized according to symptoms e.g. start with ocular then pulmonary then conclusions vis a vis enzyme therapy and/or genotype-phenotype correlations.

My recommendation would be a tighter narrative as well.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct):
none

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Discretionary Revisions (which the author can choose to ignore)
none

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: Acceptable

Statistical review: No

Declaration of competing interests:
I have no competing interests