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Disorganisation: a possible cause of apparent conjoint twinning

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Abstract

A patient with duplications of the internal organs and external structures of the lower half of the body might have traditionally been explained by incomplete twinning. The presence of a fifth digit-like structure protruding from the lower abdomen and facial and cranial abnormalities suggested that, instead, he might be an example of the disorganisation mutant. However, the presence of cardiac defects was not readily explained by invoking the presence of this mutation.

After a quiescent period of three decades, there has recently been increased interest in possible human homologues of the mouse mutant disorganisation.[1] This mutant gene "disrupts the orderly process of organogenesis and induces a great variety of developmental anomalies in structures derived from all germ layers". It is inherited in a semidominant manner. We report a male infant with multiple congenital anomalies which include three legs arising from two hemipelves, a 'digit' arising from his lower abdomen, a duplication of his GI tract with a urinary-intestinal fistula, duplicated kidneys and gonads on one side, and cardiac disease. These multiple anomalies may represent another human homologue of the mouse disorganisation mutant although 'incomplete twinning' was an alternatively suggested diagnosis.

Case report

The patient was the 2864 g product of an uncomplicated pregnancy and delivery. His left ear had an anterior tag (fig 1) and stenotic auditory canal. His right ear had a superior helical pit. His nasal passages were stenotic also. CT scan of the cranium showed focal atrophic changes involving both the parietal and frontal lobes, most pronounced on the left. An echocardiogram and cardiac catheterisation indicated a d-transposition of the great vessels and a double aortic arch with a vascular ring, all of which have since been repaired. The patient initially had respiratory problems and underwent rigid bronchoscopy to determine the cause. Severe tracheomalacia at the level of the posterior aortic arch was seen with moderate bronchomalacia and subsequently the patient underwent tracheostomy for relief of his airway obstruction and for better respiratory management.

The patient had three kidneys, the right one being the only functional kidney as shown by IVP. He had a small left kidney that was non-functional with no collecting system. He had a second, left pelvic kidney with poor uptake and no excretion. The left sided kidneys both appeared to be dysplastic. The patient had two incomplete pelves as seen on *x* ray of the lower extremities. An accessory bladder was seen in the left hemipelvis as well as two accessory gonads. A retrograde urethrogram and cystogram showed a right sided bladder with a small bladder diverticulum. The patient had a duplication of his GI tract with blind loops of bowel seen by an upper GI and a barium enema. The patient also had a fistula between the duplicated colon and the base of the bladder which has since been repaired. He also had an undescended left testicle.

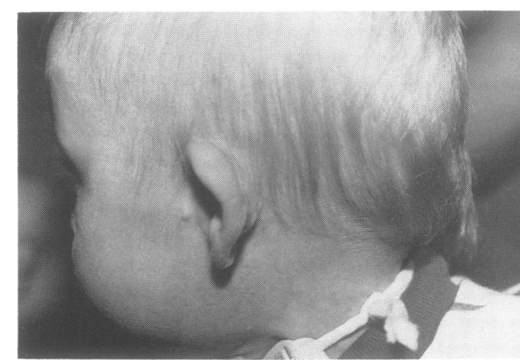

Figure 1 Patient has preauricular left ear tag.

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The patient had three lower limbs (fig 2) as well as an additional appendage which was a hamartoma that resembled an index finger protruding from the lower abdomen in the midline. This digit-like appendage contained bony material and had a fingernail. The right sided limb appeared to be a normally functioning leg. The middle limb was a small leg with no apparent spontaneous movement or neurological function. The left sided extremity extended from the pelvis and appeared to be the result of fusion of two limbs, since it was composed of a single femur, two tibias, and partial duplication of the foot (fig 3). This left sided limb also lacked neurological function. The patient had three hemivertebrae including C7, T1, and T2. His upper extremities were normal.

