Noonan syndrome

Noonan syndrome is named after the paediatrician and heart specialist Jacqueline Noonan. In 1963, she published a report on a small group of patients with typical facies, congenital heart defect, and some clinical features similar to Turner syndrome, but with normal chromosomes.

The frequency of the Noonan syndrome is estimated to be between 1:1,000 and 1:2,500 in the general population. It has not been investigated, but it is assumed that about 30–40 children per year are born in Norway with this condition. The syndrome is underdiagnosed – its features may vary from person to person, and it is not easy to make the diagnosis, which has to be based on clinical judgement as well as some objective measurable defects. It is easiest to make the clinical diagnosis in early childhood, as the characteristic facies in Noonan syndrome is continuously changing and becomes less obvious as the child grows.

At present there are no biochemical tests to prove the diagnosis, but geneticists are carrying out active research on this.

In many cases, the diagnosis is made soon after birth or in infancy, but the condition may not be diagnosed before adulthood. It is important to make the diagnosis as early as possible so that parents and child get the treatment, help, and support that they need. The Noonan syndrome is hereditary, but half the cases are caused by a new mutation (alteration of the gene). The disorder is autosomal dominant, i.e. if one of the parents has the syndrome, the abnormal gene will be passed on to 50% of the children.

Main features

About 2/3 of the children have different degrees of congenital heart defect. This may be the most serious and problematic aspect of the syndrome. The most frequently reported heart defect is pulmonary stenosis (a narrowing of the lung artery valve). Other possible heart defects are hypertrophic cardiomyopathy (thickened heart muscle), atrial septum defect (hole in the wall separating the anterior heart chambers), ventricular septum defect (hole in the wall separating the main heart chambers), or a combination of all these defects. The heart defect is usually discovered when the newborn are examined before going home from hospital. Some children need operative or medical treatment, but many manage without treatment. They should all be followed up regularly.

Facial features that may be present:

- drooping eyelids (may be pronounced)
- downward slanting eyes with high, arched eyebrows
- epicanthus (extra skin fold at the inner angle of the eyes)
- increased distance between the eyes
- broad, arched forehead

- flat, broad root of nose
- big upper lip with a deep cleft between nose and upper lip
- high palate
- short, broad neck, possibly with skin fold
- low hair line on neck
- low-set ears with large outer part of cartilage
- many pigmented birthmarks

There is considerable variation in how pronounced the facial features are, and only a few of them need to be present. As the child grows, the face gradually becomes more normal, often more triangular with a high forehead.

Short stature

The birth length and weight of children with Noonan syndrome are often normal. Some of the children may have accumulation of fluid in the tissues at birth, but this usually soon diminishes. The increase in height in both boys and girls is less than normal throughout the whole growing period.

The average final height is about 153 cm in women and about 163 cm in men.

A person's final height can be calculated from their height graph. It has not been clarified whether growth hormone can increase the height, but research on this is in progress (Sept. '95). On an average, puberty is delayed by about two years in both sexes. In 60-80% of the boys, the testicles do not descend into the scrotum, and this may be one of the reasons for reduced fertility in men. Women's fertility is normal.

Feeding problems

During the first years of life the children may have great feeding and nutrition problems and frequent respiratory tract infections. They often have a weak sucking reflex, quickly become listless, and tire of sucking the way normal newborn and infants do. Feeding takes a long time and projectile vomiting often occurs at mealtimes. Some children have to be tube fed. Projectile vomiting usually decreases in the course of the first year, but in some cases feeding problems continue for many years. It is more important to focus on the number of calories the child needs than on the total amount of food. A nutritionist or dietician can help here. Feeding problems may be a great burden on the parents. Most of the time with the child may be spent on feeding or tube feeding, after which the child immediately vomits it all up again. The child does not gain weight or grow as expected. Weighing and measuring their child among healthy children at a child health clinic may be a strain on the parents. When tube feeding is necessary over a long period, it is very important to stimulate the mouth region to maintain the sucking reflex and motor function of the mouth. A physiotherapist or special teacher can help the child and parents with this.

Motor and intellectual development

Only a few children with Noonan syndrome are seriously handicapped. Delayed motor development and speech may be seen in about 25% of the children. Many of the children have reduced muscular tone. Pronounced flexibility of joints has been reported in about 50% of Noonan patients in a research project (Sharland et al 1992). Reduced muscular tone and joint flexibility in small children are associated with delayed motor development. Studies have shown that the average age when children with Noonan syndrome sit is about 10 months. They walk alone at an average age of 21 months, and can say simple two word sentences at about 31 months. Many children with Noonan syndrome have a high palate, which influences articulation and may lead to indistinct speech. Since children with Noonan syndrome may have difficulties with articulation and have a short stature, people are apt to think they are younger than they are, or that they are mentally handicapped. It is important that those in contact with a child or young person with Noonan syndrome are aware of this problem.

