Reproductive Issues in Women with Turner Syndrome

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KEYWORDS

• Turner syndrome • Fertility • Reproduction • Pregnancy risks
• Society recommendations • Prepregnancy counseling

KEY POINTS

- Turner syndrome is one of the most common chromosomal abnormalities in female infants.
- Clinical manifestations of Turner syndrome include abnormalities of the skeletal, cardiovascular and lymphatic, endocrine, gastrointestinal, renal, and central nervous systems.
- Ovarian function sufficient to result in puberty is uncommon, and subsequent fertility is even less common in women with Turner syndrome; however, there are several options for women who desire to expand their families.
- Because of the unique pregnancy risks and complications in women with Turner syndrome it is important to be familiar with the current guidelines for preconception counseling and monitoring during gestation.

INTRODUCTION

Turner syndrome, defined as typical features in a phenotypic female with partial or complete loss of the second sex chromosome, is one of the most common chromosomal abnormalities, with an annual incidence of 1:2500 live-born female infants.[1,2] Approximately 50% of affected women are missing an entire X chromosome and have a karyotype of 45,X. About 25% have a partial deletion of 1 X chromosome, whereas about 20% have varying degrees of mosaicism, most commonly a 45,X/46,XX karyotype.[3] A small group of affected women carries an XY cell line.

In general, the phenotypic severity of Turner syndrome varies with the extent of X chromosome loss. Clinical manifestations of Turner syndrome (**Fig. 1**) may be categorized as

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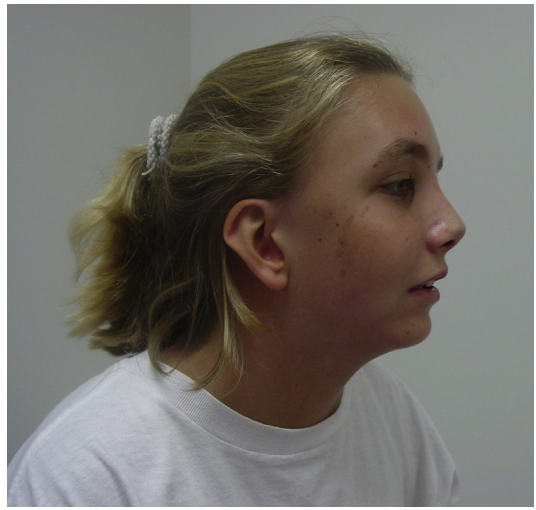

Fig. 1. Adolescent with Turner syndrome. Note the phenotypic features, including ptosis, downslanting palpebral fissures, micrognathia, low-set and posteriorly rotated ears, low posterior hairline, and pigmented nevi. (*Courtesy of* Erica Eugster, MD, Indianapolis, IN.)

abnormalities affecting multiple organ systems, including the skeletal, cardiovascular and lymphatic, endocrine, gastrointestinal, renal, and the central nervous systems (**Box 1**). Major morbidities may occur during adult life, and these result in a 3-fold increase in mortality.[4] Particularly relevant to the discussion of reproductive function is the increased prevalence of aortic root dilatation and aortic dissection, which occur in 32% and 1% to 2% of affected women, respectively.[5,6] Dissection occurs at an average age of 31.5 years, making it particularly relevant to women in their reproductive years.[7]

OVARIAN DEVELOPMENT IN WOMEN WITH TURNER SYNDROME

In normal developing women, the number of nongrowing ovarian follicles increases through the first half of gestation, reaching an average maximum of 300,000 per ovary at 18 to 22 weeks of gestation.[8] Oogonia enter meiosis, which is arrested at prophase I, forming oocytes. Oocytes are incorporated into primordial follicles starting at 14 to 20 weeks of gestation. Throughout the second half of gestation, the number of nongrowing follicles remains fairly constant, and by birth the number of follicles averages 295,000 per ovary. This number then decreases over prepubertal life, reaching about 180,000 per ovary by the age at menarche, and then declines further in an accelerating fashion until menopause (**Fig. 2**).

During the first trimester, ovarian development in fetuses with Turner syndrome is initially normal. Examination of ovaries at 14 to 18 weeks' gestation has revealed normal gonadal development.[9] Shortly thereafter, oocyte loss is accelerated in many girls with Turner syndrome, with oocyte depletion being nearly complete prenatally or by the first few months after birth. In fetuses with 46,XX karyotypes, oogonia were seen as early as 18 weeks, ovaries from 20 weeks onward were found to have primordial follicles, and preantral and antral follicles were seen at 26 weeks. In contrast, some ovaries from fetuses with 45,X karyotypes had oogonia, but no follicles were visualized.[10] There is evidence that some girls with Turner syndrome continue to