USA
PRADER-WILLI SYNDROME ASSOCIATION
Still hungry for a cure.

Medical News
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First Documented Instance of Fertility in PWS

Most of what has been written about Prader-Willi syndrome states that people with PWS are infertile, or at least that no case of fertility {pregnancy) has been documented. A recently published case, however, makes it necessary to reconsider the fertility issue and the advice given to families of teens and adults with PWS.

The scientific newsletter of the Inter- national Prader-Willi Syndrome Organisation (IPWSO) noted last spring that a Danish PWS newsletter contained a story about a woman with PWS who gave birth. The case finally appeared in a medical journal in November 1999, verifying that this birth did occur, that the mother did have PWS, and that the baby was normal. (See box, right.)

To put this news in perspective, we've asked members of PWSA ' s Scientific and Clinical Advisory Boards to offer us some guidance on the issue of fertility in PWS.

Advice for Families, Caregivers

Dr. Suzanne Cassidy, head of PWSA 's Scientific Advisory Board, comments:

"This case, the only known case of someone with PWS proven by genetic testing who became pregnant, is an important one. The relationship of the weight loss and the serotonin reuptake inhibitors to fertility is unknown. How-ever, other women with PWS who lost significant weight began to menstruate many years past the usual time for women in the general population. Since all males and females with PWS were believed to be infertile, birth control has not been considered an issue in PWS. However, care should be taken in maintaining this stance. There is no easy way to determine fertility in a female, and since this woman became pregnant when she was having sparse and infrequent periods, lack of menstruation may not be an adequate reason for reassurance."

Dr. Phillip D.K. Lee, an endocrinologist who serves on PWSA's Scientific Advisory Board, comments:

"The report of a pregnancy in a woman with PWS is not particularly surprising from a physiologic standpoint. It has been known for many years that the hormonal conditions which are required for potential fertility are present in some women with PWS and there have been occasional reports of normal puberty and menstrual cycles. In both men and women with PWS, the hormones which are relevant to fertility can be stimulated by medications such as clomiphene and, possibly, one or more of the medications involved in this report. The major limiting factors for fertility and pregnancy in PWS have been the lack of sexual interactions and the fact that men and women with PWS do not usually receive treatment, which facilitates fertility.

"The important message from this report is that although most individuals with PWS probably do not have regular or frequent sexual relationships, such interactions are certainly possible. Therefore, it is incumbent upon caretakers to offer appropriate counseling with regard to protection against sexually transmitted diseases and, particularly for women with PWS, pregnancy. This is particularly important in light of improvements in medical care for individuals with PWS and the increased likelihood for social integration. Healthcare professionals and other caretakers should also give careful consideration to the many medical and ethical issues raised by this case, including issues related to the rights to fertility, pregnancy and child-rearing and the unique considerations related to prenatal care and fetal genetic screening."

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First Documented Instance of Fertility in PWS – Continued

Dr. Moris Angulo, an endocrinologist on PWSA's Clinical Advisory Board, comments:

"Appropriate amount and pulsatile secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus is a prerequisite for both the initiation and maintenance of the reproductive axis in humans. Failure of the hypothalamus to release GnRH results in hypogonadotropic (low gonadotropins, FSH and LH) hypogonadism (sexual infantilism). In general, it is accepted that individuals with Prader- Willi syndrome (PWS) have this form of hypogonadism due to hypothalamic dysfunction. The clinical presentation of functional hypogonadism can vary from mild to severe. In the severe or complete form of hypogonadism the clinical presentation is that of primary amenorrhea (absence of menses) and absence of the larche (breast development). In the mild/moderate forms, however, near or normal sexual maturation is not unusual.

"Most girls with PWS have primary amenorrhea and immature breast development; however, cases of nor- mal or even precocious sexual development have been reported in the literature. This variety of sexual development is an index of the functioning of the hypothalamic-pituitary-gonadal axis. In general, the presence of breast development and menses is considered as a clinical marker of the functioning of this hypothalamic-pituitary-ovary axis in otherwise normal girls. Most adults with PWS are not married and have limited sexual contacts. Girls with PWS, however, with normal or near normal secondary sexual characteristics including breast development and menses may indicate a lesser degree of hypothalamic dysfunction, and therefore should be counseled about the risk of pregnancy.

"Although we do not have a comparable clinical marker for normal functioning hypothalamic-pituitary-testes axis as in females, adult males with PWS with normal penile length and testicular volume should be equally counseled in the meantime."

-Report compiled by Linda Keder
The Gathered View

Details of the Case

In 1999, the first case of a female with PWS who became pregnant and delivered a live-born child was identified by Dr. Arne Akefeldt and his co-workers in Sweden. He described a 33-year old woman who satisfied diagnostic criteria for PWS and was found to have maternal uniparental disomy for chromosome 15. She had no menstrual periods until the age of29, shortly after she was started on citalopram, a selective and potent serotonin reuptake inhibitor (same category of medication as Prozac). She then began to menstruate regularly, every four weeks. When the citalopram was discontinued her menstrual periods became sparse and infrequent, a pattern which has continued. She was subsequently started on fluoxetine (prozac) and had significant and rapid weight loss from 118 kg (260 lbs) to 55 kg (121 Ibs). At about the same time, she began having a sexual relationship with her boyfriend and became pregnant. Following an uncomplicated pregnancy, she gave birth to' a normal child by cesarean section. Genetic testing of the infant by FISH and SNRPN probe were normal, and she has done well for the four months since her birth.

Reference: Akefeldt, A. and others. (1999) "A woman with Prader-Willi syndrome gives birth to a healthy baby girl. “Letter to the editor.” *Developmental Medicine & Child Neurology* 41: 789-790.