An Overview on Turner Syndrome: Literature Review

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ABSTRACT

Background: Aneuploidy is defined as the disturbance of the normal chromosomal amount. Normally, the human cell contains 46 chromosomes, however, in fetuses with aneuploidy, it might increase or decrease beyond the normal level. Turner syndrome is a complex genetic condition in which a female fetus suffers from a complete or partial loss if an X chromosome. **Objectives:** In this paper, we will review the available literature discussing the features, diagnosis, and management of Turner syndrome. **Methodology:** We conducted the literature search within the PubMed database using the keywords: "turner syndrome" and "X-monosomy" and "genetics" and "cognitive-behavioral" and "psychosocial" with dates from 1990 to 2020. **Review:** TS constitute a partially or completely loss of X-chromosome. Almost half of the patients with TS possess a non-mosaic karyotype. Among the most commonly reported physical feature of TS include decreased adult height, infertility, increase blood pressure, and micrognathia. **Conclusion:** In conclusion, TS is one of the most common chromosomal abnormalities that affect females. Early detection through characteristic physical and clinical features could have a massive impact on the function of affected individuals later in their lives.

Key Words: *Turner syndrome, X-monosomy, genetics, cognitive-behavioral, psychosocial*

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INTRODUCTION

Aneuploidy is defined as the disturbance of the normal chromosomal amount [1]. Normally, the human cell contains 46 chromosomes [2], however, in fetuses with aneuploidy, might increase or decrease beyond the normal level (e.g. 45 or 47 chromosomes) [3]. The majority of aneuploid pregnancies in the germline end up miscarried. Among the most common abnormal chromosomes in live births are X, Y, 21, 18, and 13 [4]. The detection rate of chromosome anomalies is estimated to be 1/160 live births [4].

Turner syndrome (TS) is a complex genetic condition in which a female fetus suffers from a complete or partial loss of an X chromosome (i.e. monosomy of the X chromosome, 45, X, or 45, X0) [5]. TS typically occurs as a result of sporadic chromosomal nondisjunction and it is among the most common sexual chromosomal abnormalities with an incident rate of 1 in 2,000 live-born females [4]. There are no known environmental risks for

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the development of TS. Maternal age is not a contributing factor. TS is not usually inherited [5]. TS was first described in 1938 and by 1964, it was identified as a chromosomal abnormality.

Patients with TS typically display a characteristic physical appearance. This includes decease height, missing ovaries, webbed neck, aortic coarctation, thyroid disease and deafness [5]. Mental function is usually preserved in patients with TS. Normal intelligence is maintained while mathematical spatial visualization is usually impaired [3]. Table 1 shows the key physical findings in Turner syndrome.

Table 1. Key Physical Findings in Turner Syndrome.

Location	Feature
Eyes	Inner canthal folds, ptosis, blue sclerae
Ears, Nose, Mouth	Prominent auricles, low-set; high, narrow palate; small mandible
Neck	Low posterior hairline, webbing
Chest	Broad, widely spaced nipples; pectus excavatum
Skeleton	Cubitus valgus, short fourth metacarpal and/or metatarsal, Madelung deformity scoliosis

Due to the presence of a healthy uterus, TS patients are able to have menstrual cycles and carry children with the assessment of reproductive technology and hormonal treatment. Therefore, females with TS are usually treated with estrogen replacement therapies (ERT) and growth hormone (GH) [6]. The diagnosis of TS is usually based on the presence of physical signs and is confirmed using genetic testing [5]. Currently, there is no known cure for TS, available management only addresses symptoms [3, 4]. Normally, TS patients have a shorter life expectancy mainly because of heart problems and diabetes [5].

Due to the importance of early identification of TS as early identification and management could significantly improve the quality of life, therefore, in this paper, we will review the available literature discussing the role of MRI in emergency SCI.

METHODOLOGY:

We conducted the literature search within the PubMed database using the keywords: “turner syndrome” and “X-monosomy” and “genetics” and “cognitive-behavioral” and “psychosocial” with dates from 1990 to 2020. We also used the Google Scholar database for additional literature searches. After reading the abstracts, we manually selected the relevant papers for this review. In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics; magnetic resonance imaging and emergency spinal trauma. Exclusion criteria were all other articles that did not have one of these topics as their primary endpoint.

