PedsCases Podcast Scripts

This is a text version of a podcast from Pedscases.com on the "**An Approach to Turner Syndrome**." These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedcases.com/podcasts.

An Approach to Turner Syndrome

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Case Overview:

You are a second year medical student shadowing a pediatric endocrinologist at clinic. Your supervisor asks you to see Jenny, an engaging 8 year old, and her mother. Jenny has been referred to endocrinology by her family doctor due to her short stature. Her mother notes that she has been a fairly healthy little girl, except for having multiple ear infections over the past few years. Jenny's mother is worried about her being teased at school for being the shortest girl in class.

Objectives:

- To become familiar with clinical criteria for diagnosing Turner Syndrome
- To describe some common clinical features in girls with Turner Syndrome
- To gain exposure to the management and treatment of various medical complications commonly associated with Turner syndrome

Introduction:

Turner syndrome (TS) is a common genetic condition seen by pediatricians, and occurs in approximately 1 in 2000 to 1 in 4000 live female births.[1,2,3] The condition is generally attributed to a loss of a sex chromosome, with a karyotype of 45,X, instead of having two normal sex chromosomes.

Diagnosis:

A diagnosis of TS is based on clinical evidence as well as cytogenetic testing, and karyotyping of a patient's blood sample provides a definitive diagnosis.[1] Karyotype identifies 45, X in approximately 50% of patients. In other patients, there can be other associated karyotypes, such as mosaicism, with a second cell line with XX, XY or XXX, or there can be an abnormal second sex chromosome that results in loss of X chromosome material. A small percent of patients have Y material and there is 7-10% risk of gonadoblastoma, for which laparoscopic removal of the gonads is recommended.[1]

Prenatal findings suggestive of a diagnosis of TS in a female fetus involve the presence of cystic hygroma, hydrops, lymphedema as well as certain cardiac anomalies, such as

coarcation of the aorta on fetal ultrasound.[2,3] Prenatal screening for aneuploidy, such as first trimester screen or MSS does not accurately detect Turner syndrome. Sometimes, diagnosis occurs incidentally, when an amniocentesis or CVS is performed for other reasons, such as advanced maternal age. [1]

Neonatal features relevant to a TS diagnosis include redundant nuchal skin, a congenital heart anomaly or "puffy" hands and feet.[2]

In children, clinical diagnostic features comprise of unexplained short stature and in adolescents, with delayed puberty, a lack of breast development and primary amenorrhea with elevated levels of follicle-stimulating hormone.[2,3]

Clinical Presentation:

Common physical features that may be present upon examination in patients with TS include a webbed neck, low posterior hairline, posteriorly rotated ears, broad chest with widely spaced nipples, narrow palate with crowded teeth, cubitus valgus, hyperconvex nails, congenital heart abnormalities, short stature, decreased growth velocity and pubertal delay. [1,2,3]

Pathophysiology and Management:

A. Growth Delay

In patients with TS, a decrease in growth velocity can be noticed as early as 18 months of age.[2] Some girls may present when they do not experience the expected pubertal growth spurt. It is important to refer TS patients to a pediatric endocrinologist at the time of diagnosis. Growth may be plotted on TS-specific growth curves starting from age 2.[4] TS girls are generally offered recombinant human growth hormone. The mean adult height in TS patients is 4 feet 8 inches (143 cm), which may increase to an average of 5 feet (150 cm) when growth hormone is used.[3]

Growth hormone treatment may be initiated as soon as growth failure becomes evident, such as below the fifth percentile (height). However, it must be noted that gains in height from treatment are highly variable and depend on a number of factors such as the age of onset of treatment, dosage and duration.[1] In adolescents, estrogen may inhibit growth with its effects on the growth plate.[4] Physicians must explain to parents and children that not much is currently known about the long-term side effects of treatment, and an emphasis should be placed on realistic expectations regarding height gain, so that an informed decision can be made before initiating treatment.[2]

After starting treatment, growth velocity should be evaluated regularly, along with screening for possible complications, such as musculoskeletal complications such as scoliosis, kyphosis, dislocation of the patellae, chronic knee pain and an increased carrying angle of the arm. [1,2] Pediatricians may refer to orthopedics when necessary.

