Dear Sir,

I thank Dr Golubovsky for his interest in our paper (Matsui et al., 2003) and the new concepts regarding the genesis of hydatidiform mole.

It is generally assumed that molar pregnancy is classified into two entities, complete and partial mole, on the basis of macroscopic or cytogenetic examinations. Complete moles have a diploid chromosomal structure in which all the chromosomes are paternal as a result of fertilization of an ‘empty’ oocyte by a haploid spermatozoon (homozygous complete mole) or two sperm (heterozygous complete mole) (Kajii and Ohama, 1977; Ohama et al., 1981). On the contrary, partial moles are formed by fertilization of normal oocyte by two sperm, and the karyotype is usually triploid (Lawler et al., 1982; Ohama et al., 1986).

First, Dr Golubovsky points out that there is no convincing evidence for a reservoir of ‘empty oocytes’ through the recent IVF and assisted reproduction technique (ART) procedures. I had no data on findings of ovulated anuclear oocyte in natural conditions, while I used the term of ‘empty’ oocyte as the abnormal or inactive oocyte. In the Introduction section, I mentioned that complete mole has been shown to be the consequence of an ‘empty’ oocyte (i.e. one that has a degenerative nucleus) being fertilized by a haploid spermatozoon or two sperm.

Second, he points out the reversed dependence between the rate of complete and partial moles. In our population-based study, the diagnosis of complete and partial mole was based on the macroscopic findings, so that the possibility of misdiagnosis between complete and partial moles might be considered in some cases. However, the diagnostic criteria for complete and partial mole having remained unchanged during these two decades, the misdiagnosis between molar pregnancy and non-molar spontaneous abortion could not be considered. In our
paper, the overall incidence of molar pregnancy (complete and partial mole) in Chiba Prefecture and Japan has apparently decreased since 1991 and now it has become as low as that in Europe or the USA. These drastic changes might be a result of the decline of complete mole and some environmental or socioeconomic conditions might be connected with these drastic changes in Japan.

Third, Dr Golubovsky points out that the decline of complete mole in the beginning of the 1990s is accompanied by the drastic increase in the rate of dizygotic (DZ) twins in Japan. However, the recent widespread use of ovulation induction with IVF or ART commenced at the beginning of the 1990s. This increased use of ovulation induction might be attributed to the drastic increase of DZ twins in Japan. In my previous report, we collected and analysed data from 72 patients in Japan with hydatidiform mole co-existent with a twin live fetus. Eighteen patients were confirmed genetically to be pregnant with DZ twins of normal fetus and androgenetic mole. The incidence of ovulation induction in 18 patients was 44.4% (8/18) (Matsui et al., 2000).

Lastly, he mentions three abnormal fertilization scenarios in cases with dispermy. These fertilization scenarios were interesting, although I could not understand why the decline of complete mole was accompanied by the drastic increase in the rate of ‘sesquizygotic (SZ) twins’. If some environmental or socioeconomic conditions were decreased the incidence of complete mole scenario and increased that of SZ twins scenario, there was no evidence of the drastic increase of DZ twins without ovulation induction in Japan. In addition, in the previous genetic study of molar pregnancy (Ohama et al., 1981), ~6% of complete moles would be the product of dispermy (heterozygous complete mole). If the dispermy fertilization was the cause for developing diandric triploidy (partial mole), heterozygous complete mole and ‘SZ twins’, the incidence of partial mole would become as low as that of heterozygous complete mole.

However, there are many enigmas in the genesis of complete mole, subsequent endoreplication of one spermatozoon or fusion of two male pronuclei without female pronuclei. Although this dispermy fertilization scenario may play a role of the genesis of complete mole, further cytogenetic analysis of DZ twins, heterozygous complete mole and partial mole would be required.

References


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