**Prof. Yuval Yaron**

Obstetrician, Gynecologist, Medical Geneticist

Date: April 19, 2021

**Summary of Medical Genetic Consultation:**

Name: Na’ama Einhorn Goldman

Passport no.: 40354284

Yr. of birth: 1980

**Diagnosis:**

**Son with suspected Retinitis Pigmentosa (RP)**

**X-linked choroidermia (CHM gene mutation)**

**Following the previous consultation on March 15, 2021**

Na’ama and Yair, a healthy couple of Ashkenazi ethnicity, without blood relations between them. Na’ama has high myopia (-10). Two of her sisters, her mother, and two aunts have a similar problem. The couple have a healthy son and daughter as well as a young son (Yonatan, 6 years old) who is suspected of having RP. **A blood sample from Yonatan was send to the InVitae Lab for gene panel testing of retinal diseases.**

His exam demonstrated 3 changes:

* CHM c.877C>T (p.Arg293\*) hemizygous, Pathogenic
* USH1C c.238dup (p.Arg80Profs\*69) heterozygous, Pathogenic
* FSCN2 c.870G>C (p.Glu290Asp) heterozygous, Uncertain Significance

**Discussion**:

* **Changes in the CHM gene causes** choroidermia disease, characterized by the gradual loss of vision in males, with the appearance of night blindness in early childhood, and subsequent loss of peripheral vision and loss of visual acuity at a later stage in life. Female carriers usually are asymptomatic, though they may develop night blindness and loss of a visual field at a later stage in life.

The gene is found on the X chromosome. Males have one X chromosome and one Y chromosome and females have two X chromosomes, therefore, even in the presence of a mutation in one of the genes, they usually are healthy, or show relatively mild changes (and indeed, the women in the family have a decline in vision). A female with a mutation in one of the X chromosomes is called a carrier. In each pregnancy, carriers have a 50% risk of passing on the chromosome carrying the mutation to her offspring. A male that inherits the mutation will be affected. A female that inherits the mutation will be a carrier. All the daughters of the affected male will be carriers.

In the present case, the change in the CHM gene is a type of premature termination codon that causes the production of a truncated protein classified as a pathogenic change. In my opinion, this change explains Omer’s condition. It is advisable to receive an ophthalmologist’s assessment regarding adapting the findings to the genetic change that was identified.

* **The change in the USH1C** **gene** is classified as pathogenic as well, but defects in this gene cause Usher syndrome, which is passed on by recessive heredity, that is, if the patient has two defective copies for the gene. In the present case, Yonatan is only a carrier, and apparently this change does not cause his condition. In the future, his chances of having offspring with this disease depend on the chance that his future spouse is a carrier.
* **The change in the FSCN2** **gene** is a change whose significance is unclear, and at present, there is no particular recommendation in regard to it.

**Recommendations:**

* Follow-up with an ophthalmologist with results for clinical confirmation of the laboratory finding.
* Examine Na’ama and her sisters, Yael and Michal, for changes in the CHM gene.
* Widen the investigation of additional family members according to need.
* Each carrier may be offered a prenatal diagnosis of chorionic villus sampling, amniotic fluid, or alternatively, prenatal genetic diagnosis PGD of embryos attained by invitro fertilization.
* Repeat genetic diagnosis with the results in all cases of an irregular finding.

Sincerely,

Prof. Yuval Yaron

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Director, Unit for Prenatal Genetic Diagnosis

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