CHAPTER **24**

Down Syndrome

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HISTORY

Down Syndrome is the most common malformation pattern in humans, with an incidence of 1 in 660 live births.[1] Down Syndrome was first described in 1866 in England by Dr. John Langdon Down in an essay, "Observations on an Ethnic Classification of Idiots". Dr. Down was superintendent of an asylum for mentally retarded children in Surrey, England. He studied the mentally handicapped, and he made the first distinction between "Mongoloids." Down felt that these children looked like the people from Mongolia since they seemed to have arrested development.

In the early 1960s, the condition came to be known as "Down's Syndrome." Then in the 1970s, an American revision of scientific terms changed the name to "Down Syndrome," although "Down's" is still used in some parts of Europe.[2]

Ten years after Down's essay, the connection between maternal age and the condition was made. It was thought to be the result of degeneration of the maternal reproductive tract. The actual chromosomal abnormality of Down syndrome was proposed in 1932 by Waardenburg and then documented in 1959 by Dr. Lejeune, although Down's name is still associated with this condition.

GENETICS

Down syndrome is a trisomy of the small acrocentric G chromosome on chromosome 21.[3] This chromosome contains less than 2% of the genome, approximately 1,000 genes. The Down Syndrome phenotype is located on the 21q22 locus of the 21st chromosome, which contains about 100 genes.[3] These genes cause the full phenotype of Down Syndrome. Genes for leukemia and Alzheimer's Disease are also located on chromosome 21, and this causes a thirty-fold increased incidence of leukemia and association with Alzheimer's disease.[3]

There are 3 cytogenetic variants that cause Down Syndrome: trisomy 21, chromosomal translocation, and mosaicism. Approximately 95% of all patients with Down Syndrome have trisomy 21.[4] This abnormality occurs as a result of nondisjunction (failure of chromosomal separation during oogenesis.) Recent research has shown that in these cases, approximately 90% of the abnormal cells are the eggs, and there is a definite connection with maternal age.

The risk of having a Down Syndrome baby is one in 2,500 babies born in women under the age of thirty, but this risk increases dramatically to 1 in 200 babies born to women ages 30 to 39.[3] It is therefore recommended that women undergo amniocentesis when they are 35 years old or older.[3] The other causes of nondisjunction include viruses, excessive radiation, history of hepatitis B virus, grandparent maternal age, specific genes, and high thyroid antibody.[3]

Three to four percent of cases of Down Syndrome are caused by Robertsonian Translocation, where there is a translocation of 14/21 or translocation D. This occurs when the extra chromosome 21 is attached to chromosome 14. The number of chromosomes remains normal, but there is a triplication of the 21st chromosome material.

The third type of Down Syndrome is the Mosaic type, occurring in ~1-2% of all cases. In this type, there is a mixture of cell lines where some of them have a normal set of chromosomes (46) and others have trisomy 21 (47 chromosomes). These individuals have a milder phenotype and have higher IQs than the other types of Down Syndrome.

The risk of recurrence of Down Syndrome after one affected child is about 1% for mothers of any age, but the risk may be higher for certain translocation forms or mosaic forms. Females with Down Syndrome are fertile, however, the males are sterile.[3] Affected females have a 50% chance of having an affected child. Maternal twins are both affected, and usually only one fraternal twin is affected.[3]

The life span of an affected Down Syndrome child has increased from 9 years in 1929, to as high as 70 years in 1989.[3] This is due to advances in surgery to correct heart defects and antibiotic use to treat infections.[3]

CHARACTERISTICS

Down Syndrome presents with hypotonia and characteristic facies of a small head with brachycephaly.[3] Down Syndrome infants show muscle hypotonia throughout their first year, which decreases with age. They experience a delay in motor development that also includes hyperflexibility, lack of Moro reflex, and musculoskeletal idiosyncrasies.

The eyes have a vertical epicanthal fold with slanted palpebral fissures. The iris is speckled on the outside with Brushfield spots. Other eye complications include: myopia, cataracts, blepharitis, and ectropion (inverted eyelids). The nose is small and flattened with upturned nostrils. The ears are small and are round or square (as compared with an oval shape in non-Down Syndrome individuals). The upper helix is folded, and the lobes are small or absent. The ears are low set and the mouth is small with droopy corners, protruding tongue, and small teeth.

