A GUIDELINE FOR INVESTIGATING A SUSPECTED VACTERL ASSOCIATION

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ABSTRACT

Tibial aplasia is a rare condition. We present a case of a male infant born with unilateral tibial aplasia, right hip dislocation and an atrial septal defect. This combination of features is unusual but is consistent with an embryological field defect, the VACTERL association (1-3). We outline a strategy to investigate infants presenting with this type of limb defect in order to detect the more subtle and less evident elements of the VACTERL syndrome.

CLINICAL REPORT

Baby C is a male infant born to a 16 year old primigravida. His parents are non-consanguineous and of Black Caribbean ethnicity with no history or family history of syndromic complications. In particular there was no known cardiac disease or history of sudden death in either family. Baby C’s mother had Type I insulin-dependent diabetes that was difficult to control throughout the pregnancy with an Hba1C of 13.7. His antenatal course was uneventful: anomaly scans and antenatal serology were normal. There was no history of maternal smoking or exposure to teratogens including oestrogen-progestins or methimazole; the infant may have been exposed to cannabinoids. Baby C was delivered prematurely at 32+5 weeks gestation by emergency lower segment caesarean section, performed for fetal bradycardia. He was born in poor condition with APGAR scores of 3, 8 and 9 at 1, 5 and 10 minutes respectively and required resuscitation followed by non-invasive ventilation for 2 days. His birth weight was 2.13kg. He remained in the special care baby unit to establish feeds. At day 3 of life he became jaundiced and required phototherapy for 1 day which then resolved spontaneously.

By day 9 Baby C had an audible systolic murmur shown on echocardiogram to be a small to moderate atrial septal defect with mild right ventricular volume overload. The ECG was normal. He was reviewed at 1 month corrected gestational age in a cardiology outpatients clinic where a
repeat ECHO showed that the ASD had closed spontaneously and his ventricular function was normal and so he was discharged from follow up.

On day 25 Baby C suffered a generalised tonic clonic seizure lasting for 2 minutes. At the time of the seizure Baby C was afebrile and initial blood tests including FBC, U&E, LFTs, capillary blood gas were all normal. Lumbar puncture produced bloody taps on two attempts and the procedure was abandoned. Cranial ultrasound at the time was unchanged showing bilateral periventricular flares and a left bulky choroid. Baby C remained clinically well after this episode; no further seizures were observed. Blood culture showed no growth after 5 days. EEG and MRI performed at 1 month corrected age were normal.

Baby C’s karyotype was normal male (46, XY), no significant chromosomal anomalies or ring chromosome structures were observed. Screening ultrasound scan of the kidneys was unremarkable. Thyroid function tests and TORCH screen were also normal.

The baby had an asymmetrical deformity of the lower limbs with a fixed flexion deformity of the right knee and talipes of the right foot. Radiological imaging revealed right tibial aplasia and complete dislocation of the right hip (figure 1). The remaining skeletal survey was unremarkable. He was noted to have low vitamin D levels with a high alkaline phosphatase so treatment with Dalavat was commenced.

The development of this infant at 10 months appeared appropriate for age. At this time he was reviewed the general paediatric team and orthopaedic team. He was able to pull to stand on his left leg, however, the orthopaedic team recommended amputation of the right leg below the knee to allow best function.

Following this appointment he has undergone a below the knee amputation of his right leg. He has now started walking with support using a prosthesis and was assessed to have a stiff gait at his last clinic appointment.

DISCUSSION

This infant suffered abnormalities of the heart and right leg. These may be the collective result of a series of spontaneous malformations. Statistically the two most common congenital defects in newborns are those of the heart and those of the limbs (Manouvreir-Hanu et al 1999). Further, non-limb abnormalities may be present in 70% of persons with congenital radial or tibial deficiencies (1). Whereas limb anomalies may be identified in 1/1000 live births, tibial aplasia is rare and is estimated to occur once in every million births (7). Limb bud development is regulated by at least 20 genes (Gurrieri 2002) and it is therefore identified as a component of many syndromes. Limb malformation (the most common of which is syndactyly) may be the consequence of a range of insults including genetic and environmental ones. The history of poorly controlled maternal Type I insulin-dependent diabetes may be significant in this case: Infants of mothers with established diabetes
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ey early in pregnancy, whether type 1 or type 2, have a two to five times greater risk of congenital malformations. These typically involve the more causal part of the body, and may involve the early limb buds. Possible antenatal exposure to cannabinoids is not known to be linked to limb bud anomalies, but unidentified teratogens cannot be excluded.

Atrial septal defects are not frequent congenital malformations. Many are asymptomatic at the time of birth but they can predispose an infant to cardiac arrhythmia (sometimes fatal), pulmonary hypertension, heart failure and cerebral vascular accidents. Some have identifiable genetic defects, such as those associated with mutations in the NXX2.5 gene.

The coincidence of a rare limb anomaly with an ASD raises a further possibility that the infant’s anomalies are part of a syndromic pattern (4,6). The most likely syndrome would be VACTERL, features of which include abnormalities in the following systems: V – vertebral, A – anorectal, C – cardiac, TE- trachea-oesophageal, R- renal and L-limb abnormalities. A number of points support this association. 20-35% of VACTERL patients have lower limb defects, usually unilateral and commonly involving of the tibial developmental field (2, 3, 5, 9, 10). VACTERL cases have also been shown to be preferentially male and it is also reported that they have a higher perinatal mortality rate, lower mean birth weight and a higher frequency of fetal losses in previous pregnancies. (8)

A potential association with VACTERL is important as organ systems other than the affected leg may be initially asymptomatic. However such co-morbidities may account for significant pathology in later life or during surgery, such as anomalies of renal or cardiac anatomy. We propose that any potential association with VACTERL be approached using a number of investigations (table 1). As there are only rare cases of familial links in VACTERL syndrome it is probably not necessary to screen the first degree relatives of an index infant.

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<th>Investigation</th>
<th>Abnormality</th>
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| Skeletal survey, including chest and abdominal x-rays | Limb, hip and vertebral abnormalities
| ECHO | ASD, VSD, PDA, dextrocardia, other |
| Renal USS | Renal dysplasia, polycystic kidney, hydronephrosis, urethral atresia, other |
| Chromosomal analysis | Rare genetic association |
| Urine toxicology | Tetratogen |
| Bloods | Renal function, glucose, bone profile including vit D |

Table 1
CONCLUSIONS

An infant presenting with congenital limb abnormalities requires a careful history, examination and investigation. A careful family history needs to be ascertained. The possibility of asymptomatic or latent renal and cardiac anomalies needs to be rigorously excluded.

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REFERENCES