Turner Syndrome

Diagnostic and Management Considerations for Perinatal Clinicians

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KEYWORDS

• Turner syndrome • Monosomy X • Perinatology • Karyotype • Counseling

KEY POINTS

- Clinical features of Turner Syndrome require immediate genetic testing.
- The diagnosis of Turner Syndrome is made postnatally via 30 cell karyotype.
- Screening for cardiac and renal abnormalities is necessary soon after diagnosis.
- Counseling families after diagnosis of Turner Syndrome is challenging, but is an essential part of perinatal care for these patients.

INTRODUCTION

Turner syndrome (TS) is a common genetic condition resulting from absence of all or part of the second sex chromosome.[1,2] Patients with TS commonly exhibit cardiovascular, endocrine, renal, reproductive, autoimmune, hearing, vision, and/or psychosocial abnormalities, among other conditions.[1] Although there is a wide spectrum of disease severity, essentially all individuals require ongoing involvement with multiple subspecialists throughout their lifetimes. Early recognition and diagnosis is valuable in helping to screen for complications, establish specialty care, and provide optimal counseling for families.

The prevalence of TS is reported to be approximately 1 in 2000 to 1 in 2500 live female births.[2,3] Further, aneuploidy is a common cause of spontaneous abortion, so the incidence among all conceptions is much higher.[4] Perinatal physicians are highly likely to encounter these patients in their practice. Understanding how to recognize, diagnose, and manage individuals with TS early in life and how to appropriately counsel their families, is essential in providing optimal care to these patients.

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DIAGNOSIS

Diagnostic Criteria

Early diagnosis of TS provides the best opportunity for recognition and intervention of potential abnormalities. Delayed diagnosis can significantly impact the health-related quality of life for these patients.[1] According to the clinical practice guidelines recently published in the *European Journal of Endocrinology*, diagnosis of TS is made in phenotypic girls who have at least 1 X chromosome, complete or partial absence of the second sex chromosome, and at least 1 characteristic clinical manifestation.[1] Exceptions to these criteria include (1) individuals with a male phenotype or (2) girls with a second X chromosome having a deletion distal to Xq24.[1] Girls with such a deletion generally have premature ovarian failure but do not exhibit other clinical features of TS, neither in the neonatal period nor later in life. Clinical features that indicate TS (**Table 1**) should prompt cytogenetic testing (karyotype analysis) in the neonatal period. When testing girls with these characteristic features, a positive result with 5% or greater mosaicism meets the genetic criteria for diagnosis.[1]

Prenatal Diagnosis

The diagnosis of TS is commonly made postnatally after characteristic features are recognized. However, some fetuses are screened prenatally because of problems during gestation or during high-risk pregnancies. In these cases, the preliminary diagnosis is usually made via karyotype analysis after chorionic villus sampling or amniocentesis. Additionally, ultrasonography can suggest a diagnosis of TS in utero, as findings of increased nuchal translucency, cystic hygroma, aortic/left-sided heart defects, brachycephaly, renal dysplasia (including horseshoe kidney), polyhydramnios, and oligohydramnios are all features that make the diagnosis of TS more likely. A mild degree of smallness for gestational age can be also be a sign of TS, as infants with TS are born with lower weights/lengths on average than other infants.[5] Regardless of the prenatal findings, karyotype should always be performed postnatally to confirm the diagnosis.

Even in the absence of significant risk factors, prenatal screening tests are more commonly being offered during pregnancy. Maternal serum triple and quadruple screens may detect TS (among other conditions) by measuring concentrations of α-fetoprotein, human chorionic gonadotropin, inhibin A, and estriol.

Table 1
Clinical features of Turner Syndrome in the neonatal period that should prompt strong consideration for postnatal karyotyping

System Affected	Clinical Manifestation
General	Failure to thrive, growth failure
Lymphatic	Cystic hygroma, hydrops, lymphedema of extremities (hands/feet)
Cardiovascular	Left-sided heart defects, especially aortic arch abnormalities and bicuspid aortic valve
Mouth	Micrognathia, high-arched palate
Head and face	Epicanthal folds, ptosis, strabismus, external ear deformities, low set ears
Chest	Shield chest, wide-spaced nipples
Neck	Neck webbing, short neck, low posterior hairline
Renal	Horseshoe kidney, collecting duct abnormality, ectopic kidney
Extremities	Edema, Madelung deformity, nail dysplasia/hypoplasia