The hands are short and broad with overly convex nails. The fifth finger often only has two phalanges and the fingers display clinodactyly. Dermatoglyphic analysis shows the fingerprints displaying ulnar loops and a distal axial triradius in 85% of affected individuals. A hallucal arch tibial pattern, which is rare in unaffected individuals, can be found in the foot prints of 50% of those with Down Syndrome.[5] A Simian crease, a single line running across the palm, is present in 50% of Down Syndrome individuals. Children with Down Syndrome tend to be short and heavy, with IQs of 25-50.

DERMATOLOGIC DISORDERS

Newborns with Down Syndrome present with acrocyanosis, (blue hands and feet), at birth and lasting for a few days afterwards.[6] They may be born with a bluish mottling of the skin called cutis marmorata (latin for marble-like skin).[6] This mottling occurs from the response of the capillaries to the skin being cool. It lasts several months longer in those with Down Syndrome than in unaffected newborns.

Children with Down Syndrome often have xerosis and chelitis.[6] Atopic dermatitis often appears behind the ears, on the cheeks, behind the knees, and in elbow creases. Seborrhea and hyperkeratosis are also found in Down Syndrome children.[6] Syringomas are benign skin tumors that arise from the sweat ducts and look like small multiple raised nodules on the skin, with varying degrees of yellowish color. They are often seen on the eyelids, neck and chest and occur more often in females than males. They are asymptomatic, but can be removed by lasers or curettage.

There have been a few instances described in the literature of milia-like idiopathic calcinosis cutis, associated with palpebral and perilesional syringomas.[7] These are whitish, round 1-2 mm diameter lesions surrounded by erythema that have been found on the hands, wrists, knees and feet. Cases have been diagnosed by histological examination revealing roundish calcified deposit surrounded by a thin fibrovascular strip.

Elastosis perforans serpiginosa, a disorder of the elastic tissue of the skin, causes deep red raised lesions in a circular or linear pattern.[6] These lesions occur on the back or sides of the neck but they may occur on the chin, the cheeks, the arms, or the knees. They arise four times more commonly in males than females and may be present for up to 10 years before disappearing on their own.[6] This condition has a high recurrence rate but may be treated with liquid nitrogen.

Vitiligo, loss of pigmentation, is not a common problem in people with Down Syndrome, but it is much more common than in the general population.[6] Acanthosis nigrans, an increase in pigmentation, is very common in Down Syndrome patients, and it most often appears on the back of the neck, the hands, and the groin.[8] It characterized by hyperkeratosis, pigmentation, and papillomatous elevation that gives the skin a velvety texture. This may resemble psoriasis and could be related to obesity. This skin disorder has also been associated with Type-II Diabetes, but it is not shown to be a factor related to its development in individuals with Down Syndrome.[8]

Folliculitis, which is usually due to a Staphlococcus infection, is described as the fungal version in Down Syndrome individuals.[9] It can be treated with itraconazole or topical selenium, or orally when the infection produces faruncles or abscesses. Scabies is a common problem in teenagers and adults with Down Syndrome for unknown reasons, and tends to be a worse infection than in the general population.

Alopecia areata is more common in people with Down Syndrome, occurring in 5-9% of the population, compared with 1-2% of the general population.[10] The gene that causes this disorder is located on chromosome 21.[10]

RADIOGRAPHIC FINDINGS

Bones of children with Down Syndrome have decreased density than those observed in unaffected children of the same age.[1] Studies have indicated that the bone density in adults with Down Syndrome is lower than the general population, thus increasing the risk for osteoporosis in adulthood, especially of the spine.[1] There was a delay in bone age and the skeleton was noted to be smaller and with abnormally small ossification centers. People with Down Syndrome also have tall, thin vertebral bodies, microcrania with delayed closing of sutures, hypoplastic facial bones, deformed teeth, gracile ribs, sometimes the absence of a twelfth rib, atlantoaxial subluxation, and only two phalanges of the fifth finger. Radiographs showing 5 mm or greater distance between C1 and C2 vertebrae are diagnostic of atlantoaxial instability.[11]

