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SHORT COMMUNICATION

Klippel–Trenaunay–Weber (KTW) syndrome: the use of *in utero* magnetic resonance imaging (MRI) in a prospective diagnosis

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The diagnosis of the Klippel–Trenaunay–Weber (KTW) syndrome is rarely made antenatally. We report the use of both ultrasound and *in utero* magnetic resonance imaging (MRI) in the prenatal diagnosis of this syndrome. This is the first report of the use of prenatal MRI in the diagnosis of this condition. There was concordance in the findings of both modalities, with limb hypertrophy, and multiple haemangiomata – both subcutaneous and internally – demonstrated with ultrasound and MRI. The patient elected to terminate the pregnancy because of associated oligohydramnios and a small fetal chest noted at 20 weeks. The postmortem examination confirmed the antenatal diagnosis. Copyright © 2001 John Wiley & Sons, Ltd.

KEY WORDS: magnetic resonance imaging (MRI); Klippel–Trenaunay–Weber (KTW) syndrome; prenatal diagnosis; ultrasound

INTRODUCTION

Klippel–Trenaunay–Weber (KTW) syndrome comprises the triad of limb hypertrophy, haemangiomata, described by Trenaunay and Klippel (1900), and arteriovenous malformations as described by Weber (1907). Prenatal diagnosis has been described but this is usually made with the help of a positive family history (Paladini *et al.*, 1998). We describe the use of prenatal ultrasound and MRI to provide the diagnosis in a patient with no family history or predisposing factors for KTW syndrome.

CASE REPORT

A 21-year-old multigravida booked at 13 weeks in her second pregnancy at the Birmingham Women's Hospital. Ultrasound scan at 13 weeks showed no apparent abnormality. The patient had taken folic acid periconceptually, there was no relevant past medical history and no known familial conditions. Her first pregnancy ended at 30 weeks in an emergency Caesarean section because of *abruptio placentae*. This child has cerebral palsy. The patient was investigated preconceptually to exclude secondary predisposing factors for *abruptio placentae*. There was mild protein C, S and antithrombin III deficiency [66 U/dl (70–140); 61 U/dl (80–115); 74 U/dl (79–131)]. The patient was therefore commenced on prophylactic Fragmin 5000 IU subcutaneously once a day from 7 weeks' gestation.

A routine anomaly scan at 20 weeks showed a multicystic lesion on the fetal back and leg and the patient was referred to the Fetal Medicine Department at the Birmingham Women's Hospital. The ultrasound findings were of a nuchal fold of 6 mm, a narrow chest (cardiothoracic ratio, 87%), a low umbilical cord insertion and marked oligohydramnios. In addition there were large subcutaneous and percutaneous multicystic lesions over the back and upper thorax extending around the body and covering the left leg to the foot (Figure 1). Colour flow Doppler studies demonstrated the vascular supply to the cystic areas but failed to show flow within the lesions. A differential diagnosis of multiple congenital teratoma, cystic hygroma or KTW syndrome was considered. In view of the diffuse nature of the findings the latter diagnosis appeared most likely. An MRI scan confirmed a 'cystic hygroma' involving the skin on the right, which extended onto the thorax on the left. Images were obtained in three orthogonal planes without the need for sedation using a rapid HASTE sequence on a 1.5-T machine. These confirmed an extensive multiloculated cystic mass extending around the thorax. The mass was larger on the right side, where it extended into the neck and scalp. There were multiple fluid levels within the locules. The mass extended into both sides of the chest. There was also a cystic mass on the lower back extending to the left buttock and leg as far as the foot. There were multiple

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Figure 1—The ultrasonographic appearance of the haemangimomata associated with the Klippel–Trenaunay–Weber (KTW) syndrome. The fetal leg (left) is shown with the femur between the caelipers. Multiloculated cystic areas are clearly seen

