Genetics

Although recognized as a hereditary disorder for over 100 years, the gene mutated in people with nail patella syndrome, called LMX1B, was only identified in 1998. LMX1B encodes a transcription factor which is primarily involved in specification of dorsal-specific structures (such as nails and patellae) in the developing limb. The proper placement of tendons and ligaments within the limb also requires the proper expression of LMX1B. LMX1B is also expressed in the anterior chamber of the developing eye and in the kidney throughout life, explaining the findings of glaucoma and kidney disease in nail patella syndrome patients. The variation in symptoms among people with nail patella syndrome is not believed to be associated with the different mutations found in LMX1B, but may be the result of variation in the genes with which LMX1B interacts.

Other conditions reported in people with Nail Patella Syndrome

There appears to be a strong association between NPS and symptoms of hypothyroidism, irritable bowel syndrome, Attention Deficit Disorder (with or without Hyperactivity) and thin tooth enamel. The precise nature of theses associations remains unclear at this time. Research into the condition continues.

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Nail Patella Syndrome UK is a UK based charitable body, dedicated to the support of NPS sufferers and their doctors. We are affiliated with NPS Worldwide Inc, a US non-profit organisation, and through them we have access to many medical professionals with expertise in dealing with NPS.

If you have internet access, there is a lot of useful information on the NPSW and the NPS(UK) websites:

www.nailpatella.org
www.npsuk.org

Nail Patella Syndrome UK has applied for registration as a UK charity. The Trustees are:

Carol Dobbins (Chairman)
Shirley Raynor FCA ATII (Treasurer)
Dr. Elizabeth Sweeney MB ChB DRCOG MRCP (Secretary)

Dr Sweeney is a Consultant Clinical Geneticist at the Royal Liverpool Children's Hospital

NPS(UK)

Nail Patella Syndrome: Information for families and their doctors

Produced by Nail Patella Syndrome UK

Nail Patella Syndrome

Nail Patella Syndrome (also called Fong's Disease, Hereditary Onychoosteodysplasia ["HOOD"] or Turner-Kieser Syndrome) is characterized by several typical abnormalities of the arms and legs as well as kidney disease and glaucoma. It has been recognized as a hereditary condition for over 100 years and is inherited in an autosomal dominant manner. That is, the risk of transmission is 50% per pregnancy, irrespective of gender (just like flipping a coin). Approximately 20% of cases are sporadic, being the result of a new mutation. The incidence is approximately 1 in 50,000 and occurs throughout the world in all ethnic groups.

Purpose of this informational booklet

Nail Patella Syndrome is a complex condition that varies greatly between each individual. The purpose of this booklet is to provide information to each specialist field of medicine that may see those with nail patella syndrome, as well as to provide contact personnel should further information be needed in the care of those diagnosed with nail patella syndrome.

Limb Involvement

Fingernails:

In the majority of people with nail patella syndrome, the finger nails are partly or entirely missing (80-100% of cases). This is most severe on the thumb and decreases in severity towards the 5th finger. The crescent "moons" at the base of the nail are often

triangular. Creases over the joint nearest the tip of the finger may be absent and fingers may seem double-jointed. The 5th finger may be slightly hooked. Toe nails can also be affected, but to a lesser extent than finger nails.

Knee:

Abnormality of the knee cap (patella) represents the second most common finding in nail patella syndrome (60-100%). In approximately half of the people the patellae are completely absent, with various degrees of size reduction reported in the remainder. If present, the patella often slips to the outside when the knee is straightened. Some of the tendons and ligaments in the leg may be missing or attached incorrectly.

Pelvis:

A feature unique to nail patella syndrome is the presence of iliac horns in approximately 80% of the people. These bony projections are clearly visible on X-ray, are sometimes palpable, but are asymptomatic. The shape of the pelvic bones may be slightly altered leading to a sway-back appearance (lordosis).

Elbows:

Many people with nail patella syndrome are unable to fully straighten their arms because the bones in the elbow joint do not meet properly. Tendons and ligaments may be misplaced and webbing sometimes forms around the elbow.

Feet and ankles:

Many children with nail patella syndrome are born with club foot deformities due to misplacement of tendons around the foot and ankle. Although these may respond to physiotherapy, surgery may be required. Due to tight heel cords (Achilles tendons) people with nail patella syndrome may tend to walk on their toes. The orthopedic findings in people with nail patella syndrome can be interpreted as a loss of patterning across the dorso-ventral axis of the limb.

Since the primary effect in the knee and elbow is mislocalization of tendons and ligaments, it is imperative that magnetic resonance imaging (MRI), in addition to X-ray, be performed prior to surgery.

Kidney Disease

The incidence of kidney disease in nail patella syndrome is approximately 30-50%. This is usually more apparent later in life, although there are reports of renal problems in childhood. The earliest sign is usually the presence of protein in the urine. Kidney disease is progressive and potentially fatal.

People with nail patella syndrome should have regular urinalysis to monitor changes in kidney function.

Eye Disease

It has recently become apparent that open angle glaucoma is also part of nail patella syndrome. Open angle glaucoma can be described as a condition caused by progressive blockage of the outflow of fluid from the front chamber of the eyes. If this is left untreated, the increase in fluid pressure results in permanent, irreversible damage to the optic nerve.

People with nail patella syndrome should have regular ophthalmologic examinations since the progression of glaucoma can be limited by treatment.