A particularly characteristic feature of Down Syndrome involves an acetabular dysplasia called "elephant ear pelvis," where there are flattened acetabular slopes and large flared ilia.[4] The acetabular angles measure 7 to 25 degrees, whereas in unaffected infants the range is 12 to 37 degrees. In a study by Caffey, during the first year of life the iliac index (the sum of the acetabular angles and the iliac angles divided by 2) is highly indicative of Down Syndrome. The normal index in newborns is 68-97 degrees with a mean of 81 degrees.[4] This value is decreased in trisomy 21 newborns to a range of 49-87 degrees with a mean of 62 degrees.[4]

Other abnormalities that occur in the feet include splaying of the metatarsals, which was noted in several instances in a study of patients with Down Syndrome. Almost all of these patients had atavistic medial cuneiforms. Metatarsus primus varus and evidence of pronation was noted along with hallux abducto valgus. In other radiographic studies, there has been an increased prevalence of biphalangeal toes and metatarsophalangeal sesamoid bones.[12] Plantarflexed tali have been found in 100% of children with Down Syndrome.[13]

ORTHOPEDIC FINDINGS

Orthopedic problems are seen in 25% of Down Syndrome patients, and 50% have gait problems. Dislocation of the hip and cervical spine instability are attributed to joint laxity. A study by Livingstone and Hirst found that there was no evidence of increased joint laxity in Down Syndrome.[14] The orthopedic problems associated with Down Syndrome seem to be related to muscle hypotonia found in these children. Hypotonia, ligamentous laxity, and joint hyperflexibility are present in 88% of children with Down Syndrome. More than 25% of Down Syndrome patients are admitted to an acute care hospital due to musculoskeletal disability. Down Syndrome patients have cervical spine, hip and patellofemoral instabilities as well as foot deformities.

Atlantoaxial instability has been found in 10-30% of patients with Down Syndrome. This may be related to ligamentous laxity of the transverse ligament that holds the odontoid process close to the anterior arch of the atlas.[11] 12% to 16% of Down Syndrome patients with instability develop neurologic symptoms, such as fatigue in walking, gait abnormalities, clumsiness, incoordination, spasticity, hyperflexion, clonus, and toe-extensor reflex.[11] Neck pain, and headache may also occur in affected individuals.

Atlantoaxial instability may lead to quadriplegia and death, and there are at least 13 cases in the literature of acute posttraumatic neurologic deficit related to atlantoaxial instability in Down Syndrome.[11] Even if radiographs are normal, children with Down Syndrome should be cautioned against any neck stressing sports activities such as collision sports due to an increased incidence of cervical spondylosis. When a patient with Down Syndrome has progressive cervical spine instability or myelopathy, surgical intervention by atlantoaxial fusion is considered. There is a high possibility of complications associated with this procedure.

Acquired hip instability is seen in about 5% of Down Syndrome patients.[11] This seems to be due to ligamentous laxity or moderate increased anteversion. Dislocation occurs in children between the ages of 2 and 10 years old. Hip instability ranges from acute dislocation to recurrent dislocation to habitual and then fixed dislocation which then may cause the patient to

become non-ambulatory. Hip clinical screening and radiographic assessment may be indicated. The nonoperative approach to hip instability would be modification of sports activities. Operative treatment includes pelvic or femoral osteotomy with capsular placation followed by rehabilitation before returning to sports activity.

Legg-Calve-Perthes Disease, where the head of the femur loses blood supply, is slightly more common in children with Down Syndrome than in the general population. The symptoms are usually a painless limp and loss of full range of motion in the involved hip. It is diagnosed through radiographs. Mild cases are treated with bedrest, orthotics, and casting, but severe cases may require surgery.

Slipped capital femoral epiphysis (SCFE or "epiphysiolysis") may also be found in Down Syndrome patients. The rounded head of the femur slides on the femoral neck and this is often associated with obesity and hypothyroidism, often found in teenagers with Down Syndrome. The symptoms of SCFE are limp associated with a pain in the hip or knee. This is treated surgically with screw placement in the femur.

