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Prenatal diagnosis of Klippel–Trenaunay–Weber syndrome: a case report

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ABSTRACT

At 20 weeks of gestation, a typical combination of a massive enlargement of the right fetal leg and multiple cystic lesions was detected at ultrasound examination. Color-coded Doppler examination revealed no arteriovenous fistulae.

These findings allowed an in utero *diagnosis of the Klippel–Trenaunay–Weber syndrome, which was confirmed after subsequent termination of the pregnancy. The severe malformation involved the upper and lower right leg. No arteriovenous fistulae were found.*

INTRODUCTION

In 1900, Klippel and Trenaunay originally described the entity of limb overgrowth, multiple cutaneous angiomata and varicose veins[1], which was confirmed by Parkes-Weber in 1918[2] and extended by the infrequent finding of arteriovenous fistulae[3].

The prenatal ultrasonic characteristics of the Klippel–Trenaunay–Weber syndrome have been established retrospectively in most of these cases[4–7], while a correct prenatal diagnosis was made only once[8].

We report a prenatal diagnosis of Klippel–Trenaunay–Weber syndrome at 20 weeks of gestation which subsequently led to termination of pregnancy.

CASE REPORT

A healthy 34-year-old gravida 2, para 1 was referred to our Level III unit for an anomaly scan at 20 weeks of gestation, because of suspected cystic structures around the right fetal leg.

The family history revealed no congenital anomalies and there was no consanguinity. Her first and uncomplicated pregnancy had resulted in a term delivery of a healthy son. Her current pregnancy had been uneventful until 20 weeks.

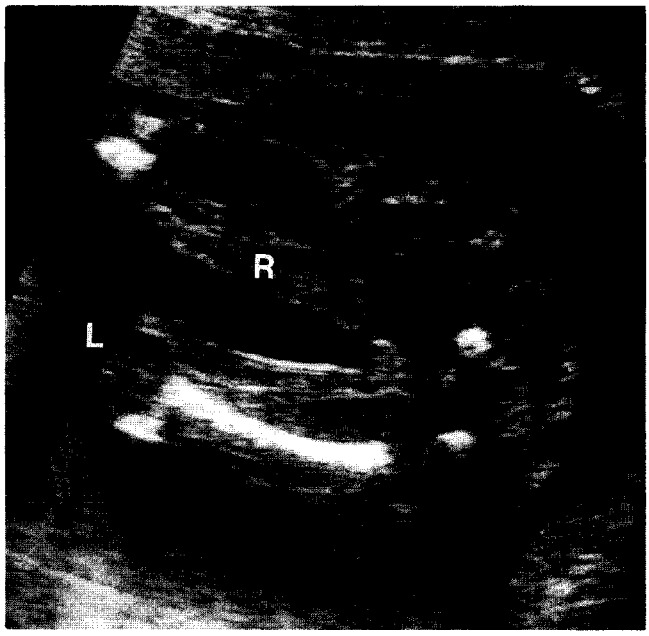

Figure 1 Sonogram of enlarged upper fetal right leg and irregular sized sonolucent cystic lesions extending into the buttock (R); normal left side (L)

On ultrasound examination, the fetus displayed a grossly enlarged upper and lower right leg which was due to numerous subcutaneous sonolucent multiloculated cystic lesions, with diameters varying between 1 and 20 mm (Figure 1). In between the cysts, more echodense tissue was seen without bony malformations. The right foot was somewhat larger (37 mm) than the left (33 mm). The cystic abnormalities extended into the right buttock and hip.

Color-coded Doppler examination of the right leg did not reveal any arteriovenous fistulae. Besides a slight cardiomegaly and thickened myocardium suggesting early signs of high-output cardiac failure, there were no additional structural defects. There was a normal amniotic fluid compartment.

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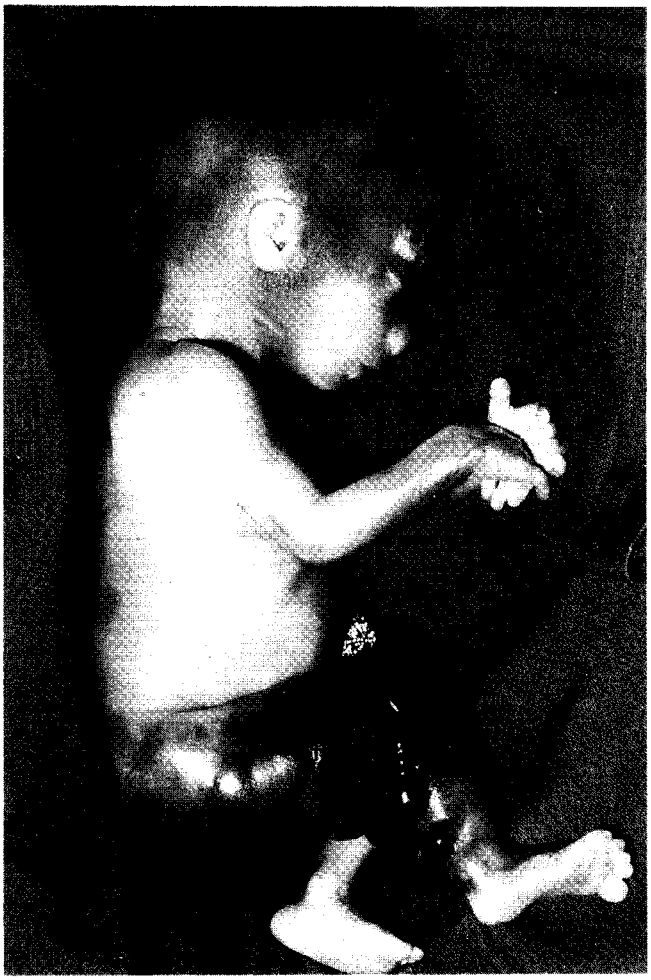