Review:

Karyotypes

As previously mentioned, TS constitutes a partial or complete loss of X-chromosome. Almost half of the patients with TS possess a non-mosaic karyotype (i.e. 45, X) [7]. Other karyotype variations of TS such as chromosomal arm deletion, isochromosomism, and mosaicism (i.e. a combination of cell lines such as 45, X and 46, XX) [8]. Multiple studies have shown that mosaicism results in a milder phenotype while other studies indicated that physical features (e.g. cardiovascular symptoms and gonadal dysfunction) have a tendency to differ in rate between karyotypes [8]. However, it remains unknown whether different karyotypes vary in the mean of their cognition and behavior.

Physical abnormalities

The most commonly reported physical features of TS include decreased adult height, infertility, increased blood pressure, and micrognathia. The risk of certain diseases is increased in patients with TS, including thyroid disease, glucose intolerance, cardiovascular diseases, and osteoporosis. By the most medically dangerous associate of TS is cardiac abnormalities. Higher mortality rates due to cardiovascular abnormalities are usually reported [4, 9].

Psychosocial Functioning

Females with TS have been noted to experience a spectrum of social functioning Impairments. This observation is particularly noted among adolescent girls with TS. Decreased social activity, deprived social coping, and higher immaturity, and hyperactivity have all been reported [10]. Due to higher rates of relationship failure and finding friends, they are more likely to be socially withdrawn [11].

Many of the psychosocial dysfunction observed in TS patients is attributed to facial disfigurements and lack of normal emotion processing [12]. Further, literature suggests that the diagnosis of autism spectrum disorders is more likely in females with TS [13].

Diagnostics

The diagnosis of TS could be obtained prior to birth using prenatal diagnostic testing such as chorionic villus sampling or amniocentesis. Using those tests, an analysis of the fetal chromosomal structure would defiantly confirm the diagnosis. TS should be clinically suspected in the presence of prodromal symptoms. For example, the presence of fetal hydrops, cystic hygroma, or cardiac defects on a prenatal ultrasound would raise the suspicion of TS [14, 15].

Post-delivery karyotype testing is often required to confirm the diagnosis. In cases where the TS is a result of mosaicism, karyotype can come back normal. If a high suspicion of TS remains despite a normal karyotype, fluorescence in situ hybridization analysis can offer an additional modality to the karyotype [14].

Later in life, patients with TS who went undiscovered might present with developmental abnormalities such as the delayed onset of puberty or amenorrhea. A high concentration of the follicle-stimulating hormone is highly indicative of TS. Anti-Mullerian hormone offers a highly sensitive marker for ovarian failure prediction [4, 16].

Growth hormone supplements

Short stature is one of the most commonly reported features of TS. Early treatment with GH is usually initiated in children with TS to preserve normal adult height. Studies have shown that girls with TS who received GH for a period of 12 months were significantly taller than those who did not. Reports suggest that GH initiation between the ages of 4 to 6 years was an important factor in determining treatment success. A sensitization phenomenon in which a diminished response to GH administration is observed in a patient receiving the therapy for 1–2 years. Thus, to compact this phenomenon, an incremental increase of GH dose is often required [16, 17].

Estrogen replacement

ERT is now considered the mainstay of treatment for estrogen insufficiency. The ideal age to start ERT in patients with TS is the age that coincides with pubertal development in the patient's peers to decrease psychosocial distress. ERT should be administered with care to GH therapy. Reports have shown that ERT can adversely affect the final adult height in a patient taking GH. Recent reports have indicated that ERT taken transdermally or intramuscularly could counteract the effect of ERT on height [14].

CONCLUSION:

In conclusion, TS is one of the most common chromosomal abnormalities that affect females. Early detection through characteristic physical and clinical features could have a massive impact on the function of affected individuals later in their lives. Early initiation of GH and ERT can help TS patients have a relatively normal life.