Patellofemoral instability occurs in 4-8% of Down Syndrome patients and may progress to pain or progressive deformity.[11] Genu valgum is a constant finding, and patellofemoral instability is often associated with long standing genu valgum.[11] Pain has been reported in 17% of patients, but patients generally respond to nonoperative treatment. Treatment for symptomatic patients includes patellar sleeve, medication, and possibly activity restriction. Operative treatments include patellar realignment by lateral release, medial reefing, and distal realignment by semitendinosis tenodesis.[11] These procedures may not be able to effectively treat ligamentous laxity. If patients experience progressive deformity, surgical intervention is a consideration but it is rarely indicated.

PODIATRIC PHENOTYPIC CHARACTERISTICS

Abnormalities include descriptions of the feet as short and stubby. There are abnormalities of the skin, partial or complete syndactyly, a poorly developed arch, a plantar crease often found between the first and second toes, the third toe is often longer than the second toe and unusual flexion of the toes. A wide space between the first and second toes, called Goldstein's sign, is present in 45% of children with Down Syndrome and this is not found in other syndromes.[15] This can be seen in fetuses during ultrasound examination.[16] In children with Down Syndrome there is increased prevalence of metatarsus primus varus with hallux valgus, increased ligamentous laxity, wide-based gait due to excessive external rotation and abduction of the hips, arthropathy, and hypotonia and slow reflex response. Down Syndrome patients have increased incidence of anhydrotic skin fissures and split toenails.[17] Increased plantarflexed first ray and wide hallucal cleft are commonly found in Down Syndrome children. Many have abnormal foot pressure points. Other foot deformities seen in Down Syndrome patients include clubfoot, hypermobile first ray, brachymetatarsia, Haglund's deformity and Tailor's bunion.

Pes plano valgus is the most common orthopedic problem in patients with Down Syndrome. It is usually asymptomatic and flexible during the first two decades of life, but it becomes more rigid and painful during the third decade. It is related to a generalized ligamentous laxity and becomes painful and disabling to the point where the patient cannot wear shoes.

Treatment

Children with Down Syndrome should be evaluated and treated early to maintain proper skeletal alignment and decrease external limb rotation. These treatments include immobilization casting, corrective shoes and splints, and surgery. Immobilization modalities may not be indicated if the child is older and delayed in learning to walk.

The open-toed straight last shoe may be used to limit pedal pronation.[3] The use of high top sneakers, rising above the ankle, with rigid, flat soles or sneakers with soles that are concave from medial to lateral are also indicated.[3] In patients with severe genu valgum the sole material inside sneakers may be split and varus wedging may be added to improve alignment of the lower limb.[3]

In a study by Selby-Silverstein, Hillstrom, and Palisanc, foot orthoses have been found to have an immediate of decreasing heel eversion on standing.[18] During gait, foot orthoses caused a more internally rotated transverse plane foot angle, decreased variability of foot function parameters and walking speed, and increased variability of ankle

moment in a group of 3-6 year old children with Down Syndrome.[18]

Foot orthoses (FOs) and shoes should be evaluated before they are dispensed to be sure they are providing the proper biomechanical alignment.[18] FOs should reduce transverse plane foot angle during gait. Knee ligament laxity and muscular support should also be evaluated and knee supports or strengthening exercises may be indicated in addition to FOs. FOs may help prevent foot pronation deformity since children using FOs walk with less pronation.[18] Physical therapy may be recommended with FOs to strengthen the hips, knees, ankles, and feet, stretch the heel cord, and improve balance by encouraging the child to shift weight during late swing phase rather than at heel contact.

CONCLUSION

Down Syndrome is the most common congenital anomaly and has numerous associated dermatologic and musculoskeletal deformities. The podiatric physician plays an important role in the care of the Down Syndrome individual. This physician should be able to identify the pathology and treat as well as educate the patient that presents for an office visit. Untreated painful feet may lead to increased morbidity and disability in patients with Down Syndrome; therefore early detection of lower extremity abnormalities as well as biomechanical management will improve the quality of life for these individuals.

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