Little systematic research has been carried out on learning difficulties and speech in this syndrome, and many text books have maintained that it is associated with general learning difficulties. Many children with speech and language problems tend to develop a generalized belief that others do not understand what they say. They do not therefore take the initiative themselves with anyone except those they know can understand them, and thus fail to experience some of the interactions with other people that are so important for the development of speech.

In a study carried out in 1992 on 50 children with Noonan syndrome in St. George's Hospital in London, it was desired to test these children's IQ, measure their ability to coordinate, and investigate their degree of self-esteem. The researchers also wanted to find out to what degree children with Noonan syndrome have emotional problems (Peter Hill, 1992). The study showed that these children's IQ was within normal limits, though in most cases in the lower range of normal. The tests seemed to indicate that some of the children understood speech better than they could express themselves verbally. Children with Noonan syndrome may therefore benefit from using signs for speech. A large number of children in the study had coordination problems when writing, eating, and fastening buttons. Many also had emotional problems, anxiety and depression being specially common. The test also indicated that children with Noonan syndrome have more intense feelings, are more active, but are also shyer than the control group of normal children.

Other characteristics

Hearing: A mild type of hearing impairment has been reported, usually as a result of fluid in the middle ear. The problem can be solved by inserting a drain.

Vision: Many of those with Noonan syndrome have a form of visual disturbance, squinting, near sight, or long sight, which may necessitate use of spectacles. The visual disturbance is usually mild.

Teeth: Children with Noonan syndrome often have dental problems. 1/3 of them have wrongly positioned teeth. The teeth often appear late and in an abnormal order. The children have many cavities, possibly because they are given a large amount of sweet food as the parents try to find something that the child will eat.

Skin: Different skin changes have been described. There may be many small, deeply pigmented birth marks. Caf□-au-lait spots are seen in some. Some may have rubor and partially lacking eyebrows.

Bleeding tendency: Slight bleeding disturbances and irregularities in blood platelet function are not uncommon. This does not usually lead to problems, even with minor operations.

Skeleton: A mild form of pigeon breast and funnel chest are typical findings in Noonan syndrome. Some may also have thoracic scoliosis (curvature of the spine to one side).

Epilepsy: Repeated attacks of epilepsy have been described in a few cases. Most of these are grand mal attacks.

Hyperthermia: Rare cases of malignant hyperthermia (seriously high body temperature) precipitated by certain anaesthetics have been reported, and this should therefore be mentioned before anaesthesia.

Autoimmune disease such as inflammation of the thyroid gland may occur in children with Noonan syndrome. This can lead to low metabolism resulting in further reduction of growth and reinforcement of other symptoms. If it occurs early, there is also a risk of inhibited development.

Follow-up and therapeutic measures

Heart defect: Regular follow-up by paediatrician at nearest children's ward.

Short stature: Regular measurement of weight and height is important, remembering the possibility of low metabolism. Blood tests to check thyroid function should be taken at intervals during the growth period.

Nutrition/feeding problems: It is important to make contact with a dietician at an early stage for advice on nutrition, and also with a special teacher/physiotherapist to help train eating and to stimulate the motor function of the mouth.

Delayed development of speech: Communication training is important. The school psychology services should be engaged early. Some services employ a speech therapist.

Hypotonia/hyperflexibility: Regular physiotherapy with pressure stimulation to counteract problems connected with hypotonia. The parents should be informed and encouraged to strengthen the child's musculature through play and interaction.

Loss of hearing: Testing as early as possible with frequent checks. In several cases it may be necessary to insert a drain because of fluid in the middle ear.

Vision: Early testing is recommended.

Teeth: The dental services should be contacted early so that the child is followed up regularly.

Orthopaedics: It may be difficult to find shoes that fit. Some shoe factories make special shoes to measure. A specialist should issue a medical certificate describing the child's need for special shoes. If the child is under 10 years old the parents pay NOK 175 a pair to cover part of the cost, and with a child over 10 years, the parents pay NOK 275 a pair. The child has a right to two pairs of shoes a year.

Special education: Children and young people with Noonan syndrome may be affected by the syndrome to very varying degrees. Most of the children need special education. Use of computers may make school work easier and give the child an increased feeling of mastery. The school psychology service can give advice on therapeutic measures after professional assessment. The child or young person's need must be documented before applying for resources to carry out the necessary therapeutic measure, and thorough documentation of this kind should be obtained early. In the case of young people it may be appropriate to apply to enter an upper secondary school on special grounds.

Association:

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Expertise available at:

- The National Hospital:
  Centre for Mental Retardation (SMR),
  The Rare Disorders Centre.
- TAKO Resource Centre for Oral Health in rare medical disorders.
- Frambu National Centre for Rare Disabilities.
- «In between» (Midt i mellom).
- Endocrinologists at regional hospitals.
- Department of Medical Genetics, Ullevål, Haukeland, and Tromsø Hospitals.