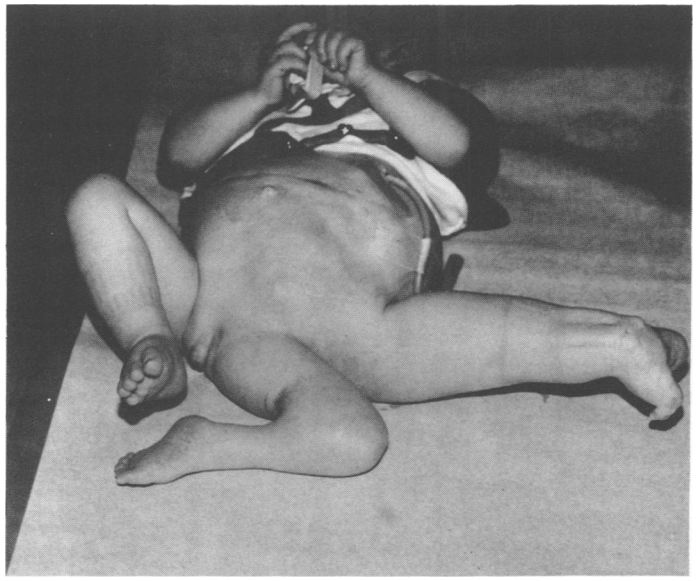

Figure 2 Patient has four lower extremities. The right extremity is normal. The middle extremity has no neurological function. The left leg is particularly interesting, extending from the pelvis and composed of a single femur, two tibias, and a bifid foot. The hamartoma has been removed before the photograph.

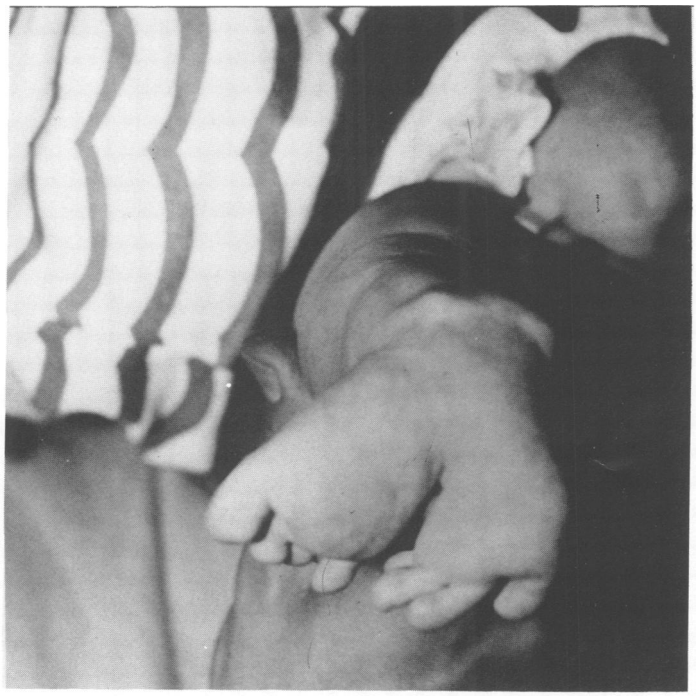

Figure 3 Close up of the bifid foot with 10 toes on the left leg.

Discussion

Although 'incomplete twinning' is an easily articulated explanation of the patient's findings, it begs the question of causality. If we only consider the lower axis of the patient, the duplicated hemipelves provide a causal explanation of three legs but not the internal duplication of the third leg. The anterior abdominal 'digit' cannot be explained by the hypothesis of incomplete twinning. In considering the internal organs, the colonic duplication and bladder fistula are very similar to defects seen in disorganisation.[2] The abnormalities of the brain (also, at 13 months, the patient's OFC is only 41 cm), ears, and narrow nasal passages are compatible with the multiple cranial abnormalities seen in disorganisation. However, the cardiac abnormalities do not match birth defects seen in disorganisation; no cardiac abnormalities were seen in 500 mouse fetuses.[2]

'Incomplete twinning' does not appear to be able to account for the range of abnormalities seen in this particular patient. Dipygus, or duplication originating in the caudal region, associated with sirenomelia may explain the limb abnormalities in this patient (see figs 13 to 28 of Potter and Craig[3]), but this explanation does not begin to account for the various other problems, including a hamartoma, colonic duplication, bladder fistula, and cranial dysmorphology. These global deformities seem to be much more likely to be associated with a single gene defect such as disorganisation.

Perhaps there are other cases of 'incomplete twinning' that are associated with more global abnormalities than can be accounted for by the simple explanation of dipygus. Possibly these cases would be better attributed to the action of the human homologue of disorganisation. The difference between the diagnosis of conjoined twins and disorganisation matters since the low penetrance of disorganisation[4] implies that either parent could be a non-penetrant carrier with a significant risk for affected offspring.

1 Winter RM, Donnai D. A possible human homologue for the mouse mutant disorganisation. *J Med Genet* 1989;**26**:417–20.
2 Hummel KP. Developmental anomalies in mice resulting from action of the gene *Disorganization*, a semi-dominant lethal. *Pediatrics* 1959;**23**:212–21.
3 Potter EL, Craig JM. *Pathology of the fetus and the infant*. 3rd ed. Chicago: Year Book Medical Publishers, 1975:220–36.
4 Hummel KP. The inheritance and expression of *Disorganization*, an unusual mutation in the mouse. *J Exp Zool* 1958;**137**:389–423.