achieved in ~50% of these cases. The risk of transmitting chromosomal anomalies needs to be considered and counseling provided, although this outcome is much less common than originally predicted. Long-term monitoring of men with KS is important given the increased risk of breast cancer, cardiovascular disease, metabolic syndrome, osteoporosis, and autoimmune disorders. Because most men with KS are never diagnosed, it is important that all internists consider this diagnosis in men with these features who might be seeking medical advice for other conditions.

■ TURNER SYNDROME (GONADAL DYSGENESIS; 45,X)

Pathophysiology TS is caused by complete or partial loss of one X chromosome and affects ~1 in 2500 women. Approximately one-half of women with TS have a 45,X karyotype, ~20% have 45,X/46,XX mosaicism, and the remainder have structural abnormalities of the X chromosome such as X fragments, isochromosomes, rings, or Y chromosome material. The clinical features of TS result from haploinsufficiency of multiple X chromosomal genes (e.g., short stature homeobox, *SHOX*), either directly or through effects on autosomal gene expression. However, imprinted genes are also proposed to be affected when the inherited X has different parental origins.

Clinical Features TS is characterized by female external genitalia, short stature, hypergonadotropic hypogonadism, infertility, and other phenotypic features (Table 390-3). Infants may present with lymphedema, nuchal folds, low hairline, or left-sided cardiac defects or later in childhood with unexplained growth failure or delayed puberty. Although limited spontaneous pubertal development occurs in up to 30% of girls with TS (10%, 45,X; 60%, 45,X/46,XX) and up to 20% have menarche, the vast majority of women with TS develop complete ovarian insufficiency. Therefore, this diagnosis should be considered in all women who present with primary or secondary amenorrhea and elevated gonadotropin levels.

TREATMENT