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Premature Ovarian Failure about Three Cases and Review of the Literature

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Abstract:- Introduction: Premature ovarian failure (PID) is clinically suspected in the presence of amenorrhea and confirmed biologically in a woman under 40 years of age by an FSH rate> 40 mIU / L twice. Its prevalence is estimated at 1 to 2% in women under 40. We report the cases of 03 patients, the first aged 25 years old, who presented with amenorrhea aged 02 years with a high FSH level on several occasions and a translocation of the somatic chromosomes 16 and 18 karyotype. And the second 30-year-old unmarried woman who presented with 14-month-old amenorrhea with repeatedly elevated FSH and a normal karyotype. And the third 34-year-old married mother of 02 children who presented with amenorrhea of 18 months with a level of FSH raised several times and a normal karyotype. Discussion: Physiological menopause secondary to depletion of follicular capital occurs on average at the age of 51 in Western countries. In 1 to 2% of women, blockage of follicular maturation or follicular depletion occurs before the age of 40, defining premature ovarian failure (POI). A basic assessment before an IOP includes: clinical examination; a karyotype; fragile X pre-mutation research; an autoimmune assessment with TSH, blood sugar, anti-TPO and anti-adrenal antibody assay, cortisol assay. In 90% of cases, no aetiology is found, and in many cases, the PID is isolated, it does not integrate into a syndrome and there are no associated signs. The management of patients with POI includes three essential areas: hormone replacement therapy, management of a possible desire to become pregnant and psychological care. A new technique of follicular activation makes it possible to consider the possibility of finally exploiting the reserve of dormant follicles to restore fertility in patients who must currently move towards egg donation Conclusion: Premature ovarian failure is a rare pathology. The therapeutic management of patients with IOP is essential to limit the harmful effects of estrogen deficiency. Less than 15% of the aetiologies of PID are elucidated.

I. INTRODUCTION

Premature ovarian failure (POI) is suspected clinically in the presence of amenorrhea and confirmed biologically in a woman aged less than 40 years by an FSH level> 40 mIU / L (or even 20 mIU / L) on two occasions [4]. Its prevalence is estimated at 1 to 2% in women under 40. In 90% of cases, no aetiology was found [2].

- *Observation 1:* 25-year-old patient from no indigeste consults for a secondary amenorrhea (02 years) she complains of hot flashes. She measures 155cm and weighs 75 kg. With family ATCD of PR among the 02 parents, 02 tents died from lupus. 1st menarche is 14 years old.

Frequently elevated FSH levels. Karyotype presence of translocation of chromosomes 16 and 18. And anti CCP positive antibodies. The rest of the normal balance sheet.

- *Observation 2:* Patient aged 30, non-indigestible, consults for secondary amenorrhea (14 months) she complains of hot flashes, She measures 160cm and weighs 65 kg. Without particulate familial ATCD. 1st menarche is 12 years old. Frequently elevated FSH levels. Karyotype and normal assessment.

- *Observation 3:* 34-year-old married patient and mother of 02 children who presented with secondary amenorrhea of 18 months. She is 152cm tall and weighs 54kg. With concept of precocious menopause in a maternal cousin of the second degree. 1st menarche is 11 years old. With repeatedly elevated FSH and normal karyotype and work-ups.

II. DISCUSSIONS

Physiological menopause secondary to depletion of follicular capital occurs on average at the age of 51 years in Western countries [5]. The age of menopause is determined by genetic factors and modulated by environmental factors, such as tobacco and polycyclic aromatic hydrocarbons [3]. In 1 to 2% of women, blockage of follicular maturation or follicular depletion occurs before the age of 40, defining premature ovarian failure (POI) [4]. The IOP reaches 1 / 10,000 in women under 20, 1 / 1,000 in women under 30 and 1% in women under 40. This prevalence is stable according to the latest epidemiological studies carried out in Great Britain, Italy, and France. In the SWAN study in the

