Drug induced VATER association: is dibenzepin a possible cause?

The VATER complex is a non-random combination of three or more vertebral, anorectal, tracheo-oesophageal, radial, and renal malformations of which the first three are nearly always present. The remainder of the complex is composed of anomalies which are sometimes associated with the other malformations. In some cases the association between sex patterns common in experimental and normal offspring is suggested. In these cases the presence of a teratogen has been implicated.

The proband is the second child of a 25 year old woman who suffered from depression and had been treated with dibenzepin (Victoril) (80 mg x 3/day) throughout her pregnancy. The mother did not smoke or drink alcohol or coffee, and had not suffered from any infection during pregnancy. The parents are not related, and the father is healthy. The family history was unremarkable. The mother had not taken any medication during her first pregnancy and gave birth to a normal baby at term. During the second pregnancy (1992), ultrasound and 2 fetoprotein measurements were not performed. The fetal heart rate near term showed no distress.

The 40 week term infant, born in February 1993, with a weight appropriate for gestational age (3260 g), presented with oesophageal atresia, right radial aplasia, lumbosacral hemivertebrae, dextroposition of the heart, and right cryptorchidism. Brain and kidney ultrasound were normal. Karyotyping and G banding studies were normal. Oesophageal malformations were surgically corrected by end to end anastomosis and fistulectomy. At the age of 3 months, physical and neurological development was normal.

Dibenepin is a tricyclic antidepressant, rarely used during the first trimester. Because of the very limited data on dibenzepin usage in pregnancy, a precise risk estimation cannot be performed.

It is noteworthy that neither extensive epidemiological studies in humans nor experimental data have shown clear evidence of an association between the use of tricyclic antidepressants in pregnancy and birth defects, and the teratogenic effect of these drugs remains uncertain and contradictory.

The VATER complex is one of the more common patterns of multiple malformations in newborns. Prenatal exposure to exogenous sex hormones, lead, and, recently, lovastatin might have a teratogenic effect. Although it is impossible to establish a causal relationship between prenatal dibenzepin exposure and VATER on the basis of a single case report, the present report adds another possible teratogenic agent and raises the possibility of a drug induced type of VATER complex. A large prospective multicentre collaborative study is needed to clarify this issue further.

PAUL MERLOB, NORAN NAOR
Department of Neonatology, Beilinson Medical Centre, Petah Tikva 49 100, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.


Kyphomelic dysplasia

A six year follow up of a child with kyphomelic dysplasia has shown some interesting and previously undescribed features. This case was originally described by Temple et al.1

Kyphomelic dysplasia is a rare condition with a generalised abnormality of skeletal growth. The definition of the condition is based on the combination of rhizomelic and mesomelic limb shortening with short, broad, and bowed long bones, the femora being most severely affected. There is metaphyseal flaring and irregularity in infancy, causing prominent joints with restricted mobility. The ribs are short and flared. Variable features include micrognathia, midface hypoplasia, long philtrum, facial haemangioma, abnormal rib number, mild platyspondyly, increased acetabular angles, and skin dimples over bony prominences.

To date 11 cases of kyphomelic dysplasia have been reported.

The subject, a male child, remained mildly dysmorphic at the age of 3 years 3 months. Rhizomelic shortening of the limbs with anterior bowing of the thighs was still evident, but had improved since infancy. His gait was abnormal with a tendency to toe walk on the left and he began to complain of intermittent left back pain. A radiograph showed flattening and fragmentation of the right capital femoral epiphysis (figure) consistent with Perthes disease.

When he was 6 years old he complained of left hip pain and radiographs showed bilateral changes of avascular necrosis of the capital femoral epiphysis. A bone scan performed as one of the investigations for Perthes disease showed a hydrometaphyseal right kidney. Further investigations showed the cause to be obstruction at the level of the vesicoureteric junction.

Changes in the hip which are similar to those in Perthes disease but always symmetrical are found in certain skeletal dysplasias and malformation syndromes, such as multiple epiphyseal dysplasia, mucopolysaccharidosis type IV, and trichorhinophalangeal syndrome.

The aetiology of Perthes disease is thought to be multifactorial. The bony changes are those of avascular necrosis owing to interruption of the blood supply to the capital femoral epiphysis. An increased incidence in congenital dislocation of the hip supports a traumatic aetiology. We believe that abnormal gait, as in this child, is likely to result in stress injury resulting in avascular necrosis of the developing femoral head. It is likely that other syndromes with severe bowing of the femora may be associated with Perthes disease.

M A R O'RELLY
CM HALL
Department of Radiology, The Hospital for Sick Children, Great Ormond Street, London WC1N 3JH.


Velo-cardio-facial syndrome and DiGeorge sequence

I was interested to read the series of articles published in the Journal of Medical Genetics regarding phenotypic overlap of the velocardiofacial syndrome and DiGeorge sequence, preceded by Judith Hall's Editorial advocating the use of the acronym CATCH 22, as suggested by Wilson et al. The attention to velocardiofacial syndrome and 22q11 is very exciting and the authors are to be congratulated on this collective body of material. I would like to respond to a number of points which, in my opinion, point out the important role of clinical diagnosis, even in conditions where molecular analysis has yielded positive results. The articles of Greenberg,2 Goldmuntz et al,3 Driscoll et al,4

The patient aged 3 years 6 months. There is bowing of both femoral shafts with flexion deformities at the knees. The capital femoral epiphysis on the right appears collapsed and fragmented. The metaphyses are flared.

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P Merlob and N Naor

*J Med Genet* 1994 31: 423
doi: 10.1136/jmg.31.5.423

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