REFERENCES

[1] Febri RR, Wiweko B, Iffanolida PA, Mutia K, Muna N, Riayati O, Jasirwan SO, Mansyur E, Yuningsih T, Muharam R, Hestiantoro A. High aneuploidy rate among 3PN embryos was not associated with sperm parameters in IVF patients. J. Adv. Pharm. Educ. Res. 2019;9(1):33-7.

[2] Mashizi M K., Golestan A T. Study of the Effect of HBX Gene of Hepatitis B Virus on Liver Cancer Progress. Entomol appl sci lett. 2020;7(3):55-65.

[3] Gravholt CH. Clinical practice in Turner syndrome. Nature clinical practice Endocrinology & metabolism. 2005;1(1):41-52.

[4] Bondy CA, Bakalov VK. Investigation of cardiac status and bone mineral density in Turner syndrome. Growth hormone & IGF research : official journal of the Growth Hormone Research Society and the International IGF Research Society. 2006;16 Suppl A:S103-8.

[5] Zinn AR, Tonk VS, Chen Z, Flejter WL, Gardner HA, Guerra R, Kushner H, Schwartz S, Sybert VP, Van Dyke DL, Ross JL. Evidence for a Turner syndrome locus or loci at Xp11. 2-p22. 1. The American Journal of Human Genetics. 1998;63(6):1757-66.

[6] Abd Al-Muhsen F, SAl-Nassir H, Mirza S, Mnati AA. Association of growth hormone gene polymorphism with birth and weaning weight of Nuimi and Awassi sheep at Kerbala province. J. Biochem. Tech. 2018;9(3):27-30.

[7] Suri M, Kabra M, Jain U, Sanders V, Saxena R, Shukla A, Singh GV, Verma IC. A clinical and cytogenetic study of Turner syndrome. Indian pediatrics. 1995;32(4):433-42.

[8] Ogata T, Matsuo N. Turner syndrome and female sex chromosome aberrations: deduction of the principal factors involved in the development of clinical features. Human genetics. 1995;95(6):607-29.

[9] Noe JA, Pittman HC, Burton EM. Congenital absence of the portal vein in a child with Turner syndrome. Pediatric radiology. 2006;36(6):566-8.

[10] McCauley E, Feuillan P, Kushner H, Ross JL. Psychosocial development in adolescents with Turner syndrome. Journal of developmental and behavioral pediatrics : JDBP. 2001;22(6):360-5.

[11] Williams J, Richman L, Yarbrough D. A comparison of memory and attention in Turner syndrome and learning disability. Journal of pediatric psychology. 1991;16(5):585-93.

[12] Lawrence K, Campbell R, Swettenham J, Terstegge J, Akers R, Coleman M, Skuse D. Interpreting gaze in Turner syndrome: impaired sensitivity to intention and emotion, but preservation of social cueing. Neuropsychologia. 2003;41(8):894-905.

[13] Ross JL, Stefanatos G, Roeltgen D, Kushner H, Cutler GB, Jr. Ullrich-Turner syndrome: neurodevelopmental changes from childhood through adolescence. American journal of medical genetics. 1995;58(1):74-82.

[14] Chernausek SD, Attie KM, Cara JF, Rosenfeld RG, Frane J. Growth hormone therapy of Turner syndrome: the impact of age of estrogen replacement on final height. Genentech, Inc., Collaborative Study Group. The Journal of clinical endocrinology and metabolism. 2000;85(7):2439-45.

[15] Attar AF, Mousavi P, Javadnoori M, Malehi AS. The Relationship between Gynecologic Age and Maternal/Fetal Weight Gain in Adolescent Pregnancies. J. Biochem. Tech. 2019;10(3):50-5.

[16] Hindmarsh PC, Dattani MT. Use of growth hormone in children. Nature clinical practice Endocrinology & metabolism. 2006;2(5):260-8.

[17] Ito Y, Fujieda K, Tanaka T, Takano K, Chihara K, Seino Y, Irie M. Low-dose growth hormone treatment (0.175 mg/kg/week) for short stature in patients with Turner Syndrome: data from KIGS Japan. Endocrine journal. 2006:0608280037-.