Figure 2 Fetus at autopsy: extensive hypertrophy with hemangiomatous lesions of right leg

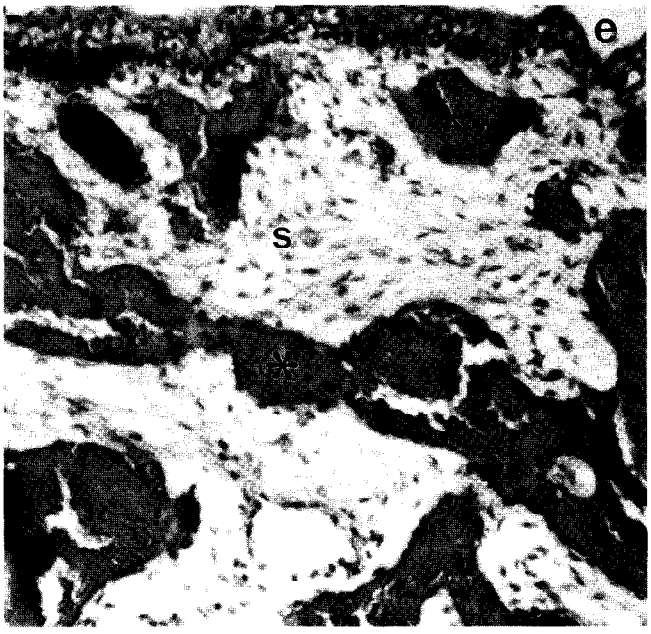

Figure 4 Microscopy of fetal skin and subcutis (× 100): epidermis (e); subcutis (s) with numerous angiomatous lesions (*)

The asymmetric limb hypertrophy and large subcutaneous cystic lesions suggested the presence of Klippel–Trenaunay–Weber syndrome. Amniocentesis revealed a normal female karyotype and a normal amniotic fluid α-fetoprotein level.

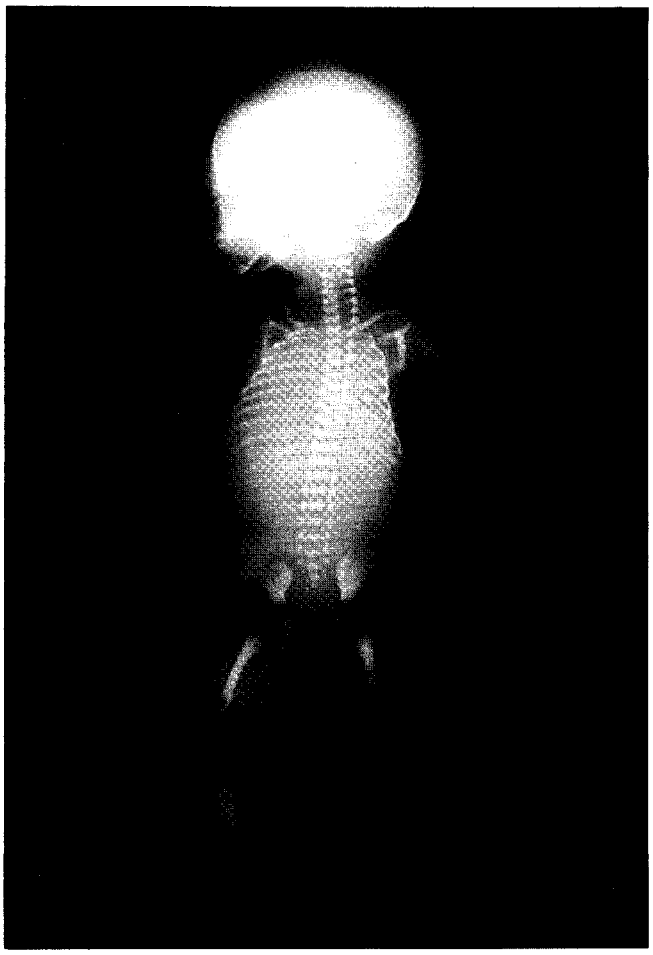

Figure 3 X-ray: soft tissue hypertrophy of right leg, without apparent bony hypertrophy

The parents were informed about the severity of the lesions, which later in childhood might require extensive surgical corrections and eventually amputation. The couple subsequently opted for termination of the pregnancy. This was carried out by means of sulprostone (Nalador®) at 21 weeks of gestation.