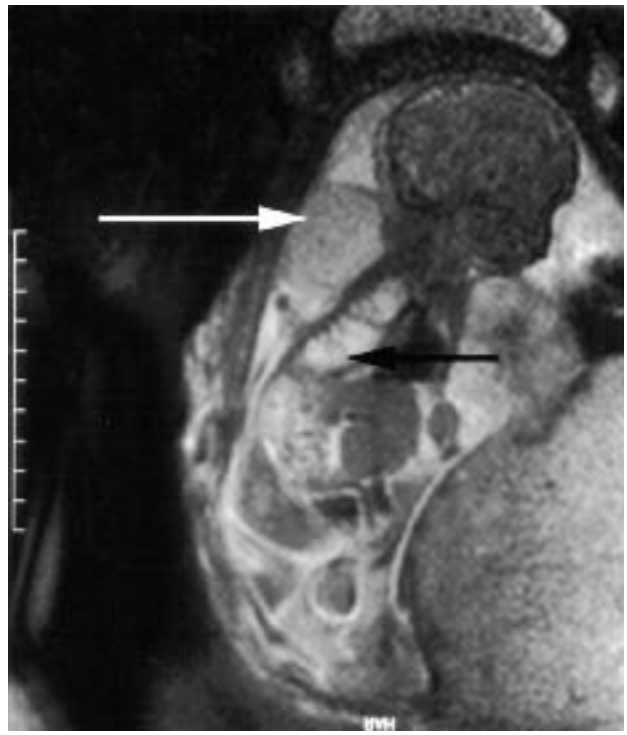

Figure 2—Klippel–Trenaunay–Weber (KTW) syndrome – haemangimomata demonstrated using magnetic resonance imaging (MRI). Images were obtained in three orthogonal planes using a rapid HASTE sequence on a 1.5-T machine. In this sagittal section, an extensive multiloculated cystic mass extending around the thorax (tail-end of black arrow) and posteriorly onto the neck is seen (white arrow). Intrathoracic extension is seen (black arrow)

serpiginous flow voids consistent with vascular channels within these masses (Figure 2). Only the left kidney was clearly identified, as a large cystic area was present extending retroperitoneally down to the bladder on the other side. A placental biopsy showed a normal male karyotype (46,XY). In view of the findings, and in particular the early onset oligohydramnios, the risk of pulmonary hypoplasia was discussed with the patient who opted for termination of pregnancy. This was performed using mifepristone (200 mg) followed 48 h later by gemeprost (1 mg) every 3 h, three doses being required. The fetus weighed 724 g. Postmortem confirmed the presence of multiple subcutaneous haemangiomata involving the chest wall, perineal area, lower abdomen and left leg. Both pleural cavities were distorted by haemangiomata on either side of the thoracic spine and the lesion extended retroperitoneally into the pelvis. Renal parenchyma was identified bilaterally. Histologically the lesions consisted of large vascular spaces with the appearance of cavernous haemangiomas. The findings confirmed the prenatal diagnosis of KTW syndrome.

DISCUSSION

KTW syndrome represents a triad of limb hypertrophy, usually affecting the lower limb (in 85% of cases), cutaneous haemangioma and arteriovenous malformations. Characteristically there is a large superficial lateral venous channel, the Klippel–Trenaunay vein. It is an uncommon, usually sporadic, condition with a prevalence of 1 : 100 000 live births (Lorda-Sanchez *et al*., 1998). There are several reports in the literature of familial cases of KTW syndrome. Whelan *et al*. (1995) reported a case of a reciprocal translocation [46,XX,t(5;11)(q13.3;p15.1)] suggesting that a single gene disorder may be a potential aetiology. There is evidence of an increased incidence of KTW syndrome with paternal age (Lorda-Sanchez *et al*., 1998) suggesting either paradominant inheritance (Happle, 1992), or autosomal-dominant inheritance with variable expression, resulting in family members having differing phenotypes ranging from manifestation of the complete KTW syndrome to severe varicose veins (Ceballos-Quintas *et al*., 1996).

