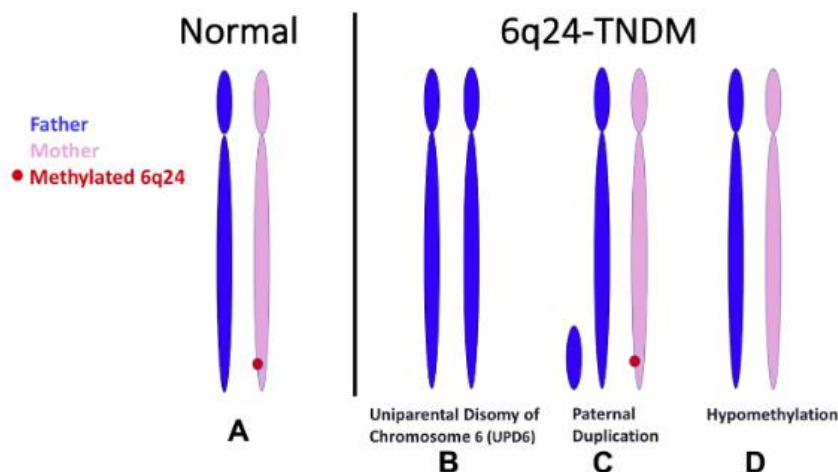


6q24-related Neonatal Diabetes



Overview:

6q24-related neonatal diabetes is caused by genetic changes (sometimes called ‘mutations’) on a region of the 6th chromosome and is the most common cause of transient neonatal diabetes. Transient neonatal diabetes is when high blood sugars appear in infancy, usually shortly after birth, but then go away for several years, and may return later in life. 6q24 is a term used to describe a region on the 6th chromosome. This region contains two important diabetes genes, these are called *PLAGL1* and *HYMAI*. Normally, people will inherit two copies of their genes, one copy from their mother and one copy from their father. At the 6q24 region, the copy inherited from the mother is usually silenced or suppressed through a process called methylation and the copy inherited from the father is active (**image A**). Sometimes, an individual can have two unsilenced or unsuppressed (unmethylated) copies of genes of the 6q24 region, leading to overexpression of the genes and causing diabetes.

Overexpression of these genes can be caused by three distinct mechanisms:

- Uniparental paternal disomy of chromosome 6 (UPD6) where there are 2 copies of 6q24, both inherited from the father (‘paternally inherited’) (**image B**);
- Paternal duplication of the 6q24 allele in which there are 3 copies of 6q24, 2 copies are inherited from the father (‘paternally inherited’) and 1 copy is inherited from the mother (‘maternally inherited’) (**image C**);
- Maternal hypomethylation, where the silencing of the copy of 6q24 inherited from the mother (‘maternally inherited’) does not happen correctly (**image D**).

Presentation:

People with 6q24-related diabetes usually develop high blood sugars in the first few days or weeks of life. In some cases, the high blood sugars will spontaneously go away in infancy and diabetes medications may be stopped during that time. Some individuals will experience low blood sugars while off all diabetes medications. Diabetes can return later in childhood or early adulthood when treatment would need to be resumed.

Some other features of 6q24-related neonatal diabetes include: very slow growth before birth (intrauterine growth restriction – IUGR), an unusually large tongue (macroglossia); a soft out-pouching around the belly-button (umbilical hernia); malformations of the brain, heart, or kidneys; weak muscle tone (hypotonia); deafness; and developmental delay.

Treatment:

In the neonatal period shortly after birth, patients with 6q24-related diabetes are often treated with insulin therapy. While treatment of 6q24-related diabetes in later life is less certain, insulin therapy is often needed. Sulfonylurea therapy has been successfully used for the treatment of some patients with 6q24-related diabetes.

Inheritance:

The inheritance pattern is varied and depends on which underlying genetic mechanism caused the 6q24-related diabetes. Most forms of 6q24-related diabetes are not inherited from a parent.

Research:

If you or a family member have 6q24-related diabetes, or think you may have it, then please contact us at monogenicdiabetes@uchicago.edu to learn more about our studies.