Fertility in McCune Albright syndrome female: A case study focusing on AMH as a marker of ovarian dysfunction and systematic review

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Background: The molecular basis of McCune Albright syndrome (MAS) is a recurrent postzygotic gain of function sporadic mutation of \textit{GNAS}, resulting in a mosaic disease. Most of girls present precocious puberty, caused by the development of recurrent ovarian cysts with autonomous hyperestrogenic stimulation. After menarche most of the patients with ovarian \textit{GNAS} mutation have menstrual disturbances and infertility.

Objectives: We wanted to focus on the fertility of MAS females and propose an appropriate management, by a detailed case report and an exhaustive review of the literature on fertility and pregnancy in MAS females.

Results:

- We present the case of a 29-year-old MAS female, who had previously undergone an unilateral ovariectomy and was managed by in vitro fertilization (IVF).
- Eight oocytes with many morphological abnormalities were retrieved after high doses stimulation (Table 1).
- The \textit{GNAS} mutation was found at a low frequency (2%) in follicular cells, but not in the endometrium nor in blood (Figure 1).
- Ovarian histopathological examination showed developing follicles of any stage (Figure 2), strongly expressing AMH by immunohistochemistry (Figure 3).

In addition, AMH was high (45.5 pmol/L) and the AMH / AFC ratio (5.69 pmol/L per follicle) was much higher than in PCOS and control patients (2.16, and 1.34 respectively) (Table 2).

Discussion: Ovarian and endometrial involvement can be responsible for infertility in MAS women. IVF and oophorectomy may be useful in management (Table 3). The genetic characterization of the different tissues may have a prognostic utility. Moreover, we propose the AMH as a marker of the ovarian activity of MAS. Further studies are needed to clarify the potential oocyte abnormalities and the risk of miscarriages in order to guide genetic counseling (Table 4).