The aetiology of KTW syndrome is unknown but there may be a mesodermal defect acting on angiogenesis leading to the formation of the haemangiomata and varicose veins characteristic of the anomaly (Baskerville *et al*., 1985). Atresia of the venous system also occurs leading to stasis, oedema, varicosities and ultimately to limb elongation and hypertrophy (Christenson *et al*., 1997). The Klippel–Trenaunay vein may represent an embryonic limb bud that has failed to regress (Howlett *et al*., 1997).

There are few cases of prenatal diagnosis of the condition in the literature. The first report of antenatally diagnosed KTW syndrome was in 1981 at 34 weeks' gestation (Hatjis *et al*., 1981). The earliest gestation at which KTW syndrome was diagnosed was at 15 weeks using three-dimensional ultrasound (Shih *et al*., 1998). It is unusual to prospectively diagnose the condition in the absence of a family history. In the present case the diagnosis was made at

20 weeks after a routine screening scan prompted referral for a fetal medicine opinion. The use of alternative imaging techniques have been reported in management of KTW syndrome postnatally and in particular MRI has been used for evaluation of lesions in children and adults (Kanterman *et al*., 1996). In one case report, perhaps surprisingly, the use of colour flow mapping prenatally was unhelpful in delineating the extent of haemangiomata (Roberts *et al*., 1999). The use of MRI in the present case is, to our knowledge, the first report of the use of MRI in the prenatal diagnosis of KTW syndrome.

The usual manifestations of the condition include the finding of large cystic areas (haemangiomata) which may only affect one limb, or variously include the thorax, perineal area or occupy the thoracic cavities, abdomen or pelvis. The haemangiomata may ultimately lead to high output failure and *hydrops fetalis*. Limb measurements may be asymmetrical. In the present case these findings were present.

The differential diagnosis is from other conditions in which body asymmetry, macrosomia and hypertrophy are features. These include Beckwith–Wiedemann syndrome, which is associated with exomphalos, generalised macrosomia or hemihypertrophy rather than haemangiomata. Proteus syndrome may be difficult to differentiate from KTW as asymmetrical overgrowth of limbs occurs, although this is usually of the hands or feet, and haemangiomata are associated also. Russell–Silver syndrome involves asymmetrical skeletal growth but abnormal limbs tend to be small giving an impression of unilateral limb hypertrophy. In addition, macrocephaly is usually a feature whereas haemangiomata are not, thus differentiation from KTW syndrome is possible.

The management of such cases needs to be on an individual basis. KTW syndrome has been reported in the paediatric literature as a benign condition with lesions tending to regress with age. However, this will often reflect the mild end of the disease spectrum with prenatally diagnosed cases having a poorer outcome. The prognosis depends on the location and size of the haemangiomata. If large, the haemangiomata may lead to life-threatening haemorrhage or shunting of blood which may cause high output cardiac failure and *hydrops fetalis*. Two case reports indicate that progression of lesions *in utero* can occur rapidly (Jorgenson *et al*., 1994; Paladini *et al*., 1998). In one case, *hydrops fetalis* developed in 1 week (Paladini *et al*., 1998).

In the present case the ultrasound and MRI findings of haemangiomata suggested a diagnosis of KTW syndrome. The associated findings of intrathoracic extensions, a small fetal chest and oligohydramnios indicated a poor prognosis with pulmonary hypoplasia likely, leading to the decision to terminate the pregnancy. One advantage with the use of *in utero* MRI in the management of KTW syndrome is the technique not only allows good definition of soft tissue lesions, it also identifies vascular malformations and their extent. Areas of low signal indicate flow voids, haemosiderin deposits or calcification, which are indicative of vascular malformations (D'Costa *et al*., 1996). The haemangiomata may not be obvious using ultrasound, making diagnosis less certain with this modality. The use of MRI in the present case allowed the diagnosis of KTW syndrome to be made with more certainty.

