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Prenatal diagnosis and hemodynamic evaluation of Klippel–Trenaunay–Weber syndrome

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ABSTRACT

Klippel–Trenaunay–Weber syndrome is a rare congenital soft-tissue anomaly which is characterized by the presence of multiple hemangiomata, arteriovenous fistulas and limb hypertrophy. We report the ultrasound findings in two cases of early prenatal diagnosis at 17 and 18 weeks of gestation. The pathogenesis of the syndrome and involvement of the cardiovascular system are discussed.

INTRODUCTION

Klippel–Trenaunay–Weber syndrome is a rare congenital anomaly originally described by Klippel and Trenaunay in 1900[1] and characterized by the presence of multiple skin hemangiomata, asymmetric limb hypertrophy and arteriovenous fistulas. In the literature, several cases have been reported in neonates but few in fetuses[2–5]. Yankowitz and colleagues[6] and Jorgenson and colleagues[7] reported the earliest known prospective intrauterine diagnoses at 17 and 19 weeks of gestation, respectively, but in the former case there was a positive family history. To the best of our knowledge, only Meholic and co-workers[5] reported a prospective case in a family with no history of the disease.

We report here two cases of prospective intrauterine diagnosis of Klippel–Trenaunay–Weber syndrome in families with negative history diagnosed at 17 and 18 weeks of gestation. In the latter case, a detailed hemodynamic evaluation was carried out.

CASE REPORTS

Case 1

A 21-year-old woman, gravida 2,1,0,0, with no family history of congenital anomalies, was referred to our unit for the presence of fetal right leg edema at 17 weeks of gestation. The ultrasound examination confirmed the presence of gross subcutaneous thickening involving the whole leg from the thigh to the foot (Figure 1). The lesion extended cephalad to the right iliac fossa, where a microcystic hemangioma was present. Limb hypertrophy and asymmetry were also noted. No other macroscopic anomaly was found on ultrasound examination. The patient was counselled about the probable diagnosis of Klippel–Trenaunay–Weber syndrome and its variable prognosis, and decided to have her pregnancy terminated. At necropsy (Figure 2), the ultrasound findings were confirmed and, in addition, hemangiomatous lesions of various sizes were found in most of the abdominal organs (intestine, liver and kidneys).

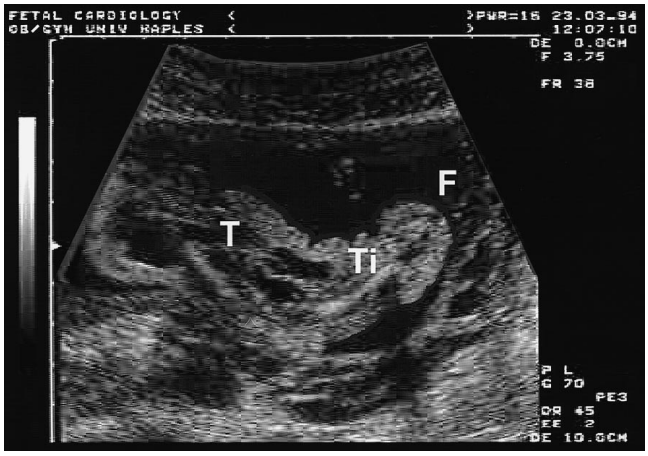

Figure 1 The right leg is shown in the picture: on the left is the multicystic hemangioma involving the whole thigh and on the right is the leg with the foot shown on a frontal plane. T, thigh; Ti, tibia; F, foot

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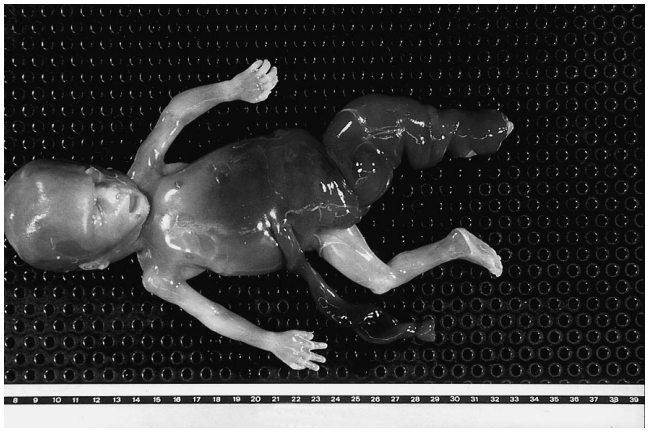