B. Cardiovascular Risk

All newly-diagnosed TS patients should be seen by a cardiologist, and those with known cardiovascular anomalies should be followed by a pediatric cardiologist. [1] Evaluations

may include an echocardiography and baseline electrocardiography, since coarctation of the aorta is a common anomaly associated with TS. [2,3] Girls with no cardiac abnormalities should be seen by a cardiologist in adolescence, before transitioning to adult cardiac care. [1]

Studies have shown a 17% to 45% prevalence of congenital heart disease in TS patients, including coarctation of the aorta, bicuspid aortic valve malformations and other left-sided defects. [2] Fatal cardiac complications in TS girls include aortic dilation, dissection or rupture. [1] It is therefore important to treat cardiac risk factors like hypertension fairly aggressively. Patients should always be encouraged to adopt a healthy diet and exercise regimen. In addition to hypertension, obesity, insulin resistance and type 2 diabetes mellitus are also common problems faced by girls and women with TS. [1,2] Therefore, glucose, liver enzymes and lipid levels should be routinely monitored. [1] Life expectancy may be reduced in TS patients on account of associated diabetes and heart disease. [2]

While few TS women go on to have children, it is important to note that pregnancy may also be a risk factor for aortic dissection. [1] The presence of cardiac abnormalities must be considered before making decisions related to family planning and assisted pregnancy.

C. Lymphatic Anomalies

Babies born with TS often have peripheral lymphedema with puffy hands and feet. Some have webbed necks, on account of prenatal cystic hygromas, i.e a flaw in the development of lymph sacs around the fetus' neck. [1] The lymphedema often resolves within the first two years of life, but can reoccur.

D. Renal Changes

Up to 40% of patients with TS have structural renal abnormalities that are visible on ultrasound. [1] These anomalies can encompass changes in the collecting system, or structural and positional changes such as horseshoe and mal-rotated kidneys. It is therefore important to conduct a renal ultrasound at the time of diagnosis. [2]

E. Hearing and Vision Concerns

Eye features sometimes observed in TS patients include hyperopia, strabismus and nystagmus.[2,4] Ophthalmologic evaluation is recommended in the first year of life.

TS patients should also be monitored for sensorineural and conductive hearing loss, as well as recurrent otitis media. [1,2] In these cases, an annual audiology evaluation is sometimes recommended.

F. Gastrointestinal Issues

Girls with TS can have abnormal craniofacial development leading to a high-arched palate, wide mandible, micrognathia and narrow maxilla. [1] This can sometimes result in feeding problems, gastroesophageal reflux and failure to thrive. [2]

G. Autoimmune Concerns

Celiac disease and thyroid dysfunction, particularly hypothyroidism, are associated with TS and can affect the growth and development of these girls.[1,2,3] Thyroid screening and transglutaminase immunoglobulin A antibody measurements are therefore recommended every 1 to 2 years from 4 years of age.[4]

H. Development, Behaviour and Learning

Girls with TS have normal intelligence, cognitive and motor development. [1,2,3] However, they are at some risk for learning, behavior and social issues.[4] With learning, there is often a deficit in math and visuospatial skills, along with attention-deficit disorder. Patients may benefit from early cognitive testing in conjunction with tutoring and learning accommodations when required. [2]

The negative psychosocial effects of TS could be on account of short stature, social isolation, social anxiety, infertility and impaired development of sexual characteristics. [1,2,3] Physicians should address their patients' concerns and offer support if needed.

I. Delayed Puberty

Gonadal dysgenesis is a hallmark characteristic of TS, with approximately 90% of patients requiring hormone-replacement therapy to initiate puberty. [1] A pediatric endocrinologist may initiate estrogen treatment at around 12 to 14 years of age, after measuring gonadotropin levels and evaluating the patient's maturity and wishes. [2] It is important to note that girls with TS are often delayed in reaching sexual milestones, which can contribute to social isolation.

J. Transitioning to Adult Care:

A pediatrician is responsible for transitioning TS girls into appropriate adult care beginning in early adolescence. This includes shifting focus from the parents to the concerns and wishes of the patient herself. [1] Patients need to be educated regarding appropriate dietary and exercise habits. Many parents and adolescent patients have questions about family planning, and may benefit from discussions surrounding egg donation, assisted reproduction and adoption.[1] As with all young adults, TS patients should be educated on sexually-transmitted diseases and safe sexual practices. Pediatricians can help refer patients to physicians experienced in working with adults with TS.

References

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