Autosomal dominant inheritance of congenital dislocation of the hip in 16 members of a family

Bir ailenin 16 üyesinde otozomal dominant kalıtım gösteren gelişimsel kalça çıkığı

Gulay CEYLANER,1 Serdar CEYLANER,1 Fulya USTUNKAN,2 Muharrem INAN3

1Intergen Genetik Center; 2Yeditepe University Medical Faculty; 3Yeditepe University Medical Faculty Orthopaedic and Traumatology Department


Anahtar sözcükler: Kalça çıkığı, doğuştan/tani/genetik; pedigri; polimorfizm, genetik.

The effect of genetic factors on hip dislocation, acetabular dysplasia, and developmental dysplasia of the hip (DDH) has long been recognized. In this report, we presented a large family that showed single gene inheritance for DDH. Pedigree analysis of a pregnant woman revealed a history of DDH in 16 members of the family. Although the pedigree showed autosomal dominant inheritance with reduced penetrance, the prevalence of DDH was considerably high, almost accounting for one-third of the family members, and skipping only one generation. Of 16 cases, three patients were diagnosed at our center. The remaining 13 patients were diagnosed at other centers. Dislocation was diagnosed very late in most of the family members, while four cases were diagnosed at birth. All family members were informed by a detailed clinical letter and recommended evaluation for DDH at every birth.

Key words: Hip dislocation, congenital/diagnosis/genetics; pedigree; polymorphism, genetic.

Developmental dysplasia of the hip (DDH) describes a spectrum of disease ranging from minor acetabular dysplasia to irreducible dislocation and may lead to premature arthritis in later life. This term has replaced the more traditional “congenital dislocation of the hip (CDH),” which assumes dislocation present at birth and does not include hips that are poorly developed or subluxed. Most developed countries report an incidence of 1.5 to 20 cases of DDH per 1000 births, the variation due in part to differences in diagnostic method and timing of evaluation. The effect of genetic factors on hip dislocation and acetabular dysplasia developmental dysplasia of the hip has long been known and still under investigation. More than 60% of infants with DDH have no identifiable risk factors while remaining cases have at least one risk factor. Having a first-degree relative with DDH is one of the described risk factors. The greater prevalence of congenital disease of the hip among the siblings and parents, especially mothers, in affected families...
is consistent with a multifactorial inheritance.\textsuperscript{[3]} We are here reporting here an example of a family with developmental dysplasia of the hip as a single gene disorder fashion as a very rare example.

**Case presentation**

A pregnant woman applied to genetics outpatient clinic because of her abnormal triple screening test results. During pedigree evaluation, sixteen people with the history of developmental dysplasia of the hip were detected. Pedigree clearly showed autosomal dominant inheritance with reduced penetrance (Figure 1). Three out of sixteen cases were evaluated and they did not have any other system abnormality and they were diagnosed as isolated DDH family after orthopedics consultation. Other thirteen family members were diagnosed at other clinics; none of them were examined at our clinic. Dislocation was diagnosed very late in some family members while four cases were diagnosed at birth.

All family members were informed by detailed clinical letter as the persons living in a village far from Ankara and evaluation for this disorder at birth was offered. Two points were accentuated in the detailed clinical letter sent to the family members. First was the importance of detection of genetic factors in family members with hip dislocation and how this will help preventive medicine by allowing early diagnosis and treatment in next generations. Second point was that their family is the largest family with DDH in the literature and if they agree with further testing, related genetic disorder can be exposed with linkage analysis.

**Discussion**

Early diagnosis is thought to improve outcome of DDH cases because nonsurgical treatments can be used to optimise development of the hip joint.\textsuperscript{[4]} Detection of high risk families is important to detect subclinical cases to threat as early as possible. On the other hand, genes and their mechanisms are not clear and such big families are useful for genetic linkage studies to detect gene localisations. Carter and Wilkinson \textsuperscript{[5]} postulated the existence of 2 genetic systems responsible for the etiology of CDH: the former, polygenic, related to dysplasia of the acetabulum; the latter, probably dominant, controlling the capsule around the hip joint. Wynne-Davies, \textsuperscript{[6]} in accordance with this hypothesis, suggested that 2 etiologic groups with congenital dislocation of the hip can be observed: one group with acetabular dysplasia, inherited through a multiple gene system (and responsible for a high proportion of cases diagnosed late), and another group with joint laxity (responsible for a high proportion of neonatal cases), revealing a genetic predisposition in which the action of unknown environmental factors appeared to be important. Autosomal dominant inheritance was firstly favored by Bornfors et al.\textsuperscript{[7]} Horton et al.\textsuperscript{[8]} observed a kindred in which 16 males and 16 females in 6 generations were affected. There were several examples of male-to-male transmission. In 27 family members, hip dislocation was associated with joint laxity. Five had joint laxity only. Six obligate heterozygotes showed no abnormality.

Mabuchi et al.\textsuperscript{[9]} described a large Japanese family in which acetabular dysplasia inherited as an autosomal dominant was the basis of osteoarthritis of the hip joint. Eight individuals in 4 generations had acetabular dysplasia manifested as pain in the hip joint during adolescence and progressing to severely crippling hip osteoarthritis before age 60 years. The patients were in general good health, height was not reduced, and there

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{pedigree.png}
\caption{Pedigree shows autosomal dominant inheritance}
\end{figure}
was no skeletal involvement suggestive of chondrodysplasia. This family is a rare example of non-syndromic hip dislocation with autosomal dominant inheritance. The penetrance is very high and just one skip generation was detected. Dislocation was diagnosed very late in some family members while four cases were diagnosed at birth. There was genetic inheritance in almost one third of the family members. Dislocation was diagnosed very late in some family members while four cases were diagnosed at birth.

Two points were accentuated in the detailed clinical letter sent to the family members. First was the importance of detection of genetic factors in family members with hip dislocation and how this will help preventive medicine by allowing early diagnosis and treatment in next generations. Second point was that their family is the largest family with DDH in the literature and if they agree with further testing, related genetic disorder can be exposed with linkage analysis.

References