In conclusion, the present case represents only the third reported prenatal diagnosis of KTW syndrome in the absence of a family history in the literature. Our literature search was performed using PubMed, Medline, the Online Mendelian Inheritance in Man (OMIM) and EMBASE databases with the keywords Klippel–Trenaunay–Weber, MRI, prenatal diagnosis and ultrasound. The case represents, as far as we are aware, the first case of the use of MRI in the antenatal management of KTW syndrome. The MRI scan was helpful in evaluating the extent of the lesions, thus adding to the confidence of the diagnosis by providing better demonstration of the vascular lesions than is possible with conventional imaging techniques antenatally.

REFERENCES

Baskerville PA, Ackroyd JS, Browse NL. 1985. The etiology of Klippel–Trenaunay–Weber syndrome. *Ann Surg* **202**: 624–627.

Ceballos-Quintal JM, Pinto-Escalante X, Castillo-Zapata Y. 1996. A new case of Klippel–Trenaunay–Weber (KTW) syndrome: evidence of autosomal dominant inheritance. *Am J Med Genet* **63**: 426–427.

Christenson L, Yankowitz J, Robinson R. 1997. Prenatal diagnosis of Klippel–Trenaunay–Weber syndrome as a cause for *in utero* heart failure and severe postnatal sequelae. *Prenat Diagn* **17**: 1176–1180.

D'Costa H, Hunter JD, O'Sullivan, O'Keefe D, Jenkins JPR, Hughes PM. 1996. Magnetic resonance imaging in macromelia and macrodactyly. *Br J Radiol* **69**: 502–507.

Happle R. 1992. Klippel–Trenaunay syndrome: is it a paradominant trait? (Letter). *Br J Dermatol* **128**: 465.

Hatjis CG, Philip AG, Anderson GG, Mann LI. 1981. The *in utero* ultrasonographic appearance of Klippel–Trenaunay–Weber syndrome. *Am J Obstet Gynecol* **139**: 972–974.

Howlett DC, Ayers AB. 1997. MRI of Klippel–Trenaunay syndrome: use of the short tau inversion recovery (STIR) sequence. *Clin Radiol* **52**: 402–405.

Jorgenson RJ, Darby B, Patterson R, Trimmer KJ. 1994. Prenatal diagnosis of the Klippel–Trenaunay–Weber syndrome. *Prenat Diagn* **14**: 989–992.

Kanterman RY, Witt PD, Hsieh PS, Picus D. 1996. Klippel–Trenaunay syndrome: imaging findings and percutaneous intervention. *AM J Roentgenol* **167**: 989–995.

Klippel M, Trenaunay P. 1900. Du naevus variqueux osteohypertophique. *Arch Gen Med* **185**: 641–672.

Lorda-Sanchez I, Prieto L, Rodriguez-Pinilla E, Martinez-Frias ML. 1998. Increased parental age and number of pregnancies in Klippel–Trenaunay–Weber syndrome. *Ann Hum Genet* **62**: 235–239.

Paladini D, Lamberti A, Teodoro A, *et al*. 1998. Prental diagnosis and haemodynamic evaluation of Klippel–Trenaunay–Weber syndrome. *Ultrasound Obstet Gynecol* **12**: 215–217.

Roberts RV, Dickinson JE, Hugo PJ, Barker P. 1999. Prenatal sonographic appearances of Klippel–Trenaunay–Weber syndrome. *Prenat Diagn* **19**: 369–371.

Shih J-C, Shyu M-K, Chang C-Y, *et al*. 1998. Application of the surface rendering technique of three-dimensional ultrasound in prenatal diagnosis and counselling of Klippel–Trenaunay–Weber syndrome. *Prenat Diagn* **18**: 298–302.

Weber FP. 1907. Angioma formation in connection with hypertrophy of limbs and hemihypertrophy. *Br J Dermatol* **19**: 231–235.

Whelan AJ, Watson MS, Porter FD, Steiner RD. 1995. Klippel–Trenaunay–Weber syndrome associated with a 5:11 balanced translocation. *Am J Med Genet* **59**: 492–494.