United States, Chinese and Japanese women have less PIDs than Caucasians and Africans with respective rates of 0.5%, 0.1%, 1 and 1.4%. The Progetto Menopausa Italia Study group showed that there was no correlation between the occurrence of an OPI and the age of the first period, the level of education or the use of oral contraception. A basic assessment of premature ovarian failure (POI) includes: looking for clinical evidence in favor of Turner syndrome, in particular short stature; Personal and / or family history of autoimmune diseases; History of mental retardation in the family; Assess whether there is an associated deafness; Sexual ambiguity in the family. For the biological assessment, it is advisable to first request: A karyotype a search for pre-mutation of fragile X; An auto-immune assessment with TSH; A blood sugar level; Anti-TPO and anti-adrenal antibody assay; Cortisol assay. The environmental causes are due to toxins or surgery. The main toxicants for the ovary, identified to date, are mainly chemotherapy and / or radiotherapy treatments. Some chemotherapy drugs can cause DNA damage which can induce programmed cell death or apoptosis of growing follicles and primordial follicles [3]. The risk differs according to the molecules and the age of administration of the treatments. Many genetic causes have been identified in recent years. To date, more than 40 different genes are recognized as involved in IOP. However, the majority of the genetic abnormalities described correspond to sporadic cases [2]. Before considering explorations of molecular genetics, the first step in the aetiological workup of IOP is to perform a karyotype. It makes it possible to highlight anomalies in the number or structure of the X chromosome or translocations between the X chromosome and autosomes [4]. Among the different cohorts of patients studied, karyotype abnormalities are present in 10 and 15% of cases of IOP. In many cases, IOP is isolated, it does not integrate into a syndrome and there is no no associated signs. Genetics in recent years have made it possible to advance our understanding of certain causes of PID, in particular through animal models that present with ovarian failure. An example is that of the NOBOX gene (Newborn OvaryhomeoBOX). This gene codes for a factor involved early in mice in folliculogenesis and in the regulation of transcription of oocyte genes. Loss of function mutations in this gene are believed to be involved in around 6% of isolated PID cases. Genetic studies have in recent years identified regions of the genome that may be linked to IOP. However, the identification of genes located in these regions is still ongoing. On the other hand, new analyzes among familial cases of PID or analyzes of patients with translocations or deletions should allow progress in the identification of new etiologies of PID. The management of patients with POI includes three essential areas: hormone replacement therapy; management of a possible desire for pregnancy; psychological care. The goal of hormone replacement therapy is to overcome estrogen deficiency. It is needed in all patients with OPI. It includes in all cases a combination of estrogen and progesterone or a progestogen. The purpose of progestin is to prevent endometrial hyperplasia which can occur if estrogen is taken alone. This treatment is a priori continued at least until the physiological age of menopause [2]. If fertility is desired, it is advisable to refer patients to a specialized center for them to benefit from in vitro fertilization with donation of oocytes. It is not helpful to stimulate the ovaries with gonadotropins or to give so-called "braking; therapy. It is therefore advisable to leave patients on non-contraceptive hormone replacement therapy [4]. For the information of patients, it is desirable to tell them that the spontaneous pregnancy rate is not zero, it is around 5% [5]. New therapeutic perspectives Follicular activation: The reproductive life of women is punctuated by the periodic recruitment of ovarian follicles from a fixed reserve of primordial follicles. These primordial follicles are said to be;dormant; because they are blocked at an immature stage for years, even decades, waiting for a signal that will trigger the growth of the follicle. The follicular activation process refers to this phenomenon of;awakening; of the primordial follicles, characterized by the growth of the oocyte, the proliferation of follicular cells, and their ability to secrete estrogen [2]. This strategy has been used to "wake up; primordial follicles from fragments of cryopreserved human ovarian cortex, and has resulted in the production of mature fertilizable oocytes in vitro in patients with ovarian failure [1]. This pioneering study, which reports the birth of a healthy baby, was reproduced by a Japanese team and makes it possible to consider the possibility of finally exploiting the reserve of dormant follicles to restore fertility in patients who currently need to guide to egg donation [5].

Psychological management should be part of the treatment of IOPs. Indeed, the rate of anxiety and even depression is higher than in the general population. A US study has shown that 89% of women experience moderate or severe emotional pain within two hours of being diagnosed. The same group from the National Institute of Health. It is higher in women with IOP than in the control population and even higher than in women with Turner syndrome. Mood disturbances often start with the onset of menstrual irregularities. To date, there is no effective preventive medical treatment for POI, especially oocyte destruction, before chemotherapy or radiotherapy, in order to preserve follicular capital. The treatments that have been suggested, in particular GnRH agonists, are not effective in randomized studies [1].

III. CONCLUSION

Premature ovarian failure is a rare condition. To date, less than 15% of the aetiologies of PID have been elucidated, despite the realization of a karyotype, a search for premutation of FMR1 and an autoimmune workup. Clinicians should be particularly vigilant if the OPI is associated with another pathology, in order to allow authentication of new etiologies. The therapeutic management of patients with OPI is essential to limit the harmful effects of estrogen deficiency. It is important to insist on taking hormone replacement therapy regularly to avoid cardiovascular and bone complications. The possibility of activating the folliculogen in vitro and the isolation of ovarian stem cells, several avenues of cell therapy are beginning to develop and seem very promising.

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