tissue in the femoral epiphysis (fig 3). The growth plate showed focal chondrocyte proliferation overlying irregular zones of chondrocyte hypertrophy with poor column formation. Ossification was irregular and trabeculae coarse. Large islands of residual cartilage were present in the metaphysis.

The findings in this baby correspond closely to those in the infants described by Winter and by Beemer et al, and support their contention that this constitutes a separate short rib syndrome. In particular, the radiological changes are not typical of any of the well recognised short rib-polydactyly syndromes, in which there may occasionally be absence of polydactyly. However, our observations of an irregular growth plate and large vascular channels in epiphyseal and metaphyseal cartilage are in keeping with other histology reports in babies with lethal short rib-polydactyly syndromes and do not appear to be specific for this particular condition.

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References


Van der Woude syndrome and limb defects: the chance of recurrence

SIR,

Küster and Lambrecht (J Med Genet 1988;25:565–7) reported the association of cleft lip and palate, lower lip pits, transverse deficiency of the hands and feet, syndactyly of the fingers, and club foot. It was speculated that the hand and limb defects could represent previously unrecorded effects of the Van der Woude syndrome. The pregnancy was significant in that there was premature rupture of the membranes from 31 to 35 weeks, when the patient was born. Amnion rupture has a well recognised association with limb deficiency, syndactyly, and club foot. There have been an extensive number of experimental studies looking at the association of amniotic sac rupture and limb deficiency and Kennedy and Persaud proposed a hypothesis based on the experimental work which indicated that the initial lesion from amniotic sac rupture is a vascular one produced by uteroplacental insufficiency either by compression of the umbilical cord or by compression of the placenta itself. Houben analysed by histological study the limb haemorrhage produced by amniocentesis in the rat and showed that the endothelial rupture of the marginal vein was the initial event, followed by blebs, perivascular oedema, and vascular congestion.

Torpin felt that the limb deficiency was the result of mesodermic fibrous strings, produced after amniotic rupture, wrapping around the limbs. This
theory remains speculative as the animal studies have shown no evidence of strings or bands as the cause of the limb deficiency. If the vascular compromise occurred at the time of premature rupture of the membranes there would be adequate time for healing of lesions and resorption of amputations. Healing in the fetus is particularly fast and relatively non-scarring. It is likely that this child’s limb defects were related to amnion rupture, and are not associated with Van der Woude syndrome.

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References

Fetal valproate phenotype is recognisable by mid pregnancy

Sir,
In the November 1987 issue of your journal, Winter et al\(^1\) reported four infants who were exposed to sodium valproate or valproic acid during pregnancy. Three surviving infants showed the characteristic facial features of the fetal valproate syndrome described by DiLiberti et al\(^2\) and confirmed by several authors.\(^3\) We report here a 22 week fetus with a large myelomeningocele and similar facial abnormalities.

The mother of this subject, a 23 year old primigravida of Iberian origin, attended a psychiatric clinic and suffered from grand mal epilepsy. She received sodium valproate (500 mg twice a day) from the age of 18 years in combination with clobazam (10 mg, three times a day). When she became pregnant, she was referred to us for prenatal diagnosis of open neural tube defect.

At 18 weeks of gestation, serum and amniotic α fetoprotein (AFP) concentrations were evaluated by radioimmunoassay. Maternal serum AFP was raised (2.9×MoM). The amniotic fluid, obtained by amniocentesis, was clear and blood free, with an AFP concentration within the normal range (<3 MoM). Ten ml of amniotic fluid were centrifuged at 14 000 g for five minutes to remove any red cell membrane contamination. Quantitative measurements of acetylcholinesterase on unfrozen material

![FIG 1 Dorsal view of the fetus.](image1)

![FIG 2 Fetal spine after dissection.](image2)
Van der Woude syndrome and limb defects: the chance of recurrence.

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