P-299

FERTILITY PRESERVATION IN PREMATURE OVARIAN INSUFFICIENCY SECONDARY TO FSH RECEPTOR GENE MUTATION : IS THERE A NEW HOPE?

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INTRODUCTION

There are very few FSHR mutation cases described in the literature[1]. When it was suspected, ovarian biopsy was often proposed as the diagnostic tool and virtually no treatment could be offered.

OBJECTIVE

Which patients should be screened for FSH receptor (FSHR) gene mutation? Are we able to offer fertility preservation for those poor prognosis patients?

CASE AND METHODS

A 19 years old patient with primary amenorrhea was referred to our center. She had moderately developed secondary sex characteristics and diminished sized ovaries. Based on the contrast between high FSH level (72.5 UI/L) and normal other ovarian reserve tests (AMH = 1.59 ng/mL and Antral Follicle Count = 16), FSHR gene mutation was screened for.

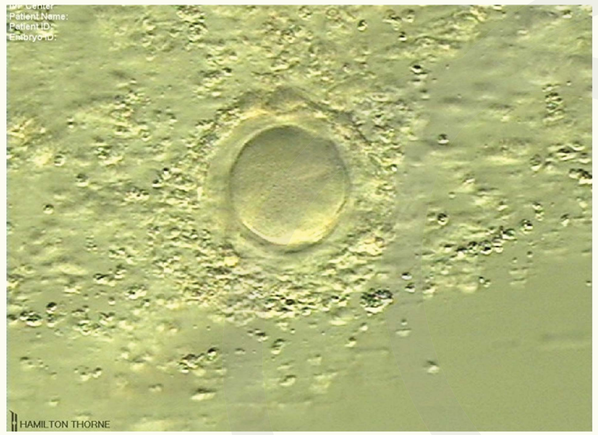
RESULTS

The patient was homozygous for exon 6 of the FSHR gene for a variant defined as c.479T>C and predicted to result in the aminoacid substitution p.Ile160Thr. This new missense mutation has been reported to be pathogenic in its heterozygous form [2]. The parents are non consanguineous French Canadian and were carrrying the same mutation on only one chromosome.

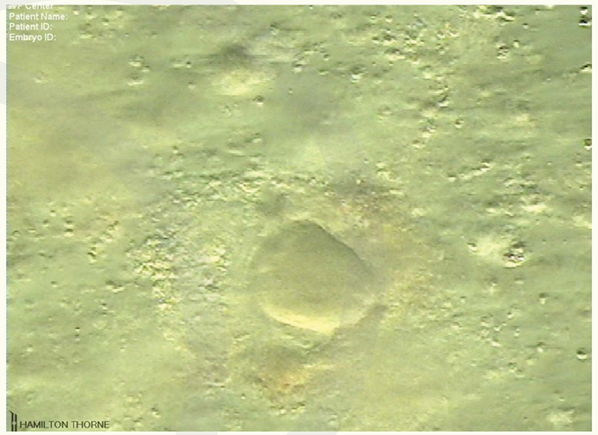
One year later, her AMH level decreased (0.59 ng/mL) and we offered fertility preservation using oocyte vitrification. After 17 days of high doses of recFSH (900 IU daily), no follicular growth was seen and estradiol levels remained low (18 follicles with maximal size of 5 mm).

In Vitro Maturation (IVM) was proposed. HCG 10.000 UI subcutaneous was used 34 hours before the oocyte retrieval. Seven immature oocytes were collected and matured in vitro. Three oocytes were successfully vitrified at metaphase II and one at metaphase I after 24h of culture (Repronex 75 UI).

Oocyte Metaphase 1, post oocyte retrieval



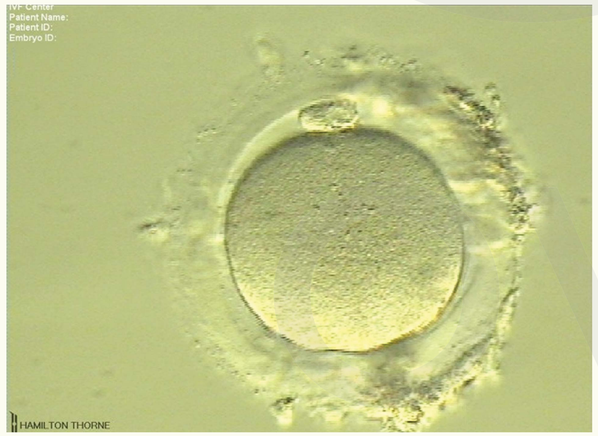
Oocyte Metaphase 1, post oocyte retrieval



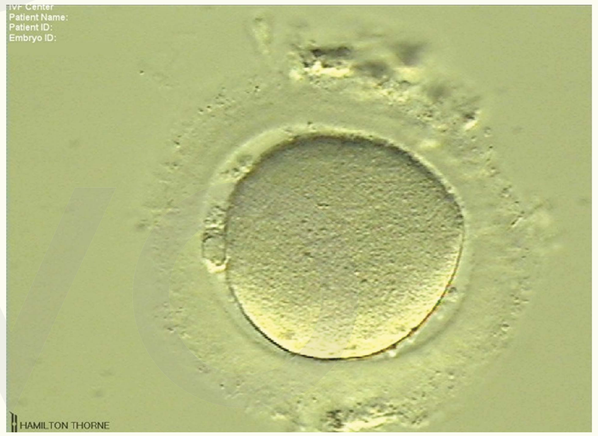
IVM

IVM

Oocyte Metaphase 2, 24h post IVM



Oocyte metaphase 2 , 24h post IVM



Further IVM were proceed carried out in order to obtain an optimal maximise the number of mature oocytes. Five days of stimulation were done before the triggering (Rec FSH 300 UI and rec LH 300 UI daily). We obtained four oocytes at metaphase II and one at metaphase I after from the second cycle. A third IVM cycle allowed for the vitrification of an additional oocyte at metaphase II.

CONCLUSIONS

POI patients secondary to FSHR gene mutation are under diagnosed due to the lack of readily available testing. AMH seems to be a relevant biomarker in order to improve their screening. The latter should be considered in patient with low AMH in future studies. New hope is arising for patients carrying the FSHR gene mutation since a first case of successful fertility preservation using oocyte vitrification following IVM is reported here. Further studies are needed to assess this original approach.

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