The 470 g female infant showed hypertrophy and extensive hemangiomatous lesions of the right leg at autopsy and on postmortem X-ray, confirming the sonographic findings (Figures 2 and 3). No arteriovenous fistulae were found. Histologically, numerous angiomatous lesions were encountered in the subcutis and underlying muscle tissue, which is pathognomonic of Klippel–Trenaunay–Weber syndrome (Figure 4). There was no pathology of other organs.

DISCUSSION

The sporadic Klippel–Trenaunay–Weber syndrome, also called angio-osteohypertrophy syndrome, involves the classic triad of asymmetric hemihypertrophy of limbs and trunk, due to bony and soft tissue hypertrophy which may extend across the mid-line, varicose veins and cutaneous hemangiomata. Arteriovenous fistulae are present in a minority of patients[4,9,10].

Also visceral angiomatosis may occur[4,6,7,10–14]. The areas of hypertrophy and the location of the arteriovenous malformations may be encountered in different parts of the body[4,7,8,11,13,15]. The severity of the phenotype is highly variable[7–9,13–15].

The exact mechanism causing Klippel–Trenaunay–Weber syndrome is not known[4,7,11,13–16]. A mesodermal defect affecting angiogenesis and associated with persistence of the embryonic vascular network, which usually regresses in the embryonic limb bud, might explain the above-mentioned vascular anomalies[13,16]. The increased vascular supply may cause the bony and soft tissue hypertrophy[8,9,11,13,16,17]. Others have suggested that a disturbance in the regulation of tissue growth factors is the underlying mechanism causing Klippel–Trenaunay–Weber syndrome[11].

Varicosis is a major component of Klippel–Trenaunay–Weber syndrome which can be caused by atresia or hypoplasia or compression of the deep venous system[9–12,17,18] or by arteriovenous fistulae[9]. Additional congenital absence of valves in the superficial veins has also been documented[11,16,17]. Secondary to venous stasis in abnormal vessels, varicose ulcers[10,11,13,15,17] and aseptic cellulitis[10,11,13,17] with secondary infection may develop, possibly because of thromboembolic episodes[17]. Another complication is mild thrombocytopenia which may be associated with persistent hemorrhage from multiple hemangiomatous (intestinal) areas[8,10–12,14,15].

Prognosis depends predominantly on the type and extent of involvement and may be relatively good in cases of mild-to-moderate disease[8,11,14,15]. No curative treatment exists for Klippel–Trenaunay–Weber syndrome. In mild forms of the disease, elastic stockings are advised to prevent edema[9–11,17]. For the bony and soft tissue hypertrophy and some of the vascular (visceral) anomalies, surgical correction has been described[4,8–12,15,18]. However, stripping of the varicose veins seems to be contraindicated because this will only worsen the clinical situation due to the atretic or obstructed deep venous system[9–12,17]. For the cutaneous manifestations of Klippel–Trenaunay–Weber syndrome, cosmetic creams or skin grafting have occasionally been successful[4,17].

Our case is another demonstration of the *in utero* diagnosis of Klippel–Trenaunay–Weber syndrome. The characteristic sonographic features, asymmetric hypertrophy with multiple echolucent cystic lesions[4–6], were limited to the same limb. The larger right foot, as demonstrated on ultrasound examination and at autopsy, supported the diagnosis. There was no visceral involvement.

An association between high-output cardiac failure and arteriovenous fistulae has been described[8–13]. In our case, slight cardiomegaly and a thickened myocardium were diagnosed on ultrasound examination as a possible early sign of cardiac failure, although no arteriovenous fistulae were demonstrated, either with color-coded Doppler examination or histologically. We suggest that this phenomenon may be an expression of an increased circulation, i.e. intravascular volume due to the angiomatous lesions in the fetal right leg.

Although the severity of the syndrome is highly variable, the parents opted for termination of pregnancy because of the extent and severity of the malformation as early as 20 weeks of gestation, which possibly would require extensive surgical intervention in childhood and associated handicaps, including eventual amputation of the right leg.

Finally no chromosomal or genetic basis for Klippel–Trenaunay–Weber syndrome has been established nor are there known teratogenic relationships. Familial cases cited by Koch were scrutinized by Gorlin and colleagues[13] and rejected as Klippel–Trenaunay–Weber syndrome either because of inadequate documentation, or diagnostic confusion with, for instance, neurofibromatosis. There is only one example of brother–sister involvement[13]. If this disorder was caused by a single gene mutation, transmission by patients to their offspring might be expected. However, most published series lack data on the offspring. In practice, the risk of recurrence is estimated to be very low.

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