Figure 2 Necropsy. The hemangioma involving the entire leg and the right part of the abdomen is evident

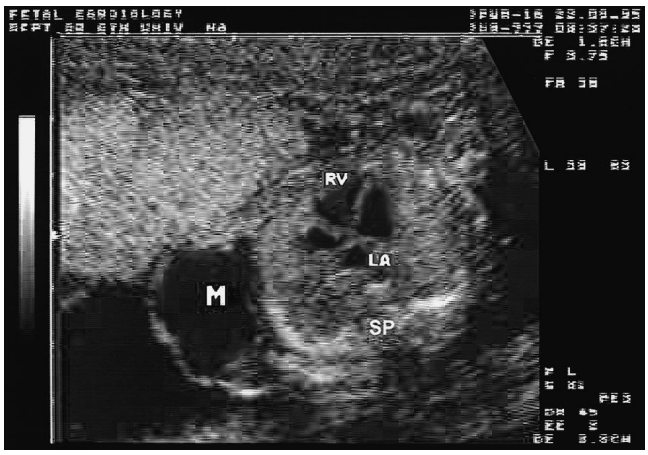

Figure 3 Transverse scan of the fetal thorax. The large cystic mass occupies the right axilla. M, mass; RV, right ventricle; LA, left atrium; SP, spine

Case 2

A 23-year-old woman, gravida 1,0,0,0, was referred to our Fetal Cardiology Unit because of a fetal 'thoracic cyst' at 18 weeks of gestation. The ultrasound examination revealed the presence of a cystic mass of 35 mm located in the right fetal axilla between the thorax and the right arm. Its walls were regular and its contents sonolucent (Figure 3). Its lumen was seen to communicate with an enlarged subcutaneous lymph vessel of the arm, but no flow could be detected by color or pulsed wave Doppler. At the level of the right groin, the subcutaneous layer appeared somewhat microcystic, with minor deformation of the cutaneous outline. This lesion was diagnosed as a hemangioma. During the same examination, clear hypertrophy of the right leg was noted.

On echocardiography, normal atrioventricular and ventriculoarterial connections were demonstrated. Analysis of peak velocities at the level of the atrioventricular and semilunar valves revealed values at the upper level for gestational age. The combined cardiac output ((cross-sectional area of aortic valve × velocity time integral of the velocity waveform) + (cross-sectional area of pulmonary valve × velocity time integral of the velocity waveform) × heart rate) was 282 ml/min, which is within the normal range for gestational age according to our and other published curves[8]. Neither fetal hydrops nor polyhydramnios were present.

The patient was counselled about the probable diagnosis of Klippel–Trenaunay–Weber syndrome and its prognosis, and elected to terminate the pregnancy. She was admitted 1 week later and, before the abortive labor was induced with prostaglandins, the ultrasound scan was repeated. The cystic mass had not increased in size, but the inguinal hemangiomatous lesion had extended to the right side of the fetal abdomen, where a 20-mm mass with the same sonographic features as the inguinal lesion was present. In addition, most of the posterior aspect of the fetal trunk showed similar hemangiomatous lesions. There was moderate polyhydramnios and mild pericardial effusion. The Doppler analysis of the central vessels and the calculation of the combined cardiac output were repeated. All values were increased and significantly above the range for 19 weeks of gestation; in particular, the combined cardiac output had reached 350 ml/min[8], leading to a diagnosis of high-output cardiac failure.

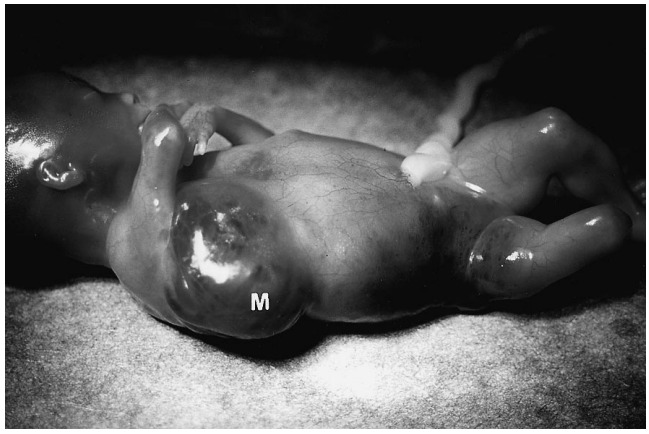

Figure 4 At necropsy, the cystic axillary mass (M) and the diffuse hemangiomatosis of the lower right part of the body is evident

Postmortem examination following termination of pregnancy confirmed the presence of gross hemangiomata of the trunk, the right flank and the groin, and hypertrophy of the right leg (Figure 4).

DISCUSSION

Klippel–Trenaunay–Weber syndrome is a well-defined pathological entity which has been widely reported in the pediatric literature as a relatively benign condition, because in most cases the hemangiomatous lesions tend to regress in the neonatal period[7,9]. However, the ultimate prognosis of the disease depends upon the location and size of the hemangiomata which may bleed, leading sometimes to life-threatening hemorrhages. Prenatal ultrasound diagnosis is feasible and has been described in a few cases, but in most of these the diagnosis was retrospective[2,3] or based on the presence of a positive family history[4]. To our knowledge, only one case of early prospective diagnosis in a family

with negative history has previously been reported, in a 17-week fetus[5].

The ultrasound diagnosis of the syndrome is based upon the association of cutaneous or subcutaneous cystic or multicystic lesions and asymmetric limb hypertrophy[5]. Additional features are represented by limb edema[6] and cardiac failure, ranging from isolated cardiomegaly[9] to severe hydrops[4]. Intrauterine ultrasound differential diagnosis includes those conditions characterized by body asymmetry and/or hypertrophy such as Proteus, CHILD (congenital hemidysplasia, ichthyosiform erythroderma and limb defects) and Beckwith–Wiedemann syndromes. The exclusion of the last condition is of the utmost importance, because familial cases with autosomal dominant inheritance have recently been described[10].

Another important issue is the natural history of Klippel–Trenaunay–Weber syndrome. Rapid progression of the hemangiomatous lesions has been reported by Jorgenson and colleagues[7]. In their case, the lesion involving only one foot at 19 weeks of gestation extended in 4 weeks to the entire leg. In our case, right leg hypertrophy, a cystic cutaneous thoracic mass and subcutaneous involvement of the right inguinal region were present at 18 weeks. One week later, the following had appeared: a large cutaneous hemangioma bulging from the right flank, extensive subcutaneous involvement of the trunk and signs of high-output cardiac failure (pericardial effusion and high combined cardiac output), as was reported also by Drose and co-workers[9]. The occurrence of this latter phenomenon, the high-output cardiac failure, is likely to be due to the development of multiple arteriovenous fistulas; in fact, only the rapid development of numerous arteriovenous fistulas may explain the acute change in cardiac output and the pericardial effusion.

However, postnatal regression of the hemangiomata has been described in several instances. This biphasic course with intrauterine growth and neonatal variable regression is similar to that of cardiac rhabdomyomata in neurofibromatosis (von Recklinghausen's disease). These tumors are also reported to reach their maximum dimensions during the third trimester of pregnancy and to regress after birth[11]. It is therefore interesting to note that the two conditions share mesodermal origin and both have been classified among congenital soft-tissue dysplasias[12]. Even though the postnatal course of Klippel–Trenaunay–Weber syndrome is completely different from that of neurofibromatosis and, above all, mental retardation is absent in the former syndrome but affects 20% of infants with neurofibromatosis, the mechanism of the reported intrauterine tumoral growth spurt may be the same for both conditions. It can be speculated that, in these diseases, possibly on genetic grounds, the maternal gestational hormonal milieu might exert an exaggerated mitotic effect on selected fetal mesodermal cellular populations, leading to the appearance of rhabdomyomata in neurofibromatosis and hemangiomata in Klippel–Trenaunay–Weber syndrome.

In conclusion, we can confirm that, in cases with no family history of congenital abnormalities, ultrasound can be used to diagnose Klippel–Trenaunay–Weber syndrome. Ultrasound demonstrated the progressive nature of the syndrome and showed that hemangiomata resulted from the formation of arteriovenous fistulas and may have had an adverse effect on cardiac function.

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