What Is Werner’s Syndrome?

Werner’s Syndrome (WS) is a very rare, autosomal recessive genetic disorder that is characterized by premature aging, beginning to show symptoms in adulthood. Otto Werner first reported Werner’s Syndrome in 1904. WS is a type of progeria, also known as Progeria adultorum, Progeria of the adult, or pangeria. There is no known cause of WS, but 90% of all afflicted persons have a lethal mutation in the WRN gene. The WRN gene is found on chromosome 8, position 12-11.2 (8p12-p11.2). In gene expression, the WRN gene encodes for a member of the RecQ family helicases. These helicases unwind DNA’s double helix during replication, recombination, transcription, and chromosomal segregation. When the DNA is unable to unwind, these vital processes are halted. The cell cycle is also primarily affected. Every time a cell divides, its’ DNA must be replicated, though since DNA replication cannot happen, a Werner’s patient undergoes very few cell divisions. Since brain and muscle cells rarely divide, WS does not majorly effect these systems. The more a person ages, the less the cells in their bodies undergo mitosis. The Telomere Theory gives one explanation why Werner’s develops into a premature aging condition. As a cell has fewer divisions, the length of a chromosome’s telomeres are never replicated by DNA’s polymerase. Thus, as a cell accumulates mitotic divisions, a cell’s telomere is shortened. (A cell has a lifespan of about 50 divisions). DNA is then damaged and left unrepaired. Then, when a cell finishes its 50 divisions, the genes that in a normal cell are covered by the longer telomere, are exposed. These new active proteins trigger deterioration of tissues and other symptoms of aging. Thus, a Werner’s patient “ages” rapidly. They show physical signs of premature aging as well as having health complications as if they were the age they looked like.

Symptoms:

The general appearance of a person with Werner’s Syndrome is a short stature—usually less than 1.60 m. The skin is very thin in areas such as fingers, ears, and toes. Muscle atrophy and a loss of muscle mass is shown. The skull is relatively large and narrows abnormally on the lower part of the face. The skin of a person affected with the condition is greatly wrinkled and a loss of fat. Most patients have calluses and ulcerations on the soles of their feet and over bony joints on the body. The person’s hair begins to gray and fall out and nail dystrophy is observed. The afflicted also has an abnormally high-pitched voice and flat feet. Most patients have increased uric acid. Werner’s syndrome patients are at risk for many other diseases as an affect of Werner’s. Bilateral cataracts are observed and the cataracts are usually posterior and subcapsular. The progressing cataracts are normally observed in the 20-40 year range. Irritation in the parathyroid glands lead to osteoporosis. Type 2 diabetes mellitus and decreased fertility are observed. Osteosclerosis of phalanges of fingers and toes and soft tissue calcification. Neoplasms and premature arteriosclerosis are observed.

Current Research:

Current Research is being conducted by many labs across the world. Mexico, Finland and Holland are the countries with the most research being done. Many American universities are testing Werner’s in labs as well as in England. Since the WRN gene is the only gene known to cause WS, but it is not mutated in all Werner’s patients, testing on this gene is the most common. Many bodies have been performing “case-control studies” that compare the mutations in WS patients who have different diseases, for example, a Werner’s patient who has heart disease, and a patient who has a malignant tumor. Some researchers believe that a minor mutation in the WRN gene happens to everyone, which causes people to age. It is the lethal mutation in WRN that causes Werner’s Syndrome. Research pertaining to the telomere theory shows that cells with no telomere loss have an enzyme, telomerase, which preserves a chromosome’s telomeres. Further research is being done to find a cure to shorten telomeres, but the challenge is too much telomerase added to a cell results in a healthy cell turning cancerous.

Prognosis:

There is no specific treatment for Werner’s syndrome. Treatment of different associated diseases and treatment of symptoms of the disease are available. Early recognition of the disease is beneficial and screening for malignancies and associated diseases should be performed regularly. There are some surgical procedures to treat the cataracts. The normal treatment of diabetes, but glitazones are said to be especially effective, and the standard treatments for malignancies and heart disease are necessary. Tests for fasting blood glucose, oral glucose, thyrotropin and oral glucose tolerance should be performed. The blood glucose level should be checked everyday because of the diabetes mellitus. Genetic counseling for the entire family is a recommended treatment because there is a 1 in 4 risk of a family member having the disease and a 1 in 2 risk of a sibling being a carrier of the disease. The lifespan of an individual is reduced and death usually occurs between 30 and 50 years old. Death has been commonly noted as one of the risk factors of malignancy, heart attacks, cerebrovascular accidents, osteoporosis, tumors, cataracts, carcinomas of organs, sarcomas, and more.

High Werner’s Frequency in Japan:

Werner’s Syndrome has shown an unusual prevalence in the Japanese. In a Japanese population, an association between a Cys1267Arg variation in the WRN was found. This could not be confirmed in Caucasians. Research was done by Dr. Makoto Goto, who found about 400 cases of in Japan, where inbreeding between cousins contributed to the high rate of the disease. Dr. Goto discussed that in Werner’s syndrome, there is an excess of soft-tissue and thyroid cancer. He discovered this cancer and other cancers by studying the inbred families. Werner’s Syndrome was greatly genetically instigated in Japan on account of the cousin-to-cousin marriages. Out of the 1,000 reported cases, over 800 cases of Werner’s Syndrome